Heavy Alcohol Use in Adolescents: Potential Influences on Nutritional Status

by
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DECLARATION

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ABSTRACT

Introduction: Adolescents are recognised as a nutritionally at-risk group, as they have high nutritional demand for growth and development, poor eating behaviour as well as a propensity for unhealthy behaviours. Heavy alcohol use, particularly in the form of binge drinking, is typical for an alarming proportion of school-going adolescents and is a plausible contributor to the nutritional challenges in adolescents, but this has not yet been fully investigated.

Aim: This study investigated the potential influences of alcohol use on the nutritional status of adolescents with alcohol use disorders (AUDs), specifically with regards to their eating behaviour and dietary intake, growth and weight status, iron status, as well as vitamin D and calcium status.

Methods: Substance use, physical activity, eating behaviour, dietary intake, growth and weight status, iron status and vitamin D and calcium status were assessed and compared in heavy drinking adolescents (meeting DSM-IV criteria for AUDs) (*n=81*) and in light/non-drinking adolescents without AUDs (non-AUDs)(*n=81*), matched for age, gender, language, socio-economic status and education. Observed dietary intake distributions were adjusted statistically to obtain usual nutrient intake distributions. Regression-adjusted differences between the groups were assessed using multi-level mixed effects linear regression, adjusting for potential confounders.

Results: Lifetime alcohol dose in standard drinks of alcohol was orders of magnitude higher in the AUDs group compared to the non-AUDs group. AUDs adolescents had a binge alcohol use pattern and a "weekends-only" style of alcohol consumption. Poor eating patterns (breakfast skipping and frequent snacking), poor food choices (energy-dense and nutrient-poor foods) and low fruit and vegetable intake (non-AUDs 90 [42.4-153.3]; AUDs 88.3 [30.0-153.0] grams per day) in both groups were reflected in the poor nutritional quality of the diet. More than half of adolescents in both groups were at risk of inadequate intakes of folate (non-AUDs 97.5%; AUDs 98.8%), vitamin C (non-AUDs 65%; AUDs 67.5%), vitamin A (non-AUDs 80%; AUDs 82.5%), vitamin E (non-AUDs 78.8%; AUDs 51.3%), magnesium (non-AUDs 98.8%; AUDs 97.5%), and phosphorus (non-AUDs 76.3%; AUDs 73.8%) and all participants were at

risk of inadequate calcium and vitamin D intakes. AUDs adolescents had a greater intake of unhealthy foods (energy-dense nutrient-poor) and a significantly greater energy intake than non-AUDs adolescents (p<0.001) that exceeded energy requirements. AUDs adolescents consumed foods high in unhealthy fats significantly more frequently (p=0.037) than the non-AUDs adolescents and had ensuing greater total fat (p<0.001), saturated fat (p<0.001) and cholesterol (p=0.009) intakes. Frequency of intake of sodium-rich foods was significantly higher in AUDs adolescents (p=0.001) and prevalence of risk of excessive sodium intake was significantly greater in the AUDs adolescents (45%) compared to non-AUDs adolescents (18.8%) (p<0.001). Anthropometric indices of growth and weight status were comparable between the groups and in line with that of the South African adolescent population. Female AUDs adolescents had increased odds (OR 2.42) of being overweight/obese compared to non-AUDs females. Physical activity in both groups was well below the WHO global recommendation. Iron store depletion (serum ferritin < 20 μg/L) was evident in a quarter of adolescents in both groups (non-AUDs 23.5%; AUDs 24.7%), with biochemical iron status measures (serum iron and total iron binding capacity) indicating a greater risk of iron store depletion in the AUDs group. Biochemical vitamin D insufficiency/deficiency (serum 25-hydroxyvitamin D < 30 ng/mL) was prevalent in both groups (non-AUDs 70.4%; AUDs 88.8%), although this was significantly greater in the AUDs group (p=0.013), with significantly lower serum 25-hydroxyvitamin D levels in the AUDs group compared to the non-AUDs group (p=0.038).

Conclusions: Heavy alcohol use in the form of binge drinking in adolescents may have the following nutrition-related influences: increased intake of energy; unhealthy fats and sodium, increased risk of overweight/obesity in females; increased risk of iron store depletion; and increased risk of vitamin D insufficiency/deficiency. Persistence of heavy alcohol use, poor food choices and dietary intake may increase the risk for adverse nutrition-related health outcomes in the AUDs adolescents.

OPSOMMING

Inleiding: Adolessente het 'n verhoogde risiko vir wanvoeding as gevolg van hul hoë voedingbehoeftes vir groei en ontwikkeling, swak eetgedrag, asook 'n geneigdheid tot verdere ongesonde gedrag. Swaar alkohol gebruik in die vorm van "*binge*" drinkery kom toenemend onder skoolgaande adolessente voor. Hierdie gedrag kan moontlik bydra tot die verhoogde voeding risiko in dié ouderdomsgroep. Hierdie moontlikheid is egter nog nie ten volle ondersoek nie.

Doel: Hierdie studie het die potensiële invloed van alkohol gebruik op die voedingstatus van adolessente met alkohol gebruik versteurings (AGVs) ondersoek, spesifiek met betrekking tot hul eetgedrag en dieetinname, groei en gewigstatus asook yster-, vitamien D- en kalsiumstatus.

Metodes: Swaar drinkende adolessente wat voldoen aan DSM-IV kriteria vir AGVs (*n=81*) en lig/nie-drinkende adolessente sonder AGVs (nie-AGVs) (*n=81*), wat afgepaar is vir ouderdom, geslag, taal, sosio-ekonomiese status en opvoedingsvlak is gewerf vir deelname aan die studie. Middel gebruik, fisiese aktiwiteit, eetgedrag, dieetinname, groei en gewigstatus, ysterstatus en vitamien D- en kalsiumstatus is tussen die twee groepe vergelyk. Waargenome dieetinname verspreidings is statisties aangepas om gewoontelike nutriëntinname te verkry. Regressie-aangepaste verskille tussen die groepe is met behulp van 'n meervoudige gemengde effekte liniêre regressie model getoets, waartydens daar vir moontlike gestrengelde faktore aangepas is.

Resultate: Leeftyd alkohol dosis, gemeet in standaard alkohol drankies, was beduidend hoër in die AGVs groep in vergelyking met die nie-AGVs groep. Alkohol gebruik in die AGVs adolessente het 'n "*binge*" patroon en 'n "slegs naweke" styl getoon. Swak eetgewoontes (oorslaan van ontbyt en gereelde peuselgewoontes), swak voedsel keuses (energie-dig en laag in nutriënte) en lae groente en vrugte inname (nie-AGVs 90.0 [42.4-153.3]; AGVs 88.3 [30.0-153.0] gram per dag), in beide groepe, is gereflekteer in die swak voeding kwaliteit van die dieet. 'n Risiko vir onvoldoende inname van folaat (nie-AGVs 97.5%; AGVs 98.8%), vitamien C (nie-AGVs 65%; AGVs 67.5%), vitamien A (nie-AGVs 80%; AGVs 82.5%), vitamien E (nie-AGVs 78.8%; AGVs 51.3%), magnesium (nie-AGVs 98.8%; AGVs 97.5%), en fosfor (nie-AGVs 76.3%; AGVs 73.8%) was teenwoordig in meer as helfte van adolessente in beide groepe, asook

'n risiko vir onvoldoende kalsium en vitamien D inname in al die deelnemers. In vergelyking met nie-AGVs adolessente, het AGVs adolessente 'n hoër inname van ongesonde voedsels (energie-dig en laag in nutriënte) gehad sowel as 'n betekenisvolle hoër totale energie inname (p<0.001), wat energie behoeftes oorskry het. Inname van voedsels hoog in ongesonde vette was betekenisvol meer gereeld in AGVs adolessente as in nie-AGVs adolessente (p=0.037) en hulle het gevolglike hoër innames van totale vet (p<0.001), versadigde vet (p<0.001) en cholesterol (p=0.009) getoon. Frekwensie van inname van natriumryke voedsels was betekenisvol meer in AGVs adolessente (p=0.001) en prevalensie van risiko vir oormatige natrium inname was betekenisvol hoër in die AGVs groep (43%) in vergelyking met die nie-AGVs groep (18.8%). Antropometriese indekse van groei en gewigstatus was vergelykbaar tussen die twee groepe en in lyn met dié van Suid-Afrikaanse adolessente. Vroulike AGVs adolessente het 'n verhoogde kans (relatiewe kansverhouding [OR] 2.42) vir oorgewig/vetsug getoon in vergelyking met vroulike nie-AGVs deelnemers. Fisiese aktiwiteit in beide groepe was heelwat laer as die WGO aanbeveling. Uitputting van ysterstore (serum ferritien < 20 μg/L) was teenwoordig in 'n kwart van adolessente in beide groepe (nie-AGVs 23.5%; AGVs 24.7%) en biochemiese ysterstatus bepaling (serum yster en totale ysterbindingskapasiteit) het gedui op 'n verhoogde risiko vir ysterstooruitputting in die AGVs groep. Biochemiese vitamien D ontoereikendheid/tekort (serum 25-hidroksievitamien D < 30 ng/mL) was grootliks teenwoordig in beide groepe (nie-AGVs 70.4%; AGVs 88.8%), maar was betekenisvol hoër in die AGVs groep (p=0.013), met betekenisvol laer serum 25-hidroksievitamien D vlakke in die AGVs groep in vergelyking met die nie-AGVs groep (p=0.038).

Gevolgtrekking: Swaar alkohol gebruik in die vorm van "*binge*" drinkery in adolessente mag die volgende voedingsverwante invloede tot gevolg hê: verhoogde energie inname, verhoogde inname van ongesonde vette en natrium, verhoogde risiko vir oorgewig/vetsug in vroulike adolessente, verhoogde risiko vir ysterstooruitputting, asook verhoogde risiko vir vitamien D ontoereikendheid/tekort. Aanhoudende swaar alkohol gebruik, swak voedsel keuses en dieetinname kan moontlik die risiko vir nadelige voedingsverwante gesondheidsuitkomste in die AGVs adolessente verhoog.

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LIST OF ABBREVIATIONS

1,25(OH)2D	1,25-dihydroxyvitamin D
25(OH)D	25-hydroxyvitamin D
ADH	alcohol dehydrogenase
AI	Adequate Intake
AMDR	Acceptable Macronutrient Distribution Range
AUDs	alcohol use disorders
BMI	body mass index
CRP	C-reactive protein
DALYs	disability-adjusted life years
DRIs	Dietary Reference Intakes
DSM-IV	American Psychiatric Association's 4th Diagnostic and Statistical Manual
DSML	Drinking Self-Monitoring Log
EAR	Estimated Average Requirement
EER	Estimated Energy Requirement
ELISA	enzyme linked immunosorbent assay
FDA	Food and Drug Administration
ICRW	International Center for Research on Women
IOM	Institute of Medicine
IU	International Units
K-SADS-PL	Schedule for Affective Disorders and Schizophrenia for School Aged Children (6-18 Years) Lifetime Version
LDH	Lifetime Drinking History
MEOS	microsomal ethanol-oxidising system
μg /L	micrograms per litre
μmol/L	micromoles per litre
mL	millilitres
MRC	Medical Research Council
NAD	nicotinamide adenine dinucleotide
NADH	reduced nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotide phosphate

NADPH	reduced nicotinamide adenine dinucleotide phosphate
NCDs	non-communicable diseases
NCHS	National Center for Health Statistics
ng	nanograms
NHANES	National Health and Nutrition Examination Survey
NIAAA	National Institute for Alcoholism and Alcohol Abuse
RDA	Recommended Dietary Allowance
ROS	reactive oxygen species
SADBDG	South African Food-Based Dietary Guidelines
SAFOODS	South African Food Data System
SD	standard deviation
SSAGA-II	Semi-Structured Assessment for the Genetics of Alcohol (SSAGA-II)
SUDs	substance use disorders
TIBC	total iron binding capacity
TLFB	Timeline Followback
UL	Tolerable Upper Intake Level
UNICEF	United Nations Children's Fund
US	United States of America
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
UVB	ultraviolet B
WHO	World Health Organization
YRBS	Youth Risk Behaviour Survey

Chapter 1

INTRODUCTION

Adolescence links childhood and adulthood and arguably incorporates some of the most critical developmental changes in the life course. It is a period during which essential physiological, psychosocial and cognitive changes occur, which may impact directly and indirectly on the nutritional status of adolescents (Stang et al., 2008). The rapid growth and development experienced by adolescents, including biological and sexual maturity, are associated with a high nutritional demand for energy, protein, vitamins and minerals (Stang et al., 2008, World Health Organization, 2005). Various individual, social, physical/environmental and macrosystem factors influence the dietary intake and eating behaviour of adolescents, with direct implications for their nutritional status (Story et al., 2002). Additionally, the attainment of greater self-efficacy occurs during this stage and adolescents consequently acquire increased control over their own food choices (Avery et al., 1992, Fitzgerald et al., 2010), contributing to the poor eating behaviour and dietary intake commonly reported in adolescents (Barquera et al., 2003, Moreno et al., 2010, Munoz et al., 1997, Pomerleau et al., 2004).

Accompanying the above-mentioned physiological and adaptive psychosocial changes, a higher preponderance to risk-taking and sensation-seeking behaviours, exposure to high-risk environments and vulnerability to experimentation are commonplace in adolescence (Dahl, 2004, United States Department of Health and Human Services, 2007). In particular, alcohol use, including harmful and risky drinking patterns, rises sharply throughout adolescence and regular and excessive exposure to alcohol is alarming and ubiquitous across the world in school-going adolescents (Reddy et al., 2010a, Substance Abuse and Mental Health Services Administration, 2006). Specifically, the episodic consumption of large quantities of alcohol, generally termed binge drinking, is at the forefront of public health concerns regarding alcohol use in adolescents, both in South Africa (Reddy et al., 2010a) and internationally (Kuntsche et al., 2004, Nelson et al., 2004). Moreover, an escalation in alcohol consumption, particularly among adolescents has been documented over the past decade (Matthews, 2010, Mcardle, 2008, Hibell et al., 2009, Reddy et al., 2010b). Adolescents face extensive physiological and psychological consequences as a result of heavy alcohol use (United States Department of Health and Human Services, 2007) and this harmful behaviour has been recognised as a possible threat to their nutritional status (World Health Organization, 2005, Stang et al., 2008).

In spite of the acknowledgment of adolescent nutritional vulnerability, this period has not generally been regarded as a high priority life stage in terms of nutrition support and interventions, with the exception of adolescent pregnancy (World Health Organization, 2005). Specifically in developing countries, like South Africa, health services and promotion focus on infant, maternal and young child nutrition-related health, with the result that nutrition-related health needs of the adolescent population may not be adequately met (World Health Organization, 2005).

Efforts to characterise and understand the impact of heavy alcohol use in adolescents have been growing in recent years. A PubMed restricted year search (titles and abstracts only) using the terms "adolescent" and ''alcohol" generated only nine publications in 1980, increasing to 51 in 1990, 141 in 2000 and 347 in 2010. However, the majority of these publications have focussed primarily on the neurological impacts of heavy alcohol use during adolescence, including neuropsychological performance (Brown et al., 2000, Ferrett et al., 2010), and structural and functional changes in the developing brain (Brown et al., 2000, Crews et al., 2000, De Bellis et al., 2000, Tapert and Brown, 1999). To date, very little work has focussed on the nutrition-related consequences of heavy alcohol use in adolescents. This paucity is concerning in view of the well-documented harmful effects of heavy alcohol use on dietary intake and the gastrointestinal tract that result in metabolic derangements and nutrient deficiencies in adults (Bode and Bode, 2003, Foster and Marriott, 2006, Lieber, 2000, Lieber, 2003). The rising prevalence of heavy alcohol use in adolescents (Hibell et al., 2009, Lim et al., 2007, Reddy et al., 2010a, United States Department of Health and Human Services, 2007) and the fact that alcohol use and nutritional health risk behaviours show a strong degree of tracking from adolescence into adulthood (Kelder et al., 1994, Serdula et al., 1993, Te Velde et al., 2007, Grant, 1998), emphasises the importance of examining these associations at an early stage in the drinking trajectory of adolescents.

As economic development improves in many developing countries, a rise in levels of alcohol consumption is expected with concomitant increases in alcohol-induced health problems (World Health Organization, 2011). According to the World Health Organization (WHO) Global Status Report on Alcohol and Health, South Africa is one of the countries with the most risky patterns of drinking (World Health

Organization, 2011) and a high alcohol-related disease burden has been reported in this country (Schneider et al., 2007).

This study therefore set out to investigate the associations between heavy alcohol use and nutritional status in adolescents to delineate the possible role of heavy alcohol use in amplifying the nutritional vulnerability in adolescents.

The first step in this research process was to critically review the relevant literature in this field (Chapter 2) in order to understand and appraise the available related evidence on alcohol use and formulate pertinent research questions for investigation in this study. The literature review includes the assessment of alcohol intake, nutritional implications of alcohol use, alcohol use in adolescents as well as nutritional risks and challenges in adolescence, with possible influences of alcohol use.

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Chapter 2

LITERATURE REVIEW

1   PERSPECTIVES ON ALCOHOL USE

1.1   Alcohol Drinking Patterns

In the past, the majority of epidemiologic studies typically used a single measure to summarise alcohol exposure into an average quantity. However, evidence has indicated that this approach does not effectively account for the health risks related to alcohol intake and that variation in alcohol drinking patterns needs to be considered (Gronbaek, 2009). According to Li (2008), the quantity of alcohol consumed, the frequency with which it is consumed, and the pattern of consumption determine the health and related impacts of alcohol use .

Alcohol use can be defined in many ways, for example, as drinking with meals, on weekends only, to intoxication, to a certain blood alcohol level, more than a certain amount per occasion and as both amount and frequency of alcohol consumed (Makela et al., 2005, Mukamal et al., 2003, Murray et al., 2002, Tolstrup et al., 2006). When considering descriptions and definitions of alcohol use in the scientific literature, it is evident that alcohol use can be broadly categorised into three drinking patterns. Firstly there is light or moderate drinking, with sensible use of alcohol and compliance with health-related guidelines for the majority of the time. Secondly there is binge or heavy episodic drinking, with frequent bingeing or heavy drinking over a short time period (acutely), usually to the point of intoxication and often beyond to unconsciousness. Lastly there is chronic alcoholism, with almost continuous drinking while awake and cumulative ingestion of large amounts of alcohol. The terms "binge alcohol use" and "heavy episodic alcohol use" are used synonymously in the literature to describe drinking large quantities over a short time period.

The National Institute for Alcoholism and Alcohol Abuse (NIAAA) in the United States of America (US) defines binge drinking as a pattern of drinking alcohol that brings blood alcohol concentration to 0.08 grams per decilitre or above. For the typical adult, binge drinking is consistent with consuming five or more drinks in males or four or more standard drinks in females in approximately two hours (National Institute for Alcoholism and Alcohol Abuse, 2004) . This NIAAA definition for binge drinking was developed in relation to adults. Children and early adolescents weigh considerably less than adults and have different body compositions. Thus they are likely to reach a blood alcohol concentration of 0.08

grams per decilitre with fewer drinks or to achieve substantially higher blood alcohol concentrations when consuming five drinks within a two hour period (Donovan, 2009). Recently new definitions for binge drinking in adolescents have been proposed using estimates of blood alcohol concentrations for intake levels of one to five standard drinks in a sample of approximately 4700 nine to 17 year olds from the 1999 to 2002 National Health and Nutrition Examination Survey (NHANES) database. Based on these findings, Donovan (2009) proposed that binge drinking should be defined as having three or more drinks in nine to 13 year olds, four or more drinks in males and three or more drinks in females aged 14 to 15 years, and five or more drinks in males and three or more drinks in females aged 16 to 17 years. Binge drinking acutely impairs brain function impacting on judgement, emotional stability and cognition with harmful consequences such as violence, unintentional death and injury and homicide (Li, 2008).

Heavy drinking is defined as frequent drinking of five or more drinks by males and four or more drinks by females per day (Li, 2008) and increases the risk of developing alcohol use disorders (AUDs). According to the current World Health Organization (WHO) Global Status Report on Alcohol and Health, harmful alcohol use is one of the world's leading health risks and is a causal factor in more than 60 major types of diseases and injuries, resulting in approximately 2.5 million deaths annually (World Health Organization, 2011b). Li (2008) indicates that many of the health problems and conditions caused by excessive, chronic drinking are the result of organ damage, including alcoholic liver disease, alcoholic pancreatitis, cardiomyopathy and impaired brain structure and function. Over the long term, excessive drinking leads to neuroadaptations that play a role in the behavioural changes seen with alcoholism, related to sensitisation, tolerance, loss of control, dependence, withdrawal and relapse (Li, 2008). Both binge drinking and heavy drinking are regarded as high risk alcohol use, with increased risk of numerous acute and chronic consequences (AUDs) that negatively affect health and life (Li, 2008). These include injuries (World Health Organization, 2011b) and non-communicable diseases (NCDs), namely diabetes mellitus (Baliunas et al., 2009) and cardiovascular disease, hypertension and stroke (Rehm et al., 2010). Specifically, a pattern of drinking which includes binge drinking has been linked to cardiovascular diseases, mainly ischaemic heart diseases (Roerecke and Rehm, 2011).

Guidelines for sensible or moderate drinking are comparable across the different countries (Foster and Marriott, 2006). The most frequently recommended alcohol limit for men and women is 24 and 20 grams per day, respectively (Foster and Marriott, 2006). In South Africa, a low risk or moderate drinking pattern is defined as no more than three standard drinks for men and no more than two standards drink per day for women (Van Heerden and Parry, 2001). A moderate drinking pattern is generally considered to be low risk in terms of engendering acute or chronic negative health and/or social and behavioural problems. This drinking pattern has also been shown to be positively associated with decreased mortality, mainly through a reduction in cardiovascular disease risk (Di Castelnuovo et al., 2006, Gronbaek, 2009).

1.2   Alcohol Intoxication

The direct and immediate effects of alcohol on the brain influence normal physiology, such as sleep-wake patterns; cognition, such as thoughts and emotions and basic motor functions, such as balance, gait and coordination (Li, 2008). Brain alcohol levels parallel blood alcohol levels because alcohol readily crosses the blood-brain barrier. Variable symptoms are directly linked to the rate of alcohol consumption and may include incoordination, euphoria, ataxia, loss of inhibitions, drowsiness, belligerence and garrulousness. As blood alcohol levels rise, the direct depressant effects of alcohol predominate and the drinker may experience lethargy along with cardiovascular symptoms, at times complicated by vomiting and pulmonary aspiration (Zeigler et al., 2005).

The ingestion of a large quantity of alcohol may result in acute alcohol intoxication, a clinically harmful condition (Vonghia et al., 2008). A number of factors can affect the extent of acute alcohol intoxication, including the quantity of alcohol ingested, the period of ingestion, body weight, tolerance to alcohol and the percentage alcohol in the beverage (Yost, 2002). Symptoms are usually linked to blood alcohol concentration (Vonghia et al., 2008). Acute alcohol intoxication can cause metabolic alterations, including hypokalaemia, hypomagnesaemia, hypoalbuminaemia, hypocalcaemia, hypophosphataemia, hypoglycaemia and lactic acidosis. Cardiovascular consequences of intoxication include volume depletion, tachycardia and peripheral vasodilation, which can contribute to hypotension and

hypothermia (Marco and Kelen, 1990). The primary life-threatening respiratory effect of acute alcohol intoxication is respiratory depression (Vonghia et al., 2008). Gastrointestinal consequences include diarrhoea, nausea, vomiting, abdominal pain secondary to gastritis, peptic ulcer, and pancreatitis (Addolorato et al., 1997, Hanck and Whitcomb, 2004), as well as motility dysfunction of the oesophagus, stomach and duodenum (Burbige et al., 1984). Acute alcoholic hepatitis may result, typically in subjects with chronic alcohol abuse and/or affected by alcoholic cirrhosis (Agarwal et al., 2004). With very high blood alcohol concentrations, alcohol poisoning may manifest with the development of stupor, coma, and death, typically secondary to respiratory depression with hypotension and respiratory acidosis (Zeigler et al., 2005).

Adolescents are more susceptible to alcohol intoxication than adults. At the initiation of alcohol use, adolescents have not yet developed a behavioural or physiological tolerance to alcohol and its effects. Due to their smaller body sizes and lower body weight compared to adults, they usually do not need to consume a very large amount of alcohol before becoming intoxicated (Spear, 2002). The social, decision-making, emotional control and judgment skills of adolescents are less developed, which makes them more prone to drink heavily and rapidly until intoxicated (Spear, 2002).

Alcohol intoxication has been associated with an increased risk of injury (Maier, 2001) and a recent study reported a strong correlation between binge drinking and violent crimes such as assault (24 to 37%), homicide (28 to 86%), robbery (7 to 72%), and sexual crimes (13 to 60%) (Brewer and Swahn, 2005).

1.3   Alcohol Use Disorders (AUDs)

According to the American Psychiatric Association's 4th Diagnostic and Statistical Manual (DSM-IV) (American Psychiatric Association, 1994), AUDs include alcohol dependence and alcohol abuse (American Psychiatric Association, 1994), with specific diagnostic criteria for each of these conditions (Box 1). Alcohol dependence is identified as the more severe condition, resulting in major physiological consequences and life impairment (Schuckit, 2009), and can be identified as repetitive problems affecting three or more areas of life (Box 1). Individuals with a family history of alcoholism have an increased risk

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for alcohol dependence (United States Department of Health and Human Services, 2007). It is thought that 40 to 60% of the risk of AUDs is attributable to genes and the remainder to gene-environment interactions (Schuckit and Smith, 2006, Timberlake et al., 2007). People diagnosed with alcohol abuse drink smaller quantities than those with the diagnosis of alcohol dependence, however, the abuse category predicts a risk of approximately 50% for continued problems (American Psychiatric Association, 1994, Hasin et al., 1996, Schuckit et al., 2005).

Box 1: American Psychiatric Association's 4th Diagnostic and Statistical Manual (DSM-IV) criteria for the diagnosis of alcohol use disorders (AUDs)

DSM-IV Criteria for Alcohol Abuse:
1. A maladaptive pattern of alcohol abuse leading to clinically significant impairment or distress, as manifested by one or more of the following, occurring within a 12-month period:
   o Recurrent alcohol use resulting in failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions or expulsions from school; or neglect of children or household).
   o Recurrent alcohol use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine).
   o Recurrent alcohol-related legal problems (e.g., arrests for alcohol-related disorderly conduct).
   o Continued alcohol use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the alcohol (e.g., arguments with spouse about consequences of intoxication or physical fights).
2. These symptoms must never have met the criteria for alcohol dependence.

DSM-IV Criteria for Alcohol Dependence:
A maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, as manifested by three or more of the following seven criteria, occurring at any time in the same 12-month period:
1. Tolerance, as defined by either of the following:
   o A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
   o Markedly diminished effect with continued use of the same amount of alcohol.
2. Withdrawal, as defined by either of the following:
   o The characteristic withdrawal syndrome for alcohol (refer to DSM-IV for further details).
   o Alcohol is taken to relieve or avoid withdrawal symptoms.
3. Alcohol is often taken in larger amounts or over a longer period than was intended.
4. There is a persistent desire or there are unsuccessful efforts to cut down or control alcohol use.
5. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
7. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the alcohol (e.g., continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

Source: (American Psychiatric Association, 1994)

2   ASSESSMENT OF ALCOHOL INTAKE

Measuring alcohol consumption is challenging and various methodological issues influence the process of obtaining estimates of alcohol use. As most commonly used methods rely on recall, both intentional and unintentional errors of recall by the respondents may result in inaccurate information. When alcohol intake is assessed, two aspects need to be considered, namely the standard drink size and the method of measurement used, which includes the reference period for which consumption data are collected (Dawson, 2003, Dufour, 1999).

2.1   Definition of a Standard Drink

Commercially available alcoholic beverages (e.g. beer, wine and spirits) are sold in various sizes and contain varying concentrations of pure alcohol (Dawson, 2003). To overcome these variations in alcohol measurement, investigations of alcohol consumption commonly use a pre-determined definition of a standard drink of alcohol (Dufour, 1999). A standard drink is the quantity of an alcoholic beverage that contains a fixed amount of pure alcohol. Since all standard drinks therefore contain a similar amount of alcohol regardless of beverage type, this concept is useful in measuring alcohol consumption (Dawson, 2003).

The challenge at present is that there is no universally accepted definition of a standard drink. Different countries have adopted a range of standard drink or unit sizes from eight grams of alcohol per standard drink in the United Kingdom to 19.75 grams per standard drink in Japan (Dawson, 2003). The NIAAA in the US has published a definition of a standard drink (Dawson, 2003). According to this guideline, a standard drink contains approximately 14.8 grams of pure alcohol, and corresponds to 355 millilitres (mL) of regular beer, 148 mL of wine, or 44 mL of 80 proof distilled spirits. The exact quantity of alcohol per standard drink varies, dependent on the beverage type. For some of the alcoholic beverages, a standard drink is the same as the typical serving or packaging sizes of the beverages, but this is not the case for all the beverage types (Dawson, 2003). A standard drink in South Africa corresponds to 340 mL of beer (1 can or small bottle), 340 mL cider (1 can or bottle), a 25 mL tot of brandy, whisky, gin, cane or vodka and a 120 mL glass of wine. Similarly, the precise quantity of alcohol per standard drink varies,

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dependent on the type of beverage, for example, a 340 mL beer (typically 5% alcohol by volume) contains ±12 grams of alcohol, a 340 mL cider (typically 6% alcohol by volume) contains ±16 grams of alcohol, a 25 mL tot of brandy, whisky, gin, cane or vodka (typically 43% alcohol by volume) contains ±11 grams of alcohol, and a 120 mL glass of wine (typically 12% alcohol by volume) contains ±11 grams of alcohol (Wolmarans et al., 1993).

2.2   Measures of Alcohol Intake

In addition to the challenges associated with defining a standard drink, the method of measurement of alcohol intake is another complexity faced during the assessment of alcohol intake (Dufour, 1999). The accuracy and validity of the measurement of alcohol use regarding the quantity, frequency and volume, depend on the method of measurement used. As with most methodology, the proposed research goals of the study should dictate the specific approach to measurement of alcohol consumption that is employed (Dufour, 1999).

Numerous measures of alcohol intake are used and reported in the literature and include frequency measures, quantity frequency measures and graduated frequency measures (Dufour, 1999). There are several factors to consider when selecting a measure of alcohol intake, including the time available for the interview, the population, the timeframe of reporting and the types of information required (Sobell and Sobell, 2003).

The five measures of alcohol intake included in the NIAAA's Guide for Clinicians and Researchers for assessing alcohol problems are as follows: 1) Alcohol Timeline Followback (TLFB), 2) Form 90, 3) Drinking Self-Monitoring Log (DSML), 4) Lifetime Drinking History (LDH) and 5) Quantity-Frequency Measures. Descriptive information on these measures is provided in Table 1. All of these measures assess alcohol intake only, while Form 90 also examines domains other than alcohol use (Sobell and Sobell, 2003).

Table 1. Descriptive information on selected measures of alcohol intake

Measure	Purpose	Drinking variables generated	Assessment timeframe	Target population	Groups used with
TLFB	Assessment of daily drinking; several dimensions of drinking can be separated and examined	Daily drinking into user-defined categories, variability, pattern, level of drinking, time to first relapse	Retrospective recall of 30-36 days before interview	Adults and adolescents	Alcohol abusers and normal drinkers; males and females; college students
Form 90	Assessment of daily drinking using a calendar and weekly grid	Same as for TLFB except uses a 90-day interval before last drink	Retrospective recall of 90 days before last drink	Adults and adolescents	Alcohol abusers; males and females
DSML	Daily recall of drinking	Same as for TLFB	Recall of daily drinking	Adults and adolescents	Alcohol abusers and normal drinkers; males and females; college students
LDH	Chronological recall of drinking patterns from adolescence to adulthood	QF average and maximum of drinking phases	Retrospective lifetime assessment of drinking	Adults and adolescents	Alcohol abusers and normal drinkers
QF measures	Assessment of drinking	QF, QF volume, volume variability	Retrospective recall of typical month or last 30 days	Adults and adolescents	Alcohol abusers and normal drinkers; college students

Source: Adapted from (Sobell and Sobell, 2003)
Abbreviations: TLFB: Alcohol Timeline Followback; DSML: Drinking Self-Monitoring Log; LDH: Lifetime Drinking History; QF: Quantity-Frequency

The TLFB method published by Sobell and Sobell (Sobell and Sobell, 1992) has been evaluated in clinical and non-clinical populations and has both clinical and research utility. The TLFB is recommended for use when relatively precise estimates of alcohol use are needed, particularly when a complete picture of drinking days, including both high and low risk days, is required, as was the case in this research. Using a calendar, respondents provide retrospective estimates of their daily drinking over a defined timeframe that can vary from 30 days up to 12 months from the interview date. A number of memory aids can be used to enhance and stimulate recall, for example a calendar. The TLFB has been shown to have good psychometric characteristics in a range of drinker groups. The target groups for this method include adolescents and adults and it has been used to measure alcohol intake in alcohol abusers and normal drinkers, males and females and college students. The TLFB allows several dimensions of a respondent's

drinking to be examined separately. These dimensions include alcohol use variability (spread), pattern (shape) and extent (quantity). A variety of continuous and categorical variables can be generated using data from the TLFB and this data are amenable to a range of statistical analyses. The TLFB provides a different and more precise level of information than indirect estimation formulae. Timeline summary data have been found to be generally reliable, but as with all methods of alcohol use assessment, exact day-by-day precision cannot be assumed or necessarily expected (Sobell and Sobell, 2003).

When quantifying alcohol-related risks, measures of both quantity and pattern of drinking is required as the relationship between these two variables is important. Drinking pattern, expressed as the frequency of heavy and binge drinking, may be more harmful than drinking pattern expressed as the average quantity of alcohol ingested per day, in terms of alcohol associated disease, alcohol-induced organ damage and the risk of AUDs (Li, 2008).

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3   PERSPECTIVES ON ALCOHOL INTAKE, ABSORPTION, METABOLISM AND ASSOCIATED NUTRITIONAL IMPLICATIONS

Alcohol use and the resultant metabolism thereof can affect nutrition through direct impacts on metabolic functioning and the gastrointestinal tract, and indirectly by impacting food and nutrient intake and energy balance, as well as via alcohol-related organ damage. It is well known that excessive, chronic alcohol consumption can result in undernutrition, metabolic derangements and nutrient deficiencies. However, very little is known about the nutritional implications of persistent binge drinking in humans, particularly adolescents. To provide some insight in this regard, relevant perspectives on the effects of chronic and experimental acute alcohol use have been included in this literature review.   Acute alcohol exposure models heavy episodic or binge drinking and is especially relevant to research examining the effects of adolescent drinking behaviours (Keiver et al., 2005).

It is important to bear in mind that the extent of the nutritional implications of alcohol use are dependent on the level of alcohol intake, the drinking pattern, the duration of alcohol use and the consequent effects on dietary intake, absorption, metabolism and excretion of nutrients (Lieber, 2003, Bode and Bode, 2003, Foster and Marriott, 2006).

3.1   Alcohol Absorption

Alcohol does not require enzymatic or mechanical digestion in the gastrointestinal tract (Ferreira and Willoughby, 2008). Upon ingestion, alcohol rapidly crosses cell membranes through simple diffusion with ensuing complete equilibration between intra- and extra-cellular concentrations (Bode, 1980, Marco and Kelen, 1990). Alcohol absorption occurs through the mucosa of the entire gastrointestinal tract, primarily in the proximal regions, namely, the stomach (approximately 70%) and duodenum (approximately 25%), while the remaining 5% of absorption occurs in the distal intestinal regions (Marco and Kelen, 1990). The rate of alcohol absorption is reduced by the presence of food in the stomach and by delayed gastric emptying (Bode and Bode, 2003). Absorption rate is also dependent on the speed at which the drink was ingested as well as gender and body size (Paton, 2005). Females are generally of smaller stature and have a smaller blood volume which results in a greater blood alcohol concentration (Paton, 2005).

3.2   Alcohol Metabolism

About 2 to 10% of ingested alcohol is excreted through the lungs, urine, and sweat and the remainder is metabolised to toxic acetaldehyde, which is degraded to acetate found predominantly in the liver (Schuckit, 2009). Alcohol must be metabolised immediately after absorption because unlike the other energy providing macronutrients (protein, carbohydrates and fat), the body is unable to store alcohol (Suter and Tremblay, 2005).

Alcohol is metabolised by alcohol dehydrogenase (ADH) found in the cytosol of hepatocytes and gastric mucosa, and by the microsomal ethanol-oxidising system (MEOS) located in the endoplasmic reticulum (Suter and Tremblay, 2005). The metabolism of alcohol via both of these systems has nutritional implications due to disturbances mainly in fat and micronutrient metabolism, as discussed in more detail in section 3.2.4.

Experimental research and human studies show increasing evidence that the gut flora is also involved in alcohol metabolism in the colon. Alcohol is transported via the bloodstream to the colonic lumen and converted to acetaldehyde by bacterial alcohol dehydrogenase (Salaspuro, 1996). The capacity of colonic bacteria to sustain the first phase of alcohol metabolism by alcohol dehydrogenase is much greater than that for the second phase, namely the conversion of acetaldehyde to acetate. Consequently the concentration of toxic acetaldehyde in the colon increases markedly, which may result in colonic mucosa damage as well as liver injury, after being absorbed into the portal blood (Bode and Bode, 2003).

3.2.1   The alcohol dehydrogenase system

At low levels of intake, alcohol is metabolised by the ADH system (Figure 1, page 22) in the cytosol of gastric mucosa and hepatocytes. Within this system, the ADH enzyme converts alcohol to acetaldehyde, which is a highly reactive and toxic compound. Hydrogen is removed from alcohol during this conversion and transferred to the cofactor nicotinamide adenine dinucleotide (NAD), thereby converting it to reduced NAD, namely NADH. NADH participates in many other essential metabolic reactions in the cell

and in the process, passes on the hydrogen to other molecules. The acetaldehyde that is formed is metabolised to acetate by a second enzyme, aldehyde dehydrogenase and finally to carbon dioxide and water through the citric acid cycle (Lieber, 2003, Suter and Tremblay, 2005, Lieber, 2000). Under most circumstances, acetaldehyde is rapidly converted to acetate and due to this rapid enzymatic conversion, the cellular concentration of acetaldehyde is usually a thousand-fold lower than that of alcohol and acetate. However, following the drinking of alcohol, acetaldehyde is found in micromolar concentrations in the circulation, whereas alcohol and acetate are found in millimolar concentrations. When the level of acetaldehyde increases, feelings of dysphoria may be experienced and there is an increased potential for toxic reactions with different cellular components (Li, 2008).

The ratio of NAD to NADH in the cell must be tightly controlled to ensure proper functioning of the cell. Excess amounts of NADH generated from alcohol metabolism, disrupts the normal cellular NAD to NADH ratio (Lieber, 2003). Several of the metabolic effects of alcohol are directly linked to the excessive production of both NADH and acetaldehyde (Suter and Tremblay, 2005) (Figure 1, page 22). When excessive amounts of NADH are generated the ability of the cell to maintain redox homeostasis is overwhelmed, which causes metabolic and other cellular disorders (Figure 1, page 22) (Lieber, 2003).

3.2.2   The microsomal ethanol-oxidising system (MEOS)

After heavy alcohol consumption, in terms of both frequency and quantity, it is mainly metabolised by the MEOS (Lieber, 2003, Suter and Tremblay, 2005) (Figure 1, page 22). The reactions that make up the MEOS involve several enzymes located in the microsomes that originate from the endoplasmic reticulum and function to transport compounds through and out of cells. Various forms of the enzyme cytochrome P450 are the primary components of the MEOS and like alcohol dehydrogenase, convert alcohol to acetaldehyde (Figure 1, page 22). Oxygen is required for the conversion of alcohol to acetaldehyde via the MEOS, as well as reduced nicotinamide adenine dinucleotide phosphate (NADPH) with the resultant formation of nicotinamide adenine dinucleotide phosphate (NADP) and water. Highly reactive, oxygen-containing molecules referred to as reactive oxygen species (ROS) or oxygen radicals, are generated as

byproducts of these reactions, with a consequent increase in oxidative stress (Lieber, 2003). The various

nutritional and hepatic implications of alcohol metabolism via the MEOS are discussed in section 3.2.4.

3.2.3   Rate of alcohol metabolism

The rate of alcohol metabolism varies considerably between persons. The average rate is approximately

30 mL in three hours and a constant quantity of alcohol is eliminated per hour (saturation kinetics). The

blood alcohol concentration does not influence the quantity of alcohol that is removed and consequently,

if alcohol is ingested at a tempo greater than the quantity being eliminated, blood alcohol concentration

will keep on rising until drinking stops (Zeigler et al., 2005). The rate of alcohol metabolism is influenced

by several factors, including age, body weight, liver size, frequency and usual quantity of alcohol intake

(Foster and Marriott, 2006). Gender is also a factor affecting the speed of alcohol metabolism with

females having less ADH activity in the gastric mucosa, slower metabolism of alcohol and sharper

increases in blood alcohol concentration when drinking (Frezza et al., 1990).

3.2.4   The effect of alcohol metabolism on lipid metabolism and hepatic function

Lipid metabolism is affected when alcohol is metabolised via both the ADH system and the MEOS. The

excessive hepatic NADH generation via the ADH pathway results in hyperlipaemia (Figure 1, page 22)

(Lieber, 2003). High levels of hepatic NADH oppose lipid oxidation and promote fatty acid synthesis

resulting in steatosis (Lieber, 2000). This condition may progress to steatohepatitis, which is

characterised by liver inflammation with concurrent fat accumulation, eventually resulting in alcoholic

liver cirrhosis (Lieber, 2003). Alcohol metabolism also promotes steatosis by enhancing hepatic uptake of

circulating lipids and reducing hepatic excretion of glycoproteins (Lieber, 2003).

Alcohol oxidation by both the ADH and MEOS systems produces acetate, which is mostly

metabolised to carbon dioxide and water (Figure 1, page 22). Only a small proportion (< 5% of a 20 gram

intake) of the acetate produced from alcohol metabolism is used for de novo lipogenesis. The largest

proportion of ingested alcohol carbons are moved to peripheral tissues in the form of acetate where

they are used as energy (Siler et al., 1999, Siler et al., 1998) at the expense of lipolysis (Suter and

Tremblay, 2005). Lipolysis is suppressed by approximately 30% after alcohol consumption, which in turn inhibits fat mobilisation (Feinman and Lieber, 1999, Jequier, 1999). The interaction of alcohol with lipid metabolism thus favours fat infiltration of the liver and lipid storage, and is therefore also relevant to the effect of alcohol use on body composition and body weight (Feinman and Lieber, 1999).

During alcohol metabolism via the MEOS, the most prominent form of cytochrome P450 involved is CYP2E1 (Lieber, 2003). After alcohol intake the activity of CYP2E1 may increase up to fourfold (Tsutsumi et al., 1989) and is thought to contribute to the development of the alcoholic liver disease (Lieber, 2000). In addition to alcohol oxidation, CYP2E1 also mediates particular processes in fatty acid and ketone (e.g. acetone) metabolism (Koop and Casazza, 1985). It has been argued that steatohepatitis can be the result of upregulated CYP2E1 activity caused by chronic heavy alcohol consumption (Lieber, 2000). In the metabolism of alcohol by CYP2E1, several types ROS are generated, which can damage hepatocytes by increasing oxidative stress, affecting fat metabolism and inactivating essential enzymes (Figure 1, page 22). The harmful effects of ROS are aggravated if the body's normal antioxidant defense systems against oxidative damage, such as glutathione and vitamin E, are impaired. Predictably, alcohol and its metabolism decrease both glutathione and vitamin E levels (Lieber, 2000). Acetaldehyde reduces glutathione concentrations in the liver (Lieber, 2000) and patients with cirrhosis have decreased liver concentrations of vitamin E (Leo et al., 1993). Alcohol metabolism via the MEOS further disturbs lipid and fatty acid metabolism, by increasing alpha-hydroxylation, liver fatty acid binding protein and fatty acid esterification (Figure 1, page 22) (Lieber, 2003).

Second to the gastric mucosa, the liver is exposed to the highest levels of intact ethanol molecules that are rapidly absorbed by the liver through the hepatic portal vein (Paton, 2005). Hepatic damage as a result of heavy alcohol use results in reduced nutrient absorption, particularly of fat-soluble vitamins due to impaired bile secretion. This damage also leads to impaired hepatic activation of nutrients (e.g. vitamin B6), changed storage of nutrients (e.g. folate) and increased nutrient degradation (e.g. vitamin A) (Lieber, 2000, Lieber, 2003).
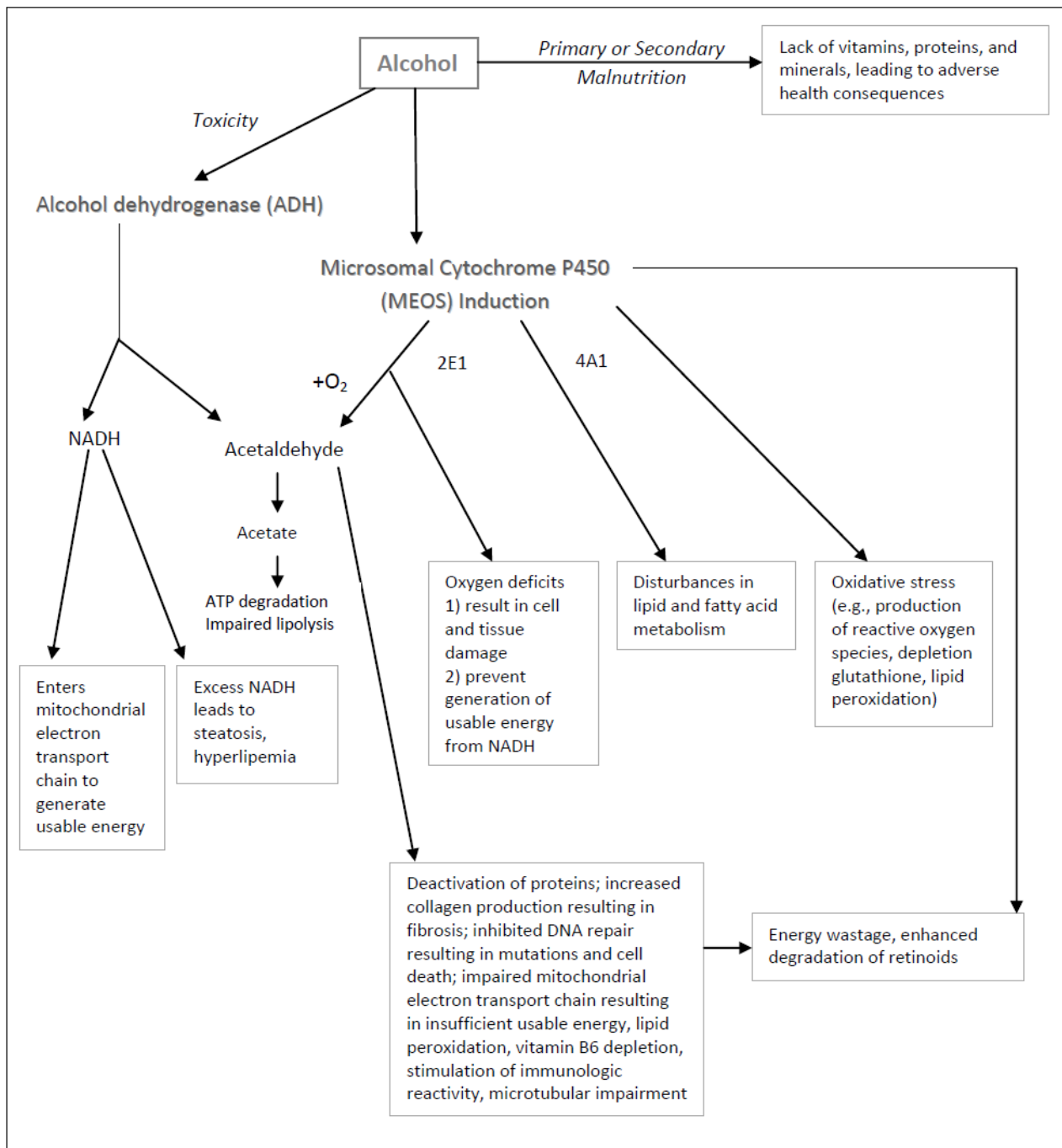
Figure 1. Summary of alcohol metabolism and resultant effects on hepatic function and nutrient metabolism
Source: Adapted from (Lieber, 2000, Lieber, 2003)

3.3   Effect of Alcohol on Mucosal Morphology

Both *chronic* and *acute* alcohol intake have been shown to affect gastrointestinal mucosal morphology.

Animal and human studies investigating the effects of *chronic* alcohol consumption on the mucosa of the

small intestine have produced conflicting findings. In experimental studies investigating the intestinal

effects of *chronic* alcohol exposure, both normal and significantly changed histology have been reported when light microscopy was used (Bode, 1980, Persson, 1991, Vaquera et al., 2002). In some studies showing normal mucosa using light microscopy, changes to mucosal structure were seen when electron microscopy and quantitative morphometry were used. Changes include goblet cell hyperplasia, decreased villi surface area, and gastric mucosal metaplasia (Bode and Bode, 2003, Bode, 1980, Persson, 1991). Endoscopic duodenal biopsies using light microscopy in *chronic* alcohol dependents have shown both normal and significantly altered intestinal histology (Bode and Bode, 2003, Dinda and Beck, 1984). In the majority of these studies the endoscopy and biopsy were performed three to fourteen days after hospital admission. This could partly explain the contradictory findings, since the well known rapid regeneration rate of intestinal epithelium following abstinence from alcohol, may have resulted in healing of lesions and damage in those who underwent endoscopy after a longer period of hospital admission. Casini et al (1999) reported changes to the matrix network and an increase in myofibroblast-like cells in the duodenal mucosa of *chronic* alcohol abusers, which may point to intestinal mucosa fibrosis. The documented epidemiological association between alcohol consumption and risk of major gastric and duodenal bleeding (Kelly et al., 1995) further supports the possibility that the mucosal injury seen in *acute* alcohol administration may in fact also occur in *chronic* exposure of the intestine to large quantities of alcohol. The inconsistent findings of studies that examined the effects of *chronic* alcohol exposure on the intestine may be partly explained by the variable study designs, including study type, alcohol dose administered, age, gender and animal type used (Bode and Bode, 2003).

Animal studies have shown that *acute* administration of alcohol dilutions that are comparable to those of commonly available alcoholic beverages causes mucosal damage in the small intestine. This damage includes haemorrhagic erosions, haemorrhage in the lamina propria and epithelial cell loss at the villi tips (Beck and Dinda, 1981). Oral or intragastric alcohol administration in animal models results in lesions being most evident in the duodenum (Baraona et al., 1974). Similar lesions were seen in volunteers three hours after oral intake of an alcohol dose of one gram per kilogram body weight (Gottfried et al., 1978). These findings are further supported by evidence from a large, prospective case-control study where intake of alcoholic beverages significantly increased the risk of duodenal bleeding in

non-predisposed persons (Kelly et al., 1995). Additionally, the relative risk of acute upper gastrointestinal bleeding has been shown to increase with rising alcohol consumption (Kaufman et al., 1999).

The exact mechanisms whereby alcohol causes these significant and damaging morphologic changes have not been fully elucidated. Early studies showed that alcohol has a direct toxic effect on the mucosal epithelium (Bode, 1980). Experimental studies suggest that the initial event in the mucosa in response to alcohol is an enhanced influx of leukocytes, which results in an increased release of injurious mediators, such as leukotrienes (Beck et al., 1988) reactive oxygen species (Dinda et al., 1996) and histamine by mast cells (Dinda et al., 1988).

The effects of alcohol on mucosal morphology may result in changes in nutrient absorption and gastrointestinal haemorrhage in the short term, with undernutrition and nutrient deficiencies with longer term use.

3.4   Effect of Alcohol on Mucosal Enzymes

Acute and *chronic* alcohol exposure can impede the activity and function of many brush border enzymes as well as enzymes in other enterocyte compartments (Bode and Bode, 2003). Enzymes, such as Na(+)-K(+)-ATPase may be inhibited with alcohol intake, resulting in a decreased absorption of substances that require active, energy-dependent transport mechanisms (Persson, 1991). Rodent studies have found both decreased and unaltered disaccharidase (lactase, sucrase, maltase and trehalase) activity after *acute* and *chronic* alcohol exposure (Bode, 1980, Persson, 1991). *Chronic*, heavy alcohol use may cause alcohol-exacerbated lactase deficiency resulting in diarrhoea (Perlow et al., 1977) and jejunal biopsies in humans have found lower than normal lactase activity in some alcoholics (Bode and Bode, 2003). *Chronic* alcohol exposure increases the activity of the enzyme, gamma-glutamyl transferase in the intestinal mucosa in animal experiments and in humans (Persson, 1991).

At this point, the effects of alcohol consumption on mucosal enzymes are not fully known and more research is needed to elucidate possible effects, and to understand the nutritional implications of the enzymatic effects that have been documented. However, based on available evidence, it is possible

that alcohol consumption, both *acute* and *chronic* may interfere with the absorptive capacity of the gastrointestinal system via effects on mucosal enzymes, for example the disaccharidases.

3.5   Effects of Chronic Alcohol Use on Absorption, Activation, Utilisation and Excretion of Specific Nutrients

In *chronic* alcoholism, primary malnutrition can result when alcohol displaces macro- and micronutrients in the diet (see section 3.7.2 for detail). Secondary malnutrition may be caused by maldigestion or malabsorption of nutrients due to the negative effects of *chronic* alcohol use on gastrointestinal function, including pancreatic insufficiency and impairment in the functioning of the small intestine. Once alcohol-related organ damage, such as liver disease and chronic pancreatitis due to direct toxic effects manifest, inefficient nutrient metabolism and retention and impaired nutrient utilisation are exacerbated. A further contributor to poor nutritional status is the impaired activation, utilisation, degradation and increased excretion of nutrients that results from *chronic* heavy alcohol use and subsequent organ damage (Lieber, 2000, Lieber, 2003).   It is important to note that studies in humans, primates, and rodents have established that alcohol can cause organ damage even in well-nourished people. Furthermore, micronutrient deficiencies can occur in alcoholics, with and without organ disease (Lieber, 2003).

A summary of the effects of *chronic* alcohol use on absorption, activation, utilisation and excretion of specific nutrients is presented in Table 2.

Table 2. Effects of chronic alcohol use on absorption, activation, utilisation and excretion of specific nutrients

Nutrient	Primary effects	Possible mechanisms and/or comments
Protein [a]	Increased faecal nitrogen excretion	Occurs in alcohol abusers with and without alcohol-related organ damage
	Reduced absorption	Alcohol impairs intestinal protein hydrolysis
	Reduced duodenal absorption	Prominent alcohol-induced mucosal damage in duodenum
Fat [a]	Steatorrhea	Occurs in alcohol abusers with and without alcohol-related organ damage
	Reduced duodenal absorption	Prominent alcohol-induced mucosal damage in duodenum
Carbohydrates [a]	Reduced duodenal absorption	Prominent alcohol-induced mucosal damage in duodenum
Folate [b]	Impaired absorption and decreased hepatic uptake	Alcohol inhibits expression of the reduced folate transporter
	Increased urinary excretion	Decreased renal conservation of circulating folate Megaloblastic anaemia is common in alcoholics
Vitamin B12 [a] [e]	Impaired absorption	Alcohol-induced pancreatic insufficiency results in insufficient luminal protease activity and alkalinity, which normally function to release vitamin B12 from the 'r' protein
Vitamin B6 [c]	Increased destruction and decreased activation	Rapid destruction by acetaldehyde in erythrocytes Hepatic damage leads so decreased activation
Thiamin [d]	Reduced absorption, phosphorylation and low circulating concentrations Impaired cellular thiamin utilisation	Due to hepatic damage in alcohol liver disease Deficiency causes Wernicke-Korsakoff syndrome, an alcohol-linked neurological disorder and plays significant role in other alcohol-induced brain injuries, such as cognitive impairments, including alcoholic dementia
Vitamin A [e]	Decreased hepatic levels	Liver disease alters the liver's ability to take up beta-carotene and/or convert it into vitamin A Alcohol promotes hepatic secretion of vitamin A
Vitamin D [f]	Decreased circulating concentrations	Impaired absorption from impaired biliary secretion, related malnutrition and reduced sun exposure Impaired renal synthesis and/or increased degradation of 1,25 dihydroxyvitamin D
Calcium and Phosphorus [g]	Disrupted metabolism and low circulating concentrations	Disturbances in calcium-regulating hormones (parathyroid hormone, $1,25(OH)_2D$, calcitonin) Contributing mechanism for harmful effects on bone
Magnesium [a]	Low circulating concentrations	Increased urinary excretion or diarrhoea
Zinc [a]	Low circulating concentrations	Increased urinary zinc excretion
Iron [h]	Deficiency and anaemia	Gastrointestinal blood loss and complications of heavy alcohol use and alcoholic cirrhosis
	Hepatic overload	In alcoholic cirrhosis, synergistic hepatotoxic effects in the development of alcoholic liver disease

Sources: [a] (Bode and Bode, 2003); [b] (Bode and Bode, 2003, Foster and Marriott, 2006, Lieber, 2000); [c] (Bode and Bode, 2003, Lieber, 2000); [d] (Bode and Bode, 2003, Martin et al., 2003); [e] (Lieber, 2003); [f] (Alvisa-Negrin et al., 2009, Malik et al., 2009, Shankar et al., 2008); [g] (Keiver et al., 2005, Lieber, 2000); [h] (Bode and Bode, 2003, Ioannou et al., 2004, Lieber, 2000)

As depicted in Table 2, *chronic* alcohol use may negatively impact the status of numerous nutrients in the body. A number of these impacts are related primarily to alcohol-related organ damage, which is a more advanced complication of *chronic* alcohol use. However, some of the impacts have been observed in drinkers without organ damage. Examples include effects on macronutrients, folate, vitamin D, calcium and phosphorus. While binge drinking over the short term is not expected to result in the

organ damage seen with *chronic* alcoholism, the impacts of *chronic* alcohol use that are not related to organ damage may inform an understanding of possible effects of binge drinking on nutritional status.

3.6   Effects of Acute Alcohol Use on Absorption, Activation, Utilisation and Excretion of Specific Nutrients

Some understanding of the effects of *acute* alcohol consumption on nutrient status has been gleaned from experimental animal and human research (Beck and Dinda, 1981, Bode and Bode, 2003, Hayashi et al., 1992, Thomson, 1984) and the following effects have been documented:

Acute exposure of the small intestine to alcohol has been shown to hinder the active transport of numerous nutrients through the epithelial layer of the mucosa (Beck and Dinda, 1981, Bode and Bode, 2003, Bode, 1980). Impaired absorption has been described for monosaccharides, lipids (fatty acids and monoglycerides) and also for vitamins, as described below (Beck and Dinda, 1981, Bode and Bode, 2003, Bode, 1980). Alcohol can interfere with the uptake of essential amino acids and decreased intestinal absorption of amino acids (e.g. alanine, glycine and methionine) following an alcohol dose has been described (Lieber, 2003, Bode and Bode, 2003).

Acute alcohol administration causes a decrease in serum folate levels (Bode and Bode, 2003). Low serum levels, indicative of folate deficiency have been reported in approximately 60 to 70% of binge drinking adults (Halsted and Keen, 1990), with reduced absorption being one of the possible causative factors (Lindenbaum, 1980).

Acute alcohol administration reduces calcium levels in both human and animal studies (Avery et al., 1983, Diez et al., 1997, Laitinen et al., 1991, Petroianu et al., 1991) and this reduction has been found to be dose-dependent (Krishnamra et al., 1987, Sampson et al., 1999) and to last for up to 24 hours with higher alcohol doses (Hemmingsen and Kramp, 1980). A recent study in a rat model found that *acute* alcohol administration at physiologically relevant doses reduced circulating ionised calcium concentrations. This alcohol-induced reduction in circulating ionised calcium increased with alcohol dose and was still evident after 48 hours, when blood alcohol was undetectable (Keiver et al., 2005). Evidence suggests that hypocalcaemia during alcohol use may be caused by an alcohol-induced shift in ionised

calcium from the extracellular into the intracellular compartment within soft tissue and bone (Peng and Gitelman, 1974). Thus, alcohol may induce hypocalcaemia through injury to, or functional impairment of cellular calcium transporters or channels. Higher doses of alcohol may therefore result in a more severe and sustained injury, and so cause a more prolonged hypocalcaemia (Keiver et al., 2005). The health implications of a prolonged decrease in blood ionised calcium concentrations are unknown.

As described above, effects of *acute* alcohol use have been documented for some nutrients, such as folate and calcium. However, at this point the *acute* effects of alcohol use on many of the other nutrients and the consequences of these effects are not known.

3.7   Effect of Alcohol Consumption on Eating Behaviour, Dietary Intake and Health

In the literature alcohol use has been shown to alter dietary intake in a number of different ways, depending on the drinking pattern, duration of drinking and quantity of alcohol consumed. Alcohol intake has a direct effect on total energy consumption via its contribution to energy intake, as well as an indirect effect on dietary intake (energy and nutrients) by influencing eating behaviour (eating occasions, foods choices and amount of food eaten) (Foster and Marriott, 2006).

3.7.1   Potential energy contribution of alcohol

On a per gram basis, alcohol is the second most energy-dense of all the macronutrients after fat, providing 29 kilojoules per gram, while fat provides 37 kilojoules per gram and carbohydrates and protein each provide 17 kilojoules per gram. Alcohol-containing beverages consist mainly of water, pure alcohol and variable quantities of carbohydrates, and for the most part they contain negligible amounts of other nutrients (Lieber, 2003). Some alcoholic drinks contain trace amounts of protein, vitamins and minerals. For example, beer contains very small amounts of B-vitamins and some minerals and wine contains some trace elements. However, the quantities of these micronutrients vary considerably between different beers and wines and depend on production methods and raw ingredients (Foster and Marriott, 2006).

Therefore, the kilojoules provided by alcoholic drinks are derived by and large from their alcohol and carbohydrate content. There is considerable variation in both the alcohol and carbohydrate content

of alcoholic drinks. Average alcohol content ranges from about four to five grams per 100 mL in beer and alcoholic coolers, to about 12 grams per 100 mL in wine and pre-mixed cocktails and 40 to 50 grams per mL in distilled spirits. Vodka, cognac and whiskey contain no carbohydrates, while dry white and red wines contain approximately 0.2 to one grams of sugar per 100 mL, dry fortified wines and beer contain about three grams and port and sweet white wines contain up to about 12 grams of sugar per 100 mL (Lieber, 2003). Due to their low nutrient content, alcoholic beverages are often considered to be "empty" kilojoules (Lieber, 2003).

An important point to consider when quantifying the energy contribution of alcohol is the thermogenic effect thereof. A recent review by Suter and Tremblay (2005) reported that the thermic effect of alcohol in healthy moderate consumers of alcohol is between 15% and 25% of the energy value of the alcohol consumed. However, heavy alcohol consumption results in an increased thermogenic effect. Suter and Tremblay (2005) explain that alcohol oxidation via the MEOS system requires NADPH. The MEOS changes the coupling of alcohol oxidation to oxidative phosphorylation by using NADPH, thereby generating heat and thus "wastage" or "loss" of energy occurs. This energy "loss" is more significant when a larger proportion of alcohol energy is metabolised via the MEOS, as is the case in heavy and chronic alcohol consumption (Suter and Tremblay, 2005). On the contrary no major energy loss is evident during alcohol oxidation via the ADH system (Lieber, 1991). In fact, oxidation of alcohol via the ADH pathway produces NADH, which can be used for ATP production (Suter and Tremblay, 2005). Thus, when alcohol is metabolised by the ADH system, 16 moles of ATP per mole of alcohol are produced (Lands and Zakhari, 1991). However, when alcohol is metabolised via the MEOS, less than 10 moles of ATP are produced per mole of alcohol (Lands, 1991). It can therefore be argued that the underweight status common in chronic alcoholics may be attributable in part to this concept of "energy wastage" (Foster and Marriott, 2006, Suter and Tremblay, 2005). The dose of alcohol which induces the MEOS varies between individuals and is not fully known (Suter and Tremblay, 2005).

3.7.2   Changes in eating behaviour and dietary intake as a result of alcohol intake

Evidence points to the fact that over the short term, alcohol consumption tends to increase subsequent food intake with a consequent increase in total energy intake (Yeomans, 2010).

The short term or acute effects of alcohol on food intake have largely been studied using laboratory-based, experimental studies that examined food intake and physiological indicators related to food intake, such as hunger, satiation and appetite after various test and pre-load meals in healthy individuals (Yeomans, 2010). On evaluation of the available evidence on the short term effects of alcohol intake on food intake, Yeomans (2010) concluded that there is a failure to compensate for energy ingested as alcohol by reducing energy intake in the form of food, and that alcohol energy is additive to energy ingested from other sources under these circumstances. Yeomans (2010) also indicated that preload studies of the effects of alcohol on subsequent food intake showed no evidence that energy ingested as alcohol results in a reduction in ensuing food intake. In fact, in most studies individuals were prone to eat more food after an alcohol pre-load than after no pre-load, which suggests that alcohol intake may promote subsequent food intake, resulting in increased energy intake. These findings were consistent for most of the studies, irrespective of the wide variety of preload beverages used, whether alcohol was administered disguised/undisguised or whether controls were matched for energy content and sensory quality (Yeomans, 2010).

There is some evidence that alcohol has the ability to enhance short term appetite (Yeomans, 2010, Foltin et al., 1993, Westerterp-Plantenga and Verwegen, 1999). Essentially, findings suggest that alcohol intake promotes short term passive over-consumption of energy (Yeomans et al., 2003) and does not seem to elicit the satiety systems that control short term food intake, fundamentally resulting in a short term failure to compensate for energy ingested as alcohol (Yeomans, 2010). However, appetite and the regulation of food intake is very complex, relevant mechanisms are not yet clearly understood and additional research is required (Yeomans, 2010, Hirschberg, 1998, Schwartz et al., 1999, Vettor et al., 2002).

A recent qualitative study in American college students, reported that binge drinking may result in eating without hunger during or after consuming alcohol. On the other hand, larger amounts may be

eaten prior to drinking in anticipation of a binge drinking occasion in order to be able to tolerate more

alcohol (Nelson et al., 2009a). In a follow-on cross-sectional study in college students (*n=3406*; mean age

24.2 years ±5.9 years) approximately 80% of participants reported alcohol-related eating "always or

usually" during the preceding year. This study also found that binge drinking was significantly associated

with poor eating behaviours (< 5 daily servings fruit and vegetables, breakfast consumed on < 5 days per

week, fast-food consumption at least several times per week), as well as unhealthy weight control

behaviour and sedentary behaviour (Nelson et al., 2009b). However, Foster and Marriot (2006) reported

that individuals who engage in binge drinking frequently avoid eating before they drink in order to get

drunk more quickly.

Epidemiologic studies in free living populations, mostly consisting of non-drinkers and moderate

alcohol consumers, have examined trends in energy intake in relation to alcohol consumption levels,

reflecting the longer term effects of alcohol intake on energy and food intake (Yeomans, 2010, Colditz et

al., 1991, De Castro and Orozco, 1990). The balance of epidemiologic evidence seems to indicate that

over the longer term energy ingested as alcohol is additive to other energy sources in the diet (Yeomans,

2010), suggesting that moderate alcohol intake may result in long term passive over-consumption of

energy (Yeomans, 2004). Positive associations were found between alcohol and energy intake in both

adult men and women in two large cohort studies, namely the Nurses' Health study and the Health

Professionals follow up study (Colditz et al., 1991). Evidence from these two large cohort studies as well

as detailed analyses of food diaries of adults (De Castro and Orozco, 1990) suggest that the alcohol

energy ingested adds to the energy from other macronutrient sources. In these longer term studies, no

consistent evidence points towards increased food intake on drinking days, as is found with short term

alcohol intake. In interpreting these results it must be borne in mind that evidence clearly indicates the

presence of inter-individual variation in the long term effects of alcohol use on food intake and that this is

also influenced by variation in the history of alcohol use (Yeomans, 2010).

Finally, with chronic alcoholism and comorbid alcohol-related illness, poor dietary intake and the

substitution of food with alcohol is most often seen (Suter and Tremblay, 2005). Hangover,

gastroduodenitis, inebriation-induced suppression of consciousness and social marginalisation are causes

of poor dietary intake. Alcohol-related diseases in chronic alcohol users are also know to affect appetite, further impacting on dietary intake. The associated emaciation, undernutrition and resultant negative effect on gastrointestinal mucosa leads to further malabsorption. The consequent poor nutritional status in chronic alcoholics increases their susceptibility to organ dysfunction and related harmful health impacts (Lieber, 2000, Lieber, 2003).

3.7.3   Nutrition-related health consequences of alcohol intake

As discussed in previous sections, excess alcohol consumption may result in the displacement of micronutrients in the diet (Ferreira and Willoughby, 2008). The requirements for certain micronutrients may also be increased as a result of the metabolism of alcohol (Van Den Berg et al., 2002) as well as organ damage in chronic excessive use of alcohol (Lieber, 2003). Although alcohol can be viewed as being energy-dense, with a high amount of energy per unit weight, it is nutrient-poor, thus potentially reducing the nutrient-density of the diet. In view of these factors, it is reasonable to speculate that heavy alcohol use may increase the risk for nutrient inadequacies and their related deficiency symptoms/syndromes with added risk of potentiating disease development, including NCDs. The relative risk for developing cardiovascular diseases, cancers and digestive diseases is demonstrated by a dose-response curve as a function of daily alcohol intake, with the risk for NCDs development increasing significantly at six or more standard drinks per day (Corrao et al., 2004).

When considering the energy density of alcohol, it is feasible that the ingestion of alcohol energy above energy requirements could result in a positive energy balance over time if food intake is increased, with ensuing weight gain. However, controversy exists as to whether the increase in energy intake that results from alcohol consumption itself is a risk factor for overweight and obesity. Epidemiological studies have provided contradictory findings. Some evidence supports a positive correlation between alcohol use and body mass index (BMI) or obesity measures (Kent and Worsley, 2009, Schroder et al., 2007, Wannamethee et al., 2005). Other studies show a J-shaped association with light to moderate drinking being linked to a reduced body size and abstinence and heavy drinking being associated with higher waist-to-hip ratio or BMI (Arif and Rohrer, 2005, Lukasiewicz et al., 2005). Accordingly, Foster and

Marriot (2006) state in a review that the majority of prospective data shows an increased risk of weight gain and obesity with heavy alcohol intake of greater than 30 grams or three drinks per day but not with light to moderate drinking. Yeomans (2010) reports that moderate alcohol consumption may be associated with a reduced risk of obesity development unless the alcohol is consumed through binge drinking, as discussed in more detail below. The inconsistencies that have been observed may be explained by the effects of confounders in studies, as well as by various methodological issues linked to studies that have measured alcohol consumption, such as misreporting of intake, which is specifically relevant in overweight/obese participants (Foster and Marriott, 2006). Cigarette smoking is an important confounder to consider in the relationship between weight and alcohol intake. The British Regional Heart Study found that the strongest effect of alcohol on weight was among non-smokers and that current smokers have a lower mean BMI compared to non-smokers at almost every level of alcohol intake (Wannamethee and Shaper, 1992, Wannamethee and Shaper, 2003). Dietary intake (as mentioned in section 3.7.2), physical activity levels, gender and genetics are also important factors that may affect the association between alcohol consumption and body weight (Yeomans, 2010, Suter and Tremblay, 2005). Tremblay et al (1995) found that alcohol intake, especially in conjunction with a high fat diet and sedentary behaviour, was associated with abdominal obesity, particularly in women.

Frequency of alcohol intake and a binge drinking pattern also seem to be factors that may affect the relationship between alcohol consumption and body weight (Yeomans, 2010, Suter and Tremblay, 2005). Frequency of intake affects the amount of alcohol consumed, with increased frequency resulting in an increased amount of alcohol consumed (Suter and Tremblay, 2005).   A positive relationship has been demonstrated between drinking frequency and waist circumference even when total alcohol consumption was controlled for (Tolstrup et al., 2008). As far as binge drinking is concerned, data from the Third NHANES indicated that this drinking pattern may be a risk factor for obesity (Arif and Rohrer, 2005). In the latter study, total intake was inversely associated with BMI but binge drinkers were more likely to be overweight or obese compared to participants who consumed the same quantity of alcohol over multiple occasions (Arif and Rohrer, 2005). Furthermore, binge drinking and binge eating have been found to be associated behaviours (Fischer and Smith, 2008, Harrell et al., 2009), with both behaviours

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classified as impulsive behaviours, and studies showing an association between impulsivity measures and binge eating (Nasser et al., 2004, Steiger et al., 1999, Wiederman and Pryor, 1996), binge drinking (Balodis et al., 2009) and obesity (Nederkoorn et al., 2006a, Nederkoorn et al., 2007, Nederkoorn et al., 2006b). It has thus been suggested that alcohol may be a component of the weight gain risk as a consequence of impulsive behavioural choices (Yeomans, 2010).

After examining this literature, it is plausible that protracted and frequent binge-drinking occasions may increase the risk for nutrition-related health consequences, including the displacement of micronutrients, weight gain, with ensuing overweight and obesity and NCD development. However, it is also clear that to further clarify the relationships between alcohol use and nutrition-related health outcomes, detailed data on alcohol use and drinking patterns are needed, including frequency, quantity and density of alcohol consumption, in combination with reliable and quantitative dietary, physical activity and lifestyle data.

3.8   Concluding Perspectives

Nutritional implications of alcohol use result from an interplay between the immediate effects on the gastrointestinal tract (digestion, absorption and haemorrhage), the metabolic impacts related to alcohol oxidation (metabolism, utilisation and excretion), the energy contribution of alcohol itself and the influence of drinking on total energy and food intake. The nutrition-related implications of this interplay depend on the frequency, pattern and quantity of alcohol used, as well as individual factors. At present, the effects of this alcohol-nutrition interplay are not known in free living adolescents who use alcohol heavily and frequently engage in binge drinking. When considering the literature reviewed, it is reasonable to speculate that several known nutrition-related problems that may result from alcohol metabolism, chronic alcoholism and acute alcohol use could plausibly also manifest in the binge drinking adolescent. These conjectures may become even more relevant when considering the usual quantities of alcohol consumed per drinking occasion by binge drinking adolescents as well as the protracted binge drinking behaviour in adolescents (see section 4 for a detailed discussion on alcohol use in adolescents).

It can be speculated that the toxic levels of acetaldehyde, NADH and acetate produced during the metabolism of large quantities of alcohol could lead to disturbances in lipid metabolism in heavy drinking adolescents, for example reduced lipolysis and increased risk for steatosis. It is also possible that the generation of ROS and oxidative stress by alcohol metabolism could initiate hepatocyte damage in adolescents who engage in frequent and protracted heavy alcohol use, with ensuing disturbances in metabolic liver functions.

The reported nutritional consequences of heavy chronic and acute/short term/binge alcohol intake on the gastrointestinal tract, dietary intake and nutrient status may inform an understanding of the nutrition-related effects of heavy alcohol use in adolescents (Table 3)

Table 3. Nutritional consequences of heavy chronic and acute/short term/binge alcohol intake

Consequences of chronic alcohol intake	Consequences of acute/short term/binge alcohol intake
Eating behaviour and dietary intake	
Contribution of alcohol energy to total energy intake	Contribution of alcohol energy to total energy intake
Poor food and nutrient intake(e.g. from hangover, gastroduodenitis or alcohol-related disease) with eventual undernutrition, emaciation	Food intake may be reduced/avoided in anticipation of alcohol use with meal disruptions and reduced nutrient intakes
Displacement of macronutrients and micronutrients with alcohol, therefore reduced nutrient-density of the diet	Displacement of macronutrients and micronutrients with alcohol, therefore reduced nutrient-density of the diet
	Ingested alcohol energy may be additive to energy intake from other sources (failure to compensate for added alcohol energy) and may promote weight gain over time and risk of overweight and obesity
	Alcohol use may promote subsequent food intake, with increased energy intake and ensuing weight gain and risk of overweight and obesity
	Eating without hunger before or after consuming alcohol (alcohol-related eating)
	Eating larger amounts prior to and in anticipation of binge drinking
Gastrointestinal-related	
Reduced nutrient absorption via disrupted absorptive mechanisms and mucosal damage e.g. folate and vitamin B12	Reduced nutrient absorption via disrupted absorptive mechanisms e.g.folate, monosaccharides, amino acids, monoglycerides and fatty acids
Damage to mucosal morphology and gastrointestinal haemorrhage, with loss of iron	Damage to mucosal morphology and gastrointestinal haemorrhage, with loss of iron
Disrupted intestinal enzyme function	Disrupted intestinal enzyme function
Reduced nutrient absorption as a result of hepatic damage, particularly fat-soluble vitamins	
	Vomiting and diarrhoea associated with excessive drinking over a short period with resultant nutrient losses and reduced nutrient absorption
Metabolism-related /nutrient levels	
Reduced circulating vitamin D levels	
Impaired renal synthesis and/or increased degradation of 1,25 dihydroxyvitamin D	
Disrupted calcium metabolism and reduced circulating calcium levels	Disrupted calcium metabolism and reduced circulating calcium levels
Disturbances in lipid and fatty acid metabolism	
Reduced vitamin E and glutathione due to oxidative effects of alcohol metabolism	
Impaired hepatic nutrient, activation and storage and increased nutrient degradation with and without alcohol-related hepatic damage e.g. vitamin B6, thiamin	
Increased urinary excretion e.g. folate, magnesium, zinc	
	Reduced circulating folate levels

Abbreviation: e.g.: example

When considering the above-mentioned potential nutritional implications of acute/short

term/binge drinking, it is important to point out that it is unlikely that *occasional binge drinking* by

adolescents will have major effects on current nutritional status. However, regular and persistent binge

drinking by adolescents is likely to have more significant nutritional implications, both in terms of nutrient metabolism and dietary and energy intake. At present it is not known for how long this high risk drinking pattern must persist before any one or combination of nutritional challenges may start to emerge. It is a matter of cause that current or past nutritional status of the binge drinking adolescent would play an important role in determining the progression of nutritional challenges in this life stage.

4   ALCOHOL USE IN ADOLESCENTS

4.1   Definition of Adolescence

The WHO defines adolescence as the age group from 10 to 19 years, while the term youth is used for the age group 10 to 24 years (World Health Organization, 2005). As in the 1989 United Nations Convention of the Rights of the Child, adolescents are sometimes categorised as children, which is defined as the group younger than 18 years of age (World Health Organization, 2005). In terms of development, adolescence is the life stage during which there is a gradual transition from childhood to adulthood, beginning with the onset of puberty. It is a period during which essential physiological, psychological and social transformations occur and adolescents must deal with many significant changes to their bodies, emotions, thoughts, perspectives and environments (Stang et al., 2008, United States Department of Health and Human Services, 2007).

Adolescents make up approximately 18% of the total world population (Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, 2008). In less developed regions, adolescents have a higher demographic weight and Africa is expected to see its adolescent population expand more rapidly than Asia and Latin America due to a lower fertility decline (World Health Organization, 2005). In South Africa, adolescents make up roughly 20% of the total population (Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, 2008).

4.2   Prevalence of Alcohol Use

Alcohol use in adolescence is described in the literature using the measures: "ever used alcohol", defined as at least one alcoholic drink on at least one day during their life; "current alcohol use", defined as having had at least one alcoholic drink on at least one day during the past month and "heavy episodic" or "binge drinking", defined as having had five or more drinks of alcohol in a row (within a couple of hours) in the past month (Eaton et al., 2010, Hibell et al., 2009, Reddy et al., 2010a).

The findings of some of the most recent studies and surveys on adolescent alcohol use in developed and developing countries, including South Africa are outlined in Table 4. Based on this evidence (Table 4), prevalence of adolescent alcohol use seems to be the highest in Europe, followed by the US. Data from developing countries shows slightly lower rates of adolescent alcohol use. These trends are in line with findings from the current WHO Global Status Report on Alcohol and Health, which describes the highest alcohol consumption levels in the developed world, including Western and Eastern Europe (World Health Organization, 2011b).

Table 4. Recent prevalence studies of adolescent alcohol use in select global areas

Country and study sample	Ever used alcohol (%)	Current user (%)	Binge/heavy episodic use (%)
United States of America, 2009 Youth Risk Behavior Survey, nationally representative sample [a]	73	42	24
2007 European survey of 15 to 16 year olds concerning substance use in 35 European countries (ESPAD), average over samples from all countries [b]	82	61	43
South Africa, 2008 Youth Risk Behaviour Survey, nationally representative sample [c]	50	35	29
Brazil, nationally representative sample [d]	not reported	34	48
Thailand, national sample [e]	49	30	6

Sources: [a] (Eaton et al., 2010); [b] (Hibell et al., 2009); [c] (Reddy et al., 2010a); [d] (Pinsky et al., 2010); [e] (Assanangkornchai et al., 2009)

When considering these statistics on heavy adolescent alcohol use, it is not surprising that it is deemed a significant public health problem both in developed (Mcardle, 2008, Miller et al., 2007) and developing countries (Parry et al., 2004c, Pinsky et al., 2010, Reddy et al., 2010a). Adolescents drink less frequently than adults, but they drink more heavily when they do drink alcohol (Substance Abuse and Mental Health Services Administration, 2006). American data indicates that on average, adolescents

drink approximately five drinks per occasion about six times a month (Substance Abuse and Mental Health Services Administration, 2006). This quantity of alcohol consumption puts the adolescent alcohol user in the binge alcohol consumption range (National Institute for Alcoholism and Alcohol Abuse, 2004, United States Department of Health and Human Services, 2007). Indeed, this binge drinking pattern is known to be highly prevalent among adolescents and young adults and results in considerable health risks in these life stages (Miller et al., 2007, Hingson et al., 2005). Evidence suggests that adolescents and young adults drink large quantities on weekends as they are seeking excitement and fun (Kuntsche and Cooper, 2010), resulting in a drinking culture characterised by heavy episodic weekend drinking, a pattern documented among adolescents in the developed and developing countries (Flisher et al., 2003, Heeb et al., 2008). Moreover, young people often drink on weekends with the intention of getting drunk (Room and Livingston, 2009). Intentional alcohol intoxication on weekends is seen as enjoyable and may in part be a compensation for day-to-day duties and demands, and an escape from everyday realities (Parker and Williams, 2003, Van Wersch and Walker, 2009).

Data from the US (Substance Abuse and Mental Health Services Administration, 2006) and South Africa (Reddy et al., 2010a) show that alcohol use, including harmful and risky drinking patterns, rises sharply throughout the adolescent period. In the most recent South African Youth Risk Behaviour Survey (YRBS), conducted in a national sample of grade 8 to 11 adolescents (*n=10270*), rates of ever using alcohol, past month binge drinking and past month alcohol use increased with age and grade (Reddy et al., 2010a). According to the 2007 Monitoring the Future study in the US, the percentage of adolescent who report drinking to intoxication at least once in the previous month rises from 6% among adolescents in the 8th grade to 18% among those in the 10th grade, with nearly one third of adolescents in the 12th grade reporting this pattern (Johnston et al., 2008). Binge or heavy episodic drinking also increases sharply during adolescence with rates being 10% in the 8th grade, 22% in the 10th grade and 26% in the 12th grade (Johnston et al., 2008).

In looking more closely at adolescent alcohol use in South Africa, certain trends in terms of ethnicity, region, gender, age of onset and binge drinking are evident. The most recent YRBS (Reddy et al., 2010a) reported that a significantly greater percentage of white (78%), mixed ancestry (67%) and

Indian (63%) adolescents had ever consumed alcohol when compared to African black participants (46%). Similarly, significantly more white (56%) and mixed ancestry (49%) adolescents were current alcohol users compared to their African black (32%) and Indian (35%) peers (Reddy et al., 2010a). Similarly, ethnic differences in adolescent alcohol use have also been documented in other regions of the world (Donath et al., 2011, Luczak et al., 2001, Rodham et al., 2005, Substance Abuse and Mental Health Services Administration, 2006). In terms of region, the Western Cape Province (53.0%) had the highest prevalence of current drinkers and along with the Northern Cape (45.6%) and Gauteng (48.1%), had a significantly greater proportion of current drinkers than the national average (34.9%) (Reddy et al., 2010a).

A substantial proportion of adolescents start using alcohol at a very young age. In South Africa, 11.9% of the national adolescent sample had used alcohol before the age of 13 years. More adolescents in younger age groups had their first drink before age 13 compared to learners in older age groups, indicating that initiation of alcohol use is now occurring at younger ages. Early initiation of alcohol use (before age 13) was significantly greater in white (27.5%), mixed ancestry (19%) and Indian (25.1%) adolescents compared to African black (9.7%) adolescents (Reddy et al., 2010a). In the US, almost a third of adolescents begin drinking before age 13 (Grunbaum et al., 2004).

In all of the alcohol use measures in the YRBS, males had significantly greater rates than females. However, this gender difference was not seen among mixed ancestry adolescents, where females had higher rates in all of the measures apart from initiation age (Reddy et al., 2010a). Gender differences in adolescent alcohol use have also been documented in Europe (Hibell et al., 2009), England (Rodham et al., 2005) and the US (United States Department of Health and Human Services, 2007), with male adolescents also mostly having higher rates of alcohol use.

In terms of binge drinking, a study examining trends in adolescent alcohol use at three sentinel sites in South Africa between 1997 and 2001 found binge drinking to be a common form of substance misuse among school-going youth of both genders, with over a third of the males in Cape Town reporting binge drinking by grade 11 (Parry et al., 2004a). In line with these findings, recent (past month) alcohol use, particularly weekend binge-drinking was reported in 32% of school-going adolescents in the Cape Town area (Flisher et al., 2003). Nationally, a significant increase in the proportion of adolescents who

reported binge drinking was reported in the YRBS in 2008 (29%) (Reddy et al., 2010a) compared to that reported in 2002 (23%) (Reddy et al., 2003). This increasing trend in adolescent binge drinking is in accordance with European surveillance (Hibell et al., 2009). Data suggests that the prevalence of binge drinking in South African adolescents is lower than in Europe, but slightly higher than in the US (Table 4). Significantly more South African males (33.5%) than females (23.7%) had engaged in binge drinking, which is in line with data reviewed from other countries in Table 4. The prevalence of binge drinking among mixed ancestry adolescents (38.6%) was significantly greater than in African black (26.4%) and Indian (23.1%) adolescents. Again the Western Cape was the worst affected province with significantly more adolescents (41.1%) practising binge drinking compared to the national average (28.5%) (Reddy et al., 2010a). Correspondingly, the most recent South African Health and Demographic Survey, which includes subjects 15 years and older, reported that 12% of male and 14% of female alcohol users engage in hazardous or harmful drinking, with hazardous drinking being especially prevalent over weekends. Rates of hazardous/harmful drinking rates are approximately 16 times higher for men over weekends compared to weekdays and about seven times greater for female alcohol users (Department of Health, 2007)

In some adolescents, early alcohol intake will result in the development of an AUD, meeting the diagnostic criteria for either alcohol abuse or dependence. According to the 2005 National Survey on Drug Use and Health in the US, almost 6% of adolescents aged 12 to 17 years meet the diagnostic criteria for alcohol abuse or dependence (Substance Abuse and Mental Health Services Administration, 2006). No similar national prevalence data for adolescents in South Africa is available, although based on regional data (Flisher et al., 2003) AUDs have been described as prevalent among South African adolescents in a report of the South African Stress and Health study (Herman et al., 2009). The risk for excessive drinking may be even higher in adolescents with alcohol dependent parents due to a combination of genetic and developmental aspects that reduce sensitivity to alcohol (United States Department of Health and Human Services, 2007).

In summary, prevalence data in South Africa indicate that heavy alcohol use by adolescents is highly prominent in the Western Cape Province and within the white and mixed ancestry population

groups in this country, and is largely characterised by a binge drinking pattern of consumption, especially on weekends. This drinking pattern is in line with international data on adolescent alcohol use patterns.

4.3   Consequences of Adolescent Alcohol Use

4.3.1   General health-related consequences

The adolescent life stage is one in which good physical health and low disease rates generally prevail (World Health Organization, 2005). Few studies have examined the general health status of adolescents with AUDs, for example the relationship between AUDs and liver injury.   As most adolescents are early in their drinking trajectory and have not had heavy alcohol exposure for extended periods of time, it can be speculated that they would not commonly display explicit signs and symptoms of the health problems known to be associated with heavy chronic drinking. However, research in this regard is equivocal. Recent findings suggest that while adolescents with AUDs engage in related problematic health behaviours, they do not yet demonstrate overt cardiovascular consequences of these behaviours (Thatcher and Clark, 2006). On the other hand, adolescent drinking has been associated with self reported health problems (Arria et al., 1995, Hansell and White, 1991, Newcomb and Bentler, 1987) and modest but demonstrable liver injury (Clark et al., 2001). Additionally, binge drinking in older adolescents has been associated with higher rates of cardiovascular disease in a large longitudinal study (Pletcher et al., 2005).

A further potential health problem involves the fact that early heavy alcohol use is associated with increased risk for future development of AUDs, adverse lifetime alcohol-related consequences and other substance abuse (Hingson et al., 2002, Hingson et al., 2001, Hingson et al., 2000). Research from the US shows that about 40% of early drinkers (initiation before age 15), report alcohol use and behaviour at some time during their lives that is consistent with an AUD diagnosis and this is four times greater than the proportion among drinkers who started after 21 years of age (Grant et al., 2004). According to a large, longitudinal study in the UK, adolescent binge drinking in both genders is associated with significant future adversity, including social adversity such as poorer educational outcomes and crime, as well as an increased risk of adult AUDs and other substance use (Viner and Taylor, 2007).

4.3.2   Neurological impacts

Research into the effects of heavy alcohol use during adolescence using adolescent animal models and human adolescent populations has expanded dramatically in recent years, focusing mainly on neurological impacts, such as alcohol-induced motor impairments (Silveri and Spear, 1998, White et al., 2002), neuropsychological performance (Brown et al., 2000, Ferrett et al., 2010) and structural and functional changes in the developing brain (Brown et al., 2000, Crews et al., 2000, De Bellis et al., 2000, Tapert and Brown, 1999). The neurological effects of alcohol use differ in adolescents and adults (Matthews, 2010). Generally adolescents are more sensitive than adults to the stimulating effects of alcohol, while they appear to be less sensitive to certain aversive effects of acute alcohol intoxication, such as ataxia, hangover and sedation and are less likely to fall asleep than adults (Doremus et al., 2003, Little et al., 1996, Silveri and Spear, 1998, Spear, 2002, Varlinskaya and Spear, 2004, White et al., 2002). The low sensitivity to these aversive effects may make adolescents more susceptible to some of the other harmful effects of alcohol use as they may be more likely to drink to the point of coma and may be more likely than adults to engage in activities that they are too impaired to perform (United States Department of Health and Human Services, 2007). In general females are more vulnerable to the effects of alcohol consumption than males, in part related to mean lower body weight and lower alcohol metabolising capacity (less ADH per unit of body mass) (Miller et al., 2007).

4.3.3   Adolescent risk-taking behaviours and other health-related behaviours

There is a 200% increase in overall morbidity and mortality rates in the period between middle childhood and late adolescence/early adulthood, which is primarily attributable to the rise in erratic, risk-taking and sensation-seeking behaviour that occurs during the pubertal period (United States Department of Health and Human Services, 2007). These high rates of risk-taking behaviours, exposure to high-risk environments and vulnerability to experimentation contribute to unintentional injuries, violence, high-risk sexual behaviour, suicide and homicide (Dahl, 2004). Adolescent alcohol abuse/dependence is a leading contributor to numerous harmful physiologic, psychologic and social health consequences, such

as injuries, interpersonal violence (Schneider et al., 2007), unplanned pregnancy, sexually transmitted

diseases, including HIV infection (Cooper and Orcutt, 1997, Cooper et al., 1994), school failure (Hill et al.,

2000), crime and violence (Valois et al., 1995), increased risk of adult alcohol dependence/abuse, illicit

drug use, social adversity (Viner and Taylor, 2007) and tobacco use (Miller et al., 2007).

A co-occurrence or clustering of unhealthy factors and risk behaviours, including increased BMI,

alcohol, tobacco and other drug use and violence may emerge during adolescence (Pasch et al., 2008).

The US Youth Risk Behavior Survey data showed that non-binge current drinkers were more likely to

engage in health risk behaviours including tobacco use, physical fighting, marijuana, cocaine and inhalant

use, have forced intercourse, be currently sexually active and use alcohol or drugs before last sexual

intercourse. Binge-drinking adolescents were even more likely than non-binge current drinkers to engage

in these and other health risk behaviours. These analyses also found a strong dose-response relationship

between binge drinking frequency and prevalence of health risk behaviours (Miller et al., 2007).

This clustering is also evident in South Africa. In the recent YRBS in South Africa, an analysis of

clustering risk behaviours using six risk behaviour domain measures, namely substance use, traffic safety,

hygiene, sexual behaviour, intentional and unintentional injury and nutrition (reflected by number of days

in past week fast-food and sweetened beverages consumed) and physical activity. These analyses

showed a clustering of risk behaviours (Reddy et al., 2010a), which is consistent with prior adolescent

health behaviour studies (Burke et al., 1997, Lytle et al., 1995). A three-cluster analysis by Reddy et al

(2010a) using the six risk behaviour domain measures found that three levels or clusters of risk taking

were present in the sample, namely lower risk, intermediate risk and higher risk. Adolescents in the

lowest risk cluster had the lowest rates for all the risk behaviour domain measures, with the exception of

the nutrition and physical activity domain, which was similar across all three clusters. In the intermediate

risk cluster adolescents had higher prevalence rates for substance use, violence, sexual and traffic safety

behaviour than the lowest risk cluster but these rates were below those of the higher risk cluster.

Adolescents in the highest risk cluster had the greatest rates for all the risk behaviour domain measures,

except for hygiene. Within the higher risk cluster rates for substance use, sexual behaviour and traffic

safety rates were found to be at least twice that of the national sample, with violent behaviour being

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greater than four times the national average. The analyses showed that the identified clusters tended to be better predictors of risk behaviour than demographic variables, such as gender, grade and ethnicity (Reddy et al., 2010a). Co-occurrence of health risk behaviours during adolescence has considerable potential to cause and exacerbate many negative health outcomes and burdens of disease later in adulthood. Ultimately, adolescents who use alcohol heavily and who also engage in other health risk behaviours are more vulnerable to adverse health outcomes.

Within the South African context, research in adults has found a relationship between environmental stressors, such as crime and violence, and substance use (Kalichman et al., 2006). Previous studies also show that community adversities, such as substance availability and violence frequently co-occur (Ward et al., 2001). In line with the findings in South African adults, a recent study in large sample of adolescents in three South African cities, found that environmental stressors were linked to both adolescent alcohol use and smoking, as well as diminished psychological and physical well-being (Brook et al., 2011).

Notwithstanding the expansion of research into the effects of heavy alcohol use in adolescence, very little work has been done on the possible nutrition-related consequences. Hence there is a paucity of information on possible short and longer term consequences of heavy alcohol use for adolescent nutritional status, in spite of the recognition that adolescents are a nutritionally at-risk group. Potential alcohol-related nutritional risks for adolescents are discussed in section 5, as relevant.

4.4   Concluding Perspectives

Heavy alcohol use and specifically binge drinking is a rising public health concern among adolescents globally, as well as in South Africa. The negative health impacts of heavy adolescent alcohol use are numerous and may also include possible effects on nutritional outcomes in this life stage. Heavy drinking by adolescents may increase their susceptibility to alcohol-related organ damage and the development of NCDs. However, at this point only a small amount of data on the possible longer term effects of heavy adolescent alcohol use are available and very little information on nutritional outcomes exists.

Heavy alcohol use increases risk for development of AUDs and early alcohol intake will result in the development of this disorder in some adolescents. Negative neurological outcomes have also been documented as consequences of heavy drinking during adolescence and reports that heavy adolescent alcohol use is strongly associated with numerous health risk behaviours is a cause for concern.

In order to add additional perspective to the problem of heavy alcohol use in South African adolescents, some reference to the South African environmental context is warranted. In South Africa, high socio-economic inequalities continue, with poverty and degradation being prevalent in many communities (Mayosi et al., 2009). Children and adolescents specifically are exposed to many environmental stressors, which have harmful effects on their current health, psychological well-being and future health (Barbarin and Richter, 2001, Ensink et al., 1997). Within these South African communities, macrosocial elements, such as economic deprivation, violence and victimisation, have been shown to be associated with alcohol use and smoking (Kalichman et al., 2006). Availability and access to substances, both legal and illegal, has also been shown to predict alcohol use and smoking within these communities (Parry et al., 2004b). Thus, the environmental context in which many adolescents in South Africa live may be regarded as one of the significant factors contributing to the problem of heavy adolescent alcohol use.

Finally, it must be borne in mind that the vulnerability of adolescents to adopting unhealthy behaviours is also dependent on a variety of individual, family and community practices and circumstances, which are closely linked to eucation, economic and social opportunities.

5   NUTRITIONAL CHALLENGES AND RISKS DURING ADOLESCENCE

5.1   Nutritional Needs and Risks in Adolescents

Globally, adolescents are recognised as a nutritionally at-risk group (World Health Organization, 2005).

High nutritional demand for growth and development (Tables 5 and 6) , coupled with well documented

poor dietary intake and eating behaviour during adolescence (World Health Organization, 2005, Kerr et

al., 2009, Moreno et al., 2010) and propensity for risk-taking behaviours are particularly important

threats to nutritional adequacy (World Health Organization, 2005).

Table 5. Estimated Energy Requirement (EER) in kilojoules per day for adolescents aged 15 years *

	Males	**Females**
Sedentary physical activity level	9337	7270
Low active physical activity level	10996	8639
Active physical activity level	12655	9920
Very active physical activity level	14696	12054

Source: (Institute of Medicine, 2002/2005)
Notes: EER = Total Energy Expenditure + 84 kilojoules per day – estimate of energy deposition during childhood
Males: reference height 1.70 metres; weight 56.3 kilograms
Females: reference height 1.62 metres; weight 52.0 kilograms
* EER for age 15 years since the mean age of adolescent sample used in this research study was 14.8 years

Table 6. The Dietary Reference Intakes for adolescents aged 14 to 18 years

	EAR		RDA / AI *		UL
	M	**F**	**M**	**F**	**M and F**
Carbohydrates (g/d)	100	100	**130**	**130**	-
Dietary Fibre (g/d)	-	-	38	26	-
Linoleic acid (g/d)	-	-	16	11	-
α-Linolenic acid (g/d)	-	-	1.6	1.1	-
Protein (g/kg/d)	0.73	0.71	**52**	**46**	-
Vitamin B6 (mg/d)	1.1	1.0	**1.3**	**1.2**	80
Vitamin B12 (μg/d)	2.0	2.0	**2.4**	**2.4**	-
Folate (μg/d)	330 [a]	330 [a]	**400 [a]**	**400 [b,a]**	800
Thiamin (mg/d)	1.0	0.9	**1.2**	**1.0**	-
Riboflavin (mg/d)	1.1	0.9	**1.3**	**1.0**	-
Niacin (mg/d)	12 [c]	11 [c]	**16 [c]**	**14 [c]**	30
Pantothenic acid (mg/d)	-	-	5	5	-
Biotin (μg/d)	-	-	25	25	-
Vitamin C (mg/d)	63	56	**75**	**65**	1800
Vitamin A (μg RE/d)	630 [d,e]	485 [d,e]	**900 [d]**	**700 [d]**	2800
Vitamin D (IU/d)	400	400	**600 [f,g]**	**600 [f,g]**	4000
Vitamin E (mg/d)	12	12	**15 [h]**	**15 [h]**	800
Vitamin K (μg/d)	-	-	75	75	-
Calcium (mg/d)	1100	1100	1300	1300	3000
Magnesium (mg/d)	340	300	**410**	**360**	350
Phosphorus (mg/d)	1055	1055	**1250**	**1250**	4000
Iron (mg/d)	7.7	7.9 [i]	**11**	**15 [i]**	45
Zinc (mg/d)	8.5	7.5	**11**	**9**	34
Fluoride (mg/d)	-	-	3	3	10
Iodine (μg/d)	95	95	**150**	**150**	1100
Selenium (μg/d)	45 [j]	45 [j]	**55**	**55**	400
Chromium (μg/d)	-	-	35	24	-
Copper (μg/d)	685	685	**890**	**890**	8000
Manganese (mg/d)	-	-	2.2	1.6	9
Potassium (g/d)	-	-	4.7	4.7	-
Sodium (g/d)	-	-	1.5	1.5	2.3
Chloride (g/d)	-	-	2.3	2.3	3.6

[a] As dietary folate equivalents (DFE). 1 DFE = 1 μg food folate = 0.6 μg of folic acid from fortified food or as a supplement consumed with food = 0.5 μg of a supplement taken on an empty stomach.

[b] In view of evidence linking folate intake with neural tube defects in the fetus, it is recommended that all women capable of becoming pregnant consume 400 μg from supplements or fortified foods in addition to intake of food folate from a varied diet.

[c] As niacin equivalents (NE), 1 mg of niacin = 60 mg of tryptophane.

[d] As retinol activity equivalents (RAEs), 1 RAE = 1 μg retinol, 12 μg B-carotene, 24 μg a-carotene, or 24 μg-B-cryptoxambine. The RAE for dietary provitamin A caroteroids is two-fold greater than retinol equivalents (RE), whereas the RAE for preformed vitamin A is the same as RE.

[e] Extrapolated from the AI for infants, 0 through 6 months

[f] Under the assumption of minimal sunlight.

[g] As international units, 40 IU vitamin D = 1 μg cholecalciferol

[h] As α-tocopherol. α -Tocopherol includes *RRR-* α -tocopherol, the only form of α -tocopherol that occurs naturally in foods, and the 2R-stereoisomeric forms of the α -tocopherol (*RRR-*, *RSR-*, *RRS-*, and *RSS-* α -tocopherol) that occur in fortified foods and supplements. It does not include the 2*S*-stereoisomeric forms of α -tocopherol (*SRR-*, *SSR-*, *SRS-*, and *SSS-* α -tocopherol), also found in fortified foods and supplements.

[i] assumed that females < 14 years do not menstruate and females > 14 years menstruate

[j] extrapolated from adult data

Sources: (Institute of Medicine, 1997, Institute of Medicine, 2001, Institute of Medicine, 2002/2005, Institute of Medicine, 2004, Institute of Medicine, 2011)

Abbreviations: M: males; F: females; g/d: grams per day; g/kg/d: grams per kilogram per day, μg/g: micrograms per day; IU/d: International Units per day

Notes:

EAR (Estimated Average Requirement): the average daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group

RDA: the average daily nutrient intake level sufficient to meet the nutrient requirement of nearly all (97 to 98 percent) healthy individuals in a particular life stage and gender group

AI: a recommended average daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate - used when a RDA cannot be determined

* RDA (Recommended Dietary Allowances) in **bold type** or AI (Adequate Intake) in ordinary type

However, adolescence has not generally been regarded as a high priority life stage in terms of nutrition support and interventions, with the exception of adolescent pregnancy (World Health Organization, 2005). Specifically in developing countries, like South Africa, health services focus on infant, maternal and young child nutrition-related health, with the result that nutrition-related health needs of the adolescent population may not be adequately met. This situation may be exacerbated by the fact that because adolescents are undergoing transition from childhood to adulthood, they may no longer receive the attention and care usually focused on children, but may not yet benefit from the protections and authority that goes with adulthood (World Health Organization, 2005).

Recognised nutritional challenges and risks in adolescence include poor eating behaviour and dietary intake, undernutrition, specifically stunting (chronic undernutrition) and underweight (chronic negative energy balance); overnutrition, specifically overweight and obesity (chronic positive energy balance), and poor iron, vitamin D and calcium nutriture (Figure 2) (World Health Organization, 2005, Cashman, 2007).
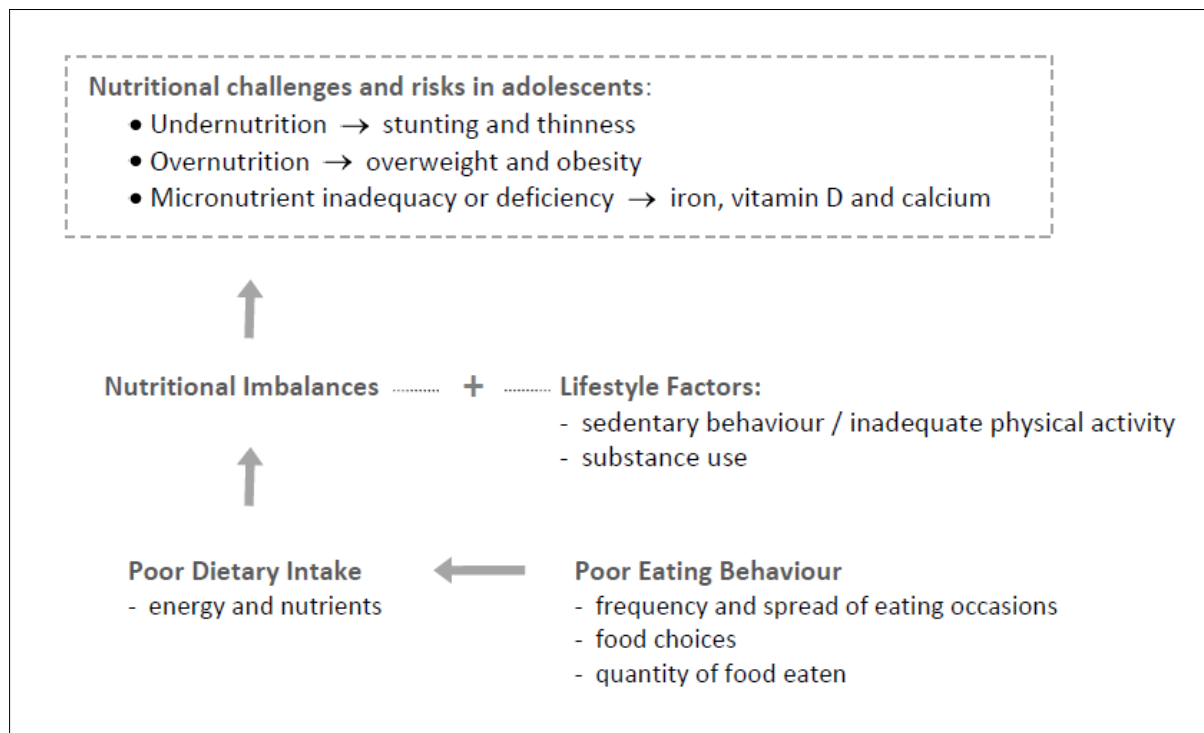
Figure 2. Outline of primary nutritional challenges risks and associated factors in adolescence

These nutritional challenges and risks are caused by poor dietary intake and eating behaviour, often in conjunction with lifestyle factors, such as predominant sedentary behaviour and substance use (Figure 2) (World Health Organization, 2005). Indeed, substance use is regarded as a possible threat to adolescent nutritional status (World Health Organization, 2005, Stang et al., 2008). Infection as a feature of malnutrition may be relatively less important in adolescents than in children under 5 years, with lifestyle factors becoming more significant (World Health Organization, 2005). The negative impacts of dietary inadequacies and overnutrition also place adolescents at an increased risk for the development of a range of chronic physical and mental disorders in adulthood, particularly if combined with other adverse lifestyle patterns, such as inadequate physical activity, smoking and alcohol use (World Health Organization, 2005). Research shows that the dietary intake and eating behaviour that predisposes to coronary heart disease, type 2 diabetes, hypertension, obesity and other chronic lifestyle diseases is set in motion during childhood and adolescence (Andersen et al., 2003, Boreham et al., 1999, Caballero, 2001, Law, 2000).   In fact, adolescents with poor diets and eating behaviour have a considerably increased risk for the premature development of NCDs such as diabetes, cardiovascular diseases, metabolic syndrome, osteoporosis and certain cancers in adulthood (De Henauw et al., 2007). Furthermore, the rising epidemic of overweight and obesity in adolescents (Lobstein et al., 2004, Moreno et al., 2005) is attributed in part to unhealthy eating behaviour (Moreno et al., 2010), overeating, a lack of physical activity and an increase in sedentary behaviour (Rey-Lopez et al., 2008).   Recent work by Ford et al (2008) found that the odds of overweight and obese adolescents reporting a diagnosis for two cardiovascular risk factors by young adulthood were 1.5 to 2 times higher than normal weight adolescents, regardless of BMI in young adulthood. There is no doubt that optimal nutritional status during adolescence is essential for growth, current and future health and ultimate developmental potential.

In the following sections (5.2 to 5.7), the primary nutritional challenges and related risk in adolescents, namely dietary intake and eating behaviour, stunting and underweight, overweight and obesity, and iron, vitamin D and calcium nutriture, as well as physical activity (Figure 2), are discussed within the context of heavy alcohol use during this life stage.

5.2   Eating Behaviour and Dietary Intake in Adolescents

5.2.1   Eating behaviour and dietary intake defined

When appraising the literature, it is evident that terminology regarding what, when and how much adolescents eat is inconsistent. Terms such as food intake, dietary intake, nutrient intake, meal pattern, dietary pattern, eating pattern, dietary trends, eating behaviour, dietary behaviour, food behaviour, dietary practices and food choices are used interchangeably, usually without clarification or definition.

For the purposes of this review the term "eating behaviour" is used and refers to the frequency and spread of eating occasions, food choices and portion sizes of food eaten (Figure 2). The term "dietary intake" is also used and for the purposes of this review refers to energy and nutrient intake (Figure 2).

5.2.2   Eating behaviour and dietary intake in adolescents

The dietary intake of adolescents is typically energy-dense and nutrient-poor with ensuing risk of nutrient inadequacies (Briefel et al., 2009, Temple et al., 2006). Eating behaviour during adolescence is characterised by increased eating frequency, meal skipping, and unhealthy food choices, including high intakes of sugar-sweetened beverages and fast-foods, as well as increased portion sizes (Moreno et al., 2010, Li et al., 2010, Temple et al., 2006). This dietary intake and eating behaviour is a cause for concern as it is associated with negative health consequences during adolescence and later in adulthood (Andersen et al., 2003, Boreham et al., 1999, Caballero, 2001, Moreno and Rodriguez, 2007, Moreno et al., 2010). When considering that various eating behaviours are often associated with each other, it is likely that some of the adverse dietary factors could cluster in the same adolescents increasing the individual risk related to each of the factors (Moreno et al., 2010). Furthermore, adolescence is characterised by greater self efficacy and within this process, adolescents acquire increased control over their own food choices and may often acquire poor eating behaviour in this progression (Avery et al., 1992, Fitzgerald et al., 2010). It is also important to consider that adolescence is a life stage during which health-related behaviours and practices that will impact significantly on future health are established.

Unhealthy diets, poor food choices and inadequate physical activity are some of the behaviours that may be initiated and established during adolescence (Kimm et al., 2002, Van Kooten et al., 2007).

International evidence

Recent work by Popkin and Duffey (2010) examined trends in frequency of eating occasions in a sample of 28404 children between the ages of two and 18 years of age, from nationally representative large US data sets across various periods between 1977 and 2006. Results showed that compared to 30 years ago, children are consuming foods more frequently throughout the day. Energy intake, especially from snacking, increased across all percentiles of the distribution and the vast majority of meals included both food and beverages (Popkin and Duffey, 2010). The Spanish AVENA (*Alimentación y Valoración del Estado Nutricional en Adolescentes*: Food and Assessment of the Nutritional Status of Adolescents) study showed that about 40% of adolescents ate four or more meals and about 40% ate five or more meals per day (Moreno et al., 2010). Similarly, in the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) study meal frequencies ranged from 4.1 to 5.1 meals per day (Moreno et al., 2008a, Moreno et al., 2008b).

In line with the higher frequency of eating occasions, the prevalence of snacking has increased among adolescents in the US in the past few decades (Jahns et al., 2001). From 1977 to 1996, data indicates a significant increase in the number of daily snacking occasions in 12 to 18 year old adolescents that resulted in a 30% increase in the energy intake from snacks, accounting for a quarter of total energy intake (Jahns et al., 2001). Energy-dense items such as cakes, cookies and savoury snacks have been shown to be popular snack choices among American children and adolescents (Sebastian et al., 2007). Findings from a recent study in the United Kingdom were similar. Data in 13 to 16 year old adolescent from the 1997 National Diet and Nutrition Survey and from a Northern Irish adolescent cohort collected later in 2005 showed that energy intake from snacks was significantly greater in the 2005 cohort. A trend towards a greater percentage energy intake from snacks was also seen in 2005 cohort compared to the 1997 cohort (Kerr et al., 2009). It has been suggested that in some individuals there may be no

compensation made for the increased energy intake from energy-dense snacks at ensuing eating occasions (De Graaf, 2006).

Meal skipping is frequently seen in adolescents, particularly in relation to breakfast. The prevalence of breakfast skipping seems to be country-specific. In the US, the practice of breakfast skipping increased from the 1960's to the 1990's when approximately a third of adolescents reportedly skipped breakfast, especially females (Siega-Riz et al., 1998). Recent evidence from an analysis of NHANES (1999 to 2006) data showed that this is still the case (Deshmukh-Taskar et al., 2010). In Europe an average of nine percent of adolescents were found to skip breakfast in the HELENA study (Moreno et al., 2008a, Moreno et al., 2008b), with prevalence being higher in some countries, for example, 12% of male and 24% of female adolescents in Sweden skip breakfast (Sjoberg et al., 2003). Prevalence findings from the Spanish AVENA study are in line with the HELENA study (Moreno et al., 2005), but a greater prevalence (20%) of breakfast skipping was reported among Italian adolescents (Turconi et al., 2008). From this information it seems that breakfast skipping during adolescence is most prominent in the US and among females. Breakfast skipping has also been reported to increase with age in female adolescents (Moreno et al., 2005). Lack of time and hunger have been reported by adolescents as reasons for skipping breakfast (Reddan et al., 2002).

Adolescents frequently consume energy-dense diets that are of poor quality in terms of essential micronutrients and that result from poor food choices, with a high consumption of sweetened beverages and unhealthy foods (Briefel et al., 2009, Burgess-Champoux et al., 2009, Li et al., 2010, Moreno et al., 2010). According to Temple (2006), adolescents are known to frequently consume "junk food", such as sweets, potato crisps, French fries and sweetened beverages, which are typically energy-dense, containing high quantities of fat and/or sugar and relatively low levels of micronutrients and dietary fibre. The widespread availability of these types of foods may negatively affect the nutritional quality of the diet (Temple et al., 2006). A study in 532 Italian adolescents reported that only 37% of the sample was deemed to have satisfactory food choices, with low intakes of fruit and vegetables as well as milk and yoghurt at breakfast and high intakes of cakes and sweets being evident in this sample (Turconi et al., 2008). Work by Sebastian et al (2009) supports this notion, showing that adolescent food choices in the

US do not meet the Dietary Guidelines for Americans, with high fat consumption and low intakes of fruits and vegetables and dairy products. The increasing prevalence of childhood obesity is associated with junk food consumption (Ebbeling et al., 2002, Ludwig et al., 2001).

The increasing trend in intake of sugar-sweetened beverages by adolescents ties in with the documented poor food choices in this life stage. Trends in the US over the past few decades show greater proportions of two to 18 year olds consuming larger quantities and more servings per day of sweetened beverages (Nielsen and Popkin, 2004). Among American adolescents, intakes of sweetened carbonated drinks increased from 3.4% to 8.8% of total energy in males and from 4.4% to 8.2% in females from the late 1970s to the late 1990s (French et al., 2003). Likewise, longitudinal results show a significant increase in consumption of sugar-sweetened beverages, including carbonated drinks, iced teas and fruit drinks, among younger males from a large, diverse sample of adolescents from Project EAT (Eating Among Teens)-II in the US. Intake of fruit juice, milk, other milk-based drinks and coffee/tea decreased with age. The same study reported that alcohol consumption increased across all groups (Nelson et al., 2009c). A significant increase in sweetened carbonated drinks has also been reported among Irish adolescents, in terms of frequency of intake and portion size ingested (Kerr et al., 2009) and a dramatic increase (> 50%) in the sales of sugar-sweetened drinks since the 1970's has been reported in Denmark (Matthiessen et al., 2003). The increased intake of sweetened beverages is reason for concern since a recent systematic review showed a positive association between increased intakes of sugar-sweetened beverages and weight gain and obesity in both children and adults (Malik et al., 2006). The result of a few short term feeding trials in adults also supported the notion that intake of sugar-sweetened beverages induce a positive energy balance and weight gain (Malik et al., 2006). A further concern in adolescents is the fact that sweetened beverages often displace more nutritious beverages such as milk, resulting in reduction in the nutritional quality of the diet (Harnack et al., 1999).

High intake of fast-foods and take-aways can be regarded as a component of the poor food choices in adolescents. Fast-food has become prominent in the diets of children and adolescents worldwide, with more meals being purchased away from home and eaten away in restaurants or fast-food stores (Mehta and Chang, 2008). A study in Benin in 13 to 19 year old adolescents found that out-

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of-home prepared foods contributed greater than 40% of the daily energy, protein, fat, carbohydrate and fibre consumption in the sample of adolescents (Nago et al., 2010). These trends have been ascribed to a number of factors including increased access to fast-food chains and restaurants and reduced prices of fast-foods (Mehta and Chang, 2008).

Although there is significant heterogeneity in portion sizes globally, literature shows a trend towards larger portion sizes in many countries worldwide (Matthiessen et al., 2003, Moreno et al., 2010, Young and Nestle, 2003). Evidence from Denmark and the US demonstrates this trend clearly. In Denmark, portion sizes of commercial energy-dense foods and beverages as well as fast-food meals high in fat and/or added sugar have increased over time particularly in past 10 years (Matthiessen et al., 2003). Portions in the US have increased over time with fast-food chains having portions two to five times larger than the original (Young and Nestle, 2003). In the US, the Food and Drug Administration (FDA) defines standard portions for food labels and the United States Department of Agriculture (USDA) defines standard portion sizes for dietary guidance. However, in reality, most portions offered in the market are twice as large as the defined USDA standard portion sizes, sometimes being up to eight times larger (Moreno et al., 2010). Nielsen and Popkin (2003) examined trends in food portion sizes consumed in the US, and reported that from 1977 to 1996, portion sizes increased both in and out of the home in all food categories apart from pizza. The energy intake and portion size of sweetened carbonated drinks increased by 206 kilojoules, salty snacks by 391 kilojoules, hamburgers by 407 kilojoules and French fries by 286 kilojoules (Nielsen and Popkin, 2003). This observed increase in portion sizes and quantity of food intake is relevant to eating behaviour during adolescence as it is a direct determinant of energy and nutrient intake, and consequently may impact on the stated nutritional challenges and risks.

South African evidence

Although there are a limited number of published studies on the dietary intake and eating behaviour of South African adolescents, available data shows concurrence with international trends (Temple et al., 2006, Venter and Winterbach, 2010, Reddy et al., 2010a). Temple et al (2006) investigated dietary intakes in a sample of adolescents from schools in Cape Town that were representative of the different

ethnic groups and socio-economic categories of the population. It was reported that 22.2% of the adolescents skipped breakfast. The large majority of foods eaten by these adolescents were unhealthy choices, including both foods brought to school (41 to 56%) and food purchased at school (70%, mostly from the school food store). Seventy percent of the adolescents who purchased food at school did not select any healthy food items, while 73% purchased two or more unhealthy items. Students from higher socio-economic schools were twice as likely to bring food to school, but were no more likely to purchase healthy foods at school (Temple et al., 2006). A recent study in middle to upper income adolescents attending public schools in the Bellville/Durbanville area of Cape Town reported that 19% of males and 17% of females had high fat intakes, using a scoring system based on the frequency of intake of foods that are sources of fat. The authors reported that these adolescents were consuming diets that do not represent the South African Food-Based Dietary Guideline of eating fats sparingly (Venter and Winterbach, 2010, Vorster et al., 2001).

Aspects of eating behaviour were also assessed in the recent YRBS (Reddy et al., 2010a). Healthy and poor food choices were examined through questions on the frequency and consumption of specified food groups. Adolescents were asked whether they had consumed specified food groups often (defined as on four or more days) in the seven days preceding the survey. Food groups included fresh fruit, uncooked vegetables, cooked vegetables, dairy products (milk or 'amasi'), meat products (chicken, lamb or beef), maize products (pap, porridge or rice), fast-foods or "luxuries" (hamburger, fried chicken, boerewors roll, hotdog, hot chips, 'gatsby', pie, 'vetkoek' or polony roll), cakes (cakes, biscuits, 'koeksisters' or donuts) and sweetened beverages. During the week preceding the survey, 58% of the sample reported consuming fresh fruit often, with 39% and 50% reporting they had eaten uncooked vegetables and cooked vegetables often, respectively. Dairy was eaten often by 44% of the adolescents, maize often by 63% and meat often by 52% of the adolescents. In the week preceding the survey fast-food or "luxuries" were eaten often by 39%, cakes often by 43% and sweetened beverages often by 50% of the sample (Reddy et al., 2010a). Although it is difficult to assess adequacy from this type of data, the findings provide an indication of the food choices being made by South African adolescents, showing that many are not consuming fruit and vegetables and dairy foods every day and that fast-foods, junk foods,

confectionary and sweetened beverages are frequently consumed. It is of concern that the proportion of adolescents who reported eating fast-foods and cakes often (on four or more days) was equal to that reported for eating uncooked vegetables often, and that the proportion consuming sweetened beverages often (on four or more days) was equal to that reported for eating cooked vegetables often. It is also of concern that the percentage of adolescents who consumed dairy foods often (on four or more days) was lower than that reported for consuming sweetened beverages often.

Ethnic differences were evident in certain of the food choices that were assessed in South African adolescents, as reported by Reddy et al (2010). Fresh fruit was eaten often by a significantly lower percentage of mixed ancestry (52%) and Indian (50%) adolescents compared to African black (59%) adolescents. Dairy foods were consumed often by a significantly higher proportion of white (62%) adolescents compared to African black (42%), mixed ancestry (50%) and Indian (51%) adolescents. Significantly more mixed ancestry (44%) and African black (44%) adolescents reported eating cakes and biscuits often compared to white (27%) and Indian (34%) adolescents. Similarly, a significantly greater percentage of Indian (59%) and mixed ancestry (57%) adolescents reported consuming sweetened beverages often compared to their African black (49%) peers (Reddy et al., 2010a). The findings suggest that adolescents of mixed ancestry seem to favour energy-dense, nutrient-poor food choices.

Findings from the few available studies in other developing countries paint a similar picture.   A study in Costa Rica reported that 50% of adolescents had cholesterol intake greater than the American Heart Association recommended guidelines, with 30% exceeding the total fat and saturated fat recommendations (Monge-Rojas, 2001). Likewise, adolescents in Benin were shown to have diets lacking in fruit and vegetables, with high intakes of sweet foods and a high percentage of total energy from fat (Nago et al., 2010).

5.2.3   Factors that influence eating behaviour in adolescents

There are many factors that influence dietary intake and eating behaviour during the adolescent years. Examining these influences from an ecological perspective promotes an improved understanding of the influence of alcohol intake on adolescent dietary intake and eating behaviour (Figure 3).

INDIVIDUAL INFLUENCES (Intrapersonal)	SOCIAL ENVIRONMENTAL INFLUENCES (Interpersonal)	PHYSICAL ENVIROMENTAL INFLUENCES (Community Setting)	MACROSYSTEM INFLUENCES (Societal)
Psychosocial Food preferences Taste and sensory perceptions of food Health and nutritional status Meanings of food Self efficacy Nutrition knowledge **Biological** Nutrition and weight history Hunger Gender Genotype **Lifestyle** Time for food preparation and convenience Cost Dieting Alcohol, smoking and other substance use Physical activity	**Family/Household/School** Demographic and cultural characteristics Education Family meals Television and computer use Household food security - food availability, affordability and access Modelling by adults (family, leaders) **Peers** Modelling Pressure to conform	Schools (tuckshops, nutrition support) Education Fast-food stores and restaurants Vending machines Convenience stores Health services Health and hygiene	Adolescents as consumers Media and advertising associated with food, eating, weight, alcohol, smoking, fashion Policy

Figure 3: Conceptual ecological framework for understanding the factors that influence adolescent dietary intake and eating behaviours
Source: Adapted from (Story et al., 2002)

From this framework it is clear there are essentially four levels of influence that need to be considered. Firstly, there are individual or intrapersonal influences, which include the psychosocial, biological and lifestyle influences. Alcohol use can be seen as an intrapersonal factor that influences dietary intake and eating behaviour. Secondly, the social environment in which the adolescent lives influences their eating behaviour and includes the interpersonal influences of family, household members, teachers and peers as well as cultural influences. On this level socio-demographics and household food security are factors that impact directly on food availability, affordability and access. Thirdly, the physical environment includes availability and access to school stores/tuckshops, fast-food retailers, food stores, vendors, liquor stores, 'shebeens' (illegal informal alcohol outlets), health services, as well as education about nutrition and health. These external influences may impact on the adolescent's decision making around food. Finally, there are macrosystem influences that encompass the

society in which the adolescent lives and include the effects of mass media, policy and advertising (Story et al., 2002).

A detailed discussion of the all the various factors that influence dietary intake and eating behaviour in adolescents, with the exception of the influence of alcohol use (see section 5.2.4), is beyond the scope this review.

5.2.4   Influence of alcohol use on eating behaviour and dietary intake in adolescents

Available evidence on the relationship between alcohol use and dietary intake and eating behaviour in adolescents includes work from the US and Israel in the 1990s. Data from the large Minnesota Adolescent Health Survey conducted in the late 1980s was used to investigate patterns of covariation of a wide range of health behaviours, including eating behaviours (Neumark-Sztainer et al., 1997). The Israeli study examined the associations between substance use and eating attitudes and behaviour in high school students (Isralowitz and Trostler, 1996). In both these studies it was observed that as a group, substance using adolescents were more likely not to eat three meals a day, to skip breakfast and to report chronic dieting and purging behaviours.

One of the few available studies that explored specific nutritional impacts of adolescent alcohol use is the work by Farrow et al (1987) on the impact of alcohol and marijuana use on physical health and nutritional status in 16 year old adolescent males. The authors concluded that health and nutritional assaults from chemical abuse in adolescents is related more to poor dietary habits and symptomatic deterioration in general health than to specific effects of chemical abuse on growth or nutritional status (Farrow et al., 1987).

As discussed in section 4.3.3, clustering of unhealthy behaviours in adolescents, including also poor eating behaviours, has been reported (Neumark-Sztainer et al., 1997, Burke et al., 1997, Paavola et al., 2004, Pronk et al., 2004). Studies among adolescents have reported that unhealthy eating behaviours in adolescents, such as consuming sweetened beverages and energy-dense snacks, skipping breakfast and other family meals are positively associated with the use of tobacco and alcohol, unsafe sex practices and watching television (Eisenberg et al., 2004, Keski-Rahkonen et al., 2003, Neumark-Sztainer et al., 1997,

Nutbeam et al., 1991). In a similar vein, Thatcher and Clark (2006) reported that adolescents with AUDs were more likely to smoke and less likely to eat a balanced diet or exercise regularly, but were not more likely to be overweight or to be hypertensive, and lipid levels were also not significantly raised.

Importantly, alcohol use (Grant, 1998), eating behaviours (Kelder et al., 1994, Te Velde et al., 2007) and weight status (Serdula et al., 1993) show a strong degree of tracking from adolescence into adulthood. These adolescent behaviour patterns are therefore not transient in nature and likely have important impacts on long term behaviour patterns and health outcomes.

The effects of alcohol consumption on dietary intake and eating behaviour and the nutrition-related consequences thereof were alluded to in section 3.7. Most of this evidence is from adult studies and little information on the relationships between alcohol use and dietary intake and eating behaviour in adolescents is available, particularly for binge drinking. However, since short term/acute alcohol exposure models binge drinking (Keiver et al., 2005), it is reasonable to speculate that some aspects discussed in section 3.7 may also be relevant to adolescent alcohol use. Specific aspects to be considered in adolescent alcohol users and adolescent binge drinkers include the following:

- The effects of binge drinking on eating behaviour, such as eating without hunger or eating more in anticipation of binge drinking (Nelson et al., 2009a), making unhealthy food choices (Nelson et al., 2009b), as well as avoidance eating before drinking to get drunk more quickly (Foster and Marriott, 2006)

- The increases in food intake subsequent to acute alcohol use, with failure to compensate for energy ingested as alcohol and thus consequent increases in total energy intake (Yeomans, 2010)

- The displacement of nutrient-dense foods by alcohol energy (Ferreira and Willoughby, 2008), with a reduction in the nutrient-density of the diet

- Energy intake being above energy requirements as a result of alcohol consumption, increasing the risk of overweight and obesity, with total alcohol intake, frequency of intake and a binge drinking pattern as potential determinants (Suter and Tremblay, 2005, Yeomans, 2010, Yeomans et al., 2003)

5.3   Underweight and Stunting in Adolescents

5.3.1   Assessment of underweight and stunting

Anthropometric measurements are used to assess underweight and stunting in all life stages, including

adolescence (Gibson, 2005a).   Body weight and linear height are commonly used measurements in

adolescents and are measured using standardised techniques (World Health Organization, 1995).

Anthropometric indices of growth and weight status are then derived from these raw measurements, for

example, height-for-age, weight-for-age, weight-for-height and BMI-for-age, where BMI is calculated as

weight (kilograms) divided by height^2 (meters). These indices are evaluated by comparison to the

distribution of reference data using *Z*-scores or percentiles. In low income countries, *Z*-scores should be

used since they can be calculated accurately beyond the limits of the original reference data (Gibson,

2005a, Gibson, 2005f).

For the interpretation of anthropometric indices of growth and weight status in adolescents, the

WHO currently recommends using the recently released WHO growth reference for ages five to 19 years

(Onis et al., 2007). The references previously recommended by the WHO for children above five years of

age (National Center for Health Statistics (NCHS)/WHO international growth reference) (World Health

Organization, 1995) have several shortcomings (Wang et al., 2006). Specifically, the BMI-for-age

reference developed in 1991 (Must et al., 1991), only starts at age 9 years and covers a limited percentile

range. Additionally, weight-for-age used in these references is inadequate for monitoring growth beyond

childhood due to its inability to differentiate between relative height and body mass. The new WHO

references provide BMI-for-age reference values to complement height-for-age reference values in the

assessment of underweight or thinness (low BMI-for-age) and stunting (low height-for-age) in school-

aged children and adolescents. The new references are also closely aligned with the WHO Child Growth

Standards at five years and result in a smooth transition in the interpretation of indices when a child

reaches five years, for height-for-age, weight-for-age and BMI-for-age (Onis et al., 2007).

When using the WHO growth references, underweight is defined as -2 standard deviations (SD) of

BMI-for-age expressed in *Z*-scores of the WHO growth reference. Stunting is defined as -2SD of height-

for-age expressed in *Z*-scores of the WHO growth reference (Onis et al., 2007).

5.3.2   Prevalence of underweight and stunting in adolescents

Until fairly recently, little data on adolescent nutritional status, including underweight and stunting, were available, especially in low and middle income countries. The International Center for Research on Women (ICRW)/ United States Agency for International Development (USAID) Nutrition of Adolescent Girls Research Program was instituted in 1990. It was conducted to provide information on factors that affect and are affected by the nutritional status of adolescent males and females, in order to inform the formulation of policies and programmes. These studies made a significant contribution to the current knowledge of nutrition in adolescence (Kurz, 1996, Kurz and C., 1994).

Based on these and other studies, it is known that underweight and stunting among adolescents are widespread in many developing countries (World Health Organization, 2005). Underweight (BMI < 5th percentile of NCHS/WHO reference data) in adolescents, ranging between 10 and 19 year of age, was found to be highly prevalent in three of the 11 ICRW studies, namely, India (53%), Nepal (36%) and Benin (23%) (Kurz, 1996, Kurz and C., 1994). National data in South Africa from the most recent YRBS showed much lower rates of underweight in adolescents in this country. The national prevalence of underweight in adolescents in this survey was 8.4%, with significantly more males (12.0%) than females (4.9%) being underweight (Reddy et al., 2010a), using the weight-for-age sex-specific 2000 CDC growth reference data (Kuczmarski et al., 2000). Ethnic comparisons of underweight prevalence in this survey found that significantly more African black (12.9%) and mixed ancestry (13.3%) males were underweight compared to African black (4.6%) and mixed ancestry (5.9%) female adolescents (Reddy et al., 2010a). Even lower prevalence of underweight were reported in a sample of older adolescents and young adults (15 to 24 years) in the most recent South African Demographic and Health Survey in 2003, with 4.1% of males and 3.7% of females being underweight (Department of Health, 2007). This survey used age dependent BMI cut-offs for underweight that were developed for Brazilian children and adolescents and that correspond to an adult BMI cut-off of 17.5 kg/m^2 at age 20 years (Conde and Monteiro, 2006).

In nine of the 11 ICRW studies, stunting (height < 5th percentile NCHS/WHO reference data) in adolescents was very prevalent, with rates of 27% in urban Guatemala to 65% in rural Philippines (Kurz

and C., 1994). These studies included adolescents of varying age ranges, with most studies having a lower range of 10 or 12 years and an upper range of 18 or 19 years. In South Africa, prevalence of stunting among adolescents in 2008 was lower than the rates reported in the ICRW studies. Nationally, 13.1% of adolescents were stunted (Reddy et al., 2010a), using the height-for-age sex-specific 2000 CDC growth reference data (Kuczmarski et al., 2000), with no variation by gender. Comparison between ethnic groups, found that significantly more Indian (10.3%), mixed ancestry (13.6%) and African black (13.8%) adolescents were stunted compared to whites (4.6%) (Reddy et al., 2010a).

5.3.3   Pertinent issues relating to underweight and stunting in adolescents

In most cases, underweight and stunting develop as a result of cumulative processes that often begin in early childhood, sometimes in *utero*. Continuing undernutrition in childhood manifests as stunting and/or possible underweight in adolescence. In stunting both skeletal and somatic growth are impacted (World Health Organization, 2005).

According to the United Nations Children's Fund (UNICEF) conceptual framework, childhood undernutrition, including underweight and stunting, is caused by interplay between immediate causes (poor dietary intake and disease), underlying causes (food insecurity, poor maternal and child care and poor hygiene), as well as basic causes (lack of human, economic and organisational resources) (United Nations Children's Fund (Unicef), 1990). An in-depth discussion of these causes is beyond the scope of this review.

When considering poor diet as a cause of stunting, it is evident that multiple simultaneous nutrient deficiencies, including both macro and micronutrients may limit linear growth resulting in stunting. This inadequate dietary intake in combination with infection during pre-school years and possibly also foetal nutritional deprivation are the primary causes of stunting during adolescence (World Health Organization, 2005). It is also pertinent to mention that intrauterine exposure to alcohol results in growth retardation and stunting (Chaudhuri, 2000, Strauss, 1997), with short stature being a prominent feature of foetal alcohol spectrum disorders (Spohr and Steinhausen, 2008). In poverty-stricken countries, stunting is widespread and occurs mainly during the first two to three years of life. However,

stunting among adolescents is frequently seen in undernourished populations (World Health Organization, 2005). As soon as final height is reached, stunting becomes a permanent result of previous undernutrition and is no longer seen as a sign of present undernutrition. The adolescent growth spurt is regarded as a potential period for catching up childhood growth deficit. Even though there is some potential for catch-up growth in adolescent years, longitudinal studies show that stunting in adolescence is best prevented during foetal life or infancy (World Health Organization, 2005). Stunting is associated with delayed mental development, increased mortality and poor educational attainment (Prentice et al., 2006)

Undernutrition in adolescence does not only delay physical growth, but also delays maturation and development processes. Chronic adolescent undernutrition, specifically inadequate intake of zinc, iron and vitamin A, causes a delay in and slowing of the adolescent growth spurt, resulting in biological age lagging behind chronological age and delayed maturation and onset of puberty (World Health Organization, 2005). In emergency circumstances (e.g. refugee crises), especially when persistent, adolescents may be affected by severe undernutrition in the same way as younger children. However, in many instances therapeutic nutrition interventions are not accessible to them as would be for younger children (World Health Organization, 2005).

5.3.4   The influence of alcohol use on underweight and stunting in adolescents

There is little data on the effects of alcohol use on the development of underweight and stunting during adolescence. However, acute alcohol intoxication has been shown to produce significant reductions in growth hormone concentrations in both male and female adolescents aged 13 to 17 years (Frias et al., 2000). Growth hormones play important roles in long bone growth in adolescents and heavy alcohol use during adolescence may thus have long term adverse effects on aspects of growth in adolescents (Frias et al., 2000).

In view of the effects of alcohol consumption on dietary intake and eating behaviour as discussed in sections 5.2.4, energy intake persistently lower than energy requirements due to avoidance of eating, chronic dieting and purging behaviours could potentially result in underweight. It is also plausible that

protracted binge drinking in adolescents may displace nutrient-dense foods (Ferreira and Willoughby, 2008), resulting in a reduction in the nutrient-density of the diet, as mentioned in section 5.2.4. Furthermore, an elevated risk of nutrient deficiencies with protracted heavy drinking is possible in view of the increased requirements for certain micronutrients that may result from the metabolism of alcohol (Van Den Berg et al., 2002). If these potential impacts were to persist during adolescence, they may likely delay or slow linear growth, particularly if nutrient inadequacies occurred during the adolescent growth spurt.

5.4   Overweight and Obesity in Adolescents

5.4.1   Assessment of overweight and obesity in adolescents

As with underweight and stunting (see section 5.3.1), indices derived from anthropometric measurements are used to assess overweight and obesity by comparison of these indices with the distribution of reference data (Gibson, 2005a, Gibson, 2005f).

As mentioned in section 5.3.1, the new WHO growth reference for ages 5 to 19 years (Onis et al., 2007) are currently recommended by the WHO for assessing adolescent anthropometric indicators of weight status. Some of the limitations of the references previously recommended by the WHO for children above 5 years of age (National Center for Health Statistics (NCHS)/WHO international growth reference) (World Health Organization, 1995) were briefly discussed in section 5.3.1. The BMI-for-age reference distributions provided in the WHO references complement height-for-age in the assessment of overweight and obesity (high BMI-for-age) in school-aged children and adolescents. These reference values are also closely aligned with the recommended adult cut-offs for overweight and obesity at 19 years. When using these references, overweight/obesity is defined as +1SD of BMI-for-age expressed in Z-scores of the WHO growth reference (Onis et al., 2007).

The International Obesity Task Force (IOTF) age-dependent BMI cut-off points for overweight and obesity (BMI $\geq$25 kg/m^2) developed by Cole et al (2000), are also widely used to assess overweight and obesity in children aged 2 to 18 years (Cole et al., 2000). These age and gender specific cut off points for

BMI for overweight and obesity in children are linked to the widely accepted adult cut off points for overweight (25kg/m^2) and obesity (30 kg/m^2) at age 18 years (Cole et al., 2000).

5.4.2   Prevalence of overweight and obesity in adolescents

The increasing prevalence of overweight and obesity among children and adolescents is a widely reported and cited as a major public health issue across developed and developing countries (Reilly, 2006, Kosti and Panagiotakos, 2006). This is illustrated in the work by Wang et al (2002) in which they examined overweight trends in older children and adolescents using nationally representative data from Brazil (1975 and 1997), the US (1971 to1974 and 1988 to1994) and nationwide survey data from China (1991 and 1997). The authors found that during the study periods, the prevalence of overweight increased in Brazil from 4.1% to 13.9%, the US from 15.4% to 25.6% and China from 6.4% to 7.7% (Wang et al., 2002). A later review verified that lower- and middle-income countries, particularly those in urban settings and following a Western lifestyle, are facing a considerable and rapidly growing epidemic of childhood and adolescent obesity (Wang and Lobstein, 2006). It is important to note that adolescent overweight and obesity in developing countries varies widely according to urbanisation and income and it is clearly not only a problem limited to high income groups (World Health Organization, 2005).

These increasing trends in overweight and obesity are also evident in South African adolescents (Table 7).

Table 7. Prevalence of overweight/obesity in South African adolescents

Prevalence overweight/obesity (%)	Youth Risk Behaviour Survey 2002	Youth Risk Behaviour Survey 2008
National	21.2	25.0
Males	9.0	14.5
Females	30.3	35.0
African Black	20.4	24.5
Males	7.1	12.1
Females	30.4	36.2
Indian	35.5	30.1
Males	30.0	33.3
Females	41.0	27.2
Mixed Ancestry	16.3	22.4
Males	11.3	15.8
Females	20.7	28.3
White	29.8	35.5
Males	25.0	34.1
Females	33.7	37.3

Sources: (Reddy et al., 2010a, Reddy et al., 2003)

Both South African YRBSs show overnutrition to be a greater problem among adolescents than undernutrition (Reddy et al., 2010a, Reddy et al., 2003), with an increase from 2002 to 2008 in the national prevalence of overweight/obesity from 21.2 to 25% (Table 7). These increases are especially prominent in the white and mixed ancestry population groups (Table 7), with reduced prevalence evident in the Indian population. In both surveys, national prevalence of overweight/obesity was shown to be markedly greater in females compared to males, but an increase in prevalence was evident in both genders. The difference between males and females in overweight/obesity prevalence was prominent in the African black and mixed ancestry groups (Table 7) (Reddy et al., 2010a, Reddy et al., 2003).   The IOTF age-dependent BMI cut-off points for overweight and obesity in children and adolescents (BMI $\geq$25 kg/m^2) (Cole et al., 2000) were used in the 2002 and 2008 YRBSs to determine prevalence of overweight and obesity (Cole et al., 2000). In a younger sample of South African children and adolescents (three to 16 years) selected from five provinces, a lower prevalence of overweight/obesity was reported in females

(22.8%) and a higher prevalence in males 17.2% (Armstrong et al., 2006) compared to the prevalence rates in the most recent YRBS, also using the IOTF age-dependent BMI cut-off points for overweight and obesity (Cole et al., 2000). However, overall Armstrong et al (2006) also found that females had a greater prevalence of overweight/obesity than males (Armstrong et al., 2006). In a sample of older adolescents and young adults (15 to 24 years) in the most recent South African Demographic and Health Survey, the prevalence of overweight/obesity in males (13.8%) was similar and the prevalence in females (25.4%) was lower (Department of Health, 2007) than the rates in the recent YRBS (Reddy et al., 2010a). As mentioned in section 5.3.2, this survey used age dependent BMI cut-offs developed for Brazilian children and adolescents and these cut-offs for overweight and obesity correspond to adult BMI cut-offs for overweight ($25kg/m^2$) and obesity ($30kg/m^2$) at aged 20 years (Conde and Monteiro, 2006). In line with the findings of both YRBSs, results from this survey also showed overnutrition to be a greater problem than undernutrition in South African adolescents.

5.4.3   Pertinent issues relating to overweight and obesity in adolescents

Overweight and obesity are the result of a long term imbalance between energy ingestion (dietary intake) and total energy expenditure (the sum of sum of basal energy expenditure, thermic effect of food, physical activity, thermoregulation, and the energy expended in depositing new tissues and in producing milk (Institute of Medicine, 2002/2005)), subject to genetic and environmental influences (Kleiser et al., 2009). Although a detailed discussion on the aetiology of overweight and obesity in adolescents is beyond the scope of this review, a few pertinent points are discussed.

The development of obesity has been linked to four critical periods, namely intrauterine life, infancy, the period of adiposity rebound (ages five to seven years) and adolescence (Dietz, 1994). Possible risk factors for overweight and obesity in early life involve genetic, physical, lifestyle, and environmental conditions (Ebbeling et al., 2002, Maffeis, 2000, Reilly et al., 2005). These include birth weight (Ong, 2006), infant feeding practices (Arenz et al., 2004), postnatal and child growth (Monteiro and Victora, 2005, Ong, 2006), timing of adiposity rebound (Taylor et al., 2005), food and beverage intake

following infancy (Malik et al., 2006, Moreno and Rodriguez, 2007), physical activity levels (Wareham et al., 2005), urbanisation and high income (Wang et al., 1998).

In developing countries undergoing rapid economic growth, such as South Africa, a nutrition transition is seen with a progressive change in nutrition-related disease patterns. In these contexts, undernutrition and overnutrition often co-exist and as food scarcity declines and incomes increase, diets and lifestyles change rapidly, becoming more Westernised (World Health Organization, 2005). Major dietary changes include shifts from a traditional high carbohydrate, high fibre, low fat diet to one with a higher fat and sugar intake and a lower carbohydrate and fibre intake, with reductions in occupational, leisure and food procurement and preparation-related physical activity levels (Popkin, 2001). It is interesting to note that within these countries overweight/obesity and stunting not only co-exist, but may be interlinked, with more manifestations of overnutrition being evident in previously stunted individuals. This is aligned with Barker's hypothesis of an increased risk of overweight and NCDs risk in those exposed to undernutrition in early life (Barker, 1996, Leon et al., 1996). A high obesity risk among stunted children in developing countries was described by Popkin et al (Popkin et al, 1996). Similarly in both children and adolescents in underprivileged areas of Brazil, it was found that obesity with stunting was more widespread than obesity without stunting (Sawaya et al., 1995). Armstrong et al (2011) recently reported secular trends in the prevalence of stunting, overweight and obesity in South African children aged eight to 11 years during 1994 and 2004. Using two age- and gender-matched cohorts, it was found that moderate stunting decreased over the seven to 10 years considered, while overweight and obesity prevalence increased. Overweight/obesity with stunting was evident, with lower levels of mild stunting and similar levels of moderate stunting among overweight/obese children when compared with non-overweight/non-obese children (Armstrong et al., 2011). It is important to note that particular causal pathways of overweight/obesity are complex and although much is known, exact mechanisms under all conditions are not completely elucidated (Kleiser et al., 2009).

Overweight and obesity in adolescence may have serious health and psychosocial consequences. Health-related consequences that have been reported in overweight/obese children and adolescents include diabetes, hepatic disease, cardiovascular risk factors, asthma, chronic inflammation, orthopaedic

problems and psychosocial problems (Reilly et al., 2003). The foremost long term health issues linked to overweight/obesity in adolescence are its propensity to persist into adult life (Gordon-Larsen et al., 2004a, Power et al., 1997, Serdula et al., 1993, Srinivasan et al., 1996) and its association with cardiovascular disease risk, premature mortality and adverse socio-economic outcomes (Reilly et al., 2003). In fact, studies show that childhood and adolescent overweight and obesity have negative effects on risk factors for cardiovascular and other NCDs independently of adult overweight (Berenson et al., 1998, Mahoney et al., 1996, Must et al., 1992). The association between adolescent and adult obesity is illustrated by a recent study that analysed nationally representative, longitudinally measured height and weight data in American adolescents enrolled in wave II (1996; ages 13 to 20 years) and wave III (2001; ages 19 to 26 years) of the National Longitudinal Study of Adolescent Health (*n=9795*). The authors reported that during a five year transitional phase between adolescence and young adulthood, the percentage of adolescents becoming and remaining obese into adulthood was very high. Over the study period of five years, 12.7% of the sample became obese, 9.4% remained obese, with only 1.6% shifting from obese to non-obese (Gordon-Larsen et al., 2004a).

Obesity in childhood and adolescence is associated with increased mortality risk in adulthood (Reilly et al., 2003). This is illustrated by results from the Harvard Growth Study where males who were overweight at 13 to 18 years had an increased risk of mortality five to six decades later, compared to participants who were lean as adolescents (Must et al., 1992). This association is further supported by a 14-year longitudinal study in obese participants (*n=6000*) in Germany, which showed an increased mortality risk in all age groups, with the increased risk associated with obesity being greater in younger age groups and weakening with age (Bender et al., 1999).

5.4.4   The influence of alcohol use on overweight and obesity in adolescents

As described earlier, the associations between alcohol, diet and weight are decidedly complex. Most of the epidemiological research in this area has been done in adult populations and little is known about the effects of different drinking patterns during adolescence on energy balance and body weight.

Based on available evidence in adults, it can be speculated that heavy alcohol use in adolescents may affect total energy intake in a variety of ways. First, if alcohol energy replaces food energy (thus no change in total energy intake) dietary quality is reduced, with poor intake of essential macro- and micronutrients, even though energy needs may be met. This nutrient inadequacy increases the risk for nutrient deficiencies, which may enhance the risk for stunting (low height-for-age). Second, heavy alcohol use may result in a more significant reduction in dietary intake with energy from alcohol not compensating for the total loss of dietary energy intake. Inadequate energy and nutrient intake could manifest in the adolescent as underweight (low BMI-for-age) or possibly stunting. However, it must be borne in mind, that the greatest risk for stunting remains poor nutrition during the first two years of life (Shrimpton et al., 2001). Third, alcohol containing drinks could be ingested in addition to usual food intake, resulting in increased total energy consumption, compounding the risks for weight gain and being overweight/obese (high BMI-for-age), as has been discussed above.

According to Nelson et al (2009), it is conceivable that alcohol-related eating may be associated with overconsumption of energy and excess weight gain over time. This notion is supported by the large study in American college students cited in section 3.7.2, where binge drinking ($\geq$5 drinks in one sitting) was significantly associated with unhealthy eating behaviour, weight control behaviour and sedentary behaviour. Alcohol-related eating, that is, eating before and/or during drinking was associated with an almost 25% increase in being overweight (Nelson et al., 2009b). This is further supported by the results of an electronic school-based health survey in Dutch adolescents (*n=25176*; aged 13 to 14 years and 15 to 16 years) where alcohol use, physical inactivity and skipping breakfast were all associated with overweight (Croezen et al., 2009). The clustering of health risk behaviours discussed in sections 4.3.3 and 5.2.4 is also relevant here, as a recent study found that earlier alcohol, tobacco and other drug use, depression, increased fighting and reduced optimism may lead to unhealthy increases in weight (Pasch et al., 2008). Similarly, a large survey in Greek adolescents reported a positive and independent association between alcohol consumption and smoking and percentage of overweight females (Tzotzas et al., 2008). The authors stated that this may be due to the high energy content of alcohol or the clustering of unhealthy behaviours, such as high fat and low fibre diets, physical inactivity and television watching, as

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reported in other studies (Paavola et al., 2004, Pronk et al., 2004, Burke et al., 1997). Longer term influences of alcohol on adolescent overweight and obesity have also been reported by Oesterle et al (2004) in a longitudinal study (*n=808*; aged 10 to 24 years). In this study, adolescent chronic heavy drinkers were found to be nearly four times more likely to be overweight or obese and/or have high blood pressure at age 24 than those who did not drink heavily in adolescence (Oesterle et al., 2004).

Based on the presented evidence it can thus be argued that heavy drinking adolescents may have an increased risk of overweight and obesity due to the additive effect of alcohol energy to total energy intake resulting in a persistent positive energy balance, but also due to unhealthy eating behaviours and food choices that may result in further increases in energy intake. However, it must be considered that the association between alcohol intake and weight status may be influenced by physical inactivity (Pietilainen et al., 2008) and smoking (Saarni et al., 2009).

5.5   Iron Status in Adolescents

5.5.1   Dietary assessment of iron status

Dietary assessment is usually used to identify the first stages of nutritional deficiency and can indicate risk of dietary inadequacy but cannot diagnose an actual deficiency (Gibson, 2005g).   This is especially true for iron, as iron absorption depends on the absorptive capacity of enterocytes and on the form of the consumed iron. There are two forms of iron in food, haem and non-haem, with the bioavailability of haem iron being much higher than that of non-haem iron. Absorption of non-haem iron is dependent on the presence of a number of inhibitors and enhancers in the gastrointestinal tract (see section 5.5.4 for more detail). Thus, when assessing dietary iron, an attempt is needed to estimate *available* dietary iron (Fairweather-Tait, 2004, Gibson, 2005c).

For the most accurate measure of available iron, meal-based data is needed, such as a validated questionnaire that elicits dietary intake of iron (haem and non-haem) and primary inhibitors and enhancers in meals (Fairweather-Tait, 2004). For improved accuracy in estimating available dietary iron, a food composition database with complete information on haem and non-haem, phytate and polyphenol content of foods is needed for the analyses of dietary intake data. As with all dietary

analyses, the calculated values obtained will be an estimate of the true intake due to the inherent

variance of food composition data, including random and systematic errors (Gibson, 2005d). A number of

predictive algorithms have been developed to estimate iron bioavailability from different diets, which

allow for the major dietary factors that affect iron absorption (Hallberg and Hulthen, 2000, Murphy et al.,

1992, Reddy et al., 2000). A significant limitation of applying these algorithms is the lack of food

composition data for the content of enhancers and inhibitors of iron absorption. This is particularly true

for the more detailed algorithms that take into consideration the effects of all the known enhancers and

inhibitors of iron absorption (Gibson, 2005c). A further factor to be considered in the assessment of iron

intake is the fortification of foods with iron, as averages in products may result in substantial errors in

calculated iron intake (Fairweather-Tait, 2004). Food fortification legislation in South Africa requires

millers to fortify white and brown bread flour and maize meal with iron (fortificant requirement for

electrolytic iron is 35.7143 milligrams per kilogram of flour and maize meal).

5.5.2   Biochemical assessment of iron status

The determination of iron status is challenging as iron status is a function of iron provided and lost over

previous months or years (Fairweather-Tait, 2004). Information on commonly used biochemical and

haematological indicators for the assessment of iron status is summarised in Table 8. Despite the fact

that a variety of indicators are available for the detection of iron deficiency and iron deficiency anaemia,

there are many challenges and possible inaccuracies in establishing iron status (Fairweather-Tait, 2004)

(Table 8). According to Gibson (2005c), a well-founded approach is to use several different biochemical

indicators of iron status rather than using any single indicator. This minimises the misclassification that

may occur as a result of overlapping normal and abnormal values for a single indicator (Gibson, 2005c).

Table 8. Commonly used biochemical and haematological indicators for the assessment of iron status

Indicators	General information about the indicators	Comments	
Haemoglobin (Hb)	Used in diagnosis of anaemia and iron deficiency	Some misclassification will occur if used on its own to assess iron deficiency, since the range of Hb values for non-anaemic individuals overlap with iron deficiency values	May also reflect deficiency in folate, vitamin B12, vitamin B6 and copper.
Haematocrit (Hct)	Used in diagnosis of anaemia and iron deficiency	Decreases after impairment of Hb formation Subject to more technical errors of measurements than Hb Hct and Hb only both reduced in severe iron deficiency	Thus, not diagnostic of iron deficiency specifically
Mean cell Volume (MCV); mean cell haemoglobin (MCH); mean cell haemoglobin concentration (MCHC)	Used in diagnosis of different types of anaemia Obtained from Hb, Hct and erythrocyte counts	In iron deficiency anaemia: reduced MCV, MCH and MCHC (microcytic, hypochromic) Macrocytic anaemia (vitamin B12 and folate deficiency): elevated MCV and MCH, normal MCHC Anaemia of chronic infection: MCV, MCH and MCHC are normal (normocytic, normochromic)	
Red cell distribution width	Used in diagnosis of different types of anaemia	Increases in iron deficiency anaemia, vitamin B12 deficiency, co-existing iron and folate deficiencies, co-existing iron and vitamin B12 deficiencies, haemoglobinopathies Useful for differentiating between microcytic anaemia due to iron deficiency or from haemoglobinopathies	
Serum iron	Reflects iron in transit from reticulo-endothelial system to bone marrow	Influenced by: *age, gender, biological variation, chronic diseases, infection, inflammation, neoplastic conditions, increased erythropoiesis, decreased erythropoiesis	
Total iron binding capacity (TIBC)	Sum of all unoccupied iron binding sites on the iron transport protein, transferrin In this test, exogenous iron is added to serum and the total quantity of iron that saturates all the transferrin iron binding sites is determined Closely linked to the transferrin concentration	Closely linked to the transferrin concentration As iron stores are diminished, TIBC of serum increases due to an increase in transferrin synthesis in response to enhanced iron absorption Increase in TIBC occurs before any indication of an insufficient supply of iron to erthropoietic precursor cells Influenced by factors marked with asterisk (*) above	
Transferrin saturation	Measure of the iron supply to erythropoietic tissue in bone marrow Calculated as serum iron divided by TIBC, expressed as a percentage	Reduced saturation signifies an insufficient rate of iron delivery to maintain normal haemoglobin synthesis Influenced by factors marked with asterisk (*) above	
Serum ferritin	Reflects the total quantity of storage iron in uncomplicated iron deficiency and in healthy persons	When once iron stores become depleted, levels no longer reflect the severity of the iron deficiency Influenced by: age, gender, biological variations, acute and chronic infections, increased erythropoiesis, decreased erythropoiesis, acute or chronic liver disease and neoplasms	
Serum transferrin receptor	Sensitive indicator of the extent of tissue iron deficiency Expressed by cellular surfaces in proportion to their requirement for iron	Levels rise in proportion to the deficit in functional iron since the cellular expression of transferrin receptor increases in response to a reduction in iron availability to tissues, as a consequence of iron storage depletion Influenced by: age, gender, biological variations, cigarette smoking, malaria, pregnancy, high altitudes, increased erythropoiesis, decreased erythropoiesis and vitamin B12 and folate deficiencies Not significantly influenced by anaemia of chronic disease and infection and inflammation	

Sources: (Gibson, 2005c, Woods and Ronnenberg, 2006)

Cut-off points used in the interpretation of biochemical indicators of iron status are age and gender specific, depending on the laboratory assay used (Gibson, 2005c). Relevant cut-off points, based on gender and age for the specific assays are provided by laboratories. These cut-off values are generally based on ranges associated with clinical signs, or impairment in a biochemical or physiologic function, as reported in the clinical literature, and also take the precision of the assay into account (Gibson, 2005h).

It must also be borne in mind that biomarkers of iron status are affected by the acute phase response. Conditions of inflammation increase hepcidin levels resulting in iron-deficient erythropoiesis, since hepcidin obstructs the release of iron from enterocytes and the reticulo-endothelial system. Persistent inflammation may cause anaemia of chronic disease and thus raised ferritin levels in anaemia do not exclude iron deficiency in the presence of inflammation (Zimmermann and Hurrell, 2007). As a consequence of these interactions, biomarkers of infection, such as C-reactive protein (CRP), are often included in studies assessing iron status in order to aid the interpretive validity of the iron biomarkers. Notably the degree of increase in CRP levels that invalidates using serum ferritin to detect iron deficiency is unclear and CRP values higher than 10 to 30 milligrams (mg) per litre have been used (Zimmermann and Hurrell, 2007).

All of the indicators mentioned in Table 8 would be suitable for biochemical and haematological iron status assessment in adolescents. The combination of serum iron, total iron binding capacity (TIBC) and transferrin saturation is widely used in biochemical iron status assessment. These three indicators are interrelated and helpful for distinguishing between nutritional iron deficiency and anaemia of chronic infection. With nutritional iron deficiency, serum iron is low and TIBC is increased with resultant low transferrin saturation. Serum ferritin is used to determine a deficient, excess or normal iron status and a quantitative relationship between serum ferritin and storage iron has been established (Gibson, 2005c). Serum ferritin levels up to and including 12 micrograms per litre are found in the absence of stainable iron in bone marrow and indicate depleted iron stores (Woods and Ronnenberg, 2006).

5.5.3   Prevalence of iron deficiency in adolescents

Iron deficiency is recognised as a common health problem among adolescents globally, especially females (Ahmed et al., 2000, Ferrari et al., 2011, Halterman et al., 2001, World Health Organization, 2005, Zimmermann and Hurrell, 2007). When considering the iron deficiency prevalence estimates, it should be borne in mind that in developed countries, iron deficiency data is most often derived from nationally representative samples using specific biomarkers of iron status, while in developing countries, haemoglobin measurements from target populations and selected samples are most often used due mostly to resource limitations. Prevalence estimates of iron deficiency anaemia using only haemoglobin measurements do not account for other causes of anaemia, such as infections and other nutritional deficiencies and may thus overestimate iron deficiency anaemia (Zimmermann and Hurrell, 2007).

In a review on the global prevalence of anaemia in the 1980's, the estimated prevalence among adolescents was 6% and 27% in developed countries and developing countries, respectively. Prevalence in Africa, Latin America, Oceania and the Caribbean was greater among adolescent males (Demaeyer and Adiels-Tegman, 1985). In the multicountry ICRW/USAID research studies on adolescent nutritional status conducted in the 1990's, anaemia was reported to be the most pervasive nutritional problem among adolescents, with higher prevalence rates being reported in developing countries. In four of the six ICRW studies in which anaemia was assessed in adolescents, it was found to be very prevalent, namely India (55%), Nepal (42%), Cameroon (32%) and Guatemala (48%) (Kurz and C., 1994). In the early 2000's, the WHO estimated that 48% of children between five and 14 years were anaemic and that the frequency of iron deficiency in developing countries was approximately 2.5 times greater than that of anaemia (World Health Organization, 2001). A study in Bangladesh published in 2000 reported that 32% of a large sample of 11 to 16 year old girls had iron deficiency anaemia (Ahmed et al., 2000). Data from the Third NHANES (1988 to 1994) in the US showed that in six to 16 year olds, iron deficiency without anaemia was more prevalent than iron deficiency with anaemia. Prevalence of iron deficiency was 3% in six to 11 year olds, with the greatest prevalence (8.7%) being among 12 to 16 year old females, of which only 1.5% had iron deficiency with anaemia. In this analysis, ethnic and socio-economic comparisons found that prevalence of iron deficiency was greater than 5% among Mexican American children, children of other ethnic

backgrounds and children below the poverty level (Halterman et al., 2001).   A higher prevalence of iron deficiency (21%) has been reported in female adolescents (11 to 18 years) in the United Kingdom (Heath and Fairweather-Tait, 2002) compared to the rate reported in American female adolescents (8.7%) mentioned above (Halterman et al., 2001). These prevalence estimates confirm iron nutriture as a nutritional vulnerability in adolescents in developed and developing countries.

In South Africa, data on iron deficiency are scant. Due to the scarcity of current prevalence data on adolescent iron deficiency, data from other life stages, including children and pregnant women, are included in this review in order to provide additional perspectives on conceivable rates of iron deficiency in adolescents. A national survey in the 1990's among six to 71 month old children, reported a prevalence of anaemia at 21% and iron deficiency anaemia at 5% (Labadarios and Middelkoop, 1995). The prevalence of iron deficiency as such has also been reported in regional studies in South Africa in various life stage samples. An early study in six to 74 year olds in rural Kwazulu-Natal reported that 42% of males and 53% of females were anaemic, largely due to low iron intake (Mayet et al., 1985). In preschool children in Kwazulu-Natal in the 1990's, an iron deficiency prevalence of 19.8% was found, with 18.9% of mothers being iron deficient, but not necessarily anaemic (Oelofse et al., 1999). Lower prevalence rates of iron deficiency were reported in children under five years (5.1%) and pregnant women (9 to 12%) in a more recent study that examined the burden of disease attributable to iron deficiency in South Africa (Nojilana et al., 2007). At present, there is no nationally representative data on the prevalence of iron deficiency among South African adolescents.

When considering the available data showing iron deficiency in various life stage groups in South Africa, and considering the vulnerability of children and adolescents to iron deficiency, it is reasonable to suggest that adolescents in this country may also be vulnerable to iron deficiency.

5.5.4   Perspectives on dietary needs and intake of iron in adolescents

Adolescents have increased iron requirements due to their rapid rate of linear growth, increase in blood volume and the onset of menarche that occurs during adolescence (Institute of Medicine, 2001, Zimmermann and Hurrell, 2007) as reflected in the iron intake recommendations for male and female

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adolescents (Table 6 in section 5.1, page 49).   The Dietary Reference Intakes (DRIs) for iron were derived from iron balance studies conducted in various population groups. For adolescents, these recommendations are based on the quantity of dietary iron intake required to maintain an appropriate level of iron storage, with additional quantities of iron added for the rapid linear growth and onset of menstruation mentioned above. The DRIs for iron are based on chronological age, however specific iron needs during adolescence are variable and dependent on sexual maturation stage. The recommendations in the DRIs are based on the assumption that females younger than 14 years do not menstruate and females older than 14 years do menstruate (Institute of Medicine, 2001, Stang et al., 2008). Nutritional iron deficiency occurs when the iron supply is inadequate to meet physiological needs. Toxicity occurs when there is dysfunction in the homeostatic mechanisms regulating iron absorption or when there is chronic exposure to high iron levels (Fairweather-Tait, 2004).

When considering dietary iron intake, the form of the dietary iron as well as the range of physiological host and dietary factors known to affect iron absorption, either by enhancing or inhibiting its absorption (Table 9), need to be borne in mind, as mentioned in section 5.5.1.

Table 9: Factors known to affect iron absorption

Host factors	Dietary Factors
Enhancing	Enhancing
Iron deficiency anaemia	Meat, poultry fish
Low body iron stores	Vitamin C
Gastric acid	Alcohol
Bile and pancreatic secretions	Inhibitory
Pregnancy	Phytates
Hypoxia (high altitude)	Polyphenols and other flavonoids
Increased erythropoiesis (e.g. after blood loss)	Tea and coffee
Homozygosity for C282Y mutation of HFE gene	Eggs
Inhibitory	Calcium and dairy foods
Rapid gastric emptying	Other transition metals (e.g. zinc, copper)
Previous high intake of iron	
High body stores	

Source: (Fairweather-Tait, 2004)
Abbreviation: HFE: haemochromatosis protein gene

Haem iron is the form of iron that is obtained from haemoglobin and myoglobin in animal foods and non-haem iron is the form of iron found in both plant foods and animal tissues (Fairweather-Tait, 2004). Haem iron absorption is more efficient and uniform than non-haem iron (Hallberg et al., 1997). Furthermore, non-dairy animal proteins also enhance non-haem iron absorption (Cook and Monsen, 1975, Glahn et al., 1996), therefore iron absorption from meat is higher than from plant foods. In meat-eating populations haem iron is estimated to contribute 10 to 15% of total iron intake and may constitute 40% or more of total absorbed iron (Carpenter and Mahoney, 1992, Hunt, 2002). Non-haem iron is less well absorbed (2 to 5%) and all non-haem food iron in the common gastrointestinal iron pool is absorbed to the same extent, which is dependent on iron status and the balance between enhancers and inhibitors of iron absorption (Hurrell and Egli, 2010, Gallagher, 2008). Thus, dietary intake of iron may seem adequate, but if total intake is primarily non-haem iron and the diet is high in inhibitors of iron absorption, the ingested dietary iron may be poorly absorbed, which would make the dietary iron intake inadequate. This can be seen as especially pertinent in population groups with increased iron needs, such as adolescents.

The possible negative effect of calcium on iron absorption is important to consider bearing in mind the importance of calcium nutrition for bone health and other key functions. Single-meal studies of iron absorption have shown large effects of certain dietary constituents on iron absorption (Fairweather-Tait, 2004). However, apparent exaggeration of the effect of inhibitors and enhancers on iron absorption in single meal studies has been demonstrated (Cook et al., 1991) and findings from longer term intervention, cross-sectional and prospective studies examining iron absorption are not always consistent with findings from single meal studies (Fairweather-Tait, 2004). A cross-sectional study in six European countries showed a weak but consistent negative association between calcium ingestion and serum ferritin. However, this association was not reliant on simultaneous intake of calcium and iron and a dose-response effect was not seen (Van De Vijver et al., 1999). The majority of intervention studies have found no effect of calcium on iron nutrition and in general, do not confirm the findings of a substantial negative effect seen in single-meal studies (Minihane and Fairweather-Tait, 1998, Sokoll and Dawson-Hughes,

1992). Thus, in the context of a varied diet, the negative effect on calcium on iron nutrition is less important than absorption studies with single meals would suggest.

As a result of all the factors that influence iron absorption, mean daily iron intake and iron stores (from serum ferritin concentrations) are not well correlated (Fairweather-Tait, 2004). This is supported by the results of a recent large study in Japanese females aged 18 to 25 years (*n=1019*) where no significant correlation between iron intake and biochemically diagnosed iron deficiency (using serum ferritin levels) was found (Asakura et al., 2009).

5.5.5   Pertinent issues relating to iron deficiency in adolescents

The higher iron needs that accompany rapid growth during adolescence, as well as growing dietary independence and reduced parental protection may result in poorer dietary choices that may lead to a lower dietary intake of iron in adolescents. Since iron is found in many foods, and its intake is directly associated with energy intake (Institute of Medicine, 2001), the risk of iron deficiency is greatest when iron requirements exceed energy needs, as in adolescents and also infants, young children and menstruating and pregnant women (Zimmermann and Hurrell, 2007).

Adiposity in adolescent females has been linked to risk for iron deficiency. This was demonstrated using the 2003 to 2004 NHANES dataset, where it was found that heavier-weight female adolescents had a greater risk for iron deficiency and that inflammation from excess adiposity plays a role in this risk. The two groups had similar dietary iron intake, age of and time since first menarche, physical activity and poverty status, and these factors did not independently predict iron deficiency (Tussing-Humphreys et al., 2009).

Food security is also a factor known to affect iron deficiency risk, especially in children and adolescents. Analyses of data from the NHANES (1999 to 2004) showed the odds of iron deficiency anaemia in adolescents, aged 12 to 15 years, from food insecure households to be 2.95 times that of children from food secure households (Eicher-Miller et al., 2009).

Iron deficiency is associated with insufficient iron-dependent functioning with regards to oxygen transport, gene transcription, oxidative metabolism and nuclear metabolism (Beard et al., 1996). Chronic

iron deficiency may ultimately manifest in anaemia, characterised by decreases in mean cell volume, low haemoglobin levels and the appearance of microcytic hypochromic erythrocytes (Institute of Medicine, 2001). Thus, anaemia is a term that encompasses a wide range of haematological abnormalities and while all forms of anaemia are reflected in low haemoglobin concentrations, a number of non-dietary factors can also produce this effect. Nonetheless, dietary iron deficiency is the principal cause of anaemia (World Health Organization, 2001).

Poor iron status is also associated with impaired immunity and reduced work performance (Beard et al., 1996). Iron deficiency may affect cognitive function in children (Pollitt et al., 1985) and adolescents (Ballin et al., 1992) and in severe and prolonged deficiency this may be only partly reversible (World Health Organization, 2005). In school children, iron deficiency has been shown to result in reduced motor activity and school performance as well as social inattention (Grantham-Mcgregor and Ani, 2001). This is supported by findings from the Third NHANES (1988-1994), where average math scores were lower in school-aged children and adolescents (six to 16 years) with iron deficiency with and without anaemia, compared to those with normal iron status. Participants with iron deficiency had more than twice the risk of achieving a lower than average mathematics score compared to participants with normal iron status (Halterman et al., 2001).

The consequences of iron deficiency anaemia also extend to effects on disability-adjusted life years (DALYs) and mortality. It was estimated that in 2000 in South Africa, between 0.9% and 1.3% of all DALYs were attributable to iron deficiency anaemia, with about 7.3% of perinatal deaths and almost 5% of maternal deaths being ascribed to iron deficiency anaemia (Nojilana et al., 2007)

5.5.6   The influence of alcohol use on iron status in adolescents

Alcohol use is known to affect iron metabolism and as stated in Table 2 (section 3.5, page 26), can result in either iron deficiency or excess of iron in the body (Ballard, 1997). However, there is a paucity of information on the association between iron status and alcohol use in adolescents. Data from the first NHANES (1971 to 1973) showed that drinking frequency was positively associated with serum iron levels and with transferrin saturation in males, with mean serum iron values being within the normal

biochemical ranges for male and female drinkers and non-drinkers (Friedman et al., 1988). In more recent work in a large sample of 18 to 25 year old females in Japan, alcohol drinking status, classified as non-drinkers (no alcohol), drinkers (alcohol intake: 0 to <1% of total energy intake) and drinkers (alcohol intake: ≥1% of total energy intake), was not associated with prevalence of iron deficiency (Asakura et al., 2009). Although very limited, these findings suggest that alcohol use may be associated with increased iron status in males, but not in females.

The relationship between alcohol consumption, iron overload, iron deficiency and iron deficiency anaemia in adults was also examined using data from the Third NHANES (1988-1994). Non-drinkers were compared to participants with a daily consumption of less than one or one; greater than one and up to two; or greater than two alcohol drinks over the preceding year (Ioannou et al., 2004). Consumption of two or more drinks per day was associated with an elevated risk of iron overload while consumption of up to two drinks was associated with decreased risk of iron deficiency (Ioannou et al., 2004). Lieb et al (2011) reported that chronic alcohol users have no major abnormalities of iron metabolism. Therefore, research on associations between alcohol use and iron status is equivocal.

With heavy alcohol use, blood loss and subsequent iron deficiency are caused by gastrointestinal bleeding (Ballard, 1997). The link between alcohol use and gastrointestinal bleeding was demonstrated in a study in adults by Kaufman et al (1999). These researchers reported that compared with participants who drank less than one drink per week, the relative risk of acute upper gastrointestinal bleeding increased with increasing alcohol consumption, rising to 2.8 among those who drank 21 or more drinks per week (Kaufman et al., 1999).   A recent survey in the United Kingdom (*n=6750*) found that 26% of patients (> 16 years of age) who were hospitalised with acute upper gastrointestinal bleeding had a history of alcohol excess (Hearnshaw et al., 2011). According to Lieber (2000), iron deficiency has been documented in adult alcoholics with the causes cited being poor dietary iron intake and blood loss from gastrointestinal lesions. Furthermore, alcohol is known to interfere with the proper incorporation of iron into the hemoglobin molecules in erythrocytes and this may contribute to iron deficiency anaemia (Ballard, 1997).

At this point, is not known whether heavy alcohol use during adolescence impacts on iron status in any way. When considering the available evidence, it is plausible that adolescent alcohol use may have no influence on iron status or that it may increase risk of iron overload. However, risk of iron overload could perhaps be regarded as less likely since iron needs increase during adolescence and iron deficiency is a recognised nutritional risk (see sections 5.5.3 and 5.5.4). It could also be speculated that heavy alcohol use, specifically binge drinking during adolescence may impact negatively on iron status. This is conceivable in view of the evidence that acute alcohol administration results in damage to mucosal morphology (reduced absorption) and intestinal haemorrhagic erosions (see section 3.3), with blood and consequent iron loss and the effects of chronic alcohol use on iron status (see section 3.5), as well as the documented iron deficiency risk in adolescents.

5.6   Vitamin D and Calcium Status in Adolescents

5.6.1   Assessment of vitamin D status

Vitamin D: Dietary indicators

Dietary vitamin D intake on its own is not seen to provide a good reflection of vitamin D status since this nutrient is obtained from both endogenous synthesis and dietary sources (Prentice et al., 2006). Furthermore, estimation of dietary intake of vitamin D requires a food composition database with adequate information on vitamin D content of foods. One of the most extensively cited nutrient databases, namely the USDA Nutrient Database, is not complete for vitamin D (Holden et al., 2008, Millen and Bodnar, 2008). The variable vitamin D content of fortified foods and quantification of the contribution of vitamin D supplements to dietary intake of individuals are further challenges in the accurate estimation of dietary vitamin D intake. Sunlight exposure questionnaires or diaries have also been used to estimate individual-specific sun exposure for vitamin D status assessment (Millen and Bodnar, 2008). However, no validated sunlight exposure questionnaires are available (Mccarty, 2008). For the purposes of this dissertation, the term vitamin D refers to either or both vitamin D_2 and vitamin D_3 and its metabolites.

Vitamin D: Biochemical indicators

Information on commonly used biochemical indicators for the assessment of vitamin D status and

detection of vitamin D insufficiency and deficiency is summarised in Table 10.

Table 10. Biochemical indicators of vitamin D status

Indicators	General information about the indicators	Comments
25-hydroxyvitamin D (25(OH)D)	Circulating concentrations reflect the sum of vitamin D from cutaneous synthesis and dietary intake, thus indication of medium to longer term vitamin D availability from both endogenous and dietary sources [a]	In vitamin D insufficiency and deficiency, concentration is reduced and remains low until reserve is repleted Most abundant circulating metabolite of vitamin D and has longest half-life of all the vitamin D derivatives [a] Regarded as a robust reliable marker of vitamin D status [a] [b] Influenced by seasonal effects, age, gender, race and ethnicity, latitude, smoking, obesity, anticonvulsant medications [a]
1,25-dihydroxyvitamin D (1,25(OH)$_2$D)	Circulating concentrations are under homeostatic control and reflect immediate physiological needs Levels are approximately 0.1% of the concentration of 25(OH)D [a]	In vitamin D insufficiency and deficiency, concentration is normal or increased, due to enhanced renal production in response to elevations in parathyroid hormone levels Not regarded as a useful marker of overall vitamin D status due its short half life [a]
Serum alkaline phosphatase	Activity in serum can be used as an indirect measure of vitamin D status [a]	Activity increases in osteomalacia in adults and rickets in children Useful for diagnosis of clinical vitamin D deficiency, not useful for detection of subclinical vitamin D deficiency Influenced by various diseases states, e.g. hyperparathyroidism, Paget's disease, cholestasis [a]
Serum parathyroid hormone	Considered a functional index of vitamin D status in the normocalcemic state Concentration inversely related to serum 25(OH)D concentration [a]	Levels increase in vitamin D deficiency when calcium absorption is reduced, in order to induce skeletal calcium mobilisation and maintain calcium homeostasis [a] Seen to have more limited value as a status marker of vitamin D compared to serum 25(OH)D [b] Influenced by age and season [a]

Sources: [a] (Gibson, 2005e); [b] (Seamans and Cashman, 2009)

Serum 25-hydroxyvitamin D (25(OH)D) levels is regarded as the best measure of vitamin D status

in humans (Table 10). Accordingly, this measure would be the preferred measure to assess vitamin D

status in adolescents, bearing in mind factors regarding the interpretation of this measure in defining

vitamin D status. While vitamin D deficiency is commonly defined as a 25(OH)D level of less than or equal

to 20 nanograms per millilitre (ng/mL), other cut-offs have been used to define vitamin D status and there has been much debate in the literature about optimal serum 25(OH)D levels for the attainment and maintenance of bone mass (Docio et al., 1998, Holick, 2007, Malabanan et al., 1998). In view of current data, there is some agreement that in adults, vitamin D deficiency is a circulating 25(OH)D concentration of less than 20 ng/mL and vitamin D insufficiency is a 25(OH)D concentration of 20 to 29 ng/mL. Concentrations of 30 ng/ mL and above are considered sufficient (Dawson-Hughes et al., 2005, Holick, 2007, Holick and Chen, 2008). This is based on data showing that intestinal calcium absorption is maximal above 32 ng/mL (Heaney et al., 2003) and that parathyroid hormone levels in adults carry on declining and reach their nadir at between 30 and 40 ng/mL (Chapuy et al., 1996, Holick et al., 2005, Thomas et al., 1998). Other researchers have reported 25(OH)D levels of 32 ng/mL and above as being sufficient (Hollis, 2005, Hollis, 2010).

Likewise, absolute consensus has not been reached regarding the concentration of 25(OH)D that defines vitamin D insufficiency in infants and children (Wagner and Greer, 2008). According to Holick and Chen (2008) it has been assumed that children have requirements similar to that of adults. In line with this assumption, a 25(OH)D concentration of greater or equal to 20 ng/mL is the lower end of the range recommended by the American Pediatric Endocrine Society as being adequate in children (Wagner and Greer, 2008). This is also the 25(OH)D concentration that was used for establishing the Institute of Medicine's (IOM) Recommend Dietary Allowance for vitamin D to meet the requirements of nearly all children and adolescents (Institute of Medicine, 1997, Institute of Medicine, 2011). At this point in time the cut-offs used in adults to define vitamin D status based on circulating 25 (OH)D levels, namely vitamin D deficiency (< 20 ng/mL), insufficiency (20 to 29.9 ng/mL) and sufficiency ($\geq$ 30 ng/mL) are being used to define vitamin D status in children (Poopedi et al., 2011).

5.6.2   Assessment of calcium status

Calcium: Dietary indicators

Dietary intake of calcium can be assessed by measuring food consumption using validated dietary intake assessment methods such as the 24 hour recall method, dietary records or food frequency questionnaires (Gibson, 2005g). As is the case with all nutrient intake analyses, the calculated calcium values based on the analyses of the food consumption data will be an estimate due to the inherent variance of food composition data (including random and systematic errors) (Gibson, 2005d). Dietary intake data can thus reflect risk for calcium deficiency, but cannot diagnose an absolute deficiency.

Calcium: Biochemical and other indicators

Biochemical and other indicators for calcium status assessment that have been considered and used include serum calcium, serum ionised calcium and various biomarkers of bone formation and bone resorption. However, there are no satisfactory tests to assess body calcium status on a routine basis as calcium levels are under strict homeostatic control and remain in balance under most conditions. Serum calcium levels only decrease after interference with calcium absorption or following extended periods of calcium deprivation (Gibson, 2005b). The interactions of the three calcitropic hormones, parathyroid hormone, 1,25 hydroxycholecalciferol and calcitonin are responsible for this homeostatic control of serum calcium concentrations (Weaver and Heaney, 2006).

Serum ionised calcium is the physiologically active form of calcium in blood and is frequently used to assess disturbances in calcium metabolism. Reduced concentrations occur in hypoparathyroidism and vitamin D-deficient rickets and elevations indicate functional hypercalcaemia (Gibson, 2005b). Several biochemical indicators of bone remodelling can be used to assess small changes in the rate of bone formation and degradation as a result of dietary influences. The sensitivity and specificity of these indicators differ and their value in assessing calcium stores is limited (Gibson, 2005b). Indirect assessments of the bone mineral content of the skeleton provide an indication of its calcium content, since the mineral content of the skeleton relates directly to its calcium content and almost all of the calcium in the body is stored in the skeleton. Non-invasive techniques such as dual X-ray absorptiometry

and computerised tomography can be used to assess skeletal bone mineral content. These techniques, although expensive and not widely accessible, provide a reliable indirect measure of body calcium stores and can be used to monitor the response to changes in calcium intakes over relatively long time periods (Gibson, 2005b).

Calcium status has been assessed adolescents using dual X-ray absorptiometry, as well as dietary calcium intakes using a 24-hour dietary recall and food frequency questionnaires (Mcveigh et al., 2007, Yang et al., 2010).

5.6.3   Prevalence of vitamin D deficiency in adolescents

Vitamin D deficiency has been found to be widespread in certain subpopulations (using various cut-off points), even among those living in countries with abundant sunshine (Lips, 2010, Mithal et al., 2009). Specifically, adolescents are a life stage group that appear to be at risk of vitamin D deficiency (Cashman, 2007; Lips 2010). This is concerning in view of the fact that adolescents experience accelerated skeletal growth and adequate vitamin D status is required to enhance intestinal calcium absorption and support bone development (Cashman et al., 2011).

A high prevalence of inadequate vitamin D status in older children and adolescents is common and continues to be reported globally. Recent studies of vitamin D status in various samples of adolescents in developed and developing countries have shown that 16% to 54% of adolescents have circulating 25(OH)D levels of less than or equal to 20 ng/mL (Gordon et al., 2004, Lapatsanis et al., 2005, Looker et al., 2002, Olmez et al., 2006, Tylavsky et al., 2005). This threshold has been linked to sub-optimal calcium absorption (Institute of Medicine, 2011, Abrams et al., 2009) and poorer adolescent bone strength and growth (Cashman et al., 2008, Viljakainen et al., 2006). In sunny countries, vitamin D deficiency is common when solar skin exposure is limited by body coverings. Studies in Turkey, India, Lebanon, Saudi Arabia, the United Arab Emirates and Australia found that between 30 and 50% of children, adolescents and adults had 25(OH)D concentrations below 20 ng/mL (El-Hajj Fuleihan et al., 2001, Marwaha et al., 2005, Mcgrath et al., 2001, Sedrani, 1984).

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At present, there is no nationally representative data on vitamin D status among South African adolescents and data is limited to small studies in selected population sub-groups, with many of the studies using different analytical methods for serum 25(OH)D quantification. A number of small studies have measured serum 25(OH)D concentrations in young children with active rickets and have reported mean 25(OH) levels ranging from 10.4 ng/mL to 19.5 ng/mL (Bhimma et al., 1995, Daniels et al., 2000, Pettifor et al., 1978). A small study in the Northern Province of South Africa in healthy black children and adolescents found mean circulating 25(OH)D levels to be approximately 50 ng/mL in six to nine year olds (*n=17*), 46 ng/mL in 10 to 13 year olds (*n=26*) and 36 ng/mL in 14 to18 year olds (*n=15*). The same study found that in healthy albino children circulating 25(OH)D levels were approximately 41 ng/mL in six to nine year olds (*n=30*), 34 ng/mL in 10 to 13 year olds (*n=36*) and 36 ng/mL in 14 to18 year olds (*n=16*)(Cornish et al., 2000). In a recent assessment of vitamin D status in a cohort of healthy 10 year old urban children (*n=475*) in the greater Johannesburg area, 7% were vitamin D deficient (serum 25(OH)D < 20 ng/mL), and 19% were Vitamin D insufficient (20 to 29 ng/mL) (Poopedi et al., 2011). White children had significantly higher serum 25(OH)D concentrations than their black counterparts (48 versus 37 ng /mL, respectively). Seasonal variations in 25(OH)D concentrations were seen only in white children, with concentrations being significantly higher in white compared to black children during the autumn and summer months (Poopedi et al., 2011).

This limited South African data suggest that children in the northern parts of the country generally seem to have an adequate vitamin D status. Black children appear to be somewhat worse off in terms of vitamin D status and more susceptible to seasonal variations, which is likely due to the documented reduced vitamin D3 synthesis with increased skin pigmentation (Clemens et al., 1982). Little is known about the vitamin D status of adolescents in the southern parts of the country, some of which lies above 30 degrees south latitude where little or no dermal vitamin D3 can be produced during winter months (Holick and Chen, 2008).

5.6.4   Perspectives on dietary needs and intake of vitamin D in adolescents

Vitamin D needs and recommendations in adolescents

The principal physiologic function of vitamin D in humans is to maintain intracellular and extracellular calcium homeostasis in order to ensure its availability for essential functions in bone and dental health, as well as for regulatory functions in numerous metabolic processes. This is achieved through the action of 1,25-dihydroxyvitamin D (1,25(OH)$_2$D), a biologically active form of vitamin D, on regulating calcium and phosphorus metabolism in the bone and intestine. Furthermore, vitamin D is responsible for maintaining extracellular calcium and phosphorus concentrations in a supersaturated state in order to ensure the mineralisation of bone (Weaver and Heaney, 2006, Holick, 2006b).

Humans obtain vitamin D from dietary sources and supplements, but primarily from sunlight exposure (Deluca, 2004, Holick, 2006a). Solar ultraviolet B (UVB) radiation enters the skin and converts 7-dehydrocholesterol to previtamin D3, which swiftly converts to vitamin D3 (cholecalciferol). Excessive solar exposure does not result in vitamin D3 toxicity, as any excess previtamin D3 or vitamin D3 is destroyed by solar exposure (Holick, 2007). Most natural foods contain only small amounts of vitamin D and these quantities are generally inadequate to maintain vitamin D sufficiency. Consequently, the dietary content of vitamin D is usually insufficient to maintain an adequate vitamin D status and cutaneous synthesis of vitamin D3 on exposure to UVB radiation is essential to maintain adequate vitamin D status, unless fortified foods are eaten or supplements are used (Pettifor, 2005). Thus, if there is insufficient UVB sunlight exposure for adequate cutaneous synthesis of vitamin D, it becomes an essential nutrient (Cashman et al., 2011).

Any interference with the penetration of UVB sunlight into the skin and anything that reduces the transmission of UVB sunlight to the surface of the earth will influence the cutaneous synthesis of vitamin D3 (Chen et al., 2007, Holick and Chen, 2008). Sunscreen absorbs UVB radiation and topical application of a factor 15 sunscreen has been shown to absorb 99% of UVB sunlight (Matsuoka et al., 1987). Increased skin pigmentation distinctly decreases vitamin D3 synthesis as melanin is very effective in absorbing UVB sunlight (Clemens et al., 1982). Season, latitude and time of day impact cutaneous vitamin D3 synthesis. The quantity of UVB photons that reach the earth's surface is affected by the angle at which sun strikes

the earth. Only small amounts, if any, vitamin D3 synthesis occurs when during winter, early morning and late afternoon, when the zenith angle is increased (Holick and Chen, 2008, Webb et al., 1988). Little or no vitamin D3 can be produced at latitudes above approximately 30 degrees north and south during winter months (Holick and Chen, 2008). In Africa, seasonal effects on cutaneous synthesis of vitamin D3 would be expected in countries that are located at latitudes greater than 30 degrees north and south, such as South Africa, Egypt, Morocco, Libya, Tunisia and Algeria (Prentice et al., 2009). An earlier study in Cape Town found only limited vitamin D synthesis *in vitro* in the winter months from April through to September (Pettifor et al., 1996). Furthermore, even with plentiful sunshine, the degree of UVB skin exposure also depends on living and working environments and clothing (Schoenmakers et al., 2008).

The relative contributions of dietary sources and cutaneous synthesis exposure to UVB sunlight to vitamin D status are still uncertain and this has made it challenging for scientific authorities to establish dietary vitamin D requirements (Cashman et al., 2011). It is thus not surprising that a range of authoritative dietary guidelines for vitamin D for specific age groups have been formulated and there is considerable variation in these recommendations (Nordic Council of Ministers, 2004, Scientific Committee for Food, 1993, United Kingdom Department of Health, 1991).

Very recently, the US DRIs committee for calcium and vitamin D of the Food and Nutrition Board of the IOM set an Estimated Average Requirement (EAR) of 10 micrograms (μg) (400 International Units [IU]) and a Recommended Dietary Allowance (RDA) of 15 μg (600 IU) for vitamin D for children aged one to 18 years (Institute of Medicine, 2011) (Table 6 in section 5.1, page 49). The previous DRIs for vitamin D included only an Adequate Intake (AI) and Tolerable Upper Intake Level (UL) (Institute of Medicine, 1997). For the establishment of the new recommendations, the DRI committee used evidence of serum 25(OH)D levels that benefited bone health, such as maximising calcium absorption, positive outcomes on bone mineral content and prevention of rickets. However, the committee pointed out that the confounding effect of sunlight exposure has not yet been addressed adequately and advised that it would be ideal if the relative contribution made by sunlight exposure to overall serum 25(OH)D levels could be quantified in formulating the EAR. The committee did, however propose that due to the public health concerns related to sun exposure and skin cancer risk, vitamin D requirements cannot be based on a

"recommended" or conventional level of sun exposure (Institute of Medicine, 2011). As is, the committee in establishing the recent EAR and RDA for vitamin D, followed an approach that focused on identifying the vitamin D intakes that will maintain serum 25 (OH)D levels above selected cut-offs when cutaneous synthesis is considerably *reduced* or *absent* (Institute of Medicine, 2011). The appropriateness of the RDA recommendation is supported by recent work by Cashman et al (2011) who found in white Danish female adolescents that in the absence of significant amounts of sun exposure, a daily intake of about 18.8 micrograms (750 IU) of vitamin D would permit 97.5% of these adolescent females to achieve a serum 25(OH)D concentration of greater or equal to 20 ng/mL (Cashman et al., 2011). This is in line with the serum concentration used to establish the RDA resulting in a recommendation of 15 micrograms to meet the requirements of nearly all children and adolescents (Institute of Medicine, 2011). Abrams et al (2009) also suggests that based on current data, it seems that intakes of approximately 10 to 20 micrograms (400 to 800 IU) of vitamin D per day should achieve a serum 25(OH)D level of greater or equal to 20 ng/mL in most children.

Vitamin D intake in adolescents

Dietary sources of vitamin D include fatty fish, some fish liver oils, organ meats, egg yolks and also fortified foods, for example margarine and milk (Holick, 2006b). Data from national surveys in the developed world on vitamin D intakes are limited (Gibson, 2005e) and similarly in Africa dietary vitamin D intake data are scarce (Prentice et al., 2009). From the little available data on food patterns and sources of intakes of other nutrients, the contribution of dietary sources to vitamin D intake does not seem to be substantial on this continent (Prentice et al., 2009). This is primarily because few naturally occurring food sources are rich in vitamin D and in many areas these are consumed infrequently or not at all (Bwibo and Neumann, 2003, Mackeown et al., 1998, Murphy et al., 1995).

5.6.5   Perspectives on dietary needs and intake of calcium in adolescents

Calcium needs and recommendations in adolescents

Calcium is the dominant mineral in bone, accounting for approximately 40% of bone mineral content and almost all of total body calcium is found in bone. The remaining 1% is found in soft tissues where it functions as a fundamental intracellular messenger and as co-factor for extracellular enzymes and proteins (Weaver and Heaney, 2006). Calcium provides structural strength to bone, but also serves as a reservoir to supply calcium for the maintenance of extracellular calcium homeostasis (Power et al., 1999).

The IOM DRIs committee for calcium and vitamin D recently also set an EAR of 1100 mg and a RDA of 1300 mg for calcium for children aged nine to 18 years (Table 6 in section 3.5, page 49). The previous DRIs for calcium included only an AI and UL. As with the DRIs for other nutrients, the EAR is set to meet the calcium needs of 50% and the RDA is set to meet the calcium needs of 97.5% of this age group (Institute of Medicine, 1997). The new reference intakes were set based on evidence that adolescents need higher levels of calcium to support bone growth than adults. The focus for this life stage in estimating the EARs and calculating RDAs was to determine the level of calcium intake consistent with bone accretion and positive calcium balance. The average calcium accretion was determined through bone measures such as dual X-ray absorptiometry and the average calcium retention was estimated by calcium balance studies. This data then enabled an estimation of the calcium intake required to support bone accretion and net calcium retention (Institute of Medicine, 2011). Data from a recent study provided the bone calcium accretion levels for children and adolescents that ranged from 92 to 210 mg/day (Vatanparast et al., 2010). The committee reported that a strong body of evidence from rigorous studies substantiates the importance of vitamin D and calcium in promoting bone growth and maintenance (Institute of Medicine, 2011).

Calcium intake in adolescents

Milk and other dairy products, such as cheese and yoghurt are excellent sources of readily available calcium. Canned fish with bones, such as salmon and fortified soyamilk substitutes are regarded as good sources. Leafy green vegetables contain good amounts of calcium, however the absorption of calcium

from these foods is lower than from dairy foods. Poor calcium sources include nuts, wholegrains and meats. Therefore, calcium is not widely distributed in different foods and if dairy foods are not eaten regularly, ingestion of available calcium may be inadequate (Weaver and Heaney, 2006).

Evidence indicates that most adolescents do not consume sufficient amounts of calcium (Harel et al., 1998, Morgan et al., 1985). Adolescent females have been reported to be twice as likely to have a deficient calcium intake (Key and Key, 1994). Analyses of recent NHANES data (2005 to 2006) found that among 14 to 18 year olds, 56% of males and only 10% of females had a calcium intake above the AI of 1300 mg per day from the 1997 DRIs for calcium (Moshfegh et al., 2009). Using the slightly lower EAR of 1100 mg per day published by the IOM in 2011 may have yielded sufficient intakes in a slightly greater proportion of adolescents. Either way, these findings support the notion of poor calcium intake by adolescents. Results from a recent study in low income urban African American adolescents were analogous, with approximately half (55%) of this sample consuming less than 1300 mg of calcium per day (Wang et al., 2010). Dietary calcium intake data from Africa is limited, but available data shows that intakes by infants, children and adults are substantially lower than recommendations (Prentice et al., 2009). Daily intakes of 200 to 300 mg have been reported in South Africa, The Gambia, Kenya, Egypt and Nigeria (Thacher et al., 2006). Intake of dairy foods is nominal in many African countries and typical diets are high in oxalates, tannins and phytates that are known to decrease calcium absorption (Prentice et al., 2009). Currently, very little is known about the calcium and vitamin D status of South African adolescents.

5.6.6   Pertinent issues relating to vitamin D and calcium deficiency in adolescents

The skeleton starts developing in *utero* and continues to develop throughout childhood and adolescence, until skeletal maturity is attained (Harel, 2008). The quantity of bone mass accrued when skeletal maturity is reached is referred to as the peak bone mass and this is usually achieved by early adulthood (Mughal and Khadilkar, 2011). Peak bone mass is a significant determinant of risk for fractures and osteoporosis in later life (Johnston and Slemenda, 1994, Mughal and Khadilkar, 2011).

Adolescence is characterised by rapid growth and more than 90% of peak bone mass is accrued during this period (Harel, 2008). According to Mughal and Khadilkar (2011), the increase in height occurs first in adolescents, followed by the increase in bone mineral content. An increase in bone width also occurs as new bone is deposited at the periosteal surface in adolescent males and females, and additionally on the endocortical surface in females. Bone strength parameters, including mass, size and shape, adapt continuously throughout life via bone modelling and remodelling. This happens in response to mechanical loading primarily from muscular contractions and involves an increase in the mineral mass and cross-sectional area of the particular of bone under stress (Mughal and Khadilkar, 2011). Bone modelling and remodelling during adolescence improves bone quality and establishes the skeleton's peak bone strength (Harel, 2008). Interactions of multiple calcitropic hormones such as growth hormone, gonadal hormones and insulin-like growth factor are also at play during bone mass accretion in adolescence (Davies et al., 2005).

The development of the human skeleton necessitates a sufficient supply of many different nutrients. Bone tissue is made up of hydroxyapatite ($(Ca)10(PO4)6(OH)2$) crystals and other ions that are rooted in fibrils of collagen and a ground substance of proteoglycans and glycoproteins. The formation of bone therefore requires sufficient supplies of energy, amino acids and the key bone-forming minerals, calcium, phosphorus, magnesium and zinc and of other ions, for example, copper, manganese and boron. Vitamins are also required for bone formation, including vitamin D, C, and K, that are involved in cartilage and bone metabolism and/or calcium and phosphate homeostasis and crystal and collagen formation (Prentice et al., 2006).

During childhood and adolescence, a primary physiological responsibility of $1,25(OH)_2D$ (activated vitamin D) is to ensure adequate intestinal calcium absorption to meet the needs of skeletal growth and development (Pettifor, 2005). Activated vitamin D is needed for the production of calbindin, a calcium-binding protein involved in transcellular calcium transport for absorption (Weaver, 2002). In the absence of vitamin D, only approximately 10 to 15% of dietary calcium is absorbed (Holick, 2007). Serum 25(OH)D concentrations of 30 ng/mL or less are associated with a significant reduction in intestinal calcium absorption (Heaney et al., 2003) and an increase in parathyroid hormone (Chapuy et al., 1997, Holick et

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al., 2005, Thomas et al., 1998). Therefore, in childhood and adolescence, the primary pathophysiological effect of vitamin D deficiency is a decrease in intestinal calcium absorption below the levels required to maintain a positive calcium balance that is adequate in size to meet the demands of the growing skeleton (Pettifor, 2005).

Severe and prolonged clinical vitamin D deficiency in early childhood results in rickets in infants and children and osteomalacia in adults. Rickets begins with suboptimal bone mineralisation at the growth plate and progresses with associated physiological disturbances, resulting in irreversible damage to skeletal structure. Similarly, osteomalacia is defective mineralisation and softening of bone in adults (Institute of Medicine, 2011). There are a spectrum of causes of rickets, with pure vitamin D deficiency at one end and dietary calcium deficiency at the other end of the spectrum. In the middle of these two extremes, a combination of vitamin D insufficiency and poor dietary calcium intake combine synergistically, preventing sufficient calcium absorption to meet the requirements of the growing child (Pettifor, 2005). It has been suggested that a serum 25(OH)D concentration of less than 12 ng/mL in children and adolescents is associated with an elevated risk of rickets (Institute of Medicine, 2011). However, rickets is less of a problem in adolescents and is found primarily in younger children. Less severe vitamin D deficiency and insufficiency leads to hyperparathyroidism with increased bone turnover and loss (Lips, 2001, Ooms et al., 1995). Growth retardation in children is also associated with vitamin D deficiency (Holick and Chen, 2008).

Osteoporosis is another skeletal condition linked to calcium and vitamin D nutriture and is characterised by compromised bone strength due to decreased bone mass and bone quality. Reduced bone mass, reflected in low bone mineral density, increases bone fragility, resulting in increased risk of skeletal fracture (Institute of Medicine, 2011). Adequate calcium intake has been definitively established as protective against osteoporosis. The primary approaches for decreasing the risk for osteoporosis are to maximise development of peak bone mass during growth and to reduce bone loss later in life. Achieving optimal calcium intakes is a goal for both of these approaches (Weaver and Heaney, 2006) and the quantity of calcium deposited in the osteoid matrix during childhood and adolescence is a determinant of the risk of osteoporosis and fractures in adulthood (Matkovic et al., 1979, Sandler et al.,

1985). Peak bone mass, the maximum amount of bone that can be accumulated (Bonjour et al., 1994), is attained by age 18 years at some skeletal sites, but by approximately age 25 years at other sites (Institute of Medicine, 2011)

Attainment of peak bone mass is determined by non-modifiable factors, such as genetics and epigenetics, age, race and ethnicity, pregnancy history and chronic disease. Modifiable factors that impact on bone mass accretion include nutritional exposures in *utero*, in infancy, during childhood and adolescence, as well as weight-bearing physical activity, having a healthy body weight, not smoking, moderate alcohol use and hormonal status (Harel, 2008, Mughal and Khadilkar, 2011, Prentice et al., 2006). Excess phosphorus from soft drinks has been mentioned as a possible risk for adolescent skeletal development, however, evidence relating to this hypothesis is inconclusive (Heaney and Rafferty, 2001, Ma and Jones, 2004, Mcgartland et al., 2003, Vartanian et al., 2007).

Evidence suggests that inadequate calcium intake may translate into inadequate calcium retention and a decrease in peak bone mass in adolescents (Matkovic et al., 1990). This is illustrated by studies showing an increase in bone mineral density after calcium supplementation in children and adolescents, with doses ranging from 360 to 1000 mg per day (Johnston et al., 1992, Lloyd et al., 1996, Prentice et al., 2005, Stear et al., 2003). Greater calcium retention has also been demonstrated with an increase in calcium intake from diet and supplements in adolescent females (Jackman et al., 1997), as has greater intake of dairy products in adolescents and young adults (Merrilees et al., 2000, Teegarden et al., 1999). However, evidence supports a threshold effect of calcium on bone mass as shown in an assessment of 124 studies in children and young adults (Matkovic and Heaney, 1992). A threshold effect of calcium on bone mass at a daily calcium intake of 1480 mg for nine to 17 year olds was found (Matkovic and Heaney, 1992).

With reference to the role of vitamin D in this regard, a double-blind randomised placebo controlled one year intervention study in adolescent females found positive effects of vitamin D supplementation of 5 micrograms and 10 micrograms (200 and 400 IU) on bone mineralisation (Viljakainen et al., 2006). Results from vitamin D supplementation trials suggest that the prepubertal period may be a particularly crucial time for promoting skeletal mineralisation through vitamin D

supplementation, however, this needs confirmation through sufficiently powered randomised controlled trials (Mughal and Khadilkar, 2011).

According to Wortsman et al (2000) *obesity* may be linked to vitamin D deficiency and this may be due to the sequestration of vitamin D by the extensive body fat pool, resulting in reduced availability of vitamin D . A recent longitudinal study in Colombian schoolchildren found that serum 25(OH)D concentrations were inversely associated with the development of adiposity. Vitamin D deficient children were seen to have an adjusted 0.1 per year greater change in BMI compared to vitamin D sufficient children (p for trend=0.05) and a mean 0.03 greater annual change in subscapular-to-triceps skinfold ratio (p=0.003; p test for trend=0.01) (Gilbert-Diamond et al., 2010). Thus, adiposity may be detrimental to the development of bone strength parameters and bone mass accrual during growth (Mughal and Khadilkar, 2011).

5.6.7   The influence of alcohol use on vitamin D and calcium status in adolescents

Both chronic and acute alcohol exposure have been shown to disturb circulating concentrations of calcium levels and the calcium-regulating hormones, parathyroid hormone, $1,25(OH)_2D$ and calcitonin (Sampson et al., 1997, Turner, 2000). Disturbances in calcium homeostasis by alcohol occur partly via effects on vitamin D and also via alcohol-mediated inhibition of intestinal calcium transport independant of vitamin D (Krawitt et al., 1975, Sampson, 1997). Alcohol is known to change the concentration of calcium-regulating hormones, however, it is not known if these aberrations contribute to the initial reduction in calcium levels or perhaps just maintain the low levels by failing to respond appropriately. Specifically, the calcium and parathyroid hormone relationship seems to be influenced by alcohol in such a way that during alcohol-induced hypocalcaemia, levels of parathyroid hormone do not increase and at times decrease (Diez et al., 1997, Keiver et al., 2000, Keiver and Weinberg, 2003, Laitinen et al., 1994, Laitinen et al., 1992, Thomas et al., 1990). It is also possible that alcohol reduces the serum levels around which calcium is regulated or that it disrupts the ability of parathyroid hormone to respond to reduced circulating calcium levels (Keiver et al., 2005). Considering the documented effects of alcohol use on calcium homeostasis and vitamin D homeostasis, it could be speculated that alcohol-induced

hypocalcaemia in heavy drinking adolescents may impact on their long term bone health, particularly in the case of frequent and protracted binge drinking.

This possibility is supported by evidence from chronic alcohol users in whom associations between alcoholism and reduced bone density and bone mass, increased fracture susceptibility and increased osteonecrosis (Lieber, 2000) have been established. Depressed bone synthesis has also been reported in alcohol exposed experimental animal models (Sibonga et al., 2007) and in alcoholics (Santori et al., 2008). Alcohol abuse disturbs osteoblastic activity and the decrease in bone mass and strength following heavy alcohol intake is primarily due to a bone remodeling imbalance, with a predominant reduction in bone synthesis (Turner, 2000, Wezeman et al., 2007, Maurel et al., 2011). An additional effect of alcohol is the alteration of bone mineral metabolism, including parathyroid hormone, vitamin D, testosterone, cortisol and insulin-like growth factor 1 levels, both directly and indirectly (Alvisa-Negrin et al., 2009). Other factors, such as inadequate dietary intake, social marginalisation (Gonzalez-Reimers et al., 2005, Santolaria et al., 2000), protein deficiency (Molina-Perez et al., 2000), and inadequate physical activity (Alvisa-Negrin et al., 2009) also contribute to bone loss in alcoholics. It is evident that there is general consensus regarding the effect of alcohol on bone synthesis, but results regarding its effects on bone resorption are less established (Dai et al., 2000, Diamond et al., 1989, Schnitzler and Solomon, 1984, Turner, 2000).

When considering the relationships between heavy alcohol use, vitamin D and calcium status and skeletal health in adolescents, it is important to note that increased alcohol consumption has been associated with reduced bone mineral density in adolescent males (Fehily et al., 1992). In line with this, alcohol and smoking were found to have a significant inverse association with bone mineral density in a recent four year prospective study in 109 high school students (Korkor et al., 2009). These findings are further supported by experimental animal data. Studies in adolescent rodent models have shown that chronic alcohol intake reduces bones mineral density, inhibits bone growth, degrades cancellous bone structure and negatively affects biomechanical strength (Hogan et al., 1997, Sampson et al., 1997, Sampson et al., 1996, Wezeman et al., 1999, Wezeman et al., 2003). In addition, intermittent binge-like alcohol exposure in adolescent and young adult rats has significant negative effects on bone integrity, for

example trabecular structure, bone mass and functional strength capacities of bone (Callaci et al., 2006, Lauing et al., 2008, Wezeman et al., 2007) and has been found to increase osteoclastic resorption (Wezeman et al., 2000). A recent laboratory investigation in adolescent rats using binge drinking models demonstrated that binge alcohol exposure can produce disturbances of normal bone gene expression patterns that persist well beyond the phase of active intoxications (Callaci et al., 2010). Research in rodents from the same laboratory also demonstrated that bone loss, induced by binge alcohol exposure, can be prevented with an effective dose of vitamin D, even during high blood alcohol levels that have been shown to disturb osteoblast functions (Wezeman et al., 2007). In summary, binge alcohol exposure can produce both short and long term skeletal harm in the adolescent rat. It can be speculated that these findings may have relevance for peak bone mass attainment and future risk of skeletal disease in human adolescents who engage in repeated binge drinking episodes. Within this context it must also be borne in mind that heavy episodic drinking behaviours that begin during late adolescence tend to continue into early adulthood (Mccarty et al., 2004), increasing the time that alcohol-related skeletal damage may be taking place.

In view of the evidence discussed it is reasonable to speculate that repeated alcohol-induced disruptions in calcium and vitamin D homeostasis, in combination with possible poor calcium and vitamin D intake and status during adolescence (see sections 5.6.4 and 5.6.5), may have implications for maximising peak bone mass, thereby influencing the risk of osteoporosis in later life.

5.7   Physical Activity

5.7.1   Assessment of physical activity

When considering assessment of physical activity levels it needs to be considered that physical activity for health benefits consists of several components, for example, duration, intensity, frequency and type. Furthermore, physical activity can be performed in different domains, for example, occupational physical activity, discretionary or leisure time physical activity and/or transport-related physical activity (Armstrong and Bull, 2006).

Methods for physical activity assessment range from complex validated instruments (Armstrong and Bull, 2006) and structured questionnaires (Fulton et al., 2009), to single questions about participation and frequency of participation in physical activity (Kujala et al., 2007). Research in adolescents has used a variety of these methods to assess physical activity (Reddy et al., 2010a, Mcveigh et al., 2004). For example, in the YRBS in South Africa, the frequency and duration of physical activity were assessed via questions relating to vigorous and moderate physical activity. Sufficient vigorous physical activity was considered as having engaged in sports such as soccer, netball, rugby, basketball or running for at least 20 minutes on three or more days in the week preceding the survey. Sufficient moderate physical activity was considered as having engaged in activities such as walking, slow bicycling, skating, pushing a lawn mower, mopping, polishing or sweeping the floors for at least 30 minutes on five or more days in the seven days preceding the survey. Physical activity at less than these defined levels was regarded as insufficient and participants reported if they not engaged in any physical activity in the preceding week, as per the definitions of vigorous or moderate physical activity above (Reddy et al., 2010a).

5.7.2   Physical activity in adolescents

The WHO global recommendation for physical activity for health for five to 17 year olds is an accumulation of 60 minutes of moderate to vigorous physical activity daily (World Health Organization, 2011a). This recommendation is supported by scientific evidence showing that adequate physical activity provides fundamental health benefits for children and adolescents, contributing to the health of musculoskeletal tissues, including bones, muscles and joints, and facilitating the maintenance of a healthy body weight. Additionally, physical activity also promotes the health of the cardiovascular system as well as neuromuscular awareness and has been associated with psychological benefits in young people through improvement of their control over feelings of anxiety and despair, and helping with social development by providing opportunities (World Health Organization, 2011a). Promotion of physical activity also reduces the risk for the development of NCDs and contributes to improved quality of life (Stafford et al., 1998).

Beneficial effects of exercise during childhood appear to track into adulthood, with most benefits being seen when activity starts during the prepubertal and peripubertal phase (Bass et al., 1998, Bradney et al., 1998, Kannus et al., 1995, Lloyd et al., 2000). This is further supported by longitudinal data showing that adolescents with a healthy participation in physical activity are more likely to be active adults (Vanreusel et al., 1997) and that the converse also applies with low physical activity in adolescence also tracking into adulthood (Gordon-Larsen et al., 2004b).

When considering the profile of physical activity in adolescents, a concerning trend of decreasing physical activity levels is evident. Declining levels of physical activity during adolescence have been well documented in developed countries (Gordon-Larsen et al., 2004b, Kimm et al., 2002), and less than 15% of school children in eight developing countries reported having engaged in frequent physical activity (five days and more per week, minimum 60 minutes per day) (Peltzer, 2010). When considering the consequences of sedentary behaviour in adolescence, evidence of a direct association between sedentary behaviour (mainly television watching) and adiposity in adolescents has been reported (Must and Tybor, 2005). Prospective studies that adjusted for dietary intake reported an inverse association between physical activity and increases in BMI (Elgar et al., 2005, Jago et al., 2005) and adiposity (Moore et al., 2003, Moore et al., 1995). A review of longitudinal studies of sedentary behaviour and physical activity among youth and their association to weight and adiposity reported an inverse relationship with physical activity and a positive association with sedentary behaviour (Must and Tybor, 2005).

In line with these findings, both YRBSs in South Africa reported low levels of physical activity (Reddy et al., 2010a, Reddy et al., 2003). Furthermore, a significant decrease in sufficient moderate physical activity (34% to 29%) and a significant increase in "insufficient" or "no physical activity" (38% to 42%) among adolescents was found from 2002 to 2008 (Reddy et al., 2010b). In 2008, physical inactivity in the Western Cape in general (51.6%) and in the mixed ancestry group specifically (46.5%) was higher than the national prevalence (42%). More females (46.2%) participated in insufficient or no physical activity than males nationally (36.7%), while in the Western Cape 57.6% of females and 44.9% of males and in the mixed ancestry population 50.9% of females and 41.7% of males, participated in insufficient or no physical activity. In terms of sedentary activity, almost a third of adolescents (29.3%) reported

watching television for more than 3 hours per day (Reddy et al., 2010a). It is well established that sufficient physical activity is a factor that threads through many components of adolescent health, including nutritional health.

5.7.3   The influence of alcohol use on physical activity in adolescents

When considering the very limited available research (mostly cross-sectional studies) regarding the association between physical activity and alcohol use, it is evident that there are links between physical inactivity and substance use among adolescents, including smoking and alcohol consumption, as well as initiation of alcohol use and smoking (Kristjansson et al., 2008, Aaron et al., 1995, Tur et al., 2003). Further evidence in this regard comes from the large population-based prospective twin study in which physical activity levels in adolescence predicted alcohol and illicit drug use in early adulthood (Korhonen et al., 2009). These researchers found that weekly alcohol intoxication (OR=1.9; p=0.002) was more common among persistently inactive participants. The authors concluded that persistent physical inactivity during adolescence may increase the risk of later problems due to excess alcohol use, and that sedentary lifestyle predicts illicit drug use after adjustment for familial factors (Korhonen et al., 2009). Similar associations were reported in a recent large cross-sectional survey (*n= 24593*) among school children aged 13 to 15 years from nationally representative samples in eight African countries. Leisure time sedentary behaviour was highly associated with alcohol, tobacco, and drug use among these adolescents (Peltzer, 2010).

It is important to note that the available evidence does not provide a clear indication of whether physical inactivity results in an increased risk for heavy alcohol use or whether heavy alcohol use results physical inactivity, or whether a combination of these two possibilities explain the reported associations.

6   MOTIVATION AND RESEARCH THEMES

Adolescents have for some time been recognised as a nutritionally at-risk group only in part because of the high nutritional demand for growth and development. This risk may be aggravated by poor dietary intake and eating behaviour in this life stage. From the literature review it is evident that adolescents are specifically at risk for undernutrition, overnutrition and poor iron, vitamin D and calcium nutriture, as a consequence of poor dietary intake and eating behaviour (Figure 4).

It is evident that that the widespread heavy alcohol use by adolescents, characterised by multiple episodes of binge drinking over weekends, is a potential contributing factor to the risks of poor nutritional status in South African adolescents. Review of relevant evidence, which includes mostly research in chronic alcohol abusers and some experimental work on acute alcohol use in humans and animal models, illustrates that heavy alcohol use can influence nutritional status in several ways. These may include direct effects on metabolic functioning (disrupted nutrient metabolism and increased micronutrient needs) and the gastrointestinal tract (impaired nutrient absorption, disrupted mucosal enzyme activity, mucosal morphology damage and haemorrhage). Indirect effects may include changes in eating behaviour (food choices and meal/snack patterns), resulting in changes in energy intake (increased food intake over the short term and decreased food intake with chronic use) and micronutrient intake, as well organ damage (chronic use). Available evidence for the ubiquity and severity of adolescent alcohol intake, makes it a plausible contributor to the nutritional challenges of adolescents, but as yet, the full array of interactions has not been fully investigated (Figure 4).
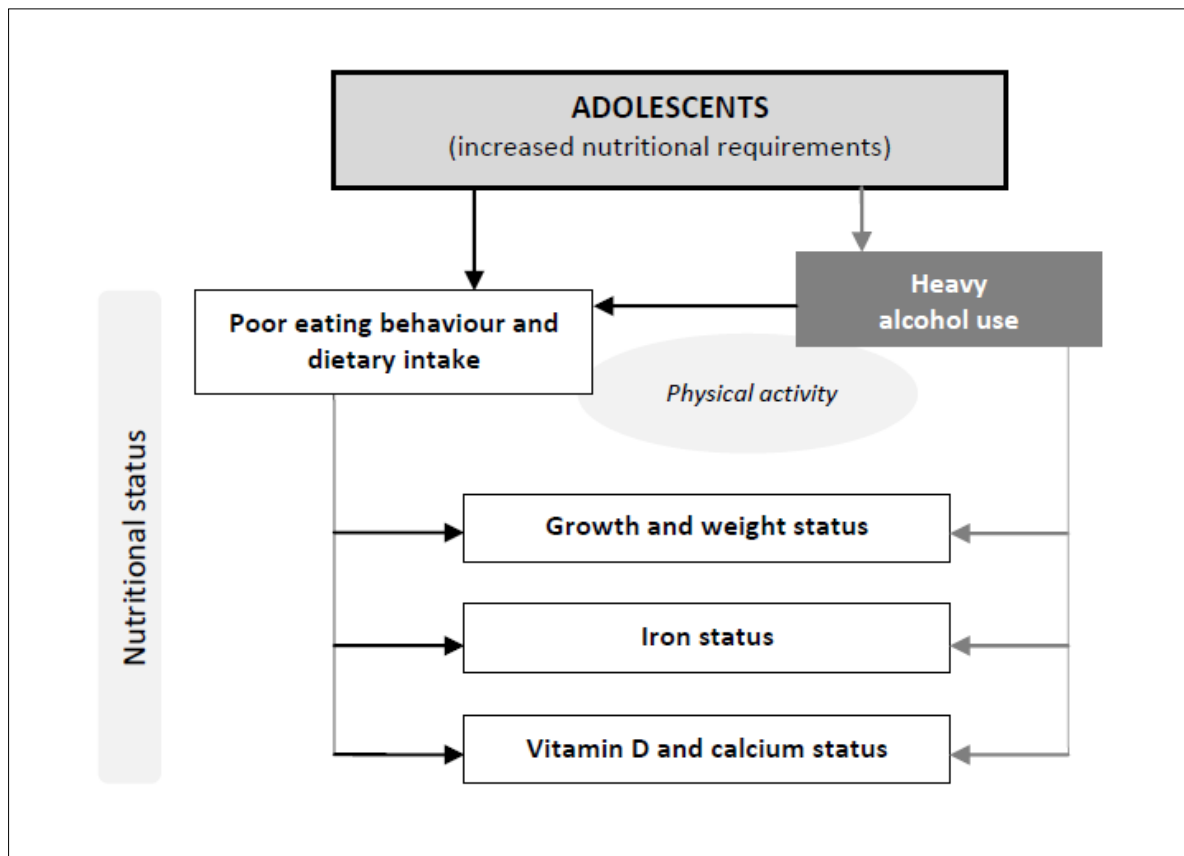
Figure 4: Conceptual framework depicting possible influences of heavy alcohol use on the nutritional status of adolescents

Pertinent specific **research questions** that are evident from Figure 4 are as follows:

1. What is the potential influence of alcohol use in adolescents on their **eating behaviour and dietary intake**?

2. What is the potential influence of alcohol use in adolescents on their **growth and weight status**?

3. What is the potential influence of alcohol use in adolescents on their **iron status**?

4. What is the potential influence of alcohol use in adolescents on their **vitamin D and calcium status**?

To our knowledge, it is not known how or if heavy alcohol use influences specific nutritional challenges in adolescents and an investigation of the stated research questions is important 1) to inform the potential for alcohol to influence nutritional status and related outcomes, and 2) subsequently to inform the need for development of focussed health promotion, intervention and programme planning

for adolescents if necessary, following confirmation of causality. By answering the stated research questions, this study endeavours to make a contribution to knowledge in this area of adolescent nutritional health.

Adolescent alcohol use is a pervasive problem in Cape Town, the largest city in the Western Cape Province of South Africa and this city provided the setting to study the nutritional status of adolescents meeting criteria for alcohol use disorders (AUDs), but with minimal other drug use histories. This study formed part of a larger study exploring the effects of heavy alcohol use on brain structure and function.

Aim: This research study investigated the potential influences of alcohol use on the nutritional status of adolescents with AUDs, specifically with regards to their eating behaviour and dietary intake, growth and weight status, iron status, as well as vitamin D and calcium status.

Study design: A cross-sectional, comparative study involving treatment-naïve heavy drinking adolescents, meeting DSM-IV criteria for alcohol use disorders (AUDs group) and light/non-drinking adolescents without alcohol use disorders (non-AUDs group), matched for age (within 1 year), gender, language, socio-economic status, smoking and level of education (within 1 year)

Study population and participants: The target population included school-going adolescents, aged 12 to 16 years, English or Afrikaans-speaking, with a lower socio-economic status, recruited from schools within a 25 kilometre radius of Tygerberg Hospital in the greater metropolitan area of Cape Town, South Africa

6.1   The Candidate's Specific Contribution

The candidate was directly involved in the conceptualisation of this specific study and was responsible for the writing of the research study protocol. The candidate collected and managed all the dietary and anthropometric data and all aspects of the collection of biochemical data, except for the actual venipuncture, which was performed by a qualified phlebotomist. The socio-demographic and substance

use data from the larger study was used. Database management and all statistical analyses pertaining to this study were done by the candidate in consultation with a biostatistician.

6.2   Outline of Chapters 3 to 6 of the Dissertation

Chapters 3 to 6 each represent one of the four research questions stated above, namely Chapter 3: Eating behaviour and dietary intake; Chapter 4: Growth and weight status; Chapter 5: Iron status and Chapter 6: Vitamin D and calcium status.

Each of these chapters is formatted with a view to being a stand-alone publishable paper. While methodology relevant to each of the sub-questions is addressed in turn, there is a degree of unavoidable overlap in the chapters. Chapter 4 has been published (Naude et al., 2011) while chapters 3, 5 and 6 are as yet unpublished.

To orientate the reader to the various chapters, a summary of the pertinent research questions, primary variables and assessment methods for each of the chapters, as well as an overview of the main statistical analyses, are depicted in Table 11. All the measures were conducted on participants in both the non-AUDs and AUDs groups in the study sample.

To clarify the boundaries of this research study, it is important to mention that it did not endeavour to examine the numerous other factors that influence the nutritional status of adolescents.

Table 11: Summary of the primary variables and assessment methods for each research question and an overview of main statistical analyses used

Research Questions	Primary variables (assessment methods)	Main statistical analyses
1. What is the potential influence of alcohol use in adolescents on their **eating behaviour and dietary intake?**	Socio-demographic information (self-report q) Substance use (revised version of the TLFB [a] procedure in combination with the K-SADS-PL [b]) Dietary intake: energy and nutrient intakes, fruit and vegetable intake, 10 most frequently consumed foods/energy-containing beverages (3 x 24-hour recalls), reasons for low fruit and vegetable intake (interviewer-administered q) Eating behaviour: frequency of intake of indicator foods (interviewer-administered non-quantitative food frequency questionnaire); meal and snack patterns and (interviewer-administered q)	• Adherence to normal distribution assessed for each variable and transformations applied, as appropriate • Descriptive statistics: means, standard deviations, medians and interquartile ranges • Socio-demographic and substance use variables compared between the two groups • Mann Whitney U Test used for comparisons of skewed continuous variables and Chi-square or Fisher's exact tests used for comparisons of categorical variables, as appropriate • Regression-adjusted differences between the two groups assessed using *multi-level mixed effects linear regression model*, adjusting for potential confounders. A pairing variable was created according to the matched pairs in the sample and served as the level variable in the model. *In this model the hierarchical structure of the data is explicitly considered. Regression parameters can be fixed but also random (i.e. free to vary across different contexts at a higher level of the hierarchy). Thus, for each regression parameter there is a fixed component but also an estimate of how much the parameter varies across contexts. Benefits of multilevel models: no assumption of homogeneity of regression slopes, no assumption that different cases of data are independent and suitable for analysis of data with missing fields* • Observed dietary intake distributions were used in regressions • Observed dietary intake distributions were adjusted statistically to partially remove the within-person variability, in order to obtain usual nutrient intake distributions *** • Adequacy of nutrient intakes in the two groups assessed using the EAR cut-point method for all micronutrients, except iron *** • Appropriateness of macronutrient intakes assessed using the AMDRs **** • Adequacy of iron intakes in the two groups assessed using the probability approach ***** • Nutrient adequacies in the two groups compared using the Chi-square test *** • Excessive nutrient intakes in the two groups determined using the ULs **** • Nutrient excess in the two groups compared using the Chi-square test ****
2. What is the potential influence of alcohol use in adolescents on their **growth and weight status**?	Socio-demographic information (self-report q) Substance use (revised version of the TLFB [a] procedure in combination with the K-SADS-PL [b]) Anthropometric indices (height-for-age; body mass index-for-age) Physical activity: minutes per week of regular, weekly 'organised sporting activities' (interviewer-administered q) Sedentary time: minutes per week of television and computer use (interviewer-administered q) Energy intake (3 x 24-hour recalls)	
3. What is the potential influence of alcohol use in adolescents on their **iron status**?	Socio-demographic information (self-report q) Substance use (revised version of the TLFB [a] procedure in combination with the K-SADS-PL [b]) Serum iron, transferrin, ferritin, total iron binding capacity, C-reactive protein, transferrin saturation (biochemistry) Dietary total iron, haem iron and total energy intake, top 5 foods/energy-containing beverages contributing to total iron intake (3 x 24-hour recalls) Frequencies of intake of indicator foods reflecting total iron and haem iron intake (interviewer-administered q)	
4. What is the potential influence of alcohol use in adolescents on their **vitamin D and calcium status**?	Socio-demographic information (self-report q) Substance use (revised version of the TLFB [a] procedure in combination with the K-SADS-PL [b]) Serum 25-hydroxyvitamin D (biochemistry) Calcium, vitamin D and energy intake, top 5 foods/energy-containing beverages contributing to calcium intake (3 x 24-hour recalls) Frequencies of intake of indicator foods reflecting calcium intake (interviewer-administered q)	

Abbreviations: q: questionnaire; TLFB: Timeline Followback (Sobell and Sobell, 1992); K-SADS-PL: Schedule for Affective Disorders and Schizophrenia for School Aged Children (six to 18 years) Lifetime Version (Kaufman et al., 1996)*;* AUDs: Alcohol use disorders*;* EAR: Estimated average requirement*;* AMDRs: Average macronutrient distribution ranges*;* ULs: Tolerable Upper Intake Levels
* Not relevant to research question 2; ** Only relevant to research question 1; ** * Only relevant to research question 3

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Chapter 3

EATING BEHAVIOUR AND DIETARY INTAKE

INTRODUCTION

The rapid growth and development experienced during adolescence results in greater energy and nutrient requirements in this group compared to adults. In addition, this maturational life stage is characterised by the attainment of greater self-efficacy (Avery et al., 1992). Within this process, adolescents acquire increased control over their own food choices (Fitzgerald et al., 2010), which has been associated with the acquisition of poor eating behaviour (poor food choices and meal and snack patterns) and subsequent poor dietary intake (energy and nutrients) (Stang et al., 2008).   This notion is supported by data from low and high income countries showing that the usual diet consumed by many children and adolescents is of a poor nutritional quality, which may be the result of increased consumption of energy-dense nutrient-poor foods (Barquera et al., 2003, Moreno et al., 2010, Munoz et al., 1997, Pomerleau et al., 2004). According to Temple et al (2006), adolescents frequently consume "junk food" such as sweets, crisps, French fries and sweetened beverages, which are typically high in energy, high in fat and/or sugar and sodium, while being relatively low in micronutrients and dietary fibre. Evidence from developed countries show that harmful health behaviours, including unhealthy dietary intake, poor eating behaviours and high levels of sedentary time adopted by adolescents, adversely affect their nutritional status, considerably increasing their risk for overweight and obesity and premature development of non-communicable diseases (NCDs) in adulthood (Andersen et al., 2003, Caballero, 2001, De Henauw et al., 2007, Law, 2000, Ludwig et al., 2001, Moreno et al., 2010, World Health Organization, 2005). The latter may be partially explained by the fact that health-related behaviours and practices established during adolescence may be continued into adulthood (Grant, 1998, Kelder et al., 1994, Te Velde et al., 2007). Indeed, dietary intake and eating behaviours that predispose to coronary heart disease, type 2 diabetes, hypertension, obesity and other chronic lifestyle diseases are set in motion during childhood and adolescence (Andersen et al., 2003, Boreham et al., 1999, Caballero, 2001, Law, 2000).

When considering the health behaviour of adolescents, clustering of unhealthy behaviours in this age group is commonly reported (Paavola et al., 2004, Pronk et al., 2004, Burke et al., 1997). Among others, unhealthy eating behaviours in adolescents, including excessive consumption of sweetened

beverages and energy-dense snacks, skipping breakfast and other family meals, are positively associated with the use of tobacco and alcohol, unsafe sex practices and watching television, thus a more sedentary lifestyle (Eisenberg et al., 2004, Keski-Rahkonen et al., 2003, Neumark-Sztainer et al., 1997, Nutbeam et al., 1991). Particularly concerning in adolescents is heavy alcohol use, which is regarded as a pervasive public health problem globally (Donath et al., 2011, Mcardle, 2008, Parry et al., 2004b, United States Department of Health and Human Services, 2007). South Africa is no exception and a disturbing prevalence of high risk drinking patterns among South African adolescents was reported in both the South African Youth Risk Behaviour Surveys (Reddy et al., 2010, Reddy et al., 2003) and in other studies (Parry et al., 2004b, Parry et al., 2004a, Madu and Matla, 2003). Adolescents frequently engage in binge drinking (Miller et al., 2007, Hingson et al., 2005, Parry et al., 2004b), which is commonly defined as having had five or more drinks of alcohol in a single drinking session (Eaton et al., 2010, Hibell et al., 2009, Reddy et al., 2010, Reddy et al., 2003, Miller et al., 2007). Research has shown that that binge drinking behaviour may influence eating behaviour and food choices, although evidence in this regard is very limited. A recent qualitative study in American college students reported that binge drinking may result in eating without hunger during or after consuming alcohol. On the other hand, larger amounts may be eaten prior to drinking in anticipation of a binge drinking occasion in order to be able to tolerate more alcohol (Nelson et al., 2009a). In a follow-on cross-sectional study in college students (*n=3406*; mean age 24.2 years $\pm$5.9 years) approximately 80% of participants reported alcohol-related eating "always or usually" during the preceding year. This study also found that binge drinking was significantly associated with poor eating behaviours (<5 daily servings fruit and vegetables, breakfast consumed on <5 days per week, fast food consumption at least several times per week), as well as unhealthy weight control behaviour and sedentary behaviour (Nelson et al., 2009b).

Since alcohol is a source of energy, its consumption contributes to total energy intake. Furthermore, alcohol may displace nutrient-dense foods in the diet while energy-dense food intake may increase, contributing to possible excess dietary energy (Foster and Marriott, 2006, Nelson et al., 2009b), and thus a positive energy balance as well as a reduction in micronutrient intake (Ferreira and Willoughby, 2008). The potential negative effects of binge drinking on eating behaviour may be

compounded by the direct negative effect of alcohol on the gastrointestinal tract that may result in reduced nutrient absorption as well as by the increased micronutrient needs resulting from the metabolism of alcohol. This is evident from experimental work on the effects of acute alcohol intake and health outcomes of individuals with chronic alcoholism (Bode and Bode, 2003, Lieber, 2000, Lieber, 2003, Van Den Berg et al., 2002).

It is argued that the possible impacts of binge drinking on eating behaviour and dietary intake is a concern, given that the adverse short and long term health outcomes associated with the poor eating behaviours and dietary intake typical of adolescents, mentioned above, may be compounded by persistent binge drinking. Despite these potential short and long term nutrition-related health risks, the eating behaviour and dietary intake of heavy drinking adolescents have not been well characterised.

The aim of this study was therefore to examine the eating behaviours and dietary intake of treatment-naive, 12 to 16 year old community-based adolescents with alcohol use disorders (AUDs), but without co-morbid substance use disorders (SUDs), in comparison to light/non-drinking adolescents without AUDs, from the same well-defined and homogenous study population. The inclusion of adolescents without co-morbid externalising disorders or SUDs permitted the study of dietary intake and eating behaviour in adolescents with AUDs, without the confounding influences of these factors.   It is hypothesised that eating behaviour and resulting dietary intake may be different in adolescents with AUDs compared to light/non-drinking adolescents without AUDs.

METHODS AND MATERIALS

Study Population and Participants

Convenience sampling was used to select a sample of 162 consenting English or Afrikaans speaking volunteers aged between 12 and 16 years. Learners attending schools in lower socio-economic areas within a 25 kilometre radius of Tygerberg Hospital, located in the greater metropolitan area of Cape Town, South Africa, and who met the inclusion criteria for the either the AUDs or non-AUDs groups, were eligible for participation. Screening included a structured psychiatric diagnostic interview, a developmental and medical history (from participants and at least one biological parent or legal

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guardian), a detailed physical and neurological examination assessing developmental delays and urine analysis and breathalyser testing (to confirm sobriety of participants during testing procedures). The Schedule for Affective Disorders and Schizophrenia for School Aged Children (six to 18 years) Lifetime Version (K-SADS-PL) (Kaufman et al., 1996) was used to screen for psychiatric diagnoses. The Semi-Structured Assessment for the Genetics of Alcohol (SSAGA-II) (Bucholz et al., 1994) was used to confirm AUDs diagnosis and to derive detailed substance use histories (alcohol, tobacco and all other drugs).

Participants were assigned to one of two groups: an AUDs group meeting DSM-IV criteria for alcohol dependence or alcohol abuse (American Psychiatric Association, 1994) or a non-AUDs group (non-drinking/light drinking with lifetime dose of < 100 standard drinks of alcohol or never consumed alcohol). Exclusion criteria for both groups were: mental retardation, lifetime DSM-IV diagnoses other than AUDs (as defined in the KSADS-PL, including major depression, dysthymia, mania, hypomania, cyclothymia, bipolar disorders, schizoaffective disorders, schizophrenia, schizophreniform disorder, brief reactive psychosis, panic disorder, agoraphobia, separation anxiety disorder, avoidant disorder of childhood and adolescence, simple phobia, social phobia, overanxious disorder, generalized anxiety disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, enuresis, encopresis, anorexia nervosa, bulimia, transient tic disorder, Tourette's disorder, chronic motor or vocal tic disorder, alcohol abuse and dependence (non-AUDs group only), substance abuse and dependence, post-traumatic stress disorder, and adjustment disorders), current use of sedative or psychotropic medication, current signs of or a history of foetal alcohol syndrome or exposure to heavy antenatal alcohol exposure, sensory impairment, history of traumatic brain injury with loss of consciousness exceeding 10 minutes, presence of diseases that may affect the CNS (e.g., meningitis, epilepsy), HIV [tested using the enzyme linked immunosorbent assay (ELISA)], less than 6 years of formal education, and lack of proficiency in English or Afrikaans. Prior to consent being obtained for participation in the study, a research social worker obtained collateral information from consenting parents, verifying the absence of medical, psychiatric and psychosocial problems. Participants in the two groups were individually matched for age (within 1 year), gender, language, socio-economic status and level of education (within 1 year). A total socio-economic status score was calculated for each participant

by summing the category scores for family income (1-6), reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), parent education (0-6), total assets (0-7), dwelling type (1-6) and bedroom cohabitation (1-7). During recruitment it was attempted to match the samples for smoking status, but this was not to be feasible since smoking was much more prevalent in the AUDs participants. This positive association of smoking and alcohol use is well documented (Larson et al., 2007).

Measures

   Substance use: A revised version of the Timeline Followback procedure (TLFB) (Sobell and Sobell, 1992), a semi-structured, clinician-administered assessment of lifetime history of alcohol use and drinking patterns (i.e., frequency, quantity and density of alcohol consumption, including every phase from when participants first started drinking at least once per month to the present, including all periods of abstinence) was used in combination with the K-SADS-PL to elicit alcohol-use data. It was administered by a Psychiatrist on the day of screening.   A standard drink was defined as one beer, cider or wine cooler (340 millilitres (mL)), one glass of wine (150mL) or a 45mL shot of liquor.   A similar procedure was carried out for each substance that the research participant acknowledged using.

   Dietary intake (energy and nutrients): Dietary intake was estimated using three 24-hour recalls per participant administered on non-consecutive days. The internal and external validity of this method has been found to be acceptable in adolescents aged ten years and older (Biro et al., 2002) and it has been shown to be appropriate for quantifying dietary intake of groups in developing countries (Gibson, 2005a, Gibson, 2005b).

   The energy (kilojoules (kJ)) and nutrient intakes for each participant for each day were calculated using the South African Food Data System (SAFOODS) (Medical Research Council, 2002). The average intakes over the three 24-hour recall interviews were calculated to represent the observed intake distributions for energy and nutrients. The dietary data include nutrient intake estimates from food (both naturally present and fortified) and water only and exclude nutrient intake estimates contributed by dietary supplements and medications. It is however important to bear in mind the limitations of the

vitamin D intake estimates in this study, namely the relatively high percentage of missing values for vitamin D (approximately 30 to 40 %) in the SAFOODS database (Wolmarans et al., 2010).

The energy intake variable obtained from the 24-hour recalls did not include estimated energy from alcohol intake. Average daily alcohol energy intake of the AUDs group was estimated from average daily alcohol intake (grams) per participant in the AUDs group using the alcohol-use data from the most recent phase of drinking as follows: 1) frequency of alcohol use (days per month) multiplied by average quantity of alcohol consumed (standard drinks per drinking day) to obtain average monthly standard drinks of alcohol consumed; 2) average monthly standard drinks of alcohol consumed was divided by 28 days to obtain average daily standard drinks of alcohol consumed; 3) average daily standard drinks of alcohol consumed was multiplied by 13.6 grams of alcohol per standard drink to obtain average daily alcohol intake in grams, which was converted to average daily alcohol energy (29 kilojoules per gram) to obtain average daily alcohol energy (kilojoules). Average daily alcohol energy was added to daily energy intake from the observed intake distributions for each AUD participant to represent total estimated energy intake. Daily alcohol energy for the *n=48* light drinking participants in the non-AUDs group was not calculated as their alcohol life dose was negligible (mean 5.77; SD 12.46 standard drinks), and the contribution of alcohol energy to total estimated energy intake would therefore also be negligible.

The average intake (grams per day) of 1) fruit, 2) vegetables and 3) fruit and vegetables combined was also calculated for each participant from the 24-hour recalls, using the food codes of all foods consumed by participants that appear in the fruit and vegetable food groups in the SAFOODS. These excluded avocado, potato, sweet potato and maize and is in accordance with categorisation of fruit and vegetables applied in the South African Food-Based Dietary Guidelines (SAFBDG), where potatoes, cereals, tubers and dry pulses are not classified as vegetables and avocado is classified in the fats and oils group (Love and Sayed, 2001). Many products branded as "fruit drinks' contain only small quantities of the original fruit juice and only fruit juices and vegetable juices that are 100% pure should be classified as fruit and vegetables, respectively (Agudo, 2004). It was thus decided to exclude fruit and vegetable juices from the estimation of fruit and vegetable intake, as it was observed during data collection that most of the participants could not distinguish between the pure juices and 'fruit drinks'.

To explore reasons for low fruit intake, participants who reported no fruit intake on one or more of the three 24-hour recall days were asked to report the single most important reason for their low fruit intake, with response options being: 'not available at home', 'not for sale in the area', 'too expensive', 'do not like fruit' or 'do not like vegetables' and 'other' reason. The same approach was followed to explore reasons for low vegetable intake.

In addition, the 24-hour recall data was used to determine the 10 most frequently consumed foods/energy-containing beverages (excluding alcoholic beverages) in each group.

Eating behaviour (frequency of intake of indicator foods as well as meal and snack patterns):
The weekly frequencies of intake of foods reflecting healthy and poor food choices were estimated using a non-quantitative food frequency questionnaire. The questionnaire consisted of a list of 37 food categories, with each food category consisting of either a single or multiple food items that were grouped based on similar nutritional characteristics (Table 1). Indicator foods/categories were identified by firstly listing foods most commonly consumed by South Africans in the Western Cape using scientific reports, publications as well as unpublished dietary assessment information generated in small research projects/compilation of community profiles for nutrition interventions. Identified foods/categories were then classified as either healthy choices (offer protective effects against NCDs) or as poor choices (would increase NCDs risk).   A panel of nutrition and NCDs health experts advised this process. The response categories included 'eaten in the past month' (yes/no), and if yes, 'times eaten per week' or 'times eaten per month'.

The frequency of intake recorded for each one of the 37 food categories was converted to reflect the number of times eaten per week. For further analyses the 37 food categories were grouped into 10 indicator food groups (Table 1). The weekly frequency of consumption of food categories included in each of the 10 indicator food groups were summed to obtain the weekly frequencies of intake for each indicator food group for each participant.

For assessment of meal and snack patterns, participants were asked to indicate (yes/no) whether they usually consumed the following meals/snacks on school days: snack at home before breakfast, meal at breakfast at home, snack before school, snack at first school break, snack at second school break, snack

on the way home after school, meal at lunch time (home, after care, friend), snack during early

afternoon, snack during late afternoon, meal at supper at home/friend and snack after supper.

Table 1: Indicator food groups (10) created from the 37 indicator food categories in the non-quantitative food frequency questionnaire

Indicator food group	Indicator food categories included in group	
1 Animal protein	• meats, red • meats, processed • meats, tinned • chicken, with skin • fish, tinned or smoked	• fish, fresh (not in batter) • eggs • milk, sour milk, yoghurt • cheese, yellow • meats, organ (liver and kidneys)
2 Dietary fibre - high	• legumes (beans, lentils) • bread, brown • oranges, naartjies • apples, bananas, pears • orange or yellow vegetables (sweet potato, pumpkin,butternut, carrots)	• green vegetables (spinach, beans, broccoli) • mixed vegetables • cabbage, cauliflower, lettuce • tomato (raw and cooked)
3 Dietary fibre - low	• bread, white	• rice, 'pap' [a], pasta, 'samp' [b], potato
4 Unhealthy fats	• meats, red • meats, processed • meats, tinned • chicken, with skin • eggs • cheese, yellow	• margarine, butter • fried foods, potato chips • fried foods, other (fat cakes, fish, chicken) • pies, sausage rolls, samoosas [c] • meats, organ (liver, kidneys)
5 Healthy fats	• fish, tinned or smoked • fish, fresh (not in batter)	• peanut butter, peanuts
6 Calcium	• milk, sour milk, yoghurt	• cheese, yellow
7 Fruit and vegetables	• oranges, naartjies • apples, bananas, pears • orange or yellow vegetables (sweet potato, pumpkin, butternut, carrots)	• green vegetables (spinach, beans, broccoli) • mixed vegetables • cabbage, cauliflower, lettuce • tomato (raw and cooked)
8 Energy-dense	• sugar, granulated • chocolate • sweets (boiled, jelly, lollipops) • cake, biscuits, doughnuts • juice, other (carbonated, concentrate mixed with water)	• crisps (potato-based, maize-based, wheat-based) • take outs (e.g. KFC, McDonalds) • jam, syrup, honey
9 Sodium-rich	• meats, processed • meats, tinned	• crisps (potato-based, maize-based, wheat-based) • take outs (KFC, McDonalds)
10 Iron-rich	• meats, red • meats, processed • meats, tinned • meats, organ (liver, kidneys) • chicken, with skin • fish, tinned or smoked	• fish, fresh (not in batter) • bread, white • bread, brown • breakfast cereals, ready-to-use • breakfast cereals/porridge, to be cooked

[a] 'pap' is cooked maize porridge eaten with a meal of gravy and/or vegetables and/or meat
[b] 'samp' is broken and dried maize kernels, boiled with water until soft
[c] 'samoosas' are triangular savoury pastries fried in ghee or oil, containing spiced vegetables or meat

Procedures

Recruitment procedures included oral presentations at schools and advertisement via word-of-mouth. At the pre-screening stage, adolescents who did not meet eligibility criteria for possible inclusion in the AUDs or non-AUDs groups were excluded.   Participants who met eligibility criteria were transported from their homes or schools to the testing site for complete physical and psychiatric screening for possible allocation to one of the groups or exclusion.

Demographic information was obtained and the first 24-hour recall interview was conducted after confirmation of inclusion in the study. The remaining two 24-hour recall interviews were done on a Monday to obtain Sunday intakes and one other week day thereafter, and were conducted over a period that included all seasons of the year to account for seasonal dietary variations. The 24-hour recall interviews were all conducted by a trained and standardised researcher, versed in relevant terminology and locally available food and beverages. The procedure for the 24-hour recalls included the following consecutive steps: a) listing of foods and beverages (including water) consumed by the participant in the previous 24 hours, starting from time of waking and proceeding chronologically until time of going to sleep; b) collection of detailed description of foods, preparation methods and brands where relevant and the amounts consumed; and c) final checking to recall forgotten foods. Commonly used household measures and food pictures from the Dietary Assessment and Education Kit, developed by Steyn and Senekal (Steyn and Senekal, 2004) were used to assist with food portion size estimation. Estimated food portions were converted to grams using the MRC Food Quantities Manual (Langenhoven et al., 1991). Dietary data could not be collected for Fridays and Saturdays as it was not feasible to conduct interviews on Saturdays and Sundays.

The indicator food frequency questionnaire was administered by the trained researcher during the second contact session which also involved administration of the second 24-hour recall interview. Participants were asked to recall whether they had consumed foods in the 37 specified food categories in the past month. If yes, they were asked to indicate the number of times per week the food/s was consumed, including every day (seven times per week). If the food was not consumed on a weekly basis, participants were asked to indicate the number of times per month.

The questionnaire on meal and snack patterns and reasons for low fruit and vegetable intake was administered by the trained researcher during the third contact session, which also involved administration of the third 24-hour recall interview.

Ethics

The Committee for Human Research of Stellenbosch University approved all study procedures (N06/07/128). After eligibility was established, written consent from parents and written assent from participants was obtained. Participants were compensated for their time with gift vouchers. Confidentiality of all study information was maintained with the exception of statutory reporting requirements in newly-identified or ongoing threats to the safety of minor participants.

Statistical analysis and data interpretation

All data were checked and cleaned before analysis. Descriptive statistics, including inspection of data for adherence to normal distributions, and group comparisons and regressions were computed using Stata/IC Version 11.1 for Windows (Statacorp Lp, 2009). Suitable transformations were applied to all variables with skewed distributions, as relevant. Statistical significance was defined at a level of $p \leq 0.05$.

Due to the paired nature of the data, multi-level mixed effects linear regression was used to compare groups, with adjustment for factors that could possibly confound associations between specific variable distributions being compared. A pairing variable was created according to the matched pairs in the sample and served as the level variable in the regressions. The smoking variable used in all regressions included the smoking group [light smokers (lifetime < 100 cigarettes) and regular smokers (lifetime > 100 cigarettes)] and the non-smoking group (participants who have never used tobacco).

Since no specific reference intakes are available for the South African population, the Dietary Reference Intakes (DRIs), established by the Food and Nutrition Board of the Institute of Medicine (IOM) were used to assess adequacy of dietary intake of energy (estimated energy requirement [EER]) and nutrients (Estimated Average Requirement [EAR]) (Institute of Medicine, 2000, Institute of Medicine, 2001, Institute of Medicine, 2002/2005, Institute of Medicine, 2011). Statistical adjustments to the

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observed intake distributions (Addendum 1) to obtain usual nutrient intake distribution estimates were

made using the National Research Council (NRC)/IOM method (Institute of Medicine, 2003, National

Research Council, 1986) (Addendum 2).

A summary of analyses, relevant data and statistical tests used to analyse data are presented in

Table 2.

Table 2. Summary of analyses, data and statistical tests used to analyse data

Analyses	Data	Statistical tests / Computation
a) Description of socio-demographics and substance use by groups b) Comparisons of socio-demographic and alcohol measures between groups for confirmation of group allocation and matching	*Demographic self-report questionnaire:* age, education level, gender, language, ethnicity, socio-economic status score *TLFB and K-SADS-PL:* alcohol, tobacco and other substance use	a) Means (SD) b) Continuous variables: Mann Whitney U Test Categorical variables: Chi-square or Fisher's exact tests
a) Description of energy and nutrient intakes by groups and by gender in groups b) Comparisons of energy and nutrient intakes between groups	*3 x 24-hour recall questionnaires:* energy and nutrient intakes (observed intake distributions [a])	a) Means (SD); medians (IQR) b) Comparisons between groups using multi-level mixed effects linear regression (energy and nutrient intakes as dependant variables), adjusting for gender, smoking status and total energy intake (including estimated alcohol energy). Comparison of total energy between groups was only adjusted for gender and smoking status
a) Description of adequacy of energy intake by group	*3 x 24-hour recall questionnaires:* (observed intake distributions [a])	a) Mean energy intake in each group interpreted according to the daily EER for sedentary adolescents [b] (aged 15 years): males: 9337 kJ/day, females: 7270 kJ/day. Weighted average EER for males and females of 8138 kJ/day used
a) Description of adequacy of nutrient intakes by group b) Comparisons of adequacy of nutrient intakes between groups	*3 x 24-hour recall questionnaires:* nutrient intakes (usual intake distributions [c])	a) EAR cut-point method [d] used to assess adequacy of nutrient intakes for carbohydrate, vitamin B6, vitamin B12, folate, thiamin, riboflavin, niacin, vitamin C, vitamin A, vitamin D, vitamin E, calcium, magnesium, phosphorus, zinc and copper b) Frequencies of intakes below the EARs (14 to 18 years) for each nutrient were compared between groups using the Chi-square test
a) Description of adequacy of iron intake by group b) Comparison of adequacy of iron intake between groups	*3 x 24-hour recall questionnaires:* iron intake (usual intake distributions [c])	a) Probability approach [e] used to estimate the expected proportion of participants at risk for inadequate iron intake b) Comparisons between groups using multi-level mixed effects linear regression (cumulative probabilities of inadequate iron intake as dependant variable), adjusting for gender, smoking status and total energy intake (including estimated alcohol energy)

Table 2. (continued)

Analyses	Data	Statistical tests / Computation
a) Description of appropriateness of macronutrient intakes by group b) Comparisons of appropriateness of macronutrient intakes between groups	*3 x 24-hour recall questionnaires:* macronutrient intakes, expressed as a percentage of total energy	a) AMDRs [f] used to assess appropriateness of macronutrient intakes (protein, fats and carbohydrates) b) Frequencies in the two groups of percentage macronutrient intakes below, within and above the AMDRs (4-18 years) for each macronutrient were compared between groups using the Chi-square test
a) Description of excessive nutrient intakes by group b) Comparisons of excessive nutrient intakes between groups	*3 x 24-hour recall questionnaires:* nutrient intakes (usual intake distributions [c])	a) ULs [g] used to assess excessive nutrient intakes for vitamin B6, folate, niacin, vitamin C, vitamin A, vitamin D, vitamin E, calcium, magnesium, phosphorus, sodium, zinc, iron and copper b) Frequencies of intakes exceeding the ULs (14 to 18 years) for each nutrient were compared between groups using the Chi-square test
a) Description of 10 most frequently consumed foods/energy-containing beverages (excluding alcoholic beverages) by group	*3 x 24-hour recall questionnaires*	a) Sum of frequencies [h] of intakes by participants in each group on each of the three days of the 24-hour recall, based on food codes, computed to reflect average frequency of intake per participant per week and ranked accordingly
a) Description of fruit and vegetable intake by group (excluding avocado, potato, sweet potato, maize, fruit juice and vegetable juice) b) Comparisons of fruit and vegetable intakes in grams per day between groups c) Description of reasons for low fruit intake (no fruit intake on one or more of the three 24-hour recalls) and comparisons of reasons for low fruit intake between groups. These analyses were repeated for vegetable intake.	*3 x 24-hour recall questionnaires* *Interviewer-administered questionnaire:* participants with no fruit intake on one or more of three 24-hour recalls asked to report single reason for low fruit intake and repeated for vegetable intake	a) Medians (IQR) of intakes of fruit and vegetables, based on food codes (grams per day) b) Comparisons between groups using multi-level mixed effects linear regression (fruit and vegetable intakes as dependant variables), adjusting for gender, smoking status and total energy intake (including estimated alcohol energy) c) Frequencies of reasons for low fruit intake were computed and were compared between groups using the Chi-square test; tests repeated for vegetable intake
a) Description of weekly frequencies of intake of foods in 10 indicator food groups by group b) Comparisons of weekly frequency of intake from indicator food groups between groups	*Non-quantitative indicator food frequency questionnaire:* average weekly intake frequencies of food categories in indicator food groups	a) Means (SD); medians (IQR) of weekly frequencies of consumption of foods in each of the 10 indicator food groups b) Comparison between groups using multi-level mixed effects linear regression (weekly frequencies of intakes as dependant variables), adjusting for gender and smoking status
a) Description of meal and snack patterns by group and comparisons of meal and snack patterns between groups	*Interviewer-administered questionnaire on meal and snack patterns*	a) Frequencies of with 'yes' versus 'no' answers in each of the 10 meal and snack categories were computed and were compared between groups using the Chi-square test

Abbreviations: SD: standard deviation; IQR: interquartile range; TLFB: Timeline Followback (Sobell and Sobell, 1992); K-SADS-PL: Schedule for Affective Disorders and Schizophrenia for School Aged Children (six to 18 years) Lifetime Version (Kaufman et al., 1996); SAFOODS: South African Food Data System (Medical Research Council, 2002); kJ/day: kilojoules per day; EER: Estimated Energy Requirement; EARs: Estimated Average Requirements (Institute of Medicine, 2000); AMDR: Acceptable Macronutrient Distribution Ranges (Institute of Medicine, 2002/2005): ULs: Tolerable Upper Intake Levels (Institute of Medicine, 2000, Institute of Medicine, 2001, Institute of Medicine, 2004, Institute of Medicine, 2011)

[a] See Addendum 1 for detail on observed intake distributions; [b] Based on the predominance of sedentary behaviour among South African adolescents (Reddy et al., 2010)

[c] See Addendum 2 for detail on usual intake distributions; [d] See Addendum 3 for detail of EAR cut-point method

[e] See Addendum 4 for detail on probability approach; [f] See Addendum 5 for detail on use of the AMDRs to assess adequacy of macronutrient intakes;

[g] See Addendum 6 for detail on use of ULs to assess excessive nutrient intakes; [h] Frequency refers to the number of times that a specific food code appeared in the 24-hour recall

RESULTS

Socio-demographic and substance use characteristics

A total of 184 adolescents were recruited and screened, of whom 22 were excluded as screen failures due to a range of exclusion criteria, including cannabis and methamphetamine use and DSM-IV Axis I diagnoses, resulting in a final sample of 162. The non-AUDs and AUDs groups were successfully matched for age, education level, gender, language and socio-economic status (Table 3). All except two participants from the non-AUDs group were from the mixed ancestry ethnic group. As expected, AUD adolescents had significantly greater alcohol exposure than non-AUDs adolescents (Table 3). Almost all (95%, *n=77*) adolescents in the AUDs group had a "weekends-only" style of alcohol consumption. The regular drinking frequency (days per month) and regular drinking quantity (standard drinks per month) indicates an approximate consumption of 13 drinks per drinking day (5 per month), which suggests a binge drinking pattern. A greater proportion of participants in the AUDs group smoked compared to the non-AUDs group, and lifetime tobacco dose (total number of cigarettes smoked in lifetime) was greater in the AUDs group (Table 3).

Dietary intake

Complete dietary intake data was collected for 160 participants, with two participants (1 per group) refusing participation. Participants in the AUDs group had significantly greater intake of energy excluding alcohol as well as total estimated energy including alcohol compared to the non-AUDs group (Table 4). Intakes of total fat, carbohydrate, protein, saturated fat, monounsaturated fat, cholesterol, thiamin, niacin, zinc, calcium, total iron, magnesium, phosphorus and copper were also significantly higher in the AUDs group (Table 4). The AUDs group had significantly lower intakes of dietary fibre, animal protein and vitamin B12 compared to the non-AUDs group (Table 4).

Total estimated energy intake (including and excluding alcohol) for the AUDs group was considerably greater than the EER for sedentary adolescents (weighted average EER of 8138 kilojoules), whereas energy intake in the non-AUDs group was only slightly greater than the weighted average EER (Table 4).

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All participants in the sample had inadequate intakes of calcium and vitamin D, while almost all participants in the sample had inadequate intakes of folate and magnesium. Only about a fifth and a quarter of participants in the non-AUDs and AUDs groups respectively had adequate vitamin A and phosphorus intake. Prevalence of zinc inadequacy was evident in just less than half of participants in both groups (Table 5). No differences between the two groups for adequacy of nutrient intakes using the EAR cut-point method were evident, except for vitamin E, with more participants in the non-AUDs group being having inadequate vitamin E intake (Table 5).

The prevalence of risk of inadequate iron intake was 33.7% (SD=5.3; *n=80*) in the non-AUDs group and 27.5% (SD=5.0; *n=80*) in the AUDs group according to the probability method, with significantly greater risk of inadequate iron intake (p=0.023) in the non-AUDs compared to the AUDs group (see Addendum 4, Table 1 for detail).

There was no significant difference between the two groups for percentage fat intake not in line with the Acceptable Macronutrient Distribution Range (AMDR) for fat intake (25-35%), although almost a third of participants in the non-AUDs group and 38% in the AUDs group had percentage fat intake greater than 35% of total energy. All participants in the sample had percentage protein intake within the AMDR of 10 to 30% and nearly all except five participants had carbohydrate intake within the AMDR of 45 to 65% (Table 6).

Significantly more adolescents in the AUDs group (45%; *n=36*) were at risk of excessive sodium intake (above Tolerable Upper Intake Level [UL] of 2.3 grams for 14 to 18 year olds) compared to the non-AUDs group (18.8%; *n=15*) (p<0.001). Intakes for both groups for vitamin B6, folate, vitamin C, vitamin A, vitamin D, vitamin E, calcium, magnesium, phosphorus, zinc, iron and copper were below ULs for 14 to18 year olds.

The 10 foods/energy-containing beverages (excluding alcohol) most frequently consumed were similar in the two groups (Table 7). Differences included cold drink (made from diluted concentrate), which only featured in the non-AUDs group list and hard/brick margarine, which only featured in the AUDs group list. White granulated sugar was the most frequently consumed food in both groups (Table 7).

Data from the 24-hour recall questionnaires revealed no differences in intakes of fruit and vegetables separately or fruit and vegetables combined (grams per day) between the AUDs and non-AUDs groups. A trend towards a greater fruit intake in the non-AUDs group compared to the AUDs group was evident (p=0.084) (Table 8). The reason provided by most participants in both groups for eating fruit less than once a day was that it was not available at home, followed by a dislike of fruit. For vegetables the primary reason provided in both groups was a dislike of vegetables, followed by vegetables not being available at home, with no significant differences between groups (Table 9).

The weekly frequencies of intake of foods in the indicator food groups were mostly similar in the non-AUDs and AUDs groups. In both groups, animal protein foods were consumed just more than twice a day, while high fibre and low fibre foods were eaten just less than twice a day (Table 10). Healthy fats were not eaten on a daily basis and calcium-rich foods were only eaten about once a day in both groups. Fruit and vegetables combined were eaten just more than once day, with the non-AUDs group tending to eat more fruit and vegetables than the AUDs groups (p=0.074). Energy-dense foods were consumed approximately four times a day and iron-rich foods almost three times daily in the two groups. Intakes of unhealthy fats (just more than 3 times daily) and sodium-rich foods (about 1.5 times daily) were significantly greater in the AUDs group than in the non-AUDs group (Table 10).

The meal patterns in the two groups were very similar, with the only difference being that a significantly greater percentage of adolescents in the AUDs group consumed a snack before school compared to non-AUDs group (Figure 1). About one third of adolescents in both groups skipped breakfast, with more than three quarters of participants snacking during the first school break. Snacks during the second school break and during the late afternoon were eaten by approximately two thirds of participants in both groups, with about a third in both groups also snacking after the evening meal (Figure 1).

DISCUSSION

This study reports on the eating behaviour and dietary intake of a group of treatment-naive, 12 to 16 year old community-based adolescents with "pure" AUDs (AUDs group), in comparison to a matched group of light/non-drinking adolescents without AUDs (non-AUDs group).

Poor eating behaviours (food choices and patterns) with ensuing poor dietary intake (energy and nutrients) are well documented among adolescents (Barquera et al., 2003, Moreno et al., 2010, Munoz et al., 1997, Pomerleau et al., 2004, Sebastian et al., 2009, Temple et al., 2006). It has also been reported that binge drinking may compound the poor eating behaviours and dietary intake in this age group (Nelson et al., 2009a, Nelson et al., 2009b).

Poor eating patterns reflected by breakfast skipping and frequent snacking, were found in both the non-AUDs and the AUDs groups in this study. Meal pattern data revealed that about a third of adolescents in both groups skipped breakfast. This is in line with findings from recent analyses of NHANES (1999 to 2006) data reporting that 31.5% of adolescents were breakfast skippers (Deshmukh-Taskar et al., 2010). Snacking, especially during school breaks and the late afternoon, was prevalent in both groups, with more than 80% of participants in both groups snacking during the first school break and just more than a third of participants snacking after the evening meal. Frequent snacking has also been reported in previous studies in adolescents (Jahns et al., 2001, Kerr et al., 2009). Energy-dense, nutrient-poor items such as sweets, savoury snacks and sweetened carbonated drinks have been shown to be popular snack choices among adolescents (Sebastian et al., 2007, Kerr et al., 2009). Although specific snack food choices were not assessed in this study, intake of sweetened drinks, crisps and sweets was common in both groups. It can thus be speculated that snacking in these groups may have consisted of these poor food choices.

The effects of binge drinking on altering eating patterns (eating without hunger, prior to, during or after consuming alcohol) can be significant (Nelson et al., 2009a, Nelson et al., 2009b). Usual meal and snack patterns in this study seemed to be similar in the non-AUDs and AUDs groups. However, specific alcohol-related eating, namely eating patterns immediately before, during or after binge drinking sessions were not assessed in this study and is recommended for future research in adolescents with AUDs.

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When considering the findings related to food choices, it is clear that poor food choices (defined as energy-dense and nutrient-poor foods) are a problem in both groups of adolescents. Four of the 10 most frequently consumed foods/energy-containing beverages in both groups can be regarded as energy-dense and nutrient-poor (granulated sugar, sweetened cold drinks, crisps and sweets). This is supported by high frequencies of poor food choices (low fibre, energy-dense, unhealthy fats, sodium-rich foods) reported by both groups on the food frequency. Furthermore, the 10 most frequently consumed foods/energy-containing beverages in both groups did not include good food sources of dietary fibre, healthy fats, fruit or vegetables.   Although full fat milk, white bread and chicken with skin, which feature in the top 10 most frequently consumed foods/energy-containing beverages are nutrient-dense foods, they can be viewed as poor food choices, since nutrient-similar, but lower energy versions of these foods could be selected instead, namely low fat or skim milk, brown bread and skinless chicken. Findings from the food frequency also suggest a significantly greater intake of foods high in unhealthy fats and sodium in the AUDs adolescents. These results are in line with findings by Temple et al (2006) who reported that a significant majority of foods eaten by adolescents in a school-based ethnically representative sample in Cape Town were unhealthy choices (defined as foods having most of the following characteristics: high in fat, added sugar, and sodium, low in fibre, and a low nutrient density). Data from other developing countries paint a similar picture.   A Costa Rican study reported that 30% of adolescents exceeded the American Heart Association guidelines for total fat (Monge-Rojas, 2001), with evidence of high intake of sweet foods and a high percentage of total energy from fat in adolescents in Benin (Nago et al., 2010).

The low fruit and vegetable intakes in both groups in this study further illustrate the inclination of these adolescents to poor food choices. As mentioned, these foods do not feature in the 10 most frequently consumed items in either of the two groups. This low frequency of fruit and vegetable intakes derived from the 24-hour recalls is in line with the low frequency of intake of fruit and vegetables (about once a day) reported on the food frequency. Further confirmation of poor fruit and vegetable intake is provided by the low quantity consumed (grams per day). The total fruit and vegetables intakes (grams per day) in both the non-AUDs (90 grams per day) and AUDs groups (88 grams per day) were markedly lower than the theoretical-minimum-risk distribution level of intake (600 grams per day for > 14 years of

age) reported in the WHO Comparative Quantification of Health Risks (Lock et al., 2004). While not significantly different, the non-AUDs group tended to have better intakes of fruit and vegetables. The main reasons for poor intake of fruit (availability) and vegetables (dislike), reported in both groups are replicable findings among children and adolescents (Rasmussen et al., 2006, Nago et al., 2010, Sebastian et al., 2009).

Consideration of the food choices (based on frequency of intake) of participants in both groups within the context of the SAFBDG (for > 5 years of age) (Vorster et al., 2001), reveals the following areas of concern: "eat plenty of vegetables and fruits every day", "eat fats sparingly", "use salt sparingly" and "use food and drinks containing sugar sparingly and not between meals". Non-adherence to these guidelines by adolescents in both groups may predict an increased risk of negative nutrition-related health outcomes.

When considering the energy and nutrient intake results, it is clear that the poor food choices are translated into diets significantly higher in energy, protein, carbohydrates, fat, saturated fat and cholesterol in the AUDs group compared to the non-AUDs group, with a poor micronutrient quality in both groups. Although poor food choices were evident in both the non-AUDs and AUDs group, with significant differences only for frequency of unhealthy fats and sodium intake, energy intake (excluding and including alcohol) in the AUDs group was significantly greater than in the non-AUDs group. The higher energy intake excluding alcohol energy corresponds with findings suggesting that over the short term, alcohol consumption tends to increase subsequent food intake with a resultant increase in total energy intake from food (Yeomans, 2010). Our findings suggest that binge drinking is influencing energy intake by increasing carbohydrate, fat, protein and alcohol energy intakes in this group to a level where energy consumption exceeded daily requirements (weighted average EER) by more than 2000 kilojoules. Energy consumption in the non-AUDs group was more in line with requirements in our sample. Given the predictive strength of adolescent eating patterns persisting into adulthood (Kelder et al., 1994), protracted excesses of alcohol and other food types in the AUDs group could translate into a persistent positive energy balance and result in risk of overweight/obesity (see Chapter 4).

Turning the focus to fat intake, nearly a third of the non-AUDs group and 38% of the AUDs group had fat intakes greater than 35% of total energy (AMDR) reflecting the poor food choices made by adolescents in both groups. The greater frequency of intake of unhealthy fats in the AUDs group (as reported on the food frequency) is reflected in the significantly higher saturated fat and cholesterol intake seen in this group. The high fat intake in this study is concerning for both groups since elevated total fat, saturated fat and cholesterol intakes translate into a potential increase in risk for NCDs, specifically for coronary heart disease (Institute of Medicine, 2002/2005). The higher frequency of intake of sodium-rich foods in AUDs group (as reported in the food frequency) is manifested in the significantly greater percentage of AUDs adolescents (45.0 % versus 18.8%) with sodium intake above the UL for sodium. The greater prevalence of excessive sodium intake in the AUDs group may increase risk for developing hypertension in later life (Dumler, 2009, He and Macgregor, 2006, He and Macgregor, 2009). The significantly greater intake of dietary fibre in the non-AUDs group may be related to the tendency towards better intakes of fruit and vegetables in this group.

Although significant higher intakes of thiamin, niacin, calcium, magnesium, phosphorus, zinc, total iron and copper and significantly lower intake of vitamin B12 in the AUDs group compared to the non-AUDs group were found, the prevalence of risk of inadequate intakes of these nutrients did not differ between groups. Risk of inadequate intakes were present in more than half of adolescents in both the non-AUDs and AUDs groups for folate, vitamin C, vitamin A, vitamin D, vitamin E, calcium, magnesium and phosphorus. The risk of inadequacy of intakes of these micronutrients is particularly concerning when considering that requirements for certain micronutrients are likely increased through alcohol metabolism (Van Den Berg et al., 2002). The low frequency of intake of milk and calcium-rich foods (approximately once daily) reflected in the 24-hour recall and food frequency may explain the high risk of inadequate intake of calcium seen in both groups. As fruit and vegetables are important sources of folate, vitamin C and vitamin A, the risk of inadequate intakes of these vitamins could be ascribed to the low intakes of fruit and vegetables seen in both groups (24-hour recall and food frequency data). The lower prevalence of inadequate vitamin E intake observed in the AUDs group could be explained by the greater total consumption of fat in this group. In terms of food sources, this difference may also be

related to the hard/brick margarine intake in the AUDs group, as this margarine featured only in the AUDs group's top 10 most frequently consumed foods/ energy-containing beverages. The high risk of inadequate intake of vitamin D needs to be interpreted with caution in light of the mentioned limitations in the SAFOODS (Wolmarans et al., 2010).

When considering the results of this study, the inherent limitations of dietary intake methodology as well as the limitations of self-report of alcohol consumption need to be considered. Furthermore, it is important to note that nutrient intakes from supplement use were not estimated in this study and thus, findings related to nutrient adequacy should be interpreted with this mind. Finally, the use of the Chi-square test to assess differences in categorical variables does not allow for adjustment for confounders, and comparisons between groups are subject to this limitation.

CONCLUSION

Bearing in mind the mentioned limitations, it is concluded that adolescents in both the non-AUDs and AUDs groups had predominantly poor food choices (energy-dense and nutrient-poor foods). This resulted in a dietary intake that was of a poor nutritional quality, with risks of inadequate folate, thiamin, vitamin C, vitamin A, vitamin D, calcium, magnesium, phosphorus and zinc intakes in both groups. However, findings suggest that the AUDs adolescents may be somewhat worse off by way of their higher intake of the unhealthy foods (energy-dense nutrient-poor). This greater intake of unhealthy foods in the AUDs group translated into an energy intake that exceeded requirements, higher intakes of macronutrients and various micronutrients, including both unhealthy fats and sodium, with a greater prevalence of risk of excessive sodium intake in this group.

Persistence of the poor food choices and dietary intake evident in this study is likely to produce long term nutritional risks in both groups, but particularly in the AUDs group who may be at a greater risk of adverse nutrition-related health outcomes. Protracted binge drinking is likely to have more pronounced nutritional implications both in terms of food choice and dietary intake. Larger, longitudinal, well-controlled studies are recommended in order to track specific long term impacts of heavy alcohol

use during adolescence on eating behaviour and dietary intake, including alcohol-related eating, and the

ensuing nutritional health risks.

Table 3. Confirmatory analyses of socio-demographic and alcohol grouping measures and substance use characteristics of the non-AUDs and AUDs groups

	non-AUDs (*n=81*)	AUDs (*n=81*)	U/χ²	p-value
	M (SD) or %	*M (SD)* or %		
Socio-demographics				
Age	14.76 (0.78)	14.92 (0.74)	-1.19	0.235
Education level [a]	7.79 (0.85)	7.85 (0.74)	-0.43	0.666
%Male	42	42	0.00	1.000
%Female	58	58		
% Afrikaans-speaking	69	69	0.00	1.000
%English-speaking	31	31		
% Mixed ancestry	97.6	97.6		0.497
% White	1.2	0		
% Black	1.2	0		
Total Socio-economic status score [b]	28.19 (5.80)	24.85 (5.93)	1.34	0.179
Alcohol Use				
% Never consumed alcohol	41	0		
% Never intoxicated	93	0		
%Light drinker (Life dose<100 standard drinks) [c]	59	0		
% Alcohol abuse [d]		2.5		
% Alcohol dependence [e]		97.5		
% Weekends-only drinking style in most recent drinking phase [f]		95%		
Drinking onset age (years) in participants that have drunk alcohol	12.25 (1.66)	12.04 (1.70)	0.57	0.567
Alcohol lifetime dose [g]	5.77 (12.46)	1493.69 (1511.53)	-11.04	**<0.001**
Age of first intoxication		12.83 (1.15)		
Age of onset of regular drinking		12.91 (1.11)		
Regular drinking duration (months)		23.78 (15.91)		
Regular drinking frequency (days/month) in most recent drinking phase		5.01 (2.87)		
Regular drinking quantity/month (standard drinks) [h]		65.78 (57.96)		
Tobacco Use				
% Never smoked tobacco	59	17		**<0.001**
% Light smokers (lifetime <100 cigarettes)	35	31		
% Regular smokers (lifetime >100 cigarettes)	6	52		
Smoking onset age (years) in light smokers	12.53 (1.62)	12.44 (1.96)	-0.19	0.846
Smoking onset age (years) in regular smokers	13 (0.71)	12.36 (1.46)	0.96	0.339
Lifetime tobacco dose of all smokers [i]	86.42 (442.80)	1417.59 (2762.60)	-7.02	**<0.001**

Abbreviation: AUDs: alcohol use disorders
Notes: For all variables not presented as percentages, means are presented with standard deviations in parentheses. Continuous variables compared using Mann Whitney U Test and categorical variables compared using Chi-square or Fisher's exact tests.
[a] Years of successfully completed education
[b] Total Socio-economic status score: Sum of Family income (1-6), Reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), Parent education (0-6), Total assets (0-7), Dwelling type (1-6) and Bedroom cohabitation (1-7) – Maximum=41
[c] Less than 100 standard drinks of alcohol consumed in lifetime
[d] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol abuse
[e] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol dependence
[f] Style of drinking followed in the most recent phase of drinking
[g] Total number of standard drinks of alcohol consumed in lifetime
[h] Average standard drinks of alcohol consumed per month
[i] Total number of cigarettes smoked in lifetime

Table 4. Estimated daily intakes of dietary energy and nutrients (observed intake distributions [a]) in the non-AUDs and AUDs groups, and comparisons between groups

	Group		Males		Females	
	non-AUDs *(n=80)*	AUDs *(n=80)*	non-AUDs *(n=33)*	AUDs *(n=47)*	non-AUDs *(n=33)*	AUDs *(n=47)*
Energy (kJ) [b]	**8965 *** (7240-10661)	**10063 *** (8245-11683)	9461 (8010-10835)	11206 (9622-12496)	8342 (7003-9944)	9291 (7923-10941)
Total Energy (kJ) [c]	**8965 *** (7240-10661)	**11028 *** (9072-13014)	9461 (8010-10835)	11684 (10181-13521)	8342 (7003-9944)	10481 (8847-11726)
Dietary fibre (g)	**14.0 *** (10.5-17.2)	**13.7 *** (11.1-17.3)	14.6 (12.4-17.3)	16.8 (14.7-20.3)	12.7 (10.1-17.1)	12.5 (10.4-14.6)
Fat (g)	**78.0 *** (61.3-106.0)	**87.1 *** (64.8-119.6)	84.4 (65.3-101.3)	96.5 (72.8-127.1)	72.8 (59.5-106.8)	81.4 (63.5-114.5)
CHO (g)	**267.9 *** (235.7-308.8)	**306.6 *** (251.9-343.6)	290.4 (250.6-342.6)	337.5 (298.1-368.1)	255.6 (207.7-297.5)	281.7 (233.6-318.7)
Protein (g)	**66.2 *** (54.9-80.1)	**70.1 *** (54.9-87.7)	66.6 (55.8-85.6)	76.6 (64.3-91.0)	62.1 (51.3-78.1)	65.9 (50.9-82.9)
Plant protein (g)	24.2 (17.0-29.1)	26.6 (21.2-31.3)	25.6 (20.1-30.0)	30.6 (26.2-34.5)	22.1 (16.2-28.6)	24.1 (19.2-29.2)
Animal protein (g)	**39.8 *** (29.7-48.1)	**35.9 *** (28.3-54.0)	41.3 (33.2-51.1)	36.5 (32.0-55.8)	37.5 (28.3-47.2)	35.2 (26.4-53.8)
SF (g)	**25.8 *** (18.9-32.8)	**27.0 *** (20.7-35.2)	28.0 (20.0-33.5)	27.6 (22.6-39.7)	24.3 (18.3-31.1)	26.3 (19.8-33.2)
MUF (g)	**28.2 *** (21.7-36.0)	**30.2 *** (23.6-40.4)	30.1 (23.3-36.5)	33.0 (25.3-44.8)	27.1 (21.6-34.1)	28.7 (23.5-36.4)
PUF (g)	18.9 (14.6-24.7)	22.8 (15.5-33.6)	18.6 (14.5-23.3)	26.4 (17.4-35.0)	20.6 (14.6-27.9)	20.9 (14.5-31.9)
Chol (mg)	**204.2 *** (148.2-271.8)	**223.6 *** (149.2-290.0)	240.1 (174.5-292.4)	225.9 (156.3-348.9)	184.8 (139.8-259.4)	221.2 (138.1-275.9)
Sugar, added (g)	90.9 (75.6-115.7)	101.1 (81.0-132.9)	97.0 (74.6-127.8)	102.2 (85.1-140.0)	90.2 (75.7-111.4)	97.7 (74.0-127.1)
Protein (%)	12.8 (11.2-14.5)	11.6 (10.4-13.8)	12.5 (11.6-14.2)	11.3 (10.4-13.2)	12.8 (10.8-14.7)	12.1 (10.0-14.1)
Plant protein (%)	4.4 (0.9)	4.5 (1.0)	4.6 (1.1)	4.8 (0.9)	4.4 (0.8)	4.3 (1.0)
Animal protein (%)	7.8 (6.0-8.7)	6.6 (5.1-8.6)	7.7 (6.0-8.7)	6.1 (4.8-7.7)	7.8 (6.0-8.7)	6.8 (5.1-9.1)
Fat (%)	32.9 (5.5)	33.6 (6.5)	31.2 (5.2)	32.7 (5.6)	34.0 (5.4)	34.2 (7.0)
SF (%)	10.5 (2.0)	10.4 (2.1)	10.3 (2.0)	10.1 (2.0)	10.7 (2.0)	10.6 (2.2)
MUF (%)	11.4 (2.0)	11.7 (2.5)	11.1 (1.8)	11.6 (2.3)	11.6 (1.8)	11.7 (2.7)
PUF (%)	8.1 (6.2-9.5)	8.4 (6.5-10.8)	7.0 (5.5-8.3)	8.7 (6.0-10.2)	8.9 (6.5-10.4)	8.1 (6.8-11.0)
CHO (%)	53.7 (5.3)	53.6 (6.9)	55.3 (5.2)	54.5 (5.9)	52.7 (5.1)	53.0 (7.5)
Vit B6 (mg)	1.7 (1.2-2.1)	1.8 (1.3-2.3)	1.7 (1.3-2.1)	2.0 (1.4-2.7)	1.6 (1.1-2.1)	1.6 (1.3-2.2)
Vit B12 (µg)	**3.3 *** (2.2-4.0)	**3.2 *** (2.2-4.4)	3.4 (2.8-4.5)	3.7 (2.3-4.3)	3.2 (2.0-3.8)	3.1 (2.1-4.4)
Folate (µg)	188.9 (138.6-231.1)	235.4 (174.6-303.7)	193.6 (162.4-237.3)	300.5 (237.0-319.8)	182.8 (131.1-225.9)	200.0 (157.2-260.5)
Thiamin (mg)	**1.0 *** (0.8-1.2)	**1.1 *** (0.8-1.3)	1.1 (0.9-1.4)	1.2 (1.0-1.4)	0.9 (0.7-1.1)	1.0 (0.8-1.2)
Riboflavin (mg)	2.3 (1.4-4.1)	2.8 (1.8-4.1)	2.5 (1.6-4.4)	3.3 (2.2-4.5)	1.8 (1.3-4.0)	2.5 (1.7-3.9)

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Table 4. (continued)

	Group		Males		Females	
	non-AUDs *(n=80)*	**AUDs** *(n=80)*	**non-AUDs** *(n=33)*	**AUDs** *(n=47)*	**non-AUDs** *(n=33)*	**AUDs** *(n=47)*
Niacin (mg)	**17.6 *** (14.8-21.2)	**17.7 *** (14.4-24.2)	18.0 (16.1-25.0)	21.6 (15.5-26.1)	17.5 (14.3-20.1)	15.9 (13.1-21.0)
Vit C (mg)	46.6 (29.2-97.8)	51.1 (32.5-100.9)	46.6 (24.7-106.0)	51.7 (35.2-142.9)	45.0 (29.6-87.6)	48.7 (29.2-96.9)
PA (mg)	4.7 (3.6-5.9)	5.2 (3.9-6.2)	4.9 (3.9-6.4)	5.6 (4.9-6.8)	4.6 (3.3-5.5)	4.7 (3.3-5.8)
Vit A (μg RE)	394.3 (244.8-645.5)	371.9 (251.8-585.4)	447.0 (275.0-734.9)	430.8 (249.4-543.5)	358.8 (215.5-542.3)	337.5 (252.2-621.5)
Vit D (IU)	99.2 (64.6-160.1)	120.1 (83.6-193.6)	123.3 (95.2-180.5)	134.9 (86.5-216.3)	83.6 (60.3-131.3)	112.9 (83.1-163.4)
Vit E (mg)	9.8 (7.5-13.3)	12.3 (8.8-17.9)	9.8 (7.5-12.3)	13.4 (9.9-17.2)	9.8 (7.5-14.1)	11.2 (8.2-18.6)
Ca (mg)	**450.1 *** (347.8-614.1)	**460.0 *** (334.1-627.1)	525.4 (391.1-651.4)	508.9 (442.8-722.0)	438.1 (318.4-564.8)	415.9 (330.7-534.1)
Mg (mg)	**202.4 *** (170.0-252.3)	**230.5 *** (186.0-255.2)	220.2 (187.9-256.0)	253.6 (233.1-298.6)	184.4 (164.7-235.9)	200.4 (180.1-240.2)
P (mg)	**863.6 *** (702.3-1074.1)	**936.4 *** (759.4-1133.3)	919.8 (808.8-1128.0)	1052.1 (883.7-1232.7)	815.4 (661.3-1061.4)	866.7 (729.5-1063.9)
Na (g)	1.9 (1.5-2.4)	2.3 (1.8-2.8)	2.0 (1.6-2.5)	2.7 (2.1-3.1)	1.8 (1.3-2.4)	2.1 (1.7-2.5)
K (g)	1.9 (1.6-2.2)	2.1 (1.8-2.4)	2.0 (1.6-2.2)	2.2 (1.8-2.6)	1.8 (1.6-2.2)	2.0 (1.7-2.2)
Zn (mg)	**8.5 *** (6.8-11.0)	**8.6 *** (6.9-11.0)	8.7 (7.1-11.0)	9.2 (7.8-11.0)	8.3 (6.6-11.1)	7.9 (6.3-10.3)
Fe (mg)	**9.5 *** (7.5-11.5)	**10.0 *** (8.2-13.1)	10.5 (8.5-14.3)	11.9 (9.0-15.8)	9.1 (7.0-13.0)	9.3 (7.4-11.4)
Cu (μg)	**1084.0 *** (872.2-1297.7)	**1172.9 *** (966.8-1434.8)	1109.0 (887.4-1310.7)	1442.7 (1104.3-1549.3)	1067.1 (860.8-1245.2)	1069.6 (911.5-1236.4)
Mn (mg)	1.8 (1.5-2.1)	1.9 (1.6-2.4)	1.9 (1.6-2.2)	2.3 (1.9-2.7)	1.7 (1.5-2.1)	1.8 (1.4-2.2)

Abbreviations: AUDs: alcohol use disorders; g: grams; mg: milligrams; μg: micrograms; CHO: carbohydrate; SF: saturated fat; MUF: monounsaturated fat; PUF: polyunsaturated fat; Chol: cholesterol; Vit: vitamin; PA: pantothenic acid; RE: retinol equivalents

Notes: Means are presented with standard deviations in parentheses for fat (%), saturated fat (%), monounsaturated fat (%), carbohydrate (%) and plant protein (%). For all other variables, medians are presented with interquartile ranges in parentheses.
[a] See Addendum 1 for detail on observed intake distributions
[b] Energy intake, excluding estimated average daily alcohol energy
[c] Total estimated energy intake, including average daily alcohol energy estimated from average daily alcohol intake (grams) per participant in the AUDs group
* Significant differences between groups in intakes of energy (excluding alcohol) (p=0.036), total estimated energy including alcohol (p<0.001), total fat (p<0.001), carbohydrate (p=0.010), protein (p<0.001), saturated fat (p<0.001); monounsaturated fat (p=0.002), cholesterol (p=0.009), thiamin (p=0.001), niacin (p<0.001), zinc (p<0.001), calcium (p=0.007), total iron (p<0.001), magnesium (p=0.008), phosphorus (p<0.001), copper (p=0.049), dietary fibre (p=0.029), animal protein (p=0.003) and vitamin B12 (p=0.011), using multi level mixed-effects linear regression, adjusting for gender, smoking status and total estimated energy including alcohol (comparison of total energy between groups was only adjusted for gender and smoking status)

Table 5. Prevalence of risk of inadequate nutrient intakes in the non-AUDs and AUDs groups using the EAR cut-point method [a], and comparisons between groups

Nutrients	EARs 14-18 years Males	EARs 14-18 years Females	non-AUDs Group (*n=80*) Prevalence below EAR (%)	AUDs Group (*n=80*) Prevalence below EAR (%)
Carbohydrate (g)	100	100	0	0
Vitamin B6 (mg)	1.1	1.0	13.8	8.8
Vitamin B12 (µg)	2.0	2.0	10	2.5
Folate (µg)	330	330	97.5	98.8
Thiamin (mg)	1.0	0.9	42.5	36.3
Riboflavin (mg)	1.1	0.9	5.0	7.5
Niacin (mg)	12	11	3.8	2.5
Vitamin C (mg)	63	56	65.0	67.5
Vitamin A (µg RE)	630	485	80.0	82.50
Vitamin D (IU)	400	400	100	100
Vitamin E (mg)	12	12	**78.8***	**51.3***
Calcium (mg)	1100	1100	100	100
Magnesium (mg)	340	300	98.8	97.5
Phosphorus (mg)	1055	1055	76.3	73.8
Zinc (mg)	8.5	7.3	46.3	42.5
Copper (µg)	685	685	2.5	1.3

Abbreviations: AUDs: alcohol use disorders; EAR: Estimated Average Requirement
Notes: Usual nutrient intake distributions used (Addendum 2)
[a] See Addendum 3 for detail the EAR cut-point method
* Significant difference between groups in risk of inadequate vitamin E intakes (p<0.001), using Chi-square test

Table 6: Comparisons of percentage macronutrient intakes with the AMDRs [a] (4 to 18 year olds) in the non-AUDs (*n=80*) and AUDs (*n=80*) groups, and comparisons between groups

	AMDR 4-18 years	Prevalence below AMDR %non-AUDs *n*	Prevalence below AMDR %AUDs *n*	Prevalence within AMDR %non-AUDs *n*	Prevalence within AMDR %AUDs *n*	Prevalence above AMDR %non-AUDs *n*	Prevalence above AMDR %AUDs *n*
Protein (%)	10 - 30%	0	0	100.0	100.0	0	0
		0	*0*	*80*	*80*	*0*	*0*
Fat (%)	25 - 35 %	1.3	1.3	70.0	61.3	28.8	37.5
		1	*1*	*56*	*49*	*23*	*30*
Carbohydrate (%)	45 - 65%	0	5.0	100.0	93.8	0	1.3
		0	*4*	*80*	*75*	*0*	*1*

Abbreviation: AUDs: alcohol use disorders; AMDR: Acceptable Macronutrient Distribution Range
Notes: Macronutrient distribution of energy intake, excluding estimated average daily alcohol energy
[a] See Addendum 5 for detail on use of the AMDRs
No significant differences between groups using Chi-square test

Table 7: Ten most frequently consumed foods/energy-containing beverages (frequency of intake per week) in the non-AUDs and AUDs groups

non-AUDs Group (*n=80*)			AUDs Group (*n=80*)		
Rank	Foods	Intake freq per wk [a]	Rank	Foods	Intake freq per wk [a]
1	Sugar, white, granulated	10.76	1	Sugar, white, granulated	10.03
2	Milk, full fat	7.64	2	Bread, white	8.84
3	Bread, white	7.12	3	Milk, full fat	6.50
4	Cold drink, carbonated, sweetened	5.10	4	Cold drink, carbonated, sweetened	5.78
5	Rice, white	4.40	5	Snack, savoury, wheat, maize crisps	5.43
6	Snack, savoury, wheat, maize crisps	4.38	6	Rice, white	4.40
7	Sweets, hard boiled and soft jelly types	3.59	7	Sweets, hard boiled and soft jelly types	4.38
8	Cold drink, diluted concentrate	3.09	8	Margarine, polyunsaturated	3.82
9	Margarine, polyunsaturated	3.03	9	Chicken, meat and skin	3.53
10	Chicken, meat and skin	2.80	10	Margarine, brick/hard	3.00

Abbreviation: AUDs: alcohol use disorders

Notes: Includes only non-alcohol energy-containing beverages

[a] Average frequency of intake of foods (times per participant per week) in each group based on three 24-hour recall questionnaires

Table 8. Fruit and vegetable intake (grams per day) in the non-AUDs and AUDs groups and comparisons between groups

	non-AUDs Group *n=80*	AUDs Group *n=80*
	Median (IQR)	Median (IQR)
Fruit and vegetables (grams per day)	90.0 (42.4-153.3)	88.3 (30.0-153.0)
Vegetables (grams per day)	48.3 (16.7-90.0)	40.0 (7.9-70.8)
Fruit (grams per day)	16.8 (0.0-55.0)	0.0 (0.0-91.7)

Abbreviation: AUDs: alcohol use disorders

Notes: Excludes avocado, potato, sweet potato, maize, fruit juice and vegetable juice

No significant differences between groups, using multi level mixed-effects linear regression, adjusting for gender, smoking status and total estimated energy including alcohol

Table 9. Main reasons (%) for non-daily consumption of fruit / vegetables in the non-AUDs (*n=80*) and AUDs (*n=80*) groups, and comparisons between groups

	% non-AUDs Group (*n*)	% AUDs Group (*n*)
Main reason for eating fruit less than once daily:	*n=67* [a]	*n=70* [a]
Not available at home	68.1 *(47)*	74.3 *(52)*
Not for sale in the area	0 *(0)*	1.4 *(1)*
Too expensive	0 *(0)*	1.4 *(1)*
Do not like fruit	31.9 *(22)*	22.9 *(16)*
Main reason for eating vegetables less than once daily:	*n=66* [a]	*n=72* [a]
Not available at home	47.0 *(31)*	40.3 *(29)*
Not for sale in the area	0 *(0)*	0 *(0)*
Too expensive	0 *(0)*	0 *(0)*
Do not like vegetables	53.0 *(35)*	59.7 *(43)*

Abbreviation: AUDs: alcohol use disorders

Notes: Participants with no fruit intake on one or more of three days of the 24-hour recalls were asked to report single reason for low fruit intake, and repeated for vegetable intake

No significant differences between groups, using Chi-square test

[a] The balance of the participants in each of the groups had reported fruit/vegetable intake at least once on each of the three days of the 24-hour recalls

Table 10: Frequencies of intake (times eaten per week) of indicator food groups in the non-AUDs and AUDs groups, and comparisons between groups

	non-AUDs Group (*n=81*)		AUDs Group (*n=81*)	
Indicator Food Group	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**
Animal protein	17.6 (4.0)		18.7 (4.9)	
Dietary fibre - high	11.7 (6.2)		11.7 (6.1)	
Dietary fibre - low		12.0 (10.0-13.0)		12.0 (10.0-13.0)
Unhealthy fats	**19.7 *** (5.8)		**22.7 *** (5.5)	
Healthy fats	2.3 (2.2)		2.6 (2.3)	
Calcium-rich	8.0 (2.6)		7.5 (3.4)	
Fruit and vegetables		9.0 (5.1-14.0)		8.0 (5.0-11.6)
Energy-dense	26.4 (7.1)		28.3 (6.1)	
Sodium-rich	**8.4 *** (3.3)		**10.7 *** (3.2)	
Iron-rich	18.8 (4.6)		20.0 (5.2)	

Abbreviations: AUDs: alcohol use disorders; SD: standard deviation; IQR: interquartile range

* Significant differences between groups in frequencies of indicator food groups reflecting unhealthy fats (p=0.037) and sodium-rich foods (p=0.001), using multi level mixed-effects linear regression model, adjusting for gender and smoking status.

Smoking variable used in regressions included the smoking group [light smokers (lifetime <100 cigarettes) and regular smokers (lifetime >100 cigarettes)] and the non-smoking group (participants who have never used tobacco)
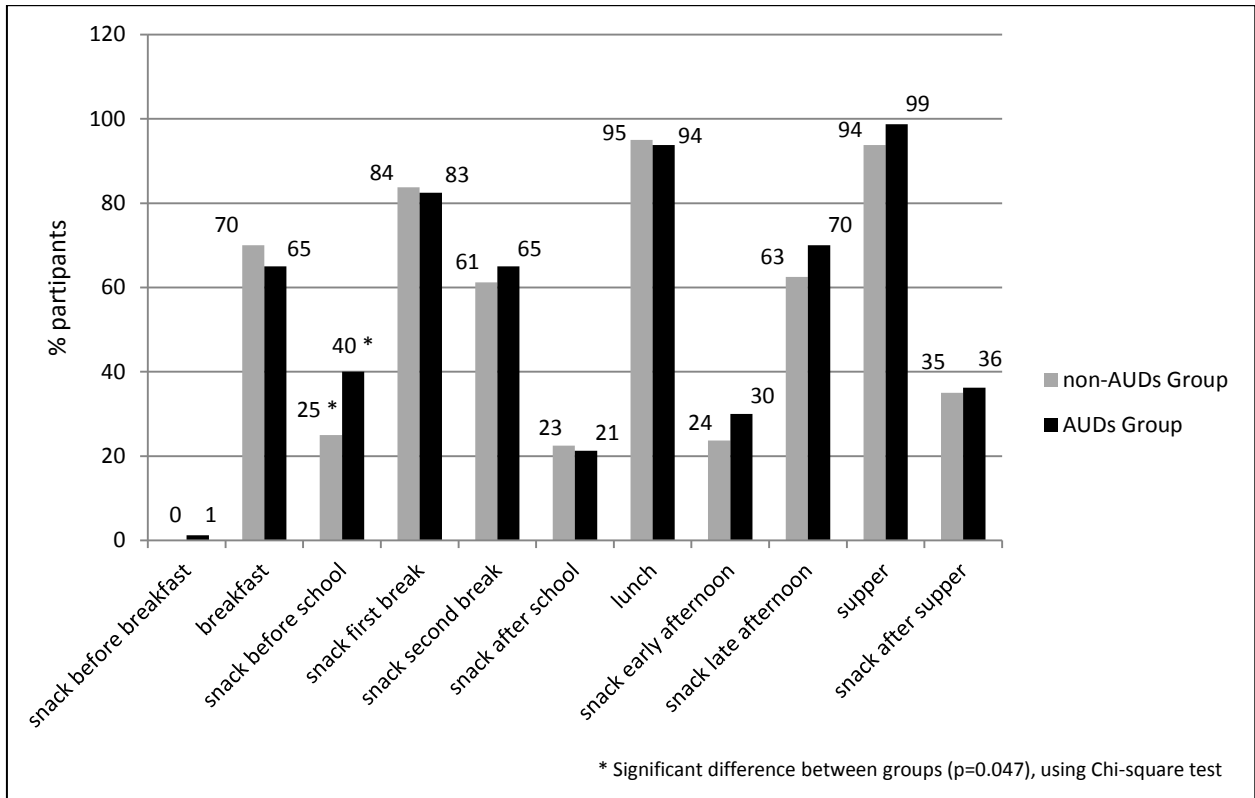
Figure 1. Meal and snack patterns (% yes) in non-AUDs (*n=80*) and AUDs (*n=80*) groups on school days

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Chapter 4

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GROWTH AND WEIGHT STATUS

INTRODUCTION

Heavy alcohol consumption during the crucial developmental period of adolescence is an important

public health concern in both in developed (Mcardle, 2008, Miller et al., 2007) and developing countries

(Parry et al., 2004, Reddy et al., 2010). Adolescent alcohol abuse/dependence has many known harmful

health and social consequences, such as school failure (Hill et al., 2000), crime and violence (Valois et al.,

1995), increased risk of adult alcohol dependence/abuse, illicit drug use, social adversity (Viner and

Taylor, 2007) cardiovascular disease (Pletcher et al., 2005), and is also strongly associated with a wide

range of other health risk behaviours (Miller et al., 2007). Examination of the effects of heavy alcohol use

during adolescence has expanded in recent years (Matthews, 2010), however, the consequences for

adolescent nutritional status are largely unknown at this time.

The 2008 South African Youth Risk Behaviour Survey (YRBS) reports that 35% of a national sample

of grade 8 to 11 adolescents (*n=10 270*) reported drinking alcohol on one or more days in the month

preceding the survey. Nationally, 29% of adolescents had engaged in past month binge drinking, a

significant increase from the rate of 23% in the 2002 YRBS (Reddy et al., 2003). Significantly more

learners in the Western Cape Province (41%) had engaged in binge drinking in the past month when

compared to the national average of 29% (Reddy et al., 2010).

Globally, adolescents are recognised as a nutritionally at-risk group (World Health Organisation,

2005). High nutritional demand for growth and development, poor eating behaviour during adolescence

(Kerr et al., 2009, Moreno et al., 2010, World Health Organisation, 2005), and a propensity for risk-taking

behaviours are all threats to nutritional adequacy (World Health Organisation, 2005). Adolescent eating

patterns are typically characterised by high consumption of sweetened beverages, increased intake of

energy-dense nutrient-poor foods, and frequently skipping meals, particularly breakfast (Briefel et al.,

2009, Burgess-Champoux et al., 2009, Li et al., 2010, Moreno et al., 2010). South African adolescents are

no exception (Venter and Winterbach, 2010, Temple et al., 2006). Poor nutrition during this life stage,

which is also characterised by the adolescent growth spurt, may be associated with stunting (chronic

undernutrition), underweight (chronic negative energy balance), or being overweight or obese (chronic

positive energy balance)(World Health Organisation, 2005).

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Alcohol is energy-dense and energy provided by alcoholic drinks is derived from the alcohol (29 kilojoules per gram) and the carbohydrates (17 kilojoules per gram) they contain, with most drinks containing negligible amounts of other nutrients (Lieber, 2003). Heavy alcohol use may affect total energy intake in a variety of ways. First, if alcohol energy replaces food energy (thus no change in total energy intake) dietary quality is reduced, with poor intake of essential macro- and micronutrients, even though energy needs may be met. This nutrient inadequacy increases the risk for nutrient deficiencies, which may enhance the risk for stunting (low height-for-age) (Onis et al., 2007). Second, heavy alcohol use may result in a more significant reduction in dietary intake with energy from alcohol not compensating for the total loss of dietary energy intake. Inadequate energy and nutrient intake could manifest in the adolescent as underweight (low body mass index (BMI)-for-age) or possibly stunting (Onis et al., 2007). However, it must be borne in mind, that the greatest risk for stunting remains poor nutrition during the first two years of life (Shrimpton et al., 2001). Third, alcohol containing drinks could be ingested in addition to usual food intake, resulting in increased total energy consumption, compounding the risks for weight gain and being overweight/obese (high BMI-for-age) (Onis et al., 2007).

A recent review examined the outcomes of preload studies of the effects of alcohol on subsequent food intake in adults, and reported that in the short term, energy ingested as alcohol is additive to energy consumed from other sources, suggesting that alcohol promotes short term passive over-consumption of energy (Yeomans, 2010). According to Yeomans (2010), alcohol is very inefficient at triggering the satiety mechanisms involved in short term control of food intake. Adult studies have further found alcohol use to be positively associated with BMI or obesity (Kent and Worsley, 2009, Schroder et al., 2007, Wannamethee et al., 2005). The work by Oesterle and colleagues (2004), namely that chronic heavy drinkers aged 10 to 24 years were nearly four times more likely to be overweight or obese at age 24, suggests that this may be true for adolescents . The positive association between alcohol and tobacco use and unhealthy eating habits such as consuming sweetened carbonated drinks, sweets and snacks, as reported in adolescents (Eisenberg et al., 2004, Keski-Rahkonen et al., 2003, Neumark-Sztainer et al., 1997, Nutbeam et al., 1991), further compounds these risks. As such, it is reasonable to speculate that dietary changes associated with heavy alcohol use in adolescence may

include a higher intake of energy-dense foods, thus contributing to increased total energy intake. Thus, heavy alcohol use during adolescence may promote overweight and obesity via the additive effect of alcohol energy as well as dietary changes favouring energy-dense items, resulting in a persistent positive energy balance.

The 2002 and 2008 YRBSs in South Africa show overnutrition to be a greater problem in this age group than undernutrition, with an increase in the prevalence of overweight and obesity nationally from 2002 to 2008 (21 to 25%), especially in the mixed ancestry population (16.6 to 22.4%). The prevalence of overweight and obesity was consistently greater in females nationally, in the Western Cape Province, and in the mixed ancestry population group (Reddy et al., 2010, Reddy et al., 2003). This follows a widely recognised global trend in which overweight exceeds underweight in females in more than half of the world's developing countries (Mendez et al., 2005).

Heavy alcohol ingestion can compound the problem of positive energy balance in usual dietary intake, increasing the risk for weight gain. Thus, it is argued that heavy alcohol use during adolescence may increase the risk for overweight and obesity. At this time, studies investigating the association between heavy alcohol use, energy balance, growth and weight status of adolescents are lacking internationally, with no such studies having been conducted in South Africa.

The current study examines anthropometric indices of growth and weight status in treatment-naive, 12 to 16 year old community-dwelling adolescents with alcohol use disorders (AUDs) in comparison to matched light/non-drinking adolescents without AUDs, both groups without co-morbid substance use disorders (SUDs) or psychiatric disorders, as part of a larger study exploring the effects of heavy alcohol use on brain structure and function. The inclusion of adolescents without co-morbid externalizing disorders or SUDs, allows us to study the effects of AUDs on growth and weight indices without the confounding effects of other substance abuse or externalising disorder risk factors. It is hypothesised that anthropometric indices of growth and weight status may be different in adolescents with AUDs compared to light/non-drinking adolescents without AUDs.

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METHODS AND MATERIALS

Study Population and Participants

This study examined adolescents with relatively 'pure' AUDs, without concomitant drug use or psychiatric (including externalising) diagnoses. The sample (*n=162*) consisted of low socio-economic status English or Afrikaans-speaking adolescents (ages 12 to 16 years) from schools within a 25-km radius of Tygerberg Hospital located in the greater metropolitan area of Cape Town, South Africa. Screening procedures included a structured psychiatric diagnostic interview, a developmental and medical history (from participants and at least one biological parent or legal guardian) and a detailed physical and neurological examination assessing developmental delays. The Schedule for Affective Disorders and Schizophrenia for School Aged Children (six to 18 years) Lifetime Version (K-SADS-PL) (Kaufman et al., 1996) was used to screen for psychiatric diagnoses. The Semi-Structured Assessment for the Genetics of Alcohol (SSAGA-II) (Bucholz et al., 1994) was used to confirm AUDs diagnosis and to derive detailed substance use histories (alcohol, tobacco and all other drugs).

Participants were assigned to one of two groups: an AUDs group meeting DSM-IV criteria for alcohol dependence or alcohol abuse (American Psychiatric Association, 1994) or a light/non-drinking non-AUDs group (lifetime dose of < 100 standard drinks of alcohol or never consumed alcohol). Exclusion criteria for both groups were: mental retardation, lifetime DSM-IV diagnoses other than AUDs (as defined in the KSADS-PL, including major depression, dysthymia, mania, hypomania, cyclothymia, bipolar disorders, schizoaffective disorders, schizophrenia, schizophreniform disorder, brief reactive psychosis, panic disorder, agoraphobia, separation anxiety disorder, avoidant disorder of childhood and adolescence, simple phobia, social phobia, overanxious disorder, generalized anxiety disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, enuresis, encopresis, anorexia nervosa, bulimia, transient tic disorder, Tourette's disorder, chronic motor or vocal tic disorder, alcohol abuse and dependence, substance abuse and dependence, post-traumatic stress disorder, and adjustment disorders), current use of sedative or psychotropic medication, current signs of or a history of fetal alcohol syndrome or exposure to heavy antenatal alcohol exposure, sensory impairment, history of traumatic brain injury with loss of consciousness exceeding 10

minutes, presence of diseases that may affect the CNS (e.g., meningitis, epilepsy), HIV [tested using the enzyme linked immunosorbent assay (ELISA)], less than 6 years of formal education, and lack of proficiency in English or Afrikaans. Prior to consent being obtained for participation in the study, a research social worker obtained collateral information from consenting parents, verifying the absence of medical, psychiatric and psychosocial problems. Participants in the two groups were matched for age (within 1 year), gender, language, socio-economic status and level of education (within 1 year). A total socio-economic status score was calculated by summing the category scores for family income (1-6), reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), parent education (0-6), total assets (0-7), dwelling type (1-6) and bedroom cohabitation (1-7). During recruitment it was attempted to match the samples on smoking status, but this was not to be feasible since smoking was much more prevalent in the AUDs participants. This positive association of smoking and alcohol use is well documented (Larson et al., 2007).

Measures

Substance use: A revised version of the Timeline Followback procedure (TLFB) (Sobell and Sobell, 1992), a semi-structured, clinician-administered assessment of lifetime history of alcohol use and drinking patterns (i.e., frequency, quantity and density of alcohol consumption, including every phase from when participants first started drinking at least once per month to the present, including all periods of abstinence) was used in combination with the K-SADS-PL to elicit alcohol-use data. It was administered by a Psychiatrist on the day of screening. A standard drink was defined as one beer or wine cooler (340ml), one glass of wine (150ml) or a 45ml shot of liquor.   A similar procedure was carried out for each substance that the research participant acknowledged using.

Anthropometry: Weights and heights were measured according to standard anthropometric techniques (World Health Organisation, 1995) by a trained research assistant. Weight was measured using a digital weighing scale (Camry ED-301, China) and shoes and heavy outer layers of clothing were removed. Height was measured using a wall-mounted stadiometer without shoes, caps and hats. Indices investigated were height-for-age (stunting) and BMI (weight/height^2)-for-age (underweight and

overweight/obesity). For comparison of anthropometric indices to reference data in developing

countries, *Z*-scores derived from the reference data were used (Gibson, 2005a). The recently released

World Health Organisation (WHO) growth reference for ages 5 to 19 years (Onis et al., 2007) were used

as reference data. Height-for-age, expressed in *Z*-scores of the WHO growth reference was used to

define stunting (<-2 standard deviations (SD), and BMI-for-age, expressed in *Z*-scores of the WHO growth

reference were used to define underweight (*Z*-score <-2 SD) and overweight and obesity (> +1 SD) (Onis

et al., 2007) using WHO AnthroPlus, Version 1.0.4 for Windows (World Health Organisation). In order to

compare the anthropometric data with findings from the most recent YRBS (Reddy et al., 2010), weight-

for-age (underweight: *Z*-score <-2 SD) and height-for-age (stunting: *Z*-score <-2SD) were also expressed in

Z-scores of the sex-specific 2000 CDC reference curves growth reference data (Kuczmarski et al., 2000)

using the Nutrition module of Epi Info (TM) 3.5.3 (Centers for Disease Control and Prevention). As in the

2008 YRBS, the International Obesity Task Force (IOTF) age-dependent BMI cut-off points for overweight

and obesity (BMI $\geq$25 kg/m^2) were used to determine prevalence of overweight /obesity (Cole et al.,

2000) for comparison purposes.

    Physical activity: A questionnaire, administered by the primary researcher, was used to estimate

active and sedentary time. Physical activity was assessed as time in minutes per week using regular,

weekly 'organised sporting activities' such as scheduled training and competitions for sports (e.g.

athletics and rugby). Physical inactivity was measured as time in minutes per week using 'television

watching' and 'computer use'. Information for each of the three domains was elicited using three

responses: participation: yes or no; if yes, number of occasions per week and minutes per occasion. The

total minutes per week was calculated for each domain. The domain for physical activity represented

total weekly active time (minutes) and the two domains for physical inactivity were added to obtain total

weekly sedentary time (minutes).

    Energy intake: Energy intake (kilojoules) was estimated by three repeated 24-hour recalls, which

has been shown to be appropriate for quantifying dietary intake in developing countries (Gibson, 2005b,

Gibson, 2005c). Furthermore, internal and external validity of this method has been found to be

acceptable in adolescents aged ten years and older (Biro et al., 2002). The 24-hour recall interviews were

all conducted by the primary researcher, who was trained and standardised and knowledgeable on terminology and locally available food and beverages, on two non-consecutive week days and on one Monday to obtain Sunday intake. No data could be collected for Fridays and Saturdays as it was not feasible to conduct interviews on Saturdays and Sundays. Commonly used household measures and food pictures from the Dietary Assessment and Education Kit, developed by Steyn and Senekal (Steyn and Senekal, 2004), were used to assist with food portion size estimation. Estimated food portions were converted to grams using the the MRC Food Quantities Manual (Langenhoven et al., 1991). The energy consumption for each participant for each day was calculated using the South African Food Data System (SAFOODS) (Medical Research Council, 2002). The average energy intake over the three 24-hour recall interviews was calculated to represent the observed intake distributions for energy (kilojoules). This energy intake variable did not include estimated energy from alcohol intake. Average daily alcohol energy intake was estimated from average daily alcohol intake (grams) per participant in the AUDs group as follows: The average daily alcohol intake (grams) was estimated from the alcohol-use data in the most recent phase of drinking as follows: 1) frequency of alcohol use (days per month) multiplied by average quantity of alcohol consumed (standard drinks per drinking day) to obtain average monthly standard drinks of alcohol consumed; 2) average monthly standard drinks of alcohol consumed was divided by 28 days to obtain average daily standard drinks of alcohol consumed; 3) average daily standard drinks of alcohol consumed was multiplied by 13.6 grams of alcohol per standard drink to obtain average daily alcohol intake in grams, which was converted to average daily alcohol energy (29 kilojoules per gram) to obtain average daily alcohol energy (kilojoules). Average daily alcohol energy was added daily energy intake from the observed intake distributions for each AUDs participant to represent total estimated energy intake (kilojoules). Daily alcohol energy for the *n=48* light drinking non-AUDs participants was not calculated as their alcohol life dose was negligible (mean 5.77 $\pm$12.46 standard drinks) and the contribution of alcohol energy to energy intake would therefore also be negligible.

Procedures

The Committee for Human Research of Stellenbosch University approved all study procedures (N06/07/128). After eligibility was established, written consent from parents and written assent from participants was obtained. Participants were transported from their homes or schools to the testing site. After physical and psychiatric screening, the participants completed demographic self-report questionnaires. On the day of screening after inclusion in the sample, weight and height measurements were taken, physical activity data was collected and the first 24-hour recall interview was conducted. The remaining two 24-hour recalls were done on a Monday and one other week day thereafter. Participants were compensated for their time with gift vouchers. Confidentiality of all study information was maintained with the exception of statutory reporting requirements in newly-identified or ongoing threats to the safety of minor participants.

Statistical analysis

All data were checked and cleaned before analysis. Descriptive statistics, including inspection of data for adherence to normal distributions, and group comparisons were computed using Stata/IC Version 11.1 for Windows (Statacorp Lp, 2009). Suitable transformations were applied to all variables with skewed distributions, as relevant. Mann Whitney U, chi-square and Fischer's exact tests were used to compare the socio-demographic and substance use variables between the non-AUDs and AUDs groups. Statistical significance was defined at a level of p≤0.05. Due to the paired nature of the data and possible confounding from the smoking imbalance between the non-AUDs and AUDs groups, a multi-level mixed effects linear regression model was used to compare anthropometric indices of growth and weight status, physical activity and energy intake between the two groups. A pairing variable was created according to the matched pairs in the sample and served as the level variable in the model. Transformed outcome variables were used where relevant. Comparisons were done with adjustment for gender, smoking status, physical activity (total weekly active time) and total estimated energy intake (including alcohol energy). Categorical physical activity variables (participate yes/no) were compared using the Chi-square or Fischer's exact tests. Prevalence of stunting, underweight and overweight/obesity using the WHO

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growth references were compared between the non-AUDs and AUDs groups using the Chi-square and Fischer's exact tests.

After confirming that assumptions for regression analyses were met, relationships between anthropometric categories and AUDs group membership were investigated for the total sample and within genders, using multi-level mixed effects logistic regression. Outcome variables were WHO anthropometric *Z*-score categories for stunting, underweight and overweight/obesity (Onis et al., 2007), and group status, gender, smoking status, physical activity and total estimated energy intake (including alcohol energy) were entered as independent variables. The pairing variable served as the level variable.

RESULTS

Demographic and substance use characteristics

A total of 184 adolescents were recruited and screened, of whom 22 were excluded as screen failures due to a range of exclusion criteria, including cannabis and methamphetamine use, and DSM-IV Axis I diagnoses, resulting in a final sample of 162. The non-AUDs and AUDs groups were successfully matched for age, education level, gender, language, ethnicity and socio-economic status (Table 1). As expected, AUDs adolescents had significantly greater alcohol exposure than non-AUDs adolescents (Table 1). There was no significant difference in age of onset of drinking and participants who had ever used alcohol started drinking around 12 years of age. Almost all (95%, *n=77*) adolescents in the AUDs group had a "weekends-only" style of alcohol consumption. The regular drinking frequency (days per month) and regular drinking quantity (standard drinks per month) indicates an approximate consumption of about 13 drinks per drinking day, which is indicative of a binge drinking pattern. A greater proportion of participants in the AUDs group smoked compared to the non-AUDs group, and lifetime tobacco dose (total number of cigarettes smoked in lifetime) was greater in the AUDs group; a significantly greater percentage of participants in the AUDs group had also experimented with cannabis. The results on cannabis and methamphetamine indicate very low use in both groups, with no other drug use, although cannabis use was significantly greater in the AUDs group compared to the non-AUDs group (Table 1).

Anthropometry, Physical Activity and Energy Intake

Complete anthropometric data sets were collected for 157 participants (non-AUDs group*: n=79*, AUDs group: *n=78*) and complete physical activity and energy intake data sets were collected for 160 participants (*n=80* per group). Heights and weights could not be obtained for five participants in the sample (non-AUDs group: *n=2*, AUDs group: *n=3*) and dietary intake and physical activity data could not be obtained for two participants (*n=1* per group). Weight, height, height-for-age and BMI-for-age, expressed in *Z*-scores of the WHO growth reference for ages five to 19 years (Onis et al., 2007), did not differ significantly between groups and there were no group by gender differences in height-for-age and BMI-for-age (Table 2). Females in the sample had a significantly greater BMI-for-age (z = 2.34; p=0.019) compared to males when adjusting for group status, smoking status, physical activity and total estimated energy intake (including alcohol). A significant positive association was found between height-for-age and total estimated energy intake (z=2.72; p=0.007) when adjusting for group status, gender, smoking status and physical activity. No significant relationship was found between BMI-for-age and total estimated energy intake (z=1.50; p=0.132). Most participants in both groups had a height-for-age within the normal WHO reference range, with one male AUDs participant having a height-for-age greater than +2SD. Body mass index-for-age was within the WHO normal reference range for approximately two thirds of participants in both groups. The proportion of stunted, thin and overweight/obese participants did not differ significantly between groups, and there was no gender by group interactions (Table 3). In both groups, more than double the numbers of females than males were overweight/obese (Table 3).

No significant differences in the number of participants engaging in organised sports (active time) were found in the total sample, nor was there a group by gender interaction (Table 2). There was also no significant difference in the total weekly active time between groups or by gender (Table 2). All participants in the sample, excepting one in the AUDs group, participated in sedentary time activities, with no differences in total weekly sedentary time between groups nor any group by gender interactions (Table 2).

Daily energy intake, excluding alcohol energy, was significantly higher in the AUDs adolescents compared to the non-AUDs adolescents for the entire group, and for males, but not for females.

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However, when estimated alcohol energy was added, energy intake in the AUDs participants was significantly higher for both males and females (Table 2)

Mixed effects logistic regression showed an increased odds ratio (OR 1.26) of AUDs participants being overweight/obese when compared to non-AUDs participants, after adjusting for gender, smoking status, physical activity (total weekly active time) and total estimated energy intake. Within the total sample, females had an increased odds ratio (OR 2.60) of being overweight/obese compared to males with adjustment for group status, smoking, physical activity and total estimated energy intake. Females with AUDs had a greater odds ratio (OR 2.42) compared to males of being overweight/obese, adjusting for smoking status, physical activity and total estimated energy intake, while no increased odds ratio was found for males with AUDs (OR 0.76) (Table 4).

DISCUSSION

The results of this study show that the growth and weight status of a group of healthy, treatment-naive adolescents with "pure" AUDs (without comorbid substance use disorders or comorbid psychiatric, including externalising, disorders) is comparable to a matched group of light/non-drinking non-AUDs adolescents and is in line with the growth and weight status of the South African adolescent population. There were a greater proportion of overweight/obese females in both groups compared to males, with this percentage being slightly greater, although not significantly so, in the AUDs group. Our analyses suggest that within this developing country setting, adolescent females with AUDs have an increased risk of being overweight/obese compared to adolescent females without AUDs, adjusting for smoking, physical activity and estimated energy intake (including alcohol energy).

When using the recommended WHO growth reference for ages 5 to 19 years, weight, height, height-for-age *Z*-scores and BMI-for-age *Z*-scores did not differ significantly between the non-AUDs and AUDs groups, and a similar prevalence of stunting, underweight and overweight and obesity were found in the groups. These anthropometric findings were compared to the findings of the 2008 YRBS (Reddy et al., 2010), in order to contextualise the findings within the South African adolescent population (Table 5). Stunting and underweight in both groups in our sample were lower than the YRBS prevalence nationally

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and in the mixed ancestry population, but similar to the stunting prevalence in the Western Cape Province. In the AUDs group, overweight and obesity prevalence was greater than in the YRBS national, provincial and mixed ancestry population prevalence, while non-AUDs group prevalence was similar to the YRBS proportions (Reddy et al., 2010).   With the same anthropometric references used in the YRBS, more overweight/obesity in the AUDs group compared to the non-AUDs group was evident, with higher prevalence in females in both groups, particularly within the AUDs group (Table 5). All indices point to the fact that prevalence of overnutrition exceeded undernutrition in this sample. Female AUDs participants showed an increased risk for overweight/obesity (OR=2.42). However, studies in larger samples are needed to confirm these findings.

Participation in physical activity was low in both groups with only a third of adolescents participating in any organised sporting activities. Average weekly active time, represented by organised regular sporting activities, was not significantly different between groups (non-AUDs group: median=0; mean=83 minutes; AUDs group: median=0, mean=104 minutes). Physical activity in both groups was well below the WHO global recommendation for physical activity (five to 17 year olds) of 60 minutes of moderate to vigorous physical activity daily (World Health Organization, 2011). It is possible that informal recreational activity such as dancing and playing sport with friends may contribute to activity levels in adolescents who are recreationally active on a regular basis. However, these low physical activity levels are in line with YRBS findings that show widespread inadequate levels of physical activity, especially in the Western Cape and among females (Reddy et al., 2010, Reddy et al., 2003). This inactivity may contribute to positive energy balance and the observed overweight/obesity prevalence.

Based on the predominance of sedentary behaviour in the total sample, the daily estimated energy requirement (EER) for sedentary adolescents (aged 15 years) was used for interpretation of energy intake data (males: 9337 kilojoules per day, females: 7270 kilojoules per day; and weighted average EER for males and females for total sample: 8138 kilojoules per day) (Institute of Medicine, 2002/2005). Total estimated energy intake (including alcohol) for the AUDs group was considerably greater than the EER for sedentary adolescents (weighted average EER as mentioned above), whereas that of the non-AUDs group was only slightly greater than the weighted average EER. Total estimated

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energy intake in females in the non-AUDs group and in both genders in the AUDs group exceeded sedentary EERs for females and males aged 15 years. As expected, total estimated energy intake (including alcohol) was significantly greater in the AUDs group compared to the non-AUDs group, since energy intake before the addition of alcohol energy was significantly higher in the AUDs group compared to the non-AUDs group. This suggests that when compared to adolescents without AUDs, adolescents with AUDs may have higher intakes of energy, possibly due to energy-dense food choices, which is then further increased by added alcohol energy.   It therefore seems reasonable to suggest that heavy drinking adolescents are ingesting alcohol energy in addition to usual food and beverage energy, resulting in diets high in total energy. Previous research showed that adolescents with AUDs were less likely to eat a balanced diet (Thatcher and Clark, 2006) and that adolescent alcohol and tobacco use is associated with consumption of energy-dense snacks and beverages (Eisenberg et al., 2004, Nutbeam et al., 1991). A recent study reported that earlier alcohol, tobacco and other drug use, depression, increased fighting and reduced optimism may lead to unhealthy increases in weight (Pasch et al., 2008). The inherent limitations of recall data for alcohol use, energy intake and physical activity are applicable to this study and the results therefore need to be interpreted with caution.

The higher frequency and risk of overweight/obesity in female adolescents as a whole, while being more pronounced in the AUDs females, is particularly relevant in view of obesity development being linked to four critical periods, namely intrauterine life, infancy, the period of adiposity rebound (ages 5 to 7 y), and adolescence (Dietz, 1994) and since the transition from adolescence to early adulthood is a period characterised by considerable increase in obesity incidence (Gordon-Larsen et al., 2004a). These findings become more pertinent in view of the substantial evidence that risk behaviours, such as alcohol use (Grant, 1998) and weight status (Serdula et al., 1993) show a strong degree of tracking from adolescence into adulthood. Longitudinal data also shows that low physical activity in adolescence tracks into adulthood (Gordon-Larsen et al., 2004b). In addition, the odds of overweight/obese adolescents reporting a diagnosis for two cardiovascular risk factors by young adulthood is 1.5 to 2 times higher than for normal-weight adolescents, regardless of BMI in young adulthood (Ford et al., 2008). Furthermore, physical inactivity (Pietilainen et al., 2008) and smoking (Saarni et al., 2009) have been

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shown to predict future obesity, in particular abdominal ("high risk") obesity by early adulthood. These adolescent behaviour patterns are therefore not transient in nature and are likely to have important impacts on long term behaviour patterns and health outcomes. Overweight/obesity results in a considerable burden of death, premature death and disability in adult South African's (Joubert et al., 2007), and is very much in line with the growing pandemic worldwide in developed as well as developing countries. This trend seems unlikely to be reversed as developing countries continue to struggle with the widespread availability of nutritionally poor, but cheap foods.

CONCLUSION

In this cross-sectional comparison, anthropometric indices of growth and weight status of participants in the non-AUDs and AUDs groups were generally comparable. However, there is an indication that adolescent females with AUDs may have an increased risk for being overweight/obese compared to similar adolescent females without these disorders within this developing setting.   Moreover, the presence of an AUDs in this adolescent sample was associated with higher energy intake, likely due to greater intakes of energy-dense food choices, exacerbated by added alcohol energy. This result is consistent with the literature suggesting that heavy alcohol use is associated with unhealthy increases in weight. The persistence of these patterns has the potential to initiate early development of nutrition-related chronic diseases and burdens in adulthood. These findings need further exploration in longitudinal, well-controlled studies, in order to elucidate the impacts of heavy alcohol use on energy balance, growth and weight status in adolescents as they age. This assessment of growth and weight status in adolescents with AUDs contributes to the understanding of possible impacts of heavy alcohol consumption on important aspects of adolescent development.

Table 1. Confirmatory analyses of socio-demographic and alcohol grouping measures and substance use characteristics of the non-AUDs and AUDs groups

	non-AUDs (n=81)	AUDs Group (n=81)		
	M (SD) or %	M (SD) or %	U/χ²	p-value
Socio-demographics				
Age	14.76 (0.78)	14.92 (0.74)	-1.19	0.235
Education level [a]	7.79 (0.85)	7.85 (0.74)	-0.43	0.666
%Male	42	42	0.00	1.000
%Female	58	58		
% Afrikaans-speaking	69	69	0.00	1.000
%English-speaking	31	31		
% Mixed ancestry	97.6	97.6		0.497
% White	1.2	0		
% Black	1.2	0		
Total Socio-economic status score [b]	28.19 (5.80)	24.85 (5.93)	1.34	0.179
Alcohol Use				
% Never consumed alcohol	41	0		
% Never intoxicated	93	0		
%Light drinker [c]	59	0		
% Alcohol abuse [d]		2.5		
% Alcohol dependence [e]		97.5		
% Weekends-only drinking style in most recent drinking phase [f]		95		
Drinking onset age (years) in participants that have drunk alcohol	12.25 (1.66)	12.04 (1.70)	0.57	0.567
Alcohol lifetime dose [g]	5.77 (12.46)	1493.69 (1511.53)	-11.04	**<0.001**
Age of first intoxication		12.83 (1.15)		
Age of onset of regular drinking		12.91 (1.11)		
Regular drinking duration (months)		23.78 (15.91)		
Regular drinking frequency (days/month) in most recent drinking phase		5.01 (2.87)		
Regular drinking quantity per month [h]		65.78 (57.96)		
Tobacco Use				
% Never smoked tobacco	59	17		**<0.001**
% Light smokers (lifetime <100 cigarettes)	35	31		
% Regular smokers (lifetime >100 cigarettes)	6	52		
Smoking onset age (years) in light smokers	12.53 (1.62)	12.44 (1.96)	-0.19	0.846
Smoking onset age (years) in regular smokers	13 (0.71)	12.36 (1.46)	0.96	0.339
Lifetime tobacco dose of all smokers [i]	86.42 (442.80)	1417.59 (2762.60)	-7.02	**<0.001**
Other Substance Use				
% Never used cannabis	89	42	34.35	**<0.001**
Lifetime cannabis dose [j]	0.12 (0.37)	4.08 (7.40)	-6.33	**<0.001**
% Never used methamphetamine	100	96		0.245
Lifetime methamphetamine dose [k]	0	1.0 (0.56)		
% Never used any other drugs	100	100		

Abbreviation: AUDs: alcohol use disorders

Notes: For all variables not presented as percentages, means are presented with standard deviations in parentheses. Continuous variables compared using the Mann Whitney U Test and categorical variables compared using the Chi-Square or Fisher's exact test.
[a] Years of successfully completed education
[b] Total Socio-economic status score: Sum of Family income (1-6), Reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), Parent education (0-6), Total assets (0-7), Dwelling type (1-6) and Bedroom cohabitation (1-7) – Maximum=41
[c] Less than 100 standard drinks of alcohol consumed in lifetime
[d] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol abuse
[e] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol dependence
[f] Style of drinking followed in the most recent phase of drinking
[g] Total number of standard drinks of alcohol consumed in lifetime
[h] Average standard drinks of alcohol consumed per month
[i] Total number of cigarettes smoked in lifetime
[j] Total number of 'joints' smoked in lifetime; [k] Total number of 'straws' (hits) of methamphetamine in lifetime

Table 2. Comparison of anthropometry, physical activity and energy intake between non-AUDs and AUDs groups

	non-AUDs Group		AUDs Group			
		%		%	p-value	z
Anthropometry						
Weight (kg)	52 (46-62)		53 (46-62)		0.745	-0.32
Height (m)	1.60 (1.56-1.65)		1.60 (1.53-1.65)		0.487	0.70
Height-for-age Z-score	-0.58 (1.03)		-0.59 (1.01)		0.672	0.42
Males	-0.73 (1.07)		-0.45 (1.14)		0.348	0.94
Females	-0.47 (0.99)		-0.69 (0.89)		0.673	-0.42
Body mass index-for-age Z-score	0.29 (1.42)		0.25 (1.38)		0.821	-0.23
Males	0.12 (1.52)		-0.11 (1.42)		0.219	-1.23
Females	0.41 (1.34)		0.52 (1.31)		0.327	0.98
Physical activity and inactivity						
Participate in physical activities (%yes) *		33		33		
Males (%yes) *		48		39		
Females (%yes) *		21		28		
Total weekly active time (minutes) [a]	0 (0-120)		0 (0-120)		0.740	-0.33
Males: weekly active time	0 (0-240)		0 (0-240)		0.382	-0.87
Females: weekly active time	0 (0-0)		0 (0-60)		0.690	0.40
Participate in sedentary activities (%yes) *		100		99		
Total weekly sedentary time (minutes) [b]	1001 (570)		1091 (569)		0.949	0.06
Males: weekly sedentary time	937 (590)		1093 (561)		0.349	0.94
Females: weekly sedentary time	1047 (558)		1089 (580)		0.327	-0.98
Energy intake						
Energy (kilojoules), excluding alcohol energy [c]	8965 (7240-10661)		10063 (8245-11683)		**0.047**	1.98
Males: energy excluding alcohol	9461 (8010-10835)		11206 (9622-12496)		**0.034**	2.11
Females: energy excluding alcohol	8342 (7003-9944)		9291 (7923-10941)		0.254	1.14
Total estimated energy (kilojoules), including alcohol energy [d]	8965 (7240-10661)		11028 (9072-13014)		**<0.001**	4.20
Males: energy including alcohol	9461 (8010-10835)		11684 (10181-13521)		**<0.001**	3.69
Females: energy including alcohol	8342 (7003-9944)		10481 (8847-11726)		**0.005**	2.81

Abbreviation: AUDs: alcohol use disorders

Notes: Variables are median and interquartile range except for height-for-age Z-score, body mass index-for-age Z-score, total weekly sedentary time, which are mean and standard deviation

n-values: Anthropometry: non-AUDs *n=79*; AUDs *n=79*; Physical activity and inactivity and Energy intake: *n=80* per group; males *n=33* and females *n=47*

Height-for-age and body mass index-for-age expressed in Z-scores of the World Health Organisation Growth Reference for ages 5 to 19 years (Onis et al., 2007)

Smoking group includes light smokers (lifetime <100 cigarettes) and regular smokers (lifetime >100 cigarettes)

Multi level mixed-effects linear regression used to compare groups, adjusting for gender, smoking status, physical activity (total weekly active time) and total estimated energy intake (including alcohol energy)

[a] Total weekly active time: sum of minutes per week spent doing regular (weekly) organised sporting activities

[b] Total weekly sedentary time: sum in minutes per week spent watching television and using a computer

[c] Energy intake, excluding estimated average daily alcohol energy

[d] Total estimated energy intake, including average daily alcohol energy estimated from average daily alcohol intake (grams) per participant in the alcohol use disorder group

* No significant differences between non-AUDs and AUDs groups using χ^2 or Fischer's exact test

Table 3. Comparison of height-for-age and BMI-for-age according to WHO Growth References (5-19 years) *Z*-score cut-offs in non-AUDs (*n=79*) and AUDs (*n=78*) groups and by gender between groups

	Groups*		Males*		Females*	
	%non-AUDs	%AUDs	%non-AUDs	%AUDs	%non-AUDs	%AUDs
	n	*n*	*n*	*n*	*n*	*n*
Height-for-Age						
Stunting < -2SD	10.1	6.4	11.8	9.1	8.9	4.4
	8	5	4	3	4	2
Body mass index-for-Age						
Underweight < -2SD	5.1	2.6	8.8	3.0	2.2	2.2
	4	2	3	1	1	1
Overweight and Obese > +1SD	25.3	29.5	17.7	18.2	31.1	37.8
	20	23	6	6	14	17

Abbreviations: AUDs: alcohol use disorders; BMI: body mass index
Notes: Body mass index (kg/m2), calculated by dividing weight (kilograms) by height (meters) squared
n-values: non-AUDs group: *n=34* males and *n=45* females; AUDs Group: *n=33* males and *n=45* females
* No significant differences between non-AUDs and AUDs groups or by gender between groups using χ^2 or Fischer's exact tests

Table 4. Multi level mixed-effects logistic regression with overweight/obesity

	Odds Ratio	p-value	95% CI	
Overweight/Obesity: Body mass index-for-age *Z*-score > +1SD				
non-AUDs Group	1.00			
AUDs Group	1.26	0.647	0.46	3.41
Males	1.00			
Females	2.61	0.053	0.99	6.87
Non-smoking	1.00			
Smoking	0.69	0.498	0.23	2.03
Total weekly active time	1.00	0.387	1.00	1.00
Total estimated energy intake (including alcohol energy)	1.00			
MALES: Overweight/Obesity: Body mass index-for-age *Z*-score > +1SD				
non-AUDs Group	1.00			
AUDs Group	0.75	0.720	0.16	3.48
Non-smoking	1.00			
Smoking	1.04	0.967	0.17	6.31
Total weekly active time	1.00	0.345	0.99	1.00
Total estimated energy intake (including alcohol energy)	1.00	0.075	1.00	1.00
FEMALES: Overweight/Obesity: Body mass index-for-age *Z*-score > +1SD				
non-AUDs Group	1.00			
AUDs Group	2.42	0.190	0.65	9.02
Non-smoking	1.00			
Smoking	0.43	0.248	0.10	1.81
Total weekly active time	1.00	0.685	1.00	1.00
Total estimated energy intake (including alcohol energy)	1.00	0.025	1.00	1.00

Abbreviation: AUDs: alcohol use disorders
Notes: Smoking group includes light smokers (lifetime <100 cigarettes) and regular smokers (lifetime >100 cigarettes)
non-AUDs group *n=79* (males *n=34* and females *n=45*); AUDs group *n=78* (males *n=33* and females: *n=45*)

Table 5. Comparison of prevalence of underweight and stunting in non-AUDs (*n=79*) and AUDs (*n=78*) groups with 2008 Youth Risk Behaviour Survey findings in the Western Cape Province (WC) (*n=1159*), nationally (*n=9862*) and for mixed ancestry population (*n=1423*)

	Groups			YRBS	
	% non-AUDs % Males %Females	**%AUDs** %Males %Females	**%WC** %Males %Females	**%National** %Males %Females	**%Mixed Ancestry**
Stunting: Height-for-age *Z*-score <-2SD	**8.9** 8.8 8.9	**10.3** 9.1 11.1	**9.7** 9.8 9.6	**13.1** 15.2 11.1	**13.6**
Underweight: Weight-for-age *Z*-score <-2SD	**7.6** 11.8 4.4	**6.4** 9.1 4.4	**6.5** 8.0 5.2	**8.4** 12.0 4.9	**9.4**
Overweight and obese: Body mass index ≥25 kg/m	**22.8** 17.7 26.7	**29.5** 18.2 37.8	**25.5** 13.7 36.3	**25.0** 14.5 35.0	**22.4**

Abbreviations: AUDs: alcohol use disorders

Notes: Height-for-age and weight-for-age according to gender-specific 2000 CDC reference (Kuczmarski et al., 2000) *Z*-score cut-offs (Epi Info (TM) 3.5.3) used in 2008 Youth Risk Behaviour Survey (Reddy et al., 2010)

Body mass index according to International Obesity Task Force cut-offs for body mass index for overweight and obesity by gender for ages 2 to 18 years (Cole et al., 2000) used in 2008 Youth Risk Behaviour Survey (Reddy et al., 2010)

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Chapter 5

IRON STATUS

INTRODUCTION

Iron deficiency is the most prevalent nutritional disorder in the world and is estimated to occur in about 66 to 80% of the world's population. Developing countries are the worse affected, particularly children and women (World Health Organization, 2000). Since iron is found in many foods and its intake is directly associated with energy intake (Institute of Medicine, 2001), the risk of deficiency is greatest when iron requirements exceed energy needs, as in adolescents and also infants, young children and menstruating and pregnant women (Zimmermann and Hurrell, 2007). Iron deficiency is recognised as a common health problem among adolescents globally (prevalence ranging between 3 and 17%), especially in females (prevalence ranging between 8.7 and 21%) (Ahmed et al., 2000, Ferrari et al., 2011, Halterman et al., 2001, World Health Organization, 2005, Zimmermann and Hurrell, 2007, Heath and Fairweather-Tait, 2002). Data on the prevalence of iron deficiency among adolescents in South Africa is very limited, with studies mostly having been done in infants, preschool children and pregnant women (Labadarios and Middelkoop, 1995, Nojilana et al., 2007, Oelofse et al., 1999).

Adolescents have high iron requirements due to their rapid rate of linear growth, increase in blood volume and the onset of menarche that occur during this life stage. They are therefore at risk of iron deficiency (Institute of Medicine, 2001), which occurs when the iron supply is inadequate to meet physiological needs (Fairweather-Tait, 2004). Iron deficiency is associated with insufficient iron-dependant functioning with regards to oxygen transport, gene transcription, oxidative metabolism and nuclear metabolism (Beard et al., 1996). Poor iron status may negatively affect cognitive function (Ballin et al., 1992, Pollitt et al., 1985) in children and adolescents as well as memory and learning processes (Beard and Connor, 2003), which in severe and prolonged deficiency may be only partly reversible (WHO, 2005). In school children iron deficiency has also been shown to result in reduced motor activity and school performance as well as social inattention (Grantham-Mcgregor and Ani, 2001). Chronic iron deficiency may ultimately manifest in anaemia, characterised by decreases in mean cell volume, low haemoglobin levels and the appearance of microcytic hypochromic erythrocytes (Institute of Medicine, 2001).

Sufficient dietary intake of iron (haem and non-haem) can be achieved if a variety of healthy food choices are made as per the recommendations of the South African Food-Based Dietary Guidelines (Chitambar and Antony, 2006, Vorster et al., 2001). Haem iron from haemoglobin and myoglobin in animal foods represents about 5 to 10% of the iron in a mixed diet of which up to 25% is absorbed. The remainder of iron in animal foods and in all plant sources of iron are in the non-haem form (Gallagher, 2008). Only about 2 to 5% of non-haem iron is absorbed (Gallagher, 2008) dependening on iron status as well as the balance between enhancers, for example non-dairy animal protein, and inhibitors, for example oxalates, of iron absorption in the diet (Hurrell and Egli, 2010).   Dietary intake of iron may thus seem adequate, but if total intake is primarily in the form of non-haem iron and the diet is high in inhibitors of iron absorption, the ingested dietary iron may be poorly absorbed. As the usual diet consumed by many adolescents is of a poor nutritional quality (Barquera et al., 2003, Moreno et al., 2010, Munoz et al., 1997), they may have an increased risk of poor iron intake.

Alcohol use is known to affect iron status and has been linked to both iron deficiency and excess of iron in the body (Ballard, 1997). Ioannou et al (2004) reported that the consumption of more than two alcoholic drinks per day by adults was associated with an elevation in the risk of iron overload. Conversely, heavy alcohol use in adults has been linked to iron deficiency, with blood loss caused by gastrointestinal bleeding and poor dietary iron intake being cited as possible reasons (Ballard, 1997, Lieber, 2000). The relative risk of acute upper gastrointestinal bleeding has been shown to increase with rising alcohol consumption (Kaufman et al., 1999).

A large body of evidence shows that exposure to hazardous levels of alcohol is typical for a disturbing proportion of school-going adolescents internationally and in South Africa (Eaton et al., 2010, Kim et al., 2008, Kuntsche et al., 2004, Lim et al., 2007, Parry et al., 2004b, Reddy et al., 2010). Adolescents use alcohol differently from adults, tending to drink less frequently but more heavily, with binge drinking over weekends being commonplace (Flisher et al., 2003, Heeb et al., 2008, Johnston et al., 2008, Substance Abuse and Mental Health Services Administration, 2006). A study examining trends in adolescent alcohol use at three sentinel sites in South Africa between 1997 and 2001 found binge drinking to be a common form of substance misuse among school-going youth of both genders, with over

a third of the males in Cape Town reporting binge drinking by grade 11 (Parry et al., 2004a). Likewise, binge drinking among South African youth was found to be prevalent in both South African Youth Risk Behaviour Surveys (YRBSs) (Reddy et al., 2010, Reddy et al., 2003).

A recent analysis of cause-specific disability-adjusted life-years (DALYs) for young people aged 10 to 24 years using data from World Health Organization's 2004 Global Burden of Disease study, reported the main risk factors for incident DALYs in 10 to 24 year olds to be alcohol (7% of DALYs), unsafe sex (4%), iron deficiency (3%), lack of contraception (2%) and illicit drug use (2%). Africa had the highest rate of DALYs in this age group, which was 2.5 times greater than in high-income countries (208 *vs* 82 DALYs per 1000 population) (Gore et al., 2011). As the greatest risk factor for DALYs, alcohol use during adolescence is likely to be an important predictor of health outcomes, as is iron deficiency, which was reported as the third greatest risk factor for DALYs.

Currently it is not known whether heavy alcohol use during adolescence influences iron status. With the rising prevalence of heavy drinking by adolescents more insight in this regard is imperative. The aim of this study therefore was to examine the iron status of treatment-naive, 12 to 16 year old community-based adolescents with alcohol use disorders (AUDs), but without co-morbid substance use disorders (SUDs), in comparison to light/non-drinking adolescents without AUDs, from the same well-defined and homogenous study population. The inclusion of adolescents without co-morbid externalising disorders or SUDs, allowed the study of the relationships between AUDs and iron status without the confounding effects of other substance abuse or externalising disorder risk factors. It is hypothesised that indicators of iron status may be different in adolescents with AUDs compared to light/non-drinking non-AUDs adolescents.

METHODS AND MATERIALS

Study Population and Participants

Convenience sampling was used to select a sample of 162 consenting English or Afrikaans speaking volunteers aged between 12 and 16 years. Learners attending schools in lower socio-economic areas within a 25 kilometre radius of Tygerberg Hospital, located in the greater metropolitan area of Cape

Town, South Africa, and who met the inclusion criteria for the either the AUDs or non-AUDs groups, were eligible for participation. Screening included a structured psychiatric diagnostic interview, a developmental and medical history (from participants and at least one biological parent or legal guardian), a detailed physical and neurological examination assessing developmental delays and urine analysis and breathalyser testing (to confirm sobriety of participants during testing procedures). The Schedule for Affective Disorders and Schizophrenia for School Aged Children (six to 18 years) Lifetime Version (K-SADS-PL) (Kaufman et al., 1996) was used to screen for psychiatric diagnoses. The Semi-Structured Assessment for the Genetics of Alcohol (SSAGA-II) (Bucholz et al., 1994) was used to confirm AUDs diagnosis and to derive detailed substance use histories (alcohol, tobacco and all other drugs).

Participants were assigned to one of two groups: an AUDs group meeting DSM-IV criteria for alcohol dependence or alcohol abuse (American Psychiatric Association, 1994) or a non-AUDs group (non-drinking/light drinking with lifetime dose of < 100 standard drinks of alcohol or never consumed alcohol). Exclusion criteria for both groups were: mental retardation, lifetime DSM-IV diagnoses other than AUDs (as defined in the KSADS-PL, including major depression, dysthymia, mania, hypomania, cyclothymia, bipolar disorders, schizoaffective disorders, schizophrenia, schizophreniform disorder, brief reactive psychosis, panic disorder, agoraphobia, separation anxiety disorder, avoidant disorder of childhood and adolescence, simple phobia, social phobia, overanxious disorder, generalized anxiety disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, enuresis, encopresis, anorexia nervosa, bulimia, transient tic disorder, Tourette's disorder, chronic motor or vocal tic disorder, alcohol abuse and dependence (non-AUDs group only), substance abuse and dependence, post-traumatic stress disorder, and adjustment disorders), current use of sedative or psychotropic medication, current signs of or a history of foetal alcohol spectrum disorders or exposure to heavy antenatal alcohol exposure, sensory impairment, history of traumatic brain injury with loss of consciousness exceeding 10 minutes, presence of diseases that may affect the CNS (e.g., meningitis, epilepsy), HIV [tested using the enzyme linked immunosorbent assay (ELISA)], less than 6 years of formal education, and lack of proficiency in English or Afrikaans. Prior to consent being obtained for participation in the study, a research social worker obtained collateral information from consenting

parents, verifying the absence of medical, psychiatric and psychosocial problems.   Participants in the two groups were individually matched for age (within 1 year), gender, language, socio-economic status and level of education (within 1 year).   A total socio-economic status score was calculated for each participant by summing the category scores for family income (1-6), reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), parent education (0-6), total assets (0-7), dwelling type (1-6) and bedroom cohabitation (1-7).   During recruitment it was attempted to match the samples for smoking status, but this was not to be feasible since smoking was much more prevalent in the AUDs participants.   This positive association of smoking and alcohol use is well documented (Larson et al., 2007).

Measures

   Substance use: A revised version of the Timeline Followback procedure (TLFB) (Sobell and Sobell, 1992), a semi-structured, clinician-administered assessment of lifetime history of alcohol use and drinking patterns (i.e., frequency, quantity and density of alcohol consumption, including every phase from when participants first started drinking at least once per month to the present, including all periods of abstinence) was used in combination with the K-SADS-PL to elicit alcohol-use data.   It was administered by a Psychiatrist on the day of screening.   A standard drink was defined as one beer, cider or wine cooler (340 millilitres (mL)), one glass of wine (150mL) or a 45mL shot of liquor.   A similar procedure was carried out for each substance that the research participant acknowledged using.

   Biochemical determination of iron status: There is no international consensus on the single or combination of biomarkers to be used to assess iron status, as each biomarker has limitations linked to either poor sensitivity or specificity, or because it is affected by conditions other than iron deficiency (Ferrari et al., 2011). The biomarkers used for the assessment of iron status in this study are presented in Table 1. As iron status biomarkers are altered by infection (Zimmermann and Hurrell, 2007), C-reactive protein (CRP) was assayed as a biomarker of infection, in order to aid the interpretive validity of the biomarkers of iron status.

Table 1. Biomarkers of iron status and infection used in this study

Indicators	Interpretation	Gender and age-specific laboratory-based cut-off points used to define iron insufficiency and inflammation
Serum iron	Reflects iron in transit from reticulo-endothelial system to bone marrow; Insensitive index of total iron stores, high variability.	< 12 μmol/L in males < 9 μmol/L in females
Total iron binding capacity (TIBC) [a]	Reflects transferrin concentration; TIBC increases when iron stores are essentially completely depleted.	> 76.1 μmol/L
Transferrin saturation	Reflects iron supply to erythropoietic tissue in bone marrow; Reduced saturation signifies depletion of iron stores and an insufficient rate of iron delivery to maintain normal haemoglobin synthesis.	< 14 %
Serum ferritin	Reflects the total quantity of storage iron in uncomplicated iron deficiency and in healthy persons; Levels up to and including 12 μg /L are found in the absence of stainable iron in bone marrow and indicate depleted iron stores.	< 20 μg /L

Sources: (Gibson, 2005a, Carlson and Litchford, 2008, Woods and Ronnenberg, 2006)
Abbreviations : μmol/L: micromoles per litre; μg /L: micrograms per litre; mg/L: milligrams per litre
[a] Serum transferrin assayed for determination of TIBC

Venous blood samples for serum iron, transferrin, ferritin and C-reactive protein (CRP) assays were collected in tubes with added clot activator and gel for serum separation from each consenting participant via venipuncture. All assays were performed on the automated Roche Modular P analyser (Roche Diagnostic GmbH, Mannheim, Germany) with the correspondent reagents according to the manufacturer's instructions. The iron assay was done with the Colorimetric method using ferrozine. The particle enhanced Immunoturbidimetric assay was used for ferritin and CRP and the Immunoturbidimetric assay was used for transferrin.   Assay-specific Roche calibrators are used for the calibration of the specific analytes. Recalibration is done after every reagent lot change and if the onboard stability of reagents expire or if quality controls are out of the acceptable range. Assayed control samples provided by the manufacturer are run once per day with the routine samples in an analytical run. Assayed BioRad Immunoassay controls are used for CRP. Control samples are provided with a certificate of analysis. The range of control values are represented graphically on a Levey-Jennings chart and if control values lie outside of the expected ranges (-2SD and +2SD) provided by the certificate of analysis, the test is regarded as invalid and results are not reported. The analytical runs for control and sample specimens were repeated. All bias on Levey-Jennings charts were reported and acted on. Pre-

assignments are done when needed and the laboratory has established its own quality control measuring range within the package insert range. This allows for strict control and for tighter reference ranges to be used, therefore earlier "fault" detection. For each reagent change, reagent parallel testing is performed and the difference between the reagents should fall within the biologically acceptable coefficient of variation. If not, further investigation takes place. Total iron binding capacity (TIBC) was calculated by the laboratory according to manufacturer's instructions by multiplying serum transferrin by a factor of 22.75 (Roche package insert Catalog number 125 806 Iron binding capacity). Transferrin saturation was calculated as the serum iron divided by the TIBC, expressed as a percentage (Gibson, 2005a).

Energy and iron intake: Dietary energy and iron intakes were estimated using three 24-hour recalls per participant. The internal and external validity of this method has been found to be acceptable in adolescents aged ten years and older (Biro et al., 2002) and it has been shown to be appropriate for quantifying dietary intake of groups in developing countries (Gibson, 2005b, Gibson, 2005c).
The total iron (milligrams (mg)) and energy (kilojoules (kJ)) intakes for each participant for each day was calculated using the South African Food Data System (SAFOODS) (Medical Research Council, 2002). The average intakes over the three 24-hour recall interviews were calculated to represent the observed intake distributions (see Addendum 1) for energy and iron. The energy intake variable obtained from the 24-hour recalls did not include estimated energy from alcohol intake. Average daily alcohol energy intake of the AUDs group was estimated from average daily alcohol intake (grams) per participant in the AUDs group using the alcohol-use data from the most recent phase of drinking as follows: 1) frequency of alcohol use (days per month) multiplied by average quantity of alcohol consumed (standard drinks per drinking day) to obtain average monthly standard drinks of alcohol consumed; 2) average monthly standard drinks of alcohol consumed was divided by 28 days to obtain average daily standard drinks of alcohol consumed; 3) average daily standard drinks of alcohol consumed was multiplied by 13.6 grams of alcohol per standard drink to obtain average daily alcohol intake in grams, which was converted to average daily alcohol energy (29 kilojoules per gram) to obtain average daily alcohol energy (kilojoules). Average daily alcohol energy was added to daily energy intake from the observed intake distributions for each AUD participant to represent total estimated energy intake. Daily alcohol energy for the *n=48* light

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drinking participants in the non-AUDs group was not calculated as their alcohol life dose was negligible (mean 5.77; SD 12.46 standard drinks), and the contribution of alcohol energy to total estimated energy intake would therefore also be negligible. The total estimated energy intake variable was reported in this study only for use when regression-adjusted differences between groups were determined. The dietary data include nutrient intake estimates from food (both naturally present and fortified) and water only and exclude nutrient intake estimates contributed by dietary supplements and medications.

The estimation of usual dietary iron intake should focus on *available* dietary iron (Fairweather-Tait, 2004, Gibson, 2005a). For these purposes, a food composition database with complete information on haem and non-haem iron as well as phytate and polyphenol content of foods is required. A predictive algorithm can be applied to estimate iron bioavailability from different diets (Hallberg and Hulthen, 2000, Murphy et al., 1992, Reddy et al., 2000). The information on haem and non-haem iron as well as primary inhibitors and enhancers of iron absorption in the SAFOODS used in this study is incomplete (Medical Research Council, 2002), and it was thus not possible to use a predictive algorithm to estimate iron bioavailability. Haem iron intake was instead estimated from the 24-hour recall data as 40% of the iron in all meat, fish and seafood (Murphy et al., 1992) consumed by participants. The 24-hour recall data was further used to determine the top five foods foods/energy-containing beverages (excluding alcoholic beverages) that contributed to total iron intake in each group.

Eating behaviour (frequency of intake of indicator foods): The weekly frequencies of intake of foods reflecting healthy and poor food choices were estimated using a non-quantitative food frequency questionnaire. The questionnaire consisted of a list of 37 food categories, with each food category consisting of either single or multiple food items that were grouped based on shared nutritional characteristics. Indicator foods/categories were identified by firstly listing foods most commonly consumed by South Africans in the Western Cape using scientific reports, publications as well as unpublished dietary assessment information generated in small research projects/compilation of community profiles for nutrition interventions. Identified foods/categories were then classified as either healthy choices (offer protective effects against non-communicable diseases [NCDs]) or as poor choices (would increase NCDs risk).   A panel of nutrition and NCDs health experts advised this process. The

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response categories included 'eaten in the past month' (yes/no), and if yes, 'times eaten per week' or 'times eaten per month'.

Eleven of the 37 food categories were grouped to reflect frequency of total iron intake (indicator group for total iron), of which seven were also grouped to reflect frequency of haem iron intake (indicator group for haem iron), as depicted in Table 2. The frequency of intake recorded for each one of the 11 food categories was converted to reflect the number of times eaten per week per participant, which were then summed to obtain the weekly frequencies of intake per participant in the non-AUDs and AUDs groups. This was repeated for the seven food categories in the indicator group reflecting haem iron intake.

Table 2: Indicator food groups reflecting total iron and haem iron derived from the indicator food categories in the non-quantitative indicator food frequency questionnaire

Indicator food group	Indicator food categories included in group	
Total iron	• meats, red	• fish, fresh (not in batter)
	• meats, processed	• bread, white
	• meats, tinned	• bread, brown
	• meats, organ (liver, kidneys)	• breakfast cereals, ready-to-use
	• chicken, with skin	• breakfast cereals/porridge, to be cooked
	• fish, tinned or smoked	
Haem iron	• meats, red	• chicken, with skin
	• meats, processed	• fish, tinned or smoked
	• meats, tinned	• fish, fresh (not in batter)
	• meats, organ (liver, kidneys)	

Notes: Food fortification legislation in South Africa requires millers to fortify white and brown bread flour and maize meal (used to make porridge) with iron and thus, breads and porridge were included in the total iron indicator food group. Most ready-to-use breakfast cereals in South Africa are also fortified with iron and were thus also included in the total iron food group.

Procedures

Recruitment procedures included oral presentations at schools and advertisement via word-of-mouth. At the pre-screening stage, adolescents who did not meet eligibility criteria for possible inclusion in the AUDs or non-AUDs groups were excluded. Participants who met eligibility criteria were transported from their homes or schools to the testing site for complete physical and psychiatric screening for possible allocation to one of the groups or exclusion.

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After confirmation of inclusion in the study, demographic information was obtained, the first 24-hour recall interview was conducted and blood samples for the biochemical determination of iron status were obtained from each participant by a phlebotomist in the morning. Tubes were transported on ice and delivered to the laboratory within two hours and serum was separated immediately from the clot and analysed promptly. The remaining two 24-hour recall interviews were done on a Monday to obtain Sunday intakes and one other week day thereafter. The 24-hour recall interviews were all conducted by a trained and standardised researcher, versed in relevant terminology and locally available food and beverages.   The procedure for the 24-hour recalls included the following consecutive steps: a) listing of foods and beverages (including water) consumed by the participant in the previous 24 hours, starting from time of waking and proceeding chronologically until time of going to sleep; b) collection of detailed description of foods, preparation methods and brands where relevant and the amounts consumed; and c) final checking to recall forgotten foods. Commonly used household measures and food pictures from the Dietary Assessment and Education Kit, developed by Steyn and Senekal (Steyn and Senekal, 2004) were used to assist with food portion size estimation. Estimated food portions were converted to grams using the MRC Food Quantities Manual (Langenhoven et al., 1991). The 24-hour recall interviews in this study were conducted over a period that included all seasons of the year to account for seasonal dietary variations. Dietary data could not be collected for Fridays and Saturdays as it was not feasible to conduct interviews on Saturdays and Sundays.

The indicator food frequency questionnaire was administered by the trained researcher during the second contact session which also involved administration of the second 24-hour recall interview. Participants were asked to recall whether they had consumed foods in the 37 specified food categories in the past month. If yes, they were asked to indicate the number of times per week the food/s was consumed, including every day (seven times per week). If the food was not consumed on a weekly basis, participants were asked to indicate the number of times per month.

Ethics

The Committee for Human Research of Stellenbosch University approved all study procedures (N06/07/128). After eligibility was established, written consent from parents and written assent from participants was obtained. Participants were compensated for their time with gift vouchers. Confidentiality of all study information was maintained with the exception of statutory reporting requirements in newly-identified or ongoing threats to the safety of minor participants.

Statistical analysis

Descriptive statistics, including inspection of data for adherence to normal distributions, and group comparisons were computed using Stata/IC Version 11.1 for Windows (Statacorp Lp, 2009). Suitable transformations were applied to all variables with skewed distributions, as relevant. Statistical significance was defined at a level of $p \leq 0.05$. The smoking variable used in all regressions included the smoking group [light smokers (lifetime < 100 cigarettes) and regular smokers (lifetime > 100 cigarettes)] and the non-smoking group (participants who have never used tobacco).

Descriptive statistics of socio-demographic and substance use variables in the non-AUDs and AUDs groups were done, including means and standard deviations. Group comparisons were done as confirmatory analyses of socio-demographic and alcohol grouping measures. For comparison of continuous variables, the Mann Whitney U Test was used and for categorical variables the Chi-square or Fisher's exact tests were used.

Descriptive analyses for biomarkers of iron status were computed for each group and by gender, including means, standard deviations, medians and interquartile ranges. Due to the paired nature of the data, multi-level mixed effects linear regression was used to compare biomarkers of iron status between the non-AUDs and AUDs groups, with adjustment for gender, serum CRP, total dietary iron intake and smoking status. Serum CRP was adjusted for to account for the influence of infection on biomarkers of iron status. A pairing variable was created according to the matched pairs in the sample and served as the level variable in the model. The iron biomarker variables (transformed if applicable) were used as the dependant variables in the regression.

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The frequencies of participants in the non-AUDs and AUDs groups with insufficient iron status (according to the defined categories for the iron biomarkers) were computed and compared between groups, including gender groups, using the Chi-square test.

Descriptive analyses for dietary intake of total iron, haem iron and energy included the medians and interquartile ranges of the observed intake distributions (Addendum 1). The above-described regression was used to examine differences in intakes of total iron, haem iron and energy intake between groups, adjusting for smoking status, gender and total estimated energy including alcohol (when energy intake was compared, total energy was not adjusted for). The observed intake distributions (Addendum1) for total iron and energy intake (transformed variables) and the calculated haem iron variable were used as dependant variables in regressions.

As no specific reference intakes are available for the South African population, the Institute of Medicine's (IOM) Dietary Reference Intakes (DRIs), were used to assess adequacy of dietary iron intake (Institute of Medicine, 2001). Using the probability approach (Addendum 4) and usual intake distributions (Addendum 2), the expected proportions of adolescents at risk for inadequate iron intake in the non-AUDs and AUDs groups were estimated (Institute of Medicine, 2000, National Research Council, 1986). To compare the risk of inadequate iron intake in the non-AUDs and AUDs groups, the usual intake distribution for total iron was standardised to z-scores. The cumulative probabilities were then calculated from the z-scores and these probabilities were compared between groups using above-described regression, adjusting for gender, smoking status and total estimated energy including alcohol.

The intake of haem iron was estimated from the 24-hour recall data as 40% of the iron in all meat, fish and seafood intake (Murphy et al., 1992). This was computed by summing 40% of the total iron intake by each participant from all food codes consumed that appeared in the 'meat and meat products' and 'fish and seafood' food groups in the SAFOODS (Medical Research Council, 2002) and compared using the above-described regression, adjusting for gender, smoking status and total estimated energy including alcohol.

Using the 24-hour recall data, the average iron intake (milligrams) for each food code was computed for each participant, after which the average intake for each group was computed and ranked.

This was done to obtain the top five foods/energy-containing beverages (excluding alcohol) that contributed to iron intake in each group.

Descriptive statistics for the weekly frequency of intake of foods in the two indicator food groups reflecting total iron and haem iron intake included means and standard deviations for each group. The above-described regression was used to examine differences in weekly frequency of intake of foods in the two indicator food groups, adjusting for smoking status and gender.

RESULTS

Demographic and substance use characteristics

A total of 184 adolescents were recruited and screened, of whom 22 were excluded as screen failures due to a range of exclusion criteria, including cannabis and methamphetamine use and DSM-IV Axis I diagnoses, resulting in a final sample of 162. The non-AUDs and AUDs groups were successfully matched for age, education level, gender, language and socio-economic status (Table 3).

As expected, AUDs adolescents had significantly greater alcohol exposure than non-AUDs (Table 3). Almost all (95%, *n=77*) adolescents in the AUDs group had a "weekends-only" style of alcohol consumption. The regular drinking frequency (days per month) and regular drinking quantity (standard drinks per month) indicates an approximate consumption of 13 drinks per drinking day, which suggests a binge drinking pattern. A greater proportion of adolescents in the AUDs group smoked compared to the non-AUDs group, and lifetime tobacco dose (total number of cigarettes smoked in lifetime) was greater in the AUDs group (Table 3).

Biochemical iron status

Blood samples for the biochemical determination of iron status could be obtained from all participants in the sample (*n=162*). Serum TIBC was significantly higher in the AUDs group compared to the non-AUDs group (Table 4). No differences between groups were found for serum iron, ferritin and transferrin saturation (Table 4). Mean and median values for all the iron biomarkers were within the indicated reference ranges (Table 1).

Significantly more AUDs adolescents had serum iron levels lower, and TIBC levels greater than the defined cut-off points when compared to the non-AUDs group (Table 5). No significant differences between groups, including gender groups, were found for any of the other indicators for frequencies below the specified cut-offs (Table 5). As raised TIBC levels reflect iron store depletion and AUDs adolescents were significantly more likely to have raised levels of this indicator, ferritin levels were further explored by determining the frequencies of adolescents with ferritin levels of 12 micrograms per litre (μg /L) or less. Although, not significantly different (p=0.152), 16% (*n=13*) of AUDs adolescents had ferritin levels less than 12 μg /L compared to 9% (*n=7*) of non-AUDs adolescents.

Iron intake

Complete dietary intake data was collected for 160 participants, with two participants (1 per group) refusing participation. Significantly greater dietary intakes of total iron and haem iron were evident in the AUDs group compared to the non-AUDs group (Table 6).

Based on the probability method, prevalence of risk of inadequate iron intake was 33.7% (SD 5.3; *n=80*) in the non-AUDs group and 27.5% (SD 5.0; *n=80*) in the AUDs group. Regression analysis showed a significantly greater risk of inadequate iron intake (p=0.023) in the non-AUDs compared to the AUDs group (Addendum 4, Table 1).

The two foods that contributed most to total iron intake were the same in both groups, namely white bread and maize-based ready-to-use breakfast cereal (Table 7). Animal sources of iron (mutton and chicken) only featured fifth in the ranking of top five foods/energy containing beverages contributing to total iron intake (Table 7).

Mean frequencies of intake of foods in the indicator food group reflecting total iron intake were 18.8 (SD 4.6) and 20.0 (SD 5.2) times per week in the non-AUDs and AUDs groups, respectively, with no difference between groups (p=0.667). Mean weekly frequencies of intake of foods in the indicator food group reflecting haem iron intake were 7.9 (SD 2.8) in the non-AUDs group and 9.1 (SD 3.0) in the AUDs group, with no difference between the groups (p=0.380).

DISCUSSION

This study reports on the iron status of a group of treatment-naive, 12 to 16 year old community-based adolescents of mixed ancestry, with "pure" AUDs (AUDs group), in comparison to a matched group of light/non-drinking adolescents without AUDs (non-AUDs group).

About a quarter of adolescents in both groups had reduced serum ferritin concentrations (< 20 μg/L), a biomarker that reflects the total amount of storage iron and is regarded as the best biochemical indicator of uncomplicated iron deficiency (Gibson, 2005a, Carlson and Litchford, 2008).   The non-significant trend for AUDs adolescents to be more likely to have serum ferritin levels of 12 μg /L or less, suggests that iron store depletion may be more pronounced in the AUDs group. This notion is further supported by the significantly higher TIBC concentrations in the AUDs group and the significantly greater proportion of these adolescents with elevated serum TIBC levels, since TIBC only increases when iron stores are essentially completely depleted (Carlson and Litchford, 2008). When considering these results it is important to bear in mind that adolescents included in this study are early in their drinking trajectory. Thus, if heavy alcohol use by these adolescents were to become regular and protracted, which is very likely (Grant, 1998, Substance Abuse and Mental Health Services Administration, 2006, Reddy et al., 2010), the trend towards iron deficiency may become significant and ultimately result in anaemia.

When considering the findings on the iron status of the AUDs adolescents in this study in the context of the literature, it is clear from the limited available information that results in this regard are inconclusive. In a large sample of 18 to 25 year old females in Japan, alcohol drinking status, classified as non-drinkers (no alcohol), drinkers (alcohol intake: 0 to <1% of total energy intake) and drinkers (alcohol intake: ≥1% of total energy intake), was not associated with prevalence of iron deficiency (Asakura et al., 2009). On the contrary, analysis of adolescent data from the first National Health and Nutrition Examination Survey (1971 to 1973), indicated that drinking frequency was positively associated with serum iron levels and with transferrin saturation in males (Friedman et al., 1988). When comparing the results of these two studies with the findings of our study, disparities in the measurement of alcohol intake need to be considered. The AUDs adolescents in our study consumed approximately 13 drinks per drinking day (binge pattern) on 5 days per month, while this level of detail was not reported in the other

two studies, which thus were not particularly useful in providing further insights in our results. When considering the associations between heavy alcohol use and iron deficiency reported in adults (Ballard, 1997, Lieber, 2000), it is possible that the binge alcohol use pattern may explain the negative association between iron status and heavy alcohol use in adolescents in this study. Ballard (1997) and Lieber (2000) indicated that poor iron status associated with heavy drinking in adults may be explained by low iron dietary intakes and/or direct effects on the gastrointestinal tract.

The results of the dietary intake of iron do not support the possibility that inadequate iron intake is associated with the poorer iron status in the AUDs group. The median intakes of total iron and haem iron were significantly greater in the AUDs group, with the non-AUDs group having greater risk of inadequate iron intake. The difference in dietary adequacy of iron intake between the groups was not reflected in the frequency of consumption of iron-rich foods, whether reflecting total or haem iron. Non-haem iron sources, namely iron fortified white bread and ready-to-use breakfast cereals (maize- and wheat-based) were among the top four sources of iron in both groups. Interestingly, crisps (maize- and wheat-based), which contain about 1.3 mg of iron per 100 grams (Medical Research Council, 2002), featured in the top five food sources of iron for the AUDs group but not in the non-AUDs group. However, due to the high fat and salt content of crisps the consumption of these snack foods should be restricted and should not be a primary iron source in any age group. The fact that haem iron sources were only fifth in the top five iron sources, provides some explanation for the iron insufficiency as reflected by the reduced serum ferritin levels in about a quarter of adolescents in both groups.

Within the context of the dietary intake results, the alternative possible explanation for poor iron status in heavy drinking adults, suggested by Ballard (1997) and Lieber (2000), namely a direct effect on the gastrointestinal tract, needs to be considered. It could be argued that the damaging effect of acute alcohol exposure on mucosal morphology (Beck and Dinda, 1981), disrupted activity of brush border enzymes as well as enzymes in other enterocyte compartments (Bode and Bode, 2003) could result in reduced iron absorption. The likelihood of gastrointestinal haemorrhage, with concomitant iron losses, being linked to the poorer iron status in the binge drinking AUDs adolescent is supported by evidence that alcohol intake significantly increases the risk of considerable duodenal bleeding in non-predisposed

people (Kelly et al., 1995), with risk for acute upper gastrointestinal bleeding increasing with rising alcohol consumption (Kaufman et al., 1999).

The possible impact of heavy alcohol use on iron status in adolescents is a concern. As mentioned in the introduction, poor iron status is associated with reduced motor activity, school performance and social inattention (Grantham-Mcgregor and Ani, 2001) as well as reduced memory and learning processes (Beard and Connor, 2003). These effects may be exacerbated by the neuropsychological risks that may be present in adolescents with AUDs, including failure to reach optimal neuromaturation and cognitive problems (Ferrett et al., 2010).

The inherent limitations of dietary methodology, as well as the limitations of self-report of alcohol consumption need to be considered in the interpretation of the results of this study. Furthermore, the use of the Chi-square test to assess differences in categorical variables does not allow for adjustment for possible confounders, thus comparisons done between the two groups using this test are subject to this limitation.

CONCLUSION

Bearing in mind these limitations, it is concluded that biochemical iron store depletion was evident in a quarter of adolescents in both groups, but that adolescents with AUDs may be more at risk of poor iron status. Dietary intake results suggest that the poorer biochemical iron status in the AUDs adolescents may possibly not be attributable to poorer iron intake in this group. It is thus speculated that direct effects on the gastrointestinal tract in heavy drinking adolescents may affect their iron status negatively.

The findings of this study provide new insights into the association between heavy alcohol use and iron status in adolescents. Further research to confirm the possible association between heavy alcohol use and poor iron status in adolescents in the longer term (with protracted heavy drinking), as well as the mechanisms involved, is recommended.

Table 3. Confirmatory analyses of socio-demographic and alcohol grouping measures and substance use characteristics of the non-AUDs and AUDs groups

	Non-AUDs (n=81)	AUDs (n=81)		
	M (*SD*) or %	*M* (*SD*) or %	U/χ^2	p-value
Socio-demographics				
Age	14.76 (0.78)	14.92 (0.74)	-1.19	0.235
Education level [a]	7.79 (0.85)	7.85 (0.74)	-0.43	0.666
%Male	42	42	0.00	1.000
%Female	58	58		
% Afrikaans-speaking	69	69	0.00	1.000
%English-speaking	31	31		
% Mixed ancestry	97.6	97.6		0.497
% White	1.2	0		
% Black	1.2	0		
Total Socio-economic status score [b]	28.19 (5.80)	24.85 (5.93)	1.34	0.179
Alcohol Use				
% Never consumed alcohol	41	0		
% Never intoxicated	93	0		
%Light drinker (Life dose<100 standard drinks) [c]	59	0		
% Alcohol abuse [d]		2.5		
% Alcohol dependence [e]		97.5		
% Weekends-only drinking style in most recent drinking phase [f]		95%		
Drinking onset age (years) in participants that have drunk alcohol	12.25 (1.66)	12.04 (1.70)	0.57	0.567
Alcohol lifetime dose [g]	5.77 (12.46)	1493.69 (1511.53)	-11.04	**<0.001**
Age of first intoxication		12.83 (1.15)		
Age of onset of regular drinking		12.91 (1.11)		
Regular drinking duration (months)		23.78 (15.91)		
Regular drinking frequency (days/month) in most recent drinking phase		5.01 (2.87)		
Regular drinking quantity/month (standard drinks) [h]		65.78 (57.96)		
Tobacco Use				
% Never smoked tobacco	59	17		**<0.001**
% Light smokers (lifetime <100 cigarettes)	35	31		
% Regular smokers (lifetime >100 cigarettes)	6	52		
Smoking onset age (years) in light smokers	12.53 (1.62)	12.44 (1.96)	-0.19	0.846
Smoking onset age (years) in regular smokers	13 (0.71)	12.36 (1.46)	0.96	0.339
Lifetime tobacco dose of all smokers [i]	86.42 (442.80)	1417.59 (2762.60)	-7.02	**<0.001**

Abbreviations: AUDs: alcohol use disorders

Notes: For all variables not presented as percentages, means are presented with standard deviations in parentheses. Continuous variables compared using the Mann Whitney U Test and categorical variables compared using the Chi-square or Fisher's exact test.

[a] Years of successfully completed education

[b] Total Socio-economic status score: Sum of Family income (1-6), Reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), Parent education (0-6), Total assets (0-7), Dwelling type (1-6) and Bedroom cohabitation (1-7) – Maximum=41

[c] Less than 100 standard drinks of alcohol consumed in lifetime

[d] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol abuse

[e] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol dependence

[f] Style of drinking followed in the most recent phase of drinking

[g] Total number of standard drinks of alcohol consumed in lifetime

[h] Average standard drinks of alcohol consumed per month

[i] Total number of cigarettes smoked in lifetime

Table 4. Concentrations of iron status biomarkers in the non-AUDs (*n=81*) and AUDs groups (*n=81*) and comparisons between groups

	Groups		Males		Females	
	non-AUDs	AUDs	non-AUDs	AUDs	non-AUDs	AUDs
Serum Iron	14.9	13.3	16.7	15.9	13.6	11.5
(umol/L)	(5.8)	(6.4)	(5.2)	(6.5)	(5.8)	(5.8)
Serum Ferritin	34.0	31.0	41.5	31.5	30.0	29.0
(μg /L)	(20.0-46.0)	(18.0-47.0)	(27.0-53.0)	(24.0-55.0)	(15.0-40.0)	(14.0-46.0)
TIBC	**68.3 ***	**70.5 ***	66.0	69.4	68.3	70.5
(umol/L)	(63.7-72.8)	(61.4-79.6)	(63.7-72.8)	(61.4-75.1)	(61.4-75.1)	(63.7-79.6)
Transferrin saturation	22.1	19.3	24.9	23.4	20.1	16.4
(%)	(8.7)	(9.7)	(7.5)	(9.8)	(9.0)	(8.7)

Abbreviations: AUDs: alcohol use disorders; umol/L: micromoles per litre; g/L: grams per litre; μg /L: micrograms per litre; TIBC: total iron binding capacity

Notes: Means are presented with standard deviations in parentheses for serum iron and transferrin saturation
Medians are presented with interquartile ranges in parentheses for serum ferritin and TIBC
n-values for genders: non-AUDs (*n=81*): *n=34* males and *n=47* females; AUDs (*n=81*): *n=34* males and *n=47* females
* Significant difference between groups for serum TIBC (p=0.045) using multi level mixed-effects linear regression model, adjusting for gender, serum CRP, total dietary iron intake and smoking status

Table 5. Prevalence of iron insufficiency in the non-AUDs (*n=81*) and AUDs (*n=81*) groups, and comparisons between groups

	Groups		Males		Females	
	%non-AUDs *n*	%AUDs *n*	%non-AUDs *n*	%AUDs *n*	%non-AUDs *n*	%AUDs *n*
Serum Iron	**18.5 ***	**35.8 ***	14.7	35.3	21.3	36.2
< 12 umol/L in males	*15*	*29*	*5*	*12*	*10*	*17*
< 9 umol/L in females						
Serum Ferritin	23.5	24.7	8.8	20.6	34.0	27.7
< 20 μg /L	*19*	*20*	*3*	*7*	*16*	*13*
TIBC	**14.8 ***	**30.9 ***	8.8	23.5	19.2	36.2
> 76.1 umol/L	*12*	*25*	*3*	*8*	*9*	*17*
Transferrin saturation	18.5	28.4	5.9	14.7	27.7	38.3
< 14 %	*15*	*23*	*2*	*5*	*13*	*18*

Abbreviations: AUDs: alcohol use disorders; umol/L: micromoles per litre; g/L: grams per litre; μg /L: micrograms per litre; TIBC: total iron binding capacity

Notes: n-values for genders: non-AUDs (*n=81*): *n=34* males and *n=47* females; AUDs (*n=81*): *n=34* males and *n=47* females
* Significant differences between groups for serum iron (p=0.013) and TIBC (p=0.015) levels, using Chi-square test

Table 6. Estimated daily dietary intakes of total iron, haem iron and energy (observed intake distributions [a]) in the non-AUDs (*n=80*) and AUDs (*n=80*) groups, and comparisons between groups

| | Median (IQR) | | | | | |
| | Group | | Males | | Females | |
	non-AUDs	**AUDs**	**non-AUDs**	**AUDs**	**non-AUDs**	**AUDs**
Total Iron (mg)	**9.5 *** (7.5-11.5)	**10.0 *** (8.2-13.1)	10.5 (8.5-14.3)	11.9 (9.0-15.8)	9.1 (7.0-13.0)	9.3 (7.4-11.4)
Haem Iron [b] (mg)	**0.9 *** (0.6-1.2)	**1.0 *** (0.5-1.5)	0.9 (0.6-1.2)	1.1 (0.6-1.6)	0.9 (0.7-1.2)	0.9 (0.5-1.4)
Total Energy (kJ) [c]	**8965 *** (7240-10661)	**11028 *** (9072-13014)	9461 (8010-10835)	11684 (10181-13521)	8342 (7003-9944)	10481 (8847-11726)

Abbreviations: AUDs: alcohol use disorders; mg: milligrams; kJ: kilojoules

Notes: All variables had skewed distributions thus medians are reported with interquartile range (IQR) in parenthesis

n-values: *n=80* per group (males *n=33* and females *n=47*)

[a] See Addendum 1

[b] Haem iron intake estimated from the 24-hour recall data by summing 40 % of the total iron intake (Murphy et al., 1992) computed by summing 40 % of the total iron intake by each participant from all food codes consumed that appeared in the 'meat and meat products' and 'fish and seafood' food groups in the SAFOODS (Medical Research Council, 2002)

[c] Total estimated energy intake, including average daily alcohol energy estimated from average daily alcohol intake (grams) per participant in the AUDs group

* Significant differences between groups for total iron (p<0.001), haem iron (p=0.005) and total energy including alcohol (p<0.001), using multi level mixed-effects linear regression model, adjusting for gender, smoking status and energy intake (when energy intake variables compared, total energy was not adjusted for)

Table 7: Top five foods/ energy-containing beverages contributing to total iron intake (milligrams per day) in the non-AUDs and AUDs groups

Rank	non-AUDs Group (*n=80*)	Iron (mg/ day) [a]	Rank	AUDs Group (*n=80*)	Iron (mg/ day) [a]
1	Bread, white	1.07	1	Bread, white	1.35
2	Breakfast cereal, ready-to-use, maize-based	0.98	2	Breakfast cereal, ready-to-use, maize-based	1.11
3	Breakfast cereal, ready-to-use, wheat-based	0.79	3	Snack, savoury, wheat, maize crisps	0.44
4	Rusk, buttermilk, white [b]	0.61	4	Breakfast cereal, ready-to-use, wheat-based	0.39
5	Mutton, loin	0.36	5	Chicken, meat and skin	0.32

Abbreviation: AUDs: alcohol use disorders mg: milligrams

Notes: Excluding alcoholic beverages

[a] Using the 24-hour recall data, the average iron intake (milligrams) for each food code was computed for each participant, after which the average intake for each group was computed and ranked

[b] Rusks are made using bread-like dough from wheat flour, usually sweetened, that is baked, then sliced into pieces and baked again until dry and crisp

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Chapter 6

VITAMIN D AND CALCIUM STATUS

INTRODUCTION

Adolescents are recognised as a nutritionally at-risk group (World Health Organization, 2005). Specific nutritional vulnerabilities pertinent to the adolescent life stage include vitamin D and calcium status within the context of rapid skeletal development and the attainment of peak bone mass that occurs during adolescence (Cashman, 2007, Mughal and Khadilkar, 2011, Weaver, 2002). The development of the human skeleton necessitates a sufficient supply of many different nutrients, although bone mass accrual is specifically dependent on adequate vitamin D status (Harel, 2008) and sufficient calcium availability (Jackman et al., 1997). Calcium is the dominant mineral in bone, accounting for approximately 40% of bone mineral content (Weaver and Heaney, 2006). This mineral provides structural strength to bone, but also serves as a reservoir to supply calcium for the maintenance of extracellular calcium homeostasis (Power et al., 1999). During childhood and adolescence, a primary physiological responsibility of 1,25-dihydroxyvitamin D (1,25(OH)$_2$D) is to ensure adequate intestinal calcium absorption to meet the needs of skeletal growth and bone development (Cashman et al., 2011, Pettifor, 2005). Adequate levels of vitamin D results in intestinal dietary calcium absorption of about 30 to 40% (Heaney et al., 2003, Holick, 2007), while the absence of vitamin D, results in absorption of only approximately 10 to 15% of dietary calcium (Holick, 2007).   The efficiency of renal calcium reabsorption is also increased in the presence of 1,25(OH)$_2$D (Dusso et al., 2005, Holick, 2007). Furthermore, a decrease in serum 25-hydroxyvitamin D (25(OH)D) concentrations induces parathyroid hormone release, which increases osteoclast activity and bone resorption (Gibson, 2005a, Harel, 2008, Holick, 2007).

Vitamin D is acquired mainly through cutaneous synthesis with ultraviolet B (UVB) sunlight exposure and also to some extent from dietary sources (Institute of Medicine, 2011). In the event of insufficient UVB sunlight exposure for adequate cutaneous synthesis of vitamin D, it becomes an essential nutrient (Cashman et al., 2011).   In Africa, seasonal effects on cutaneous synthesis of vitamin D3 would be expected in countries that are located at latitudes greater than 30 degrees north and south, such as the more southern parts of South Africa (Prentice et al., 2009). In nature only a few foods contain vitamin D, including fatty fish, some fish liver oils, organ meats, egg yolks, with some foods being fortified with vitamin D, for example margarine and milk (Holick, 2006). The main dietary sources of calcium are

dairy products, providing readily available calcium. Although leafy green vegetables contain good

amounts of calcium, the bioavailability of calcium from these foods is low (Weaver and Heaney, 2006).

The South African Food-Based Dietary Guidelines (SAFBDG) recommends the daily ingestion of at least

one to two servings of dairy (1 serving: 250 millilitres (mL) of milk drinks *or* 40 to 50 grams of cheese) for

individuals between the ages of 14 and 25 years to promote adequate intake of calcium (Department of

Health: Directorate Nutrition, 2004). A quantity of 250 to 500 mL of milk provides 27% to 55% of the

Estimated Average Requirement (EAR) for calcium for adolescents (Institute of Medicine, 2011).

Adolescents appear to be at risk of vitamin D insufficiency and deficiency (Cashman, 2007, Lips,

2010) and a high prevalence of inadequate vitamin D status in older children and adolescents continues

to be reported globally in developed and developing countries (Gordon et al., 2004, Lapatsanis et al.,

2005, Looker et al., 2002, Olmez et al., 2006, Tylavsky et al., 2005). Severe and prolonged clinical vitamin

D deficiency results in rickets in children and osteomalacia in adults (Institute of Medicine, 2011) and less

severe vitamin D deficiency and insufficiency leads to hyperparathyroidism with increased bone turnover

and loss (Lips, 2001, Ooms et al., 1995). It must further be borne in mind that accrual of more than 90%

of peak bone mass occurs during adolescence (Harel, 2008) resulting in the aforementioned increased

requirements for calcium (Harel et al., 1998, Weaver, 2002). Hence it is concerning that evidence

indicates that most adolescents do not consume sufficient amounts of calcium (Harel et al., 1998, Morgan

et al., 1985, Moshfegh et al., 2009), with females being more likely than males to have a deficient calcium

intake (Moshfegh et al., 2009, Key and Key, 1994). Peak bone mass is a significant determinant of risk for

fractures and osteoporosis in later life (Johnston and Slemenda, 1994, Mughal and Khadilkar, 2011). On

account of these factors, adolescents with insufficient vitamin D and calcium nutriture and resultant

increased risk for low bone mass, are at an increased risk for the development of osteoporosis later in life

(Neville et al., 2002, Weaver, 2002).

Alcohol per se is also known to negatively affect bone health. Inhibition of bone growth with

heavy alcohol intake has been observed in experimental animals (Wezeman et al., 2000) and also in

humans, in which a shorter stature was seen in those who drank during growth (birth to 18 years of age)

compared to those who did not (Gonzalez-Reimers et al., 2007). Alcohol abuse disturbs osteoblastic

activity and the decrease in bone mass and strength following heavy alcohol intake is primarily due to a bone remodeling imbalance, with a predominant reduction in bone formation (Turner, 2000, Wezeman et al., 2007, Maurel et al., 2011). Depressed bone synthesis has been demonstrated in experimental animal models (Sibonga et al., 2007) and alcoholics (Santori et al., 2008), who have reduced bone density and bone mass, increased fracture susceptibility and increased osteonecrosis (Lieber, 2000). Furthermore, reduced vitamin D levels have been observed in alcoholics (Alvisa-Negrin et al., 2009, Malik et al., 2009, Schnitzler et al., 2010), which may indirectly interfere with bone metabolism. Acute and chronic alcohol exposure is also known to disturb calcium homeostasis (Sampson, 1997, Turner, 2000), partly via effects on vitamin D, but also via alcohol mediated inhibition of intestinal calcium transport independent of vitamin D (Krawitt et al., 1975, Sampson, 1997).

In South Africa, the legal age limit for alcohol use is 18 years, but surveillance reveals heavy alcohol use by adolescents, and represents a significant public health concern in this country (Flisher et al., 2003, Parry et al., 2004, Reddy et al., 2010, Reddy et al., 2003). The most recent South African Youth Risk Behaviour Survey (YRBS) reported that one in two (49.6%) adolescents in the national sample of grade 8 to 11 adolescents (*n=10 270*) had ever used alcohol in their lifetime and this prevalence increased with age, with 35% of adolescents reporting current use of alcohol. In terms of region, the Western Cape Province had the highest prevalence of current drinkers (53%) (Reddy et al., 2010). Episodic consumption of large quantities of alcohol, generally termed binge drinking, is the common drinking pattern among adolescents and usually includes multiple binge drinking episodes, typically in a "weekends-only" drinking style (Flisher et al., 2003, Parry et al., 2004, Reddy et al., 2010). Nationally, 29% of adolescents in the 2008 South African YRBS reported binge drinking in the month preceding the YRBS (Reddy et al., 2010), which is a significant increase from the rate of 23% binge drinking in the 2002 YRBS (Reddy et al., 2003). In all likelihood, persistent heavy episodic drinking by adolescents is likely to be a significant predictor of health outcomes, including those related to nutritional health.

Currently there is a paucity of information on vitamin D and calcium nutriture in adolescents in South Africa, particularly in the more southern latitudes of the country. Furthermore, little is known about the association between heavy alcohol use during adolescence, specifically in the form of binge

drinking, and vitamin D and calcium nutriture. The aim of this study was therefore to examine the

biochemical vitamin D status, as well as the calcium and vitamin D intakes of treatment-naive, 12 to 16

year old community-based adolescents with alcohol use disorders (AUDs), but without co-morbid

substance use disorders (SUDs), in comparison to light/non-drinking adolescents without AUDs, from the

same well-defined and homogenous study population.   The inclusion of adolescents without co-morbid

externalising disorders or SUDs allowed the study of the relationships between AUDs and vitamin D and

calcium indicators without the confounding effects of other SUDs or externalising disorder risk factors. It

is hypothesised that indicators of vitamin D and calcium status may be different in adolescents with AUDs

compared to light/non-drinking adolescents without AUDs.

METHODS AND MATERIALS

Study Population and Participants

Convenience sampling was used to select a sample of 162 consenting English or Afrikaans speaking

volunteers aged between 12 and 16 years. Learners attending schools in lower socio-economic areas

within a 25 kilometre radius of Tygerberg Hospital, located in the greater metropolitan area of Cape

Town, South Africa, and who met the inclusion criteria for the either the AUDs or non-AUDs groups, were

eligible for participation.   Screening included a structured psychiatric diagnostic interview, a

developmental and medical history (from participants and at least one biological parent or legal

guardian), a detailed physical and neurological examination assessing developmental delays and urine

analysis and breathalyser testing (to confirm sobriety of participants during testing procedures). The

Schedule for Affective Disorders and Schizophrenia for School Aged Children (six to 18 years) Lifetime

Version (K-SADS-PL) (Kaufman et al., 1996) was used to screen for psychiatric diagnoses. The Semi-

Structured Assessment for the Genetics of Alcohol (SSAGA-II) (Bucholz et al., 1994) was used to confirm

AUDs diagnosis and to derive detailed substance use histories (alcohol, tobacco and all other drugs).

Participants were assigned to one of two groups: an AUDs group meeting DSM-IV criteria for

alcohol dependence or alcohol abuse (American Psychiatric Association, 1994) or a non-AUDs group (non-

drinking/light drinking with lifetime dose of < 100 standard drinks of alcohol or never consumed alcohol).

Exclusion criteria for both groups were: mental retardation, lifetime DSM-IV diagnoses other than AUDs (as defined in the KSADS-PL, including major depression, dysthymia, mania, hypomania, cyclothymia, bipolar disorders, schizoaffective disorders, schizophrenia, schizophreniform disorder, brief reactive psychosis, panic disorder, agoraphobia, separation anxiety disorder, avoidant disorder of childhood and adolescence, simple phobia, social phobia, overanxious disorder, generalized anxiety disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, enuresis, encopresis, anorexia nervosa, bulimia, transient tic disorder, Tourette's disorder, chronic motor or vocal tic disorder, alcohol abuse and dependence (non-AUDs group only), substance abuse and dependence, post-traumatic stress disorder, and adjustment disorders), current use of sedative or psychotropic medication, current signs of or a history of foetal alcohol spectrum disorders or exposure to heavy antenatal alcohol exposure, sensory impairment, history of traumatic brain injury with loss of consciousness exceeding 10 minutes, presence of diseases that may affect the CNS (e.g., meningitis, epilepsy), HIV [tested using the enzyme linked immunosorbent assay (ELISA)], less than 6 years of formal education, and lack of proficiency in English or Afrikaans. Prior to consent being obtained for participation in the study, a research social worker obtained collateral information from consenting parents, verifying the absence of medical, psychiatric and psychosocial problems. Participants in the two groups were individually matched for age (within 1 year), gender, language, socio-economic status and level of education (within 1 year). A total socio-economic status score was calculated for each participant by summing the category scores for family income (1-6), reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), parent education (0-6), total assets (0-7), dwelling type (1-6) and bedroom cohabitation (1-7). During recruitment it was attempted to match the samples for smoking status, but this was not to be feasible since smoking was much more prevalent in the AUDs participants. This positive association of smoking and alcohol use is well documented (Larson et al., 2007).

Measures

*Substance use***:** A revised version of the Timeline Followback procedure (TLFB) (Sobell and Sobell, 1992), a semi-structured, clinician-administered assessment of lifetime history of alcohol use and drinking patterns (i.e., frequency, quantity and density of alcohol consumption, including every phase from when participants first started drinking at least once per month to the present, including all periods of abstinence) was used in combination with the K-SADS-PL to elicit alcohol-use data. It was administered by a Psychiatrist on the day of screening. A standard drink was defined as one beer, cider or wine cooler (340mL), one glass of wine (150mL) or a 45mL shot of liquor.   A similar procedure was carried out for each substance that the research participant acknowledged using.

Biochemical determination of vitamin D status: Circulating 25(OH)D, widely regarded as the most appropriate measure of vitamin D status with levels reflecting medium to long term vitamin D availability from both endogenous and dietary sources (Gibson, 2005a). EDTA venous blood samples for the serum 25(OH)D assay were collected from each consenting participant via venipuncture. Recruitment of subjects took place across all four seasons of the year resulting in a spread of blood sampling for assessment of vitamin D status over all the seasons. The LIAISON 25 (OH) vitamin D assay (DiaSorin, Stillwater, MN, USA) was performed on the LIAISON analyser according to the manufacturer's instructions. The Liaison 25(OH)D assay is cospecific for 25(OH)D2 and 25(OH)D3 and accordingly it reports a ''total'' 25(OH)D concentration (Hollis, 2010). The LIAISON 25 OH Vitamin D assay has been validated analytically and clinically and found to be an accurate and precise method for the measurement of circulating 25(OH)D (Ersfeld et al., 2004).   This assay is standardised to a reference solution of pure 25(OH)D3 by UV quantitation (Ersfeld et al., 2004). Testing of assay specific calibrators provided by the manufacturer allow the detected relative light unit values to adjust to the assigned master curve. Recalibration is done every seven days or if quality controls are out of the acceptable range. Assayed control samples provided by the manufacturer are run once per day with the routine samples in an analytical run. Control samples are provided with a certificate of analysis. The range of control values are represented graphically on a Levey-Jennings chart and if control values lie outside of the expected ranges (-2SD and +2SD) provided by the certificate of analysis, the test is regarded as invalid and results are not reported. The analytical runs for control and sample specimens were repeated.

For the interpretation of serum 25(OH)D concentrations, it is important to note that no consensus on concentrations of 25(OH)D that define vitamin D insufficiency in infants and children (Wagner and Greer, 2008) is found in the literature. Holick and Chen (2008) have assumed that children have similar requirements to adults (Holick and Chen, 2008). In line with this assumption, a 25(OH)D concentration of greater or equal to 20 nanograms per millilitre (ng/mL) was used in establishing the Institute of Medicine (IOM) Recommend Dietary Allowance for vitamin D to meet the requirements of nearly all children and adolescents (Institute of Medicine, 1997, Institute of Medicine, 2011, Wagner and Greer, 2008). The cut-offs for circulating 25 (OH)D levels used in adults and in this study to define vitamin D status have been used to classify vitamin D status in children (Poopedi et al., 2011). These categories are based on data showing that intestinal calcium absorption is maximised above 32 ng per mL (Heaney et al., 2003) and that parathyroid hormone levels in adults continue to decline and reach their nadir at between 30 and 40 ng per mL (Chapuy et al., 1996, Holick et al., 2005, Thomas et al., 1998). The following categories were thus used to define vitamin D status based on circulating 25 (OH)D levels: vitamin D deficiency (< 20 ng/mL), insufficiency (20 to 29.9 ng/mL) and sufficiency ($\geq$ 30 ng per mL and greater) (Holick, 2007, Holick, 2008, Holick, 2009). These categories are also in line with the reference ranges recommended for the LIAISON 25 OH Vitamin D assay.

Energy, calcium and vitamin D intake: Energy, calcium and vitamin D intake was estimated using three 24-hour recalls per participant. This method of dietary intake assessment has been shown to be appropriate for quantifying dietary intake of groups in developing countries (Gibson, 2005b, Gibson, 2005c) and internal and external validity has been found to be acceptable in adolescents aged ten years and older (Biro et al., 2002).

The energy (kilojoules (kJ)), calcium (milligrams (mg) and vitamin D (International Units(IU)) intakes for each participant for each day was calculated using the South African Food Data System (SAFOODS) (Medical Research Council, 2002). The average intakes over the three 24-hour recall interviews were calculated to represent the observed intake distributions (see Addendum 1) for energy, calcium and vitamin D. The dietary data include nutrient intake estimates from food (both naturally present and fortified) and water only and exclude nutrient intake estimates contributed by dietary

supplements and medications or that obtained from sunlight. It is important to bear in mind the limitations of the vitamin D intake estimates in this study, namely the relatively high percentage of missing values for vitamin D (approximately 30 to 40 %) in the SAFOODS database (Wolmarans et al., 2010), and the lack of dietary supplement use data.

The energy intake variable obtained from the 24-hour recalls did not include estimated energy from alcohol intake. Average daily alcohol energy intake of the AUDs group was estimated from average daily alcohol intake (grams) per participant in the AUDs group using the alcohol-use data from the most recent phase of drinking as follows: 1) frequency of alcohol use (days per month) multiplied by average quantity of alcohol consumed (standard drinks per drinking day) to obtain average monthly standard drinks of alcohol consumed; 2) average monthly standard drinks of alcohol consumed was divided by 28 days to obtain average daily standard drinks of alcohol consumed; 3) average daily standard drinks of alcohol consumed was multiplied by 13.6 grams of alcohol per standard drink to obtain average daily alcohol intake in grams, which was converted to average daily alcohol energy (29 kilojoules per gram) to obtain average daily alcohol energy (kilojoules). Average daily alcohol energy was added to daily energy intake from the observed intake distributions for each AUD participant to represent total estimated energy intake. Daily alcohol energy for the *n=48* light drinking participants in the non-AUDs group was not calculated as their alcohol life dose was negligible (mean 5.77; SD 12.46 standard drinks), and the contribution of alcohol energy to total estimated energy intake would therefore also be negligible. The total estimated energy intake variable was reported in this study only for use when regression-adjusted differences between groups were determined, since differences in energy intake between groups may confound differences in nutrient intakes.

The 24-hour recall data was further used to determine the top five foods foods/energy-containing beverages (excluding alcoholic beverages) that contributed to calcium intake in each group.

Eating behaviour (frequency of intake of indicator foods): The weekly frequencies of intake of foods reflecting healthy and poor food choices were estimated using a non-quantitative food frequency questionnaire. The questionnaire consisted of a list of 37 food categories, with each food category consisting of either single or multiple food items that were grouped based on shared nutritional

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characteristics. Indicator foods/categories were identified by firstly listing foods most commonly consumed by South Africans in the Western Cape using scientific reports, publications as well as unpublished dietary assessment information generated in small research projects/compilation of community profiles for nutrition interventions. Identified foods/categories were then classified as either healthy choices (offer protective effects against non-communicable diseases [NCDs]) or as poor choices (would increase NCDs risk).   A panel of nutrition and NCDs health experts advised this process. The response categories included 'eaten in the past month' (yes/no), and if yes, 'times eaten per week' or 'times eaten per month'.

The frequency of intake recorded for each one of the 37 food categories was converted to reflect the number of times eaten per week per participant. The food categories 'milk/sour milk/yoghurt' and 'cheese' were the two food categories selected as indicators of calcium intake for the purposes of this paper, and weekly frequencies of intake for only these two food categories are reported.

Procedures

Recruitment procedures included oral presentations at schools and advertisement via word-of-mouth. At the pre-screening stage, adolescents who did not meet eligibility criteria for possible inclusion in the AUDs or non-AUDs groups were excluded. Participants who met eligibility criteria were transported from their homes or schools to the testing site for complete physical and psychiatric screening for possible allocation to one of the groups or exclusion.

After confirmation of inclusion in the study, demographic information was obtained, the first 24-hour recall interview was conducted and blood samples for the biochemical determination of 25 (OH)D were obtained in the morning from each participant by a phlebotomist. Tubes were wrapped in foil, transported on ice and delivered to the laboratory within two hours. The remaining two 24-hour recall interviews were done on a Monday to obtain Sunday intakes and one other week day thereafter. The 24-hour recall interviews were all conducted by a trained and standardised researcher, versed in relevant terminology and locally available food and beverages.   The procedure for the 24-hour recalls included the following consecutive steps: a) listing of foods and beverages (including water) consumed by the

participant in the previous 24 hours, starting from time of waking and proceeding chronologically until time of going to sleep; b) collection of detailed description of foods, preparation methods and brands where relevant and the amounts consumed; and c) final checking to recall forgotten foods. Commonly used household measures and food pictures from the Dietary Assessment and Education Kit, developed by Steyn and Senekal (Steyn and Senekal, 2004) were used to assist with food portion size estimation. Estimated food portions were converted to grams using the MRC Food Quantities Manual (Langenhoven et al., 1991). The 24-hour recall interviews in this study were conducted over a period that included all seasons of the year to account for seasonal dietary variations. Dietary data could not be collected for Fridays and Saturdays as it was not feasible to conduct interviews on Saturdays and Sundays.

The indicator food frequency questionnaire was administered by the trained researcher during the second contact session which also involved administration of the second 24-hour recall interview. Participants were asked to recall whether they had consumed foods in the 37 specified food categories in the past month. If yes, they were asked to indicate the number of times per week the food/s was consumed, including every day (seven times per week). If the food was not consumed on a weekly basis, participants were asked to indicate the number of times per month.

Ethics

The Committee for Human Research of Stellenbosch University approved all study procedures (N06/07/128). After eligibility was established, written consent from parents and written assent from participants was obtained. Participants were compensated for their time with gift vouchers. Confidentiality of all study information was maintained with the exception of statutory reporting requirements in newly-identified or ongoing threats to the safety of minor participants.

Statistical analysis

Descriptive statistics, including inspection of data for adherence to normal distributions, and group comparisons were computed using Stata/IC Version 11.1 for Windows (Statacorp Lp, 2009). Suitable transformations were applied to all variables with skewed distributions, as applicable. Statistical

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significance was defined at a level of p≤0.05. The smoking variable used in all regressions included the smoking group [light smokers (lifetime < 100 cigarettes) and regular smokers (lifetime > 100 cigarettes)] and the non-smoking group (participants who have never used tobacco).

Descriptive statistics (frequency distributions/means and standard deviations) of socio-demographic and substance use variables in the non-AUDs and AUDs groups were computed and compared for confirmation of group allocation and matching. For comparison of continuous variables, the Mann Whitney U Test was used and for categorical variables the Chi-square or Fisher's exact tests were used.

Descriptive analyses for serum 25(OH)D concentrations included medians and interquartile ranges for each group. Due to the paired nature of the data, multi-level mixed effects linear regression was used to compare serum 25 (OH)D between the two groups, with adjustment for gender, smoking status and vitamin D intake. A pairing variable was created according to the matched pairs in the sample and served as the level variable in the model. The 25(OH)D variable (transformed) was used as the dependant variable in the regression.

The frequencies of participants in the non-AUDs and AUDs groups with vitamin D sufficiency, insufficiency and deficiency (according to the defined vitamin D status categories) were computed and compared between groups, including gender groups, using the Chi-square test.

Descriptive analyses for dietary intakes of energy, calcium and vitamin D included the medians and interquartile ranges of the observed intake distributions (Addendum 1). The above-described regression was used to examine differences in intakes of energy, calcium and vitamin D between groups, adjusting for smoking status, gender and total estimated energy including alcohol (when energy intake was compared, total energy was not adjusted for). The observed intake distributions (Addendum 1) for energy, calcium and vitamin D (transformed variables) were used as dependant variables in the model.

As no specific reference intakes are available for the South African population, the Institute of Medicine's (IOM) Dietary Reference Intakes (DRIs), were used to assess adequacy of dietary intake of calcium and vitamin D (Institute of Medicine, 2011). The adequacy of calcium and vitamin D intakes were determined using usual intake distributions (Addendum 2) in accordance with the recommendation of

the IOM concerning the need to determine the usual nutrient intake distributions when assessing adequacy of dietary intake of groups in relation to the DRIs (Addendum 2) (Institute of Medicine, 2000). Adjustments to the observed intake distributions to obtain usual intake distribution estimates were made using the National Research Council (NRC)/IOM method (Institute of Medicine, 2003, National Research Council, 1986) (Addendum 2).

Using the EAR cut-point method the frequencies of intakes below the EARs for calcium and vitamin D were computed in each group to reflect the risk of inadequate intake (Institute of Medicine, 2000, Beaton, 1994) (Addendum 3). For these purposes, the EARs for 14 to 18 year olds were used for calcium (1100 mg) and vitamin D (400 IU) (Institute of Medicine, 1997, Institute of Medicine, 2011). The frequencies of usual intakes below the EARs (14 to 18 years) for each nutrient were compared between groups using the Chi-square test.

Using the 24-hour recall data, the average calcium intake (milligrams) for each food code was computed for each participant, after which the average intake for each group was computed and ranked. This was done to obtain the top five foods/energy-containing beverages (excluding alcohol) that contributed to calcium intake in each group.

Descriptive statistics for the weekly frequency of intake of foods in the two food categories, namely "milk/sour milk/yoghurt" and "cheese", included medians and interquartile ranges for each group. The above-described regression was used to examine differences in weekly frequency of intake of foods in the two food categories, adjusting for smoking status and gender. The distribution of the weekly frequency of intake of "milk/sour milk/yoghurt" could not be suitably transformed and a rank variable was created for use as the dependant variable in the regression.

RESULTS

Socio-demographic and substance use characteristics

A total of 184 adolescents were recruited and screened, of whom 22 were excluded as screen failures due to a range of exclusion criteria, including cannabis and methamphetamine use and DSM-IV Axis I diagnoses, resulting in a final sample of 162. The non-AUDs and AUDs groups were successfully matched

for age, education level, gender, language and socio-economic status. All except two participants from the non-AUDs group were from the mixed ancestry ethnic group (Table 1).

As expected, AUDs adolescents had significantly greater alcohol exposure than those without AUDs (Table 1). Almost all (95%, *n=77*) adolescents in the AUDs group had a "weekends-only" style of alcohol consumption. The regular drinking frequency (days per month) and regular drinking quantity (standard drinks per month) indicates an approximate consumption of 13 drinks per drinking day, which suggests a binge drinking pattern. A greater proportion of adolescents in the AUDs group smoked compared to the non-AUDs group, and lifetime tobacco dose (total number of cigarettes smoked in lifetime) was greater in the AUDs group (Table 1).

Biochemical vitamin D status

Blood samples for the biochemical determination of vitamin D status could be obtained from all participants in the sample, except for one in the AUDs group. Serum 25(OH)D was significantly lower in the AUDs group compared to the non-AUDs group (Table 2), although it is important to note that median 25(OH)D concentrations in both groups were within the vitamin D insufficiency category (20 to 29 ng/mL) (Table 2).   Vitamin D insufficiency and deficiency combined was found in almost 90% (*n=71*) of adolescents in the AUDs group and approximately 70% (*n=57*) of non-AUDs adolescents (Table 2). A significantly greater percentage of adolescents in the AUDs group had insufficient and deficient vitamin D status compared to the non-AUDs group. There were no significant differences in the frequencies of adolescents with sufficient, insufficient and deficient vitamin D status for gender by group comparisons (Table 2).

Vitamin D and calcium intake

Complete dietary intake data was collected for 160 participants, with two participants (1 per group) refusing participation. Regressions showed significantly higher dietary intake of energy and calcium in the AUDs group than in the non-AUDs group, while vitamin D intake did not differ significantly between the two groups (Table 3). According to the EAR cut-point method all adolescents in the sample were at

risk of inadequate calcium and vitamin D intakes, with intakes below the EARs for 14 to 18 year olds (Table 4).

The first four foods contributing most to calcium intake were the same foods in the non-AUDs and AUDs groups and included whole milk, white bread, cheddar cheese, savoury maize and wheat crisps (Table 5). Frequencies of intake of "milk/sour milk/yoghurt" (times per week) in the non AUDs (median 7; IQR 7 - 7) and AUDs (median 7; IQR 3 - 7) groups were not significantly different. There was also no difference in the frequencies of intake of "cheese" in the non-AUDs group (median 2; IQR 1 – 3) compared to the AUDs group (median 3; IQR 0.75 – 3).

DISCUSSION

This study reports on the vitamin D and calcium status of a group of treatment-naive, 12 to 16 year old community-based adolescents of mixed ancestry, with "pure" AUDs (AUDs group), in comparison to a matched group of light/non-drinking adolescents without AUDs (non-AUDs group).

Serum 25(OH)D concentrations in the adolescents with AUDs were significantly lower than in the adolescents without AUDs, although median serum levels were below the cut-off of 30 ng/mL in both groups. Furthermore, vitamin D insufficiency and deficiency, based on serum 25(OH)D concentrations, were high in both groups, but significantly more so in the AUDs group. Nearly half of AUDs adolescents (48.8%) and 42% of non-AUDs adolescents were classified as being vitamin D deficient (serum 25(OH)D levels < 20 ng/mL). These findings suggest that both groups of adolescents of mixed ancestry in Cape Town have a poor vitamin D status, which may be exacerbated by heavy alcohol use, in the form of binge drinking.

The possibility that the heavy alcohol use by these adolescents in the AUDs group may have contributed to this difference in serum 25(OH)D levels is strengthened by the fact that most of the other factors known to influence vitamin D levels were matched for in the groups or adjusted for in statistical analysis. Factors that affect circulating 25(OH)D concentrations include age, gender, smoking, ethnicity, seasonal effects and dietary intake (Gibson, 2005a). The participants in the study sample were almost exclusively of mixed ancestry ethnicity, the two groups were matched for age and gender, and smoking

and vitamin D intake were adjusted for in regression analyses. Blood samples for 25(OH)D determination were obtained across all seasons in both groups, at similar times of the year within the matched pairs. However, it should be noted that since sun exposure was not specifically estimated, it is possible that reduced sun exposure in the AUDs group could have contributed to the difference in serum 25(OH)D levels between the two groups. This may require further investigation as Malik et al (2009) indicates that reduced sunlight exposure may be the main cause of vitamin D deficiency. The very poor dietary intake of vitamin D in both groups should be noted, but the mentioned limitations in the SAFOODS database regarding vitamin D content of foods (Wolmarans et al., 2010), limits the interpretive value of these results. The lack of information on dietary supplement use also needs to be considered in this regard.

Available information on the association between vitamin D and alcohol is limited to work done in alcoholics and animal models. Alcoholics have been reported to have reduced circulating vitamin D levels (Malik et al., 2009, Alvisa-Negrin et al., 2009, Schnitzler et al., 2010), which may be related to the effect of alcohol itself on vitamin D absorption, altered biliary secretion, poor dietary intake or reduced sun exposure (Alvisa-Negrin et al., 2009). Evidence from work in rodents indicated that chronic alcohol intake may result in reduced serum $1,25 \, (OH)_2 \, D$ concentrations due to impaired renal synthesis and/or increased degradation of $1,25 \, (OH)_2 \, D$ (Shankar et al., 2008). More research is clearly needed to elucidate the different mechanisms that contribute to the reduced vitamin D levels associated with heavy alcohol intake, specifically in the form of binge drinking.

When compared to available South African information regarding 25(OH)D levels and prevalence of insufficiency/deficiency in children and adolescents, results suggest a higher prevalence of vitamin D insufficiency/deficiency in adolescents in this study sample. A small study in Polokwane (latitude of approximately 24 degrees south) in healthy black children and adolescents found mean circulating 25(OH)D levels to be approximately 50 ng/mL in six to nine year olds (*n=17*), 46 ng/mL in 10 to 13 year olds (n=26) and 36 ng/mL in 14 to18 year olds (*n=15*). The same study found that in healthy albino children circulating 25(OH)D levels were approximately 41 ng/mL in six to nine year olds (*n=30*), 34 ng/mL in 10 to 13 year olds (*n=36*) and 36 ng/mL in 14 to18 year olds (*n=16*)(Cornish et al., 2000). The levels in these studies are mostly within the vitamin D sufficiency range (serum 25(OH)D levels $\geq$ 30 ng/mL) and

much higher than the serum levels evident in this study in adolescents of mixed ancestry in Cape Town

(latitude of approximately 33 degrees south). In a recent assessment of vitamin D status in a cohort of

healthy 10 year old urban children (*n=475*) in the greater Johannesburg area (latitude of approximately

26 degrees south), 7% were vitamin D deficient (serum 25(OH)D less than 20 ng/mL), while 19% were

Vitamin D insufficient (20 to 29 ng/mL) (Poopedi et al., 2011). Seasonal variations in 25(OH)D

concentrations were seen only in white children, with concentrations being significantly higher in white

compared to black children during the autumn and summer months (Poopedi et al., 2011). The

differences in serum 25(OH)D levels between this study and the other studies mentioned may be

attributable partly to the more southerly latitude of Cape Town. To this effect, a study in Cape Town

reported only limited vitamin D synthesis in vitro in the winter months from April through to September

(Pettifor et al., 1996).

Considering the fact that serum 25 (OH)D concentrations of 30 ng/mL or less are associated with

a significant reduction in intestinal calcium absorption (Heaney et al., 2003), the combination thereof

with the low calcium intake in this study sample is of concern, especially in the AUDs group, who seem to

have a greater risk of vitamin D deficiency. The interaction of activated vitamin D ($1,25(OH)_2D$) with the

vitamin D receptor is needed for the production of calbindin, a calcium-binding protein involved in

transcellular calcium transport for intestinal absorption (Weaver, 2002), which is the dominant mode of

absorption when calcium intake is low or moderate (Weaver, 2002).

The low estimated dietary calcium intake of adolescents in this study is in line with previous

studies showing poor calcium intake in adolescents (Harel et al., 1998, Moshfegh et al., 2009). Although

calcium intake in the AUDs group was significantly greater than in the non-AUDs group, this difference

can be regarded as clinically insignificant since all participants in the sample had intake less than the EARs

for calcium for 14 to18 year olds (1100 mg). Calcium-rich foods were consumed only eight times per

week (about once daily) in both groups, which in all likelihood did not provide the one to two dairy

servings per day recommended by the SAFBDG (Department of Health: Directorate Nutrition, 2004), and

likely accounts for the low calcium intake. This is supported by the fact that calcium contribution from

milk (first in the ranking of the top five foods/energy containing beverages contributing to calcium intake)

per participant per day amounted to only about 100 to 120 mL of milk per day (120 mg of calcium per 100

mL milk) (Medical Research Council, 2002). White bread and crisps (maize- and wheat-based) also

featured as major calcium sources, being ranked second and fourth in both groups, respectively. White

bread contains 56 mg of calcium per 100 grams and average maize and wheat crisps contain 81 mg of

calcium per 100 grams (Medical Research Council, 2002), however the absorption of calcium from these

foods is lower than from dairy foods. The fact that adolescents in this sample consumed considerable

quantities of white bread and crisps may explain why they feature as main calcium sources. In view of

this poor calcium intake, dietary factors that may affect urinary calcium excretion and thus calcium status

in the body should also be considered. High protein diets may result in hypercalciuria, which is not

compensated for by increased calcium absorption (Heaney, 2000). High sodium intakes may also increase

urinary calcium excretion and has been reported to negatively affect bone density over the longer term

(Devine et al., 1995). On the other hand, high phosphorus intakes may have a hypocalciuric effect, but

since high phosphorus intake increases losses of endogenous fecal calcium simultaneously (Heaney and

Recker, 1994), the net effect on calcium balance is probably negligible.

The combination of inadequate calcium intake and poor vitamin D status seen in this adolescent

sample may have negative implications for skeletal health and attainment of peak bone mass, with heavy

alcohol use possibly increasing this risk. Firstly, the low calcium intake per se in both groups may hamper

peak bone mass attainment, as inadequate calcium intake may translate into inadequate calcium

absorption and a decrease in peak bone mass in adolescents (Matkovic et al., 1990). Secondly, the

vitamin D insufficiency and deficiency on its own may have harmful implications for bone via the effects

of hyperparathyroidism and the resultant increased osteoclast activity and bone resorption (Holick, 1996)

in these adolescents, with potentially worse impacts in the AUDs adolescents due to their increased risk

for vitamin D deficiency. Lastly, the poor vitamin D status may compound the effects of the low calcium

intake in these adolescents as absorption of calcium at low levels of intake is primarily dependent on the

presence of activated vitamin D.

The notion that alcohol use may negatively impact on bone health in adolescents is supported by

the results of a recent prospective study in 109 high school students that examined the association

between osteoporosis risk factors and attainment of bone mass over a four year period. The results showed that alcohol had a significant inverse association with bone mineral density while adequate dairy intake, defined as greater than four servings per day, had a significant positive association with bone mineral density (Korkor et al., 2009). Similarly, Neville and colleagues found a non-significant trend towards an inverse association between alcohol intake and bone mineral density (Neville et al., 2002). The negative association between alcohol intake and bone mineral density is further supported by evidence from animal models wherein intermittent binge-like alcohol exposure in adolescent and young adult rats had significant negative effects on bone integrity, including trabecular structure, bone mass and functional strength capacities of bone (Callaci et al., 2006, Lauing et al., 2008, Wezeman et al., 2007) and was found to increase osteoclastic resorption (Wezeman et al., 2000). Moreover, a recent laboratory investigation in adolescent rats using binge drinking models demonstrated that binge alcohol exposure can produce disturbances of normal bone gene expression patterns that persist well beyond the phase of active intoxication (Callaci et al., 2010). Therefore, high levels of alcohol exposure (in binges) may produce both short and long term skeletal damage in the adolescent rat. It can thus be argued that the poor vitamin D status and inadequate calcium intake, exacerbated by the repeated alcohol-induced disruptions in vitamin D and calcium homeostasis in the AUDs adolescents, may increase their risk of harmful skeletal outcomes. Furthermore, binge drinking behaviours that begin during late adolescence tend to continue into early adulthood (Mccarty et al., 2004) thereby increasing the time that alcohol-related skeletal damage may be occurring in young adults.

In interpreting the results of this research, the inherent limitations of dietary intake methodology and self-report of alcohol consumption need to be considered. Furthermore, the use of the Chi-square test to assess differences in categorical variables does not allow for adjustment for possible confounders, thus comparisons done between the two groups using this test are subject to this limitation.

CONCLUSION

Bearing in mind the mentioned limitations, it can be concluded from this cross-sectional comparative study that both groups of adolescents had a poor biochemical vitamin D status, with heavy alcohol use in

the form of binge drinking possibly increasing this risk. Furthermore, both groups had a high risk for inadequate calcium intake, possibly compounding the effects of poor vitamin D status and heavy alcohol intake. It is thus plausible to speculate that the poor calcium and vitamin D status in these adolescents, especially those with AUDs, may impact negatively on attainment of peak bone mass and consequently may increase the risk of osteoporosis later in life.

Although the findings in this non-representative sample cannot be directly extrapolated to the adolescent population in the Cape Town area, they provide some indication that vitamin D and calcium status may be less than desirable in this age group and may be compounded by heavy alcohol use, which warrants further investigation. Additionally, the findings of this study require further exploration in longitudinal, well-controlled studies, to confirm the negative associations between heavy adolescent alcohol use and vitamin D status, as well as the impacts of heavy alcohol use on skeletal development and attainment of peak bone mass in adolescents.

Table 1. Confirmatory analyses of socio-demographic and alcohol grouping measures and substance use characteristics of the non-AUDs and AUDs groups

	non-AUDs (*n=81*)	AUDs (*n=81*)		
	M (SD) or %	*M (SD)* or %	U/χ^2	p-value
Socio-demographics				
Age	14.76 (0.78)	14.92 (0.74)	-1.19	0.235
Education level [a]	7.79 (0.85)	7.85 (0.74)	-0.43	0.666
%Male	42	42	0.00	1.000
%Female	58	58		
% Afrikaans-speaking	69	69	0.00	1.000
%English-speaking	31	31		
% Mixed ancestry	97.6	97.6		0.497
% White	1.2	0		
% Black	1.2	0		
Total Socio-economic status score [b]	28.19 (5.80)	24.85 (5.93)	1.34	0.179
Alcohol Use				
% Never consumed alcohol	41	0		
% Never intoxicated	93	0		
%Light drinker (Life dose<100 standard drinks) [c]	59	0		
% Alcohol abuse [d]		2.5		
% Alcohol dependence [e]		97.5		
% Weekends-only drinking style in most recent drinking phase [f]		95%		
Drinking onset age (years) in participants that have drunk alcohol	12.25 (1.66)	12.04 (1.70)	0.57	0.567
Alcohol lifetime dose [g]	5.77 (12.46)	1493.69 (1511.53)	-11.04	**<0.001**
Age of first intoxication		12.83 (1.15)		
Age of onset of regular drinking		12.91 (1.11)		
Regular drinking duration (months)		23.78 (15.91)		
Regular drinking frequency (days/month) in most recent drinking phase		5.01 (2.87)		
Regular drinking quantity/month (standard drinks) [h]		65.78 (57.96)		
Tobacco Use				
% Never smoked tobacco	59	17		**<0.001**
% Light smokers (lifetime <100 cigarettes)	35	31		
% Regular smokers (lifetime >100 cigarettes)	6	52		
Smoking onset age (years) in light smokers	12.53 (1.62)	12.44 (1.96)	-0.19	0.846
Smoking onset age (years) in regular smokers	13 (0.71)	12.36 (1.46)	0.96	0.339
Lifetime tobacco dose of all smokers [i]	86.42 (442.80)	1417.59 (2762.60)	-7.02	**<0.001**

Abbreviation: AUDs: alcohol use disorders

Notes: For all variables not presented as percentages, means are presented with standard deviations in parentheses. Continuous variables compared using the Mann Whitney U Test and categorical variables compared using the Chi-square or Fisher's exact tests.

[a] Years of successfully completed education

[b] Total Socio-economic status score: Sum of Family income (1-6), Reversed employment category of participant's parent with the highest employment rank (Hollingshead reversed) (1-9), Parent education (0-6), Total assets (0-7), Dwelling type (1-6) and Bedroom cohabitation (1-7) – Maximum=41

[c] Less than 100 standard drinks of alcohol consumed in lifetime

[d] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol abuse

[e] Greater than 100 standard drinks of alcohol consumed in lifetime with a DSM-IV diagnosis of alcohol dependence

[f] Style of drinking followed in the most recent phase of drinking

[g] Total number of standard drinks of alcohol consumed in lifetime

[h] Average standard drinks of alcohol consumed per month

[i] Total number of cigarettes smoked in lifetime

Table 2. Serum 25-hydroxyvitamin D concentrations and prevalence of vitamin D sufficiency, insufficiency and deficiency in the non-AUDs and AUDs groups, and comparisons between groups

	Group		Males		Females	
	non-AUDs	AUDs	non-AUDs	AUDs	non-AUDs	AUDs
			median (IQR)			
Biochemistry:						
Serum 25(OH)D (ng/mL)	**25.7 *** (18.7-31.1)	**22.0 *** (18.2-25.9)	26.1 (18.7-31.3)	20.0 (15.8-25.7)	25.2 (18.2-30.6)	22.4 (19.0-25.9)
			percentage *n*			
Categories of vitamin D status:						
Vitamin D sufficiency 25(OH)D: ≥ 30 ng/mL	**29.6 **** *24*	**11.2 **** *9*	32.3 *11*	11.8 *4*	27.7 *13*	10.9 *5*
Vitamin D insufficiency 25(OH)D: 20 to 29.9 ng/mL	**28.4 **** *23*	**40.0 **** *32*	26.5 *9*	50.0 *17*	29.8 *14*	32.6 *15*
Vitamin D deficiency 25(OH)D: < 20 ng/mL	**42.0 **** *34*	**48.8 **** *39*	41.2 *14*	38.2 *13*	42.5 *20*	56.5 *26*

Abbreviations: AUDs: alcohol use disorders; IQR: interquartile range; 25(OH)D: 25-hydroxyvitamin D; ng/mL: nanograms per millilitre

Notes: All variables had skewed distributions thus medians are reported with interquartile range (IQR) in parenthesis

n-values: non-AUDs *n=81* (*n=34* males and *n=47* females); AUDs *n=80* (*n=34* males and *n=46* females);

* Significant differences between groups in serum 25 (OH)D (p=0.038), using multilevel mixed-effects linear regression, adjusting for gender, smoking status and vitamin D intake

* * Significant differences between groups in frequencies of adolescents with sufficient, insufficient and deficient vitamin D status (p=0.013), using Chi-square test

Table 3. Estimated daily intakes of dietary energy, calcium and vitamin D (observed intake distributions [a]) in the non-AUDs and AUDs groups, and comparisons between groups

	Group		Males		Females	
	non-AUDs	AUDs	non-AUDs	AUDs	non-AUDs	AUDs
			Median (IQR)			
Total Energy [b] (kJ)	**8965 *** (7240-10661)	**11028 *** (9072-13014)	9461 (8010-10835)	11684 (10181-13521)	8342 (7003-9944)	10481 (8847-11726)
Calcium (mg)	**450.1 *** (347.8-614.1)	**460.0 *** (334.1-627.1)	525.4 (391.1-651.4)	508.9 (442.8-722.0)	438.1 (318.4-564.8)	415.9 (330.7-534.1)
Vitamin D (IU)	99.2 (64.6-160.1)	120.1 (83.6-193.6)	123.3 (95.2-180.5)	134.9 (86.5-216.3)	83.6 (60.3-131.3)	112.9 (83.1-163.4)

Abbreviations: AUDs: alcohol use disorders; IQR: interquartile range; kJ: kilojoules; mg: milligrams; IU: International Units

Notes: All variables had skewed distributions thus medians are reported with interquartile range in parenthesis

n-values: *n=80* per group (males *n=33* and females *n=47*)

[a] See Addendum 1

[b] Total estimated energy intake, including average daily alcohol energy estimated from average daily alcohol intake (grams) per participant in the AUD group

* Significant differences between groups in intakes of total energy (p<0.001) and calcium (p=0.007), using multilevel mixed-effects linear regression, adjusting for gender, smoking status and total estimated energy including alcohol (comparison of total energy between groups was only adjusted for gender and smoking status)

Table 4. Prevalence of risk of inadequate calcium and vitamin D intakes in the non-AUDs and AUDs groups using the EAR cut-point method [a], and comparisons between groups

	EARs 14-18 years		non-AUDs (*n=80*)	AUDs (*n=80*)
	Males	**Females**	**Prevalence below EAR (%)**	**Prevalence below EAR (%)**
Calcium (mg)	1100	1100	100	100
Vitamin D (IU)	400	400	100	100

Abbreviations: AUDs: alcohol use disorders; EAR: Estimated Average Requirement; mg: milligrams; IU: International Units
Notes: usual nutrient intake distributions used (Addendum 2)
No differences between groups in the numbers of adolescents with risk of inadequate calcium and vitamin D intakes, using Chi-square test
[a] See Addendum 3 for detail on EAR cut-point method

Table 5: Top five foods/ energy-containing beverages contributing to calcium intake (milligrams per day) in the non-AUDs and AUDs groups

non-AUDs Group (*n=80*)			AUDs Group (*n=80*)		
Rank	**Foods**	**Calcium (mg/day) [a]**	**Rank**		**Calcium (mg/day) [a]**
1	Milk, full fat	143	1	Milk, full fat	121
2	Bread, white	50	2	Bread, white	63
3	Cheese, cheddar	47	3	Cheese, cheddar	50
4	Snack, savoury, wheat, maize crisps	21	4	Snack, savoury, wheat, maize crisps	27
5	Macaroni cheese	12	5	Custard (whole milk, custard powder)	19

Abbreviation: AUDs: alcohol use disorders; mg: milligrams
Notes: Excluding alcoholic beverages
[a] Using the 24-hour recall data, the average calcium intake (milligrams) for each food code was computed for each participant, after which the average intake for each group was computed and ranked

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Chapter 7

CONCLUSIONS AND RECOMMENDATIONS

Adolescence is a critical developmental phase in the lifecycle and adequate nutrition is needed to support growth and development, as well as short and long term nutrition-related health. Documented nutritional challenges and risks in adolescence include undernutrition (stunting and underweight), overnutrition (overweight and obesity) and poor iron, vitamin D and calcium nutriture (World Health Organization, 2005, Cashman, 2007). These nutritional challenges and risks are rooted in increased nutritional requirements, as well as the poor eating behaviour and dietary intake common in adolescents (Barquera et al., 2003, Moreno et al., 2010, Munoz et al., 1997, Pomerleau et al., 2004), often in conjunction with unhealthy lifestyle factors such as predominant sedentary behaviour and substance use, including alcohol. International and national evidence indicates clearly that heavy alcohol use during adolescence, particularly in the form of binge drinking, is a significant rising public health concern (Matthews, 2010, Nelson et al., 2004, Reddy et al., 2010, Hibell et al., 2009).

Work in adults and experimental models has indicated that alcoholism and heavy alcohol use in the form of binge drinking impacts negatively on nutritional status (Bode and Bode, 2003, Foster and Marriott, 2006, Keiver et al., 2000, Lieb et al., 2011, Lieber, 2000, Lieber, 2003, Yeomans, 2010, Halsted et al., 2002). Within the context of this evidence, the rising prevalence of heavy alcohol use by adolescents is a reason for concern, as the clustering of heavy alcohol use with poor eating behaviour and dietary intake may place alcohol-using adolescents at a greater nutritional risk. In the longer term, early heavy alcohol use may increase the risk of adult alcohol use disorders (AUDs) as well as significant adverse lifetime alcohol-related consequences (Hingson et al., 2002, Hingson et al., 2001, Hingson et al., 2000, Viner and Taylor, 2007). Furthermore, protracted heavy alcohol use may increase the risk for poor nutrition-related health outcomes in adulthood, such as non-communicable diseases (NCDs) (World Health Organization, 2010), nutrient deficiencies and metabolic derangements (Lieber, 2000, Lieber, 2003).

The potential influences of heavy alcohol use on specific short and long term nutritional risks during adolescence have not been well studied, particularly using sound and detailed alcohol use and nutritional status assessment methodology.

This cross-sectional comparative study therefore investigated the influences of heavy alcohol use on the nutritional status of adolescents with AUDs, specifically with regards to their dietary intake and eating behaviour, growth and weight status, iron status as well as vitamin D and calcium status. The study participants were school-going adolescents, aged 12 to 16 years, English or Afrikaans-speaking, with a lower socio-economic status, recruited from schools within a 25 kilometre radius of Tygerberg Hospital in the greater metropolitan area of Cape Town, in the Western Cape province of South Africa.

It is clear from the findings of this study that there were several *similarities* in the non-AUDs and AUDs groups when the measures of nutritional status employed to address the four research questions, were compared between the groups. Poor eating patterns (breakfast skipping and frequent snacking), poor food choices (energy-dense and nutrient-poor foods) and low fruit and vegetable intake in both groups were reflected in the poor nutritional quality of the diet, with risk of inadequate intakes of folate, vitamin C, vitamin A, vitamin E, magnesium and phosphorus in more than half of adolescents in both groups, and risk of inadequate calcium and vitamin D intakes in all participants. Anthropometric indices of growth and weight status were generally comparable between the groups and in line with that of the South African adolescent population, with physical activity in both groups being well below the WHO global recommendation. Biochemical iron store depletion was evident in about a quarter of adolescents in both groups and biochemical vitamin D insufficiency/deficiency was prevalent in both groups.

However, the presence of significant *differences* between the two groups for some of the measures provides evidence that heavy alcohol use in the form of binge drinking may influence the nutritional status of adolescents who engage in this behaviour to the point of an AUD diagnosis. In terms of eating behaviour and dietary intake, these influences manifested in a greater intake of unhealthy foods (energy-dense nutrient-poor) and total energy intake that exceeded requirements, possibly as a result of both poor food choices and heavy alcohol intake. The AUDs adolescents also had greater intakes of foods high in unhealthy fats and ensuing greater total fat, saturated fat and cholesterol intakes. Sodium intake and prevalence of risk of excessive sodium intake were significantly higher in the AUDs group. Furthermore, results indicate that adolescent females with AUDs may have an increased risk for being overweight/obese compared to matched adolescent females without these disorders, which may be

explained by higher total energy intake in the AUDs females primarily in the form of alcohol. Measures of biochemical iron status in the AUDs adolescents point to the possibility of higher risk of iron store depletion, which may be attributable to the direct effect of binge drinking on the gastrointestinal tract (potentially through impaired absorption and iron loss via haemorrhage), since the AUDs adolescents had a lower risk of inadequate iron intake than the non-AUDs adolescents. Finally, results suggest that the presence of an AUD may increase the already high risk of poor biochemical vitamin D status in adolescents in this sample, potentially via disruption of vitamin D homeostasis by alcohol.

The various limitations of this study have been stated in chapters 3 to 6. It is pertinent to mention that the sample size calculation was based on the main outcome (brain structure and function) of the larger study, of which this study was a component. It is possible that a larger sample size may have resulted in the detection of further significant differences between the non-AUDs and AUDs groups in this study. However, the methodological rigour employed in this study in the form of exclusion of or adjustment for potential confounders of the relationships that were investigated, the acquisition of very detailed alcohol use and drinking pattern data (frequency, quantity, pattern and style of alcohol consumption) and comprehensive quantitative dietary intake, anthropometric as well as nutritional biochemistry data, supports the gravitas of the findings.

Bearing in mind these limitations, the core conclusions of this study are that heavy alcohol use in the form of binge drinking in adolescents may have the following nutrition-related influences (Figure 1):

- increased intake of energy, unhealthy fats and sodium

- increased risk of overweight/obesity in females

- increased risk of iron store depletion

- increased risk of vitamin D insufficiency/deficiency
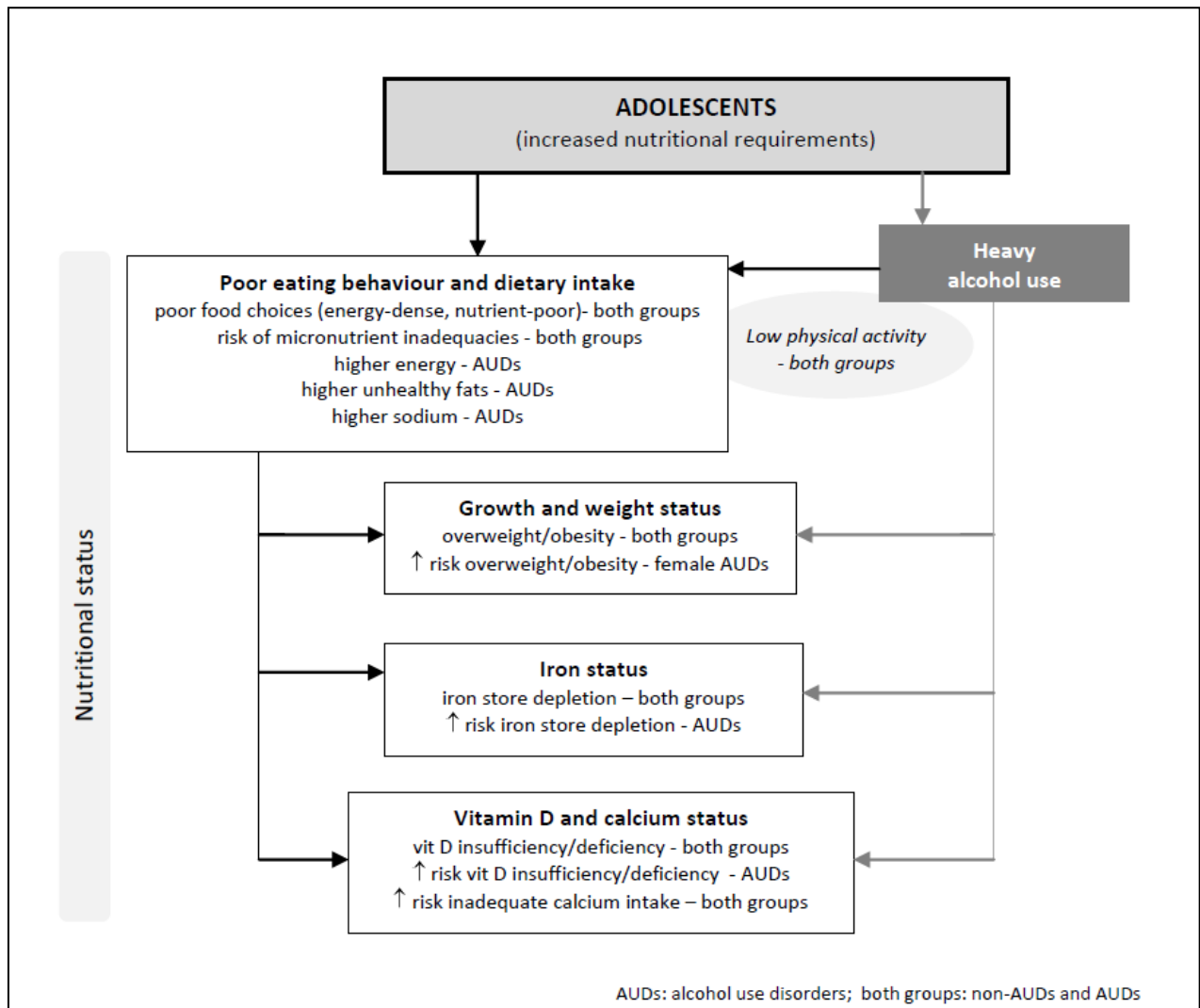
Figure 1. Conceptual framework depicting the nutrition-related influences that heavy alcohol use in the form of binge drinking may have on the nutritional status of adolescents

The fact that the adolescents in this study were still early in their potential drinking trajectory needs to be taken into account when the possible *consequences* of the identified nutritional influences of binge drinking/AUDs in adolescents are considered. If heavy alcohol use and poor eating behaviour and dietary intake do not persist in these adolescents, it is likely that that no negative long term nutrition-related consequences will occur. However, evidence supports a strong degree of tracking of adolescent alcohol use, including binge drinking into adulthood (Grant, 1998, Mccarty et al., 2004, Viner and Taylor, 2007). Similarly eating behaviours (Kelder et al., 1994, Te Velde et al., 2007), weight status (Serdula et al., 1993) and physical activity patterns (Gordon-Larsen et al., 2004) also exhibit strong tracking into adulthood.   Thus, the possibility that these adolescent behaviour patterns are not transient in nature

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and are likely to have significant impacts on long term nutritional-related and other health outcomes (NCDs, iron deficiency anaemia and osteoporosis), should not be ignored.

Despite the non-representative sample in this study, it is recommended that the potential risks identified receive attention in health promotion programmes targeted at adolescents. It is a matter of cause that such interventions should include a strong focus on the prevention, reduction and treatment of heavy alcohol use in adolescents. Further focus areas to be emphasised include increased regular physical activity, healthier food choices (nutrient-dense and lower in energy) with reduced intake of unhealthy foods (energy-dense, nutrient-poor), promotion of consumption of calcium-rich and iron-rich foods, especially haem iron sources, as well attention to vitamin D status. In this process the effects of macrosystem factors on adolescent alcohol use and nutritional health should be considered. Recommendations in this regard that were made to address alcohol abuse by the recent Western Cape Burden of Disease Reduction Project (BoDP), commissioned by the Western Cape Department of Health, include: restrictions or bans on alcohol advertising, substantial increases in alcohol cost, reduction in alcohol availability by strengthening the Liquor Act and implementation of substance-abuse prevention programmes in school curricula (Corrigall et al., 2008). Turning to nutritional health, Swinburn et al (2004) and Temple et al (2011) highlighted the need for legislative restrictions on food advertising especially to children and adolescents to address poor eating behaviour and dietary intake and risk of overweight/obesity, which is currently unregulated in South Africa. Furthermore, policy interventions around the availability of healthy foods and limited availability of poor food choices in schools are needed (Krebs and Jacobson, 2003, Temple et al., 2006). The fact that affordability and availability of healthy foods are barriers to the success of health-promotion campaigns also needs to be considered and may require government interventions in the form of taxation and subsidies (Temple and Steyn, 2011, Temple et al., 2011, Temple, 2007). It is clear that interventions seeking to address heavy alcohol use and nutritional vulnerabilities in adolescence extend across many sectors of society and are not exclusively a health issue, but a multi-sectoral issue, incorporating the health sector as well as other social sectors and the economic sector (Myers and Naledi, 2008).

Finally, it can be conclusively stated that this study provides novel insights into the potential influences of heavy alcohol use in the form of binge drinking on the eating behaviour and dietary intake, growth and weight status, iron status as well as vitamin D and calcium status of adolescents.

Recommendations for future research include longitudinal, well-controlled studies with specific reference to binge drinking-related eating, risk of overweight/obesity, iron store depletion and vitamin D insufficiency/deficiency and heavy alcohol use in adolescents. Further investigation of vitamin D insufficiency/deficiency in a representative sample of adolescents in the Western Cape is also warranted following the recommendations by Poopedi et al (2011) that studies investigating vitamin D status in southern areas of the country, where there is less sunshine during the winter months, are necessary.

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ADDENDA

ADDENDUM 1

Observed Intake Distributions

Dietary assessment methods that are designed to estimate intake of individuals include the food frequency questionnaire, 24-hour recall, diet history and weighed and estimated food records (Gibson, 2005).

When estimating dietary intake of individuals, the use of both sound methods, such as instruments that capture total nutrient intake (e.g. dietary recalls and food records) and complete food composition databases, may provide a relatively accurate reflection of an individual's intake during a specified time period. This estimation of dietary intake is regarded as the *observed* intake (Institute of Medicine, 2000, Gibson, 2005).

In this study, dietary intake was estimated using three 24-hour recalls per participant. The 24-hour recalls were administered on non-consecutive days, including a well-balanced spread of week days and one weekend day (Sunday), and over a period that included all seasons of the year to account for seasonal dietary variations. A limitation is that dietary data could not be collected for Fridays and Saturdays as it was not feasible to conduct interviews on these days.   The average intakes of the three 24-hour recall interviews were calculated to represent the *observed* intake distributions for energy and nutrients for the total sample.

The use of 24-hour recalls to estimate dietary intake provides abundant detail about the types and amounts of foods consumed and since the focus is on a single day, the magnitude of systematic errors in 24-hour recalls is decreased. However, individual diets can vary greatly from day to day. In all likelihood, an individual's *observed* intake during a particular three-day period will differ from *observed* intake in a different three-day period, and both three-day *observed* intakes will differ from true *usual* intake. Additionally, several measurement errors plague 24-hour recalls and are compounded by error resulting from the use of food composition databases. All of these factors contribute to considerable *within-person* variability and consequently, measured intake on a single day or over a three-day period is a poor estimator of *usual* (long-term) intake. Thus, an individual's *observed* mean intake over a few days

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may not be an accurate estimate of that individual's *usual* intake (Beaton et al., 1983, Institute of Medicine, 2000).

The concept of *usual* intake is also applicable to groups. On any one day, the distribution of intakes among members of a group or population will be very broad. This reflects that some members eat much more or less of a specific nutrient than *usual* on that specific day. The distribution of *usual* intakes by members of the group will be significantly narrower. However, the mean of the distribution of *observed* dietary intakes in a group is regarded as an unbiased estimate of the group's mean *usual* intake, assuming that sound dietary intake methodology was used (Institute of Medicine, 2000).

In the past, when working with dietary intake data from a group, this limitation of *observed* intakes was compensated for by averaging multiple (2 to 7) 24-hour recalls per participant in the group. However, this approach was deemed unsatisfactory since it became clear that averages over a small number of days do not accurately reflect *usual* intake distributions. Furthermore, this approach resulted in heavy respondent burden and low quality of reported intakes. Consequently, more sophisticated methods based on statistical adjustments have evolved that mitigate this limitation more effectively than averaging multiple 24-hour recalls per participant (Dodd et al., 2006). Appropriate statistical adjustments, which are discussed in detail in Addendum 2, were therefore applied to the *observed* intake distributions in this study to obtain estimated *usual* intake distributions for the study sample.

An important point to mention here relates to **regression** analyses. The dependant variable in a multiple regression analysis refers to an individual and not to a group, and as discussed, individual intakes *observed* on one day are different to *usual* intakes for that individual. While statistical adjustments can be made to the intake distribution of a group in order to estimate the *usual* intake distribution, adjustments cannot be made to individual values to estimate *usual* individual intake. Thus, *observed* intake distribution data should be used as dependant variables in multiple regression analyses (Institute of Medicine, 2000). Based on these assertions, *observed* intake distributions for energy and nutrients were used as dependant variables in the multi-level mixed effects linear regressions applied in this study.

ADDENDUM 2

Usual Intake Distributions

The duration of time that reflects *usual* dietary intake is difficult to define precisely, however, for individuals it is proposed to reflect ongoing average intake over several weeks or more. In order to determine true *usual* dietary intake, a large number of days of intake data are usually needed (Gibson, 2005, Murphy and Barr, 2011), ranging from 27 to 35 days for energy intake, and up to 390 to 474 days for vitamin A intake (Basiotis et al., 1987). Most often, the number of days of observation required to accurately characterise an individual's *usual* intake is prohibitive and it is mostly not feasible to determine an individual's true *usual* dietary intake (Murphy and Barr, 2011).   A minimum of two non-consecutive or three consecutive days of intake data on at least a representative sample of the group is needed for dietary assessment of groups in order to obtain an estimation of *usual* dietary intake using statistical adjustments (Institute of Medicine, 2000).

Since no specific reference intakes are available for the South African population, the Dietary Reference Intakes (DRIs), established by the Food and Nutrition Board of the Institute of Medicine (IOM), were used to assess adequacy of dietary intake of nutrients in this study (Institute of Medicine, 2000, Institute of Medicine, 2001, Institute of Medicine, 2002/2005, Institute of Medicine, 2011). The IOM recommends that *usual* nutrient intake distributions should be used when assessing dietary intake of groups in relation to the DRIs (Institute of Medicine, 2000).   This approach is based on the assertion that the mean of the distribution of *observed* dietary intakes in a group is an unbiased estimate of the group's mean *usual* intake, assuming that sound dietary intake methodology was used. However, the variance of the distribution of *observed* intakes is almost always too large since it contains both the between-persons (individual-to-individual) variation and the within-person (day-to-day) variation. Consequently, estimates of prevalence of inadequacy or excess generated from the *observed* intake distribution are likely to be greater than the true prevalence. For more accurate prevalence estimates, the *observed* intake distributions must be adjusted to partially remove the within-person variability in intakes. The resulting estimated *usual* intake distribution will then more closely reflect only the individual-to-individual

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variation in intakes (Institute of Medicine, 2000). There are a number of statistical methods that have

been developed to estimate *usual* intake distributions from *observed* intake distributions obtained using

24-hour recalls (Dodd et al., 2006, Institute of Medicine, 2000)

In this study adjustments to the *observed* intake distributions to obtain *usual* intake distribution

estimates were made using the National Research Council (NRC)/IOM method (Institute of Medicine,

2003, National Research Council, 1986). The IOM recommends this method for smaller samples and it is

typically applied to dietary data consisting of multiple days of intake data for a sample of participants,

preferably with an equal number of observations per participant (Institute of Medicine, 2003).

The NRC/IOM method was applied to each nutrient intake variable as follows:

1) The normality of the distributions of the nutrient intake variables was examined and natural logarithm

and square root transformations were applied as appropriate, to improve normality of the distributions.

2) A one-way ANOVA was applied to each of the transformed nutrient intake variables with the

participant ID entered as a factor variable, in order to generate the observed variance of the one day data

and the within-person variance of the one day data.

3) Since the adjustment procedure is applied to an individual participant's mean intakes over the period

of observation, both the observed variance and the within-person variance were divided by three (the

number of days of intake data per participant). This resulted in the observed variance (*Vobserved*) and

the within-person variance (*Vwithin)* for the each of the distributions.

4) The between-person variance (*Vbetween*) was then estimated by subtracting *Vwithin* from *Vobserved*

and dividing by three, that is, the number of days of intake data per participant in the sample. *Vbetween*

is seen to represent the 'true' variance of the distribution of *usual* intakes.

5) The square roots of *Vbetween* and *Vobserved* were then taken to obtain their standard deviations

(*SDbetween* and *SDobserved*).

6) Each participant's mean intake was adjusted using the following formula: Adjusted intake =

[(participant's mean – group mean) x (*SDbetween/ SDobserved*)] + group mean.

7) For use in nutrient assessment, the adjusted nutrient intake variables were transformed back to their

original units, as applicable (Institute of Medicine, 2003).

ADDENDUM 3

Assessment of nutrient adequacy and the Estimated Average Requirement (EAR) cut-point

method

The Estimated Average Requirement (EAR) is the appropriate Dietary Reference Intake to use when assessing the *adequacy* of group intakes. The EAR is defined as the average daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group. Comparing the mean nutrient intake of a group either to the EAR or the Recommended Dietary Allowance (RDA) should not be used for assessment or to imply relative nutrient *adequacy* (Institute of Medicine, 2000).

In this study, the *EAR cut-point method* was used to assess *adequacy* nutrient intakes (Institute of Medicine, 2000). This was done in both groups, namely the group of adolescents without alcohol use disorders (non-AUDs group) and the group with alcohol use disorders (AUDs group).

When using the EAR cut-point method, the distribution of usual intakes (see Addendum 2) of the nutrient in the group must be used. If *observed* intake distributions are not correctly adjusted to obtain *usual* intake distributions, the prevalence of nutrient in*adequacy* will either be overestimated or underestimated (Institute of Medicine, 2000).

The EAR cut-point method examines the prevalence of nutrient in*adequacy* in groups by estimating the proportion of individuals in the group with *usual* intakes below the EAR (the median requirement) for a specific nutrient (Institute of Medicine, 2000, Beaton, 1994). This method does not require that the distribution of *usual* intakes in the group be normal and its performance does not depend on the shape of the distribution of *usual* intakes in the group (Institute of Medicine, 2000).

The EARs for 14 to 18 year olds were used for the specific genders for each nutrient (Institute of Medicine, 2000, Institute of Medicine, 2001, Institute of Medicine, 2002/2005, Institute of Medicine, 2011). In this study, the EAR cut-point method was applied to all nutrients assessed for adequacy, except for iron. One of the assumptions of the EAR cut-point method is that the distribution of requirements of

a nutrient be approximately symmetrical. As the requirement distribution for iron is skewed, the EAR cut-point method was not used to assess *adequacy* of iron intakes and the full probability approach (see Addendum 4) was used instead (Institute of Medicine, 2000). Due to the very high correlation between energy intakes and requirements, energy adequacy cannot be assessed using either the probability approach or the cut-point method (Institute of Medicine, 2000).

It is important to note that the differences in nutrient *adequacy* between groups cannot be assessed by comparing mean intakes (Barr et al., 2002, Institute of Medicine, 2000), since the prevalence of nutrient *inadequacy* does not depend on the mean intake but rather depends on the shape and variation of the *usual* intake distribution (Institute of Medicine, 2000).

Thus, mean intakes of nutrients in the groups were *not* compared (Barr et al., 2002) to examine differences in nutrient *adequacy* between the non-AUDs and AUDs groups and determine whether the intakes of one group were "better" or "worse" than the other. Mean nutrient intakes were simply compared to assess whether intakes were higher or lower between groups, when adjusting for confounders, in order to aid the interpretation and explanation of findings from the dietary intake and eating behaviour data in this study.

ADDENDUM 4

Assessment of adequacy of iron intake and the probability approach

The probability approach and not the cut-point method should be used to assess adequacy of iron intakes since the requirement distribution for iron is skewed (Institute of Medicine, 2000). Therefore, in this study, the probability approach was used to estimate the expected proportion of participants at risk of inadequate iron intakes in the non-AUDs and AUDs groups, using the *usual* intake distribution (Addendum 2) for iron (Institute of Medicine, 2000).

The probability approach is a statistical method that combines the distribution of requirements and the distribution of usual intakes in a group, in order to obtain an estimate of the expected proportion of individuals at risk for inadequacy (National Research Council, 1986). The concept is simply that at very low intakes the risk of inadequacy is high, whereas at very high intakes the risk of inadequacy is low or negligible. Thus, with information about the distribution of requirements in the group (median, variance, and shape), a value for risk of inadequacy can be assigned to each level of intake (Institute of Medicine, 2000).

For the probability approach, the requirement distributions for iron should be obtained from published tables (Murphy et al., 2006). The estimated percentiles of the distribution of iron requirements (males and females aged 14 to 18 years) at the various levels of intake from the United States Department of Agriculture's (USDA) Continuing Survey of Food Intakes By Individuals (CSFII) 1994–1996 (United States Department of Agriculture, 1998) were used in this study. The Estimated Average Requirement (EAR) and the Recommended Dietary Allowance for iron were derived from these estimated percentiles of the distribution of iron requirements, as the 50th and the 97.5[th] percentiles, respectively (Institute of Medicine, 2001).

As mentioned above, information on the distribution of requirements in the group can be used to assign a value for risk of inadequacy to each level of *usual* intake. In these USDA tables, a risk of 1.0 (100% probability) has been assigned to all *usual* intakes falling below the 2.5th percentile of requirement and a risk of zero (0% probability) has been assigned to all *usual* intakes falling above the 97.5th

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percentile of requirement. For ranges of *usual* intakes between these extremes, the probability of inadequacy is calculated as 100 minus the midpoint of the range of percentiles of requirement, which can then be converted to a risk by dividing by 100. For example (see Table 1, Column 1 to 4), the midpoint between the level of intake between the 2.5th and 5th percentile is 3.75 (2.5th+5th/2); 100 minus 3.75 equals a probability of 96.3 %; and if divided by 100 equals a risk of 0.96. Thus, if an individual's *usual* intake falls between the range of *usual* intakes associated with the requirement between the 2.5th and 5th percentiles, the individual's risk of inadequate iron intake will be 0.96. Since there is a range of *usual* intakes in a group, the prevalence of inadequacy, i.e. the average group risk, is estimated as the weighted average of the risks at each possible intake level (Institute of Medicine, 2001).

The probability method was applied in this study as follows:

1) The number of participants in the non-AUDs group with *usual* intakes in each of the levels of *usual* intake was determined, according to their gender (See Table 1, Column 5). This was then repeated for the AUDs group (See Table 1, Column 6).

2) The risk of inadequate intake at each level was multiplied by the number of participants in the non-AUDs group with *usual* intakes in that level's range to obtain the number in the non-AUDs group with inadequate intake at each intake level (See Table 1, Column 7). This was then repeated for the AUDs group (See Table 1, Column 8).

3) The total number of participants with inadequate intakes in the non-AUDs group and the AUDs group were then determined by summing the number of participants at each level. These totals expressed as a percentage of the total number of participants in each group (*n=80*) represent an estimation of the weighted average of the risks at each possible intake level, which equates to the prevalence of risk of inadequate iron intakes in the non-AUDs and AUDs groups (Institute of Medicine, 2001). The variances of these risks were calculated using the standard formula for the variance of a proportion.   Thus, as explained, the probability approach combined the two distributions, namely the requirement distribution, which provided the risk of inadequacy at each intake level, and the *usual* intake distribution, which provided the intake levels for the group and the frequency of each (Institute of Medicine, 2000).

For the probability method to perform well, little or no correlation should be present between intakes and requirements in the group (Institute of Medicine, 2000). The probability method does not require that the distribution of *usual* intakes in the group be normal and its performance does not depend on the shape of the distribution of *usual* intakes in the group (Institute of Medicine, 2000).

To **compare** the prevalence of risk of inadequate iron intakes in the non-AUDs and AUDs groups, the *usual* intake distribution for total iron was standardised to z-scores. The cumulative probabilities were then calculated from the z-scores and these probabilities were compared between groups.

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Table 1: Prevalence of risk of inadequate iron intakes in the non-AUDs (*n=80*) and AUDs (*n=80*) groups using the probability method [a]

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8
Percentiles of Requirement Distribution	Range of Usual Intake associated with Requirement Percentiles Males 14-18y (mg/d) [b]	Range of Usual Intake associated with Requirement Percentiles Females 14-18y (mg/d) [b]	Risk of Inadequate Intake associated with Requirement Percentiles [c]	Number in non-AUDs group with intake in range	Number in AUDs group with intake in range	Number in non-AUDs group with risk of inadequate intake	Number in AUDs group with risk of inadequate intake
<2.5	<5.06	<4.63	1	1	1	1	1
2.5-5	5.06-5.42	4.63-5.06	0.96	1	1	0.96	0.96
5-10	5.43-5.85	5.07-5.61	0.93	1	3	0.93	2.79
10-20	5.86-6.43	5.62-6.31	0.85	3	1	2.55	0.85
20-30	6.44-6.89	6.32-6.87	0.75	5	3	3.75	2.25
30-40	6.90-7.29	6.88-7.39	0.65	7	4	4.55	2.6
40-50	7.30-7.69	7.40-7.91	0.55	5	3	2.75	1.65
50-60	7.70-8.08	7.92-8.43	0.45	4	3	1.8	1.35
60-70	8.09-8.51	8.44-9.15	0.35	13	14	4.55	4.9
70-80	8.52-9.03	9.16-10.03	0.25	9	7	2.25	1.75
80-90	9.04-9.74	10.04-11.54	0.15	5	5	0.75	0.75
90-95	9.75-10.32	11.55-13.08	0.08	12	12	0.96	0.96
95-97.5	10.33-10.83	13.09-14.08	0.04	4	5	0.16	0.2
>97.5	>10.83	>14.08	0	10	18	0	0
			Totals	80	80	26.96	22.01
Prevalence of risk of inadequate intakes in groups [d]						**33.7% **** (SD 5.3)	**27.5% **** (SD 5.0)

Abbreviations: AUDs: alcohol use disorders; mg/d: milligrams per day

[a] Combines the distributions of requirements and intakes in a group to produce an estimate of the expected prevalence of risk for inadequate intakes (Institute of Medicine, 2000, National Research Council, 1986).

[b] Range of *usual* intake of iron associated with requirement percentiles in 14 to 18 year old males and females, based on an 18% bioavailability (United States Department of Agriculture, 1998). The Estimated Average Requirement (EAR) and the Recommended Dietary Allowance (RDA) for iron were derived from these estimated percentiles of the distribution of iron requirements, as the 50th and the 97.5th percentiles, respectively. EAR for iron for males is 7.7 mg/day and females is 7.9mg/day; RDA for iron for males is 11 mg/day and for females is 15 mg/day.

[c] Risk of inadequate intake is the probability that requirement is greater than the *usual* intake. A probability of 1.0 has been assigned to all *usual* intakes falling below the 2.5 percentile of requirement and a probability of zero has been assigned to all *usual* intakes falling above the 97.5 percentile of requirement.

[d] Prevalence of risk of inadequate intakes in each group is the number in each group with risk of inadequate intake expressed as a percentage of the total number of participants in each group (*n=80*), which is an estimation of the weighted average of the risks at each possible intake level. Variances calculated using the standard formula for the variance of a proportion

ADDENDUM 5

Assessment of nutrient adequacy and the Acceptable Macronutrient Distribution Ranges

(AMDRs)

The AMDRs are defined as range of intakes for a specific energy source of that is associated with reduced risk of chronic diseases while contributing adequate intakes of essential nutrients. Although mainly directed at individuals, the AMDRs also allow for assessment of groups and populations (Institute of Medicine, 2002/2005).

By ascertaining the proportion of the group that falls below, within, and above the AMDRs, it is possible to determine the proportion that is outside the range and to examine adherence to recommendations. If considerable proportions of the group fall outside the range, concern for potential adverse consequences could be increased (Institute of Medicine, 2002/2005).

The AMDRs for protein, fat and carbohydrates (4 to 18 years of age) (Institute of Medicine, 2002/2005) were used to estimate the adequacy of macronutrient intakes in the two groups using *usual* intake distributions. The frequencies in the two groups of percentage macronutrient intakes below, within and above these AMDRs for each macronutrient were determined and compared between groups.

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ADDENDUM 6

Assessment of nutrient excess and the Tolerable Upper Intake Levels (ULs)

The UL is defined as the highest average daily nutrient intake level likely to pose no risk of adverse health effects to nearly all individuals in the general population. As intake increases above the UL, the possible risk of adverse effects also increases (Institute of Medicine, 2000). *Usual* intake distributions permit the determination of the proportion of a group exceeding the UL and this proportion may be at risk of harmful effects on health (Institute of Medicine, 2000).

The ULs (14 to 18 years) (Institute of Medicine, 2000, Institute of Medicine, 2001, Institute of Medicine, 2004, Institute of Medicine, 2011) were used to estimate the prevalence of excessive nutrient intakes in the non-AUDs and AUDs groups. The frequencies in the two groups of nutrient intakes exceeding the ULs were determined and compared between groups.

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ADDENDUM 7: Questionnaires and Instruments

DEM – DEMOGRAPHIC QUESTIONNAIRE (participant self-report)

GENERAL INFORMATION

<table>
<tr><td>Full name:</td><td colspan="4"></td></tr>
<tr><td rowspan="2">How would you describe your race?</td><td colspan="4">1. Black   2. Coloured   3. White</td></tr>
<tr><td colspan="4">4. Asian   5. Other(specify):   6. Refuse to answer</td></tr>
<tr><td rowspan="5">Contact numbers:</td><td>Person</td><td>Home</td><td>Work</td><td>Cell</td></tr>
<tr><td>Self</td><td></td><td></td><td></td></tr>
<tr><td>Mother</td><td></td><td></td><td></td></tr>
<tr><td>Father</td><td></td><td></td><td></td></tr>
<tr><td>(Guardian)</td><td></td><td></td><td></td></tr>
<tr><td>Residential Address:</td><td colspan="4"></td></tr>
</table>

EDUCATION

Name and area of Current School:	School: Suburb / area:

RESIDENTIAL INFORMATION

<table>
<tr><td colspan="1">How long have you lived at your current address?</td><td></td></tr>
<tr><td>How would you describe your dwelling?</td><td>1. Shack   2. Wendy house or backyard dwelling
3. Tent or traditional dwelling   4. Flat / apartment
5. Town house / semi-detached house
6. Freestanding brick house 7. Other (specify):</td></tr>
<tr><td>Which of these items do you have in your home? (mark as many as necessary)</td><td>A. Tap water   B. Flush toilet inside home   C. Electricity
D. Telephone (landline) E. Television F. Computer   G. Car</td></tr>
<tr><td>How many people sleep in the same room with you at night when you are at home?</td><td>1. one   2. two   3. three   4. four
5. five   6. more than five   7. none</td></tr>
</table>

FAMILIAL INFORMATION

Who is your primary care-giver? **(Describe the relationship, e.g. mother, father, uncle etc.)**	
What is your relationship with your BIOLOGICAL MOTHER**?**	**1. Unknown 2.Known, but irregular contact** **3. Known and regular contact 4. Living with child** **5. Deceased**
How old is she? (If deceased, specify age and reason of death)	
What is your relationship with your BIOLOGICAL FATHER**?**	**1. Unknown 2.Known, but irregular contact** **3. Known and regular contact 4. Living with child** **5. Deceased**
How old is he? (If deceased, specify age and reason of death)	
What is your parents' marital status?	**1. married 2. co-habiting 3. widowed** **4. divorced & living apart 5. divorced & living together** **6. separated 7. remarried** **8. other (specify):**

Do you live with anyone that has a current alcohol problem or uses drugs?	**1. No**	**2. Yes**
	Specify relationship	**Specify substance/s abused**

Do you live with anyone that used to have an alcohol problem or used drugs in the past?	**1. No**	**2. Yes**
	Specify relationship	**Specify substance/s abused**

SEXUAL HISTORY:

GIRLS ONLY:	
How old were you when you had your first period?	
Have you ever been pregnant?	Yes No
Have you ever terminated a pregnancy?	Yes No
Have you had a child / children?	Yes No
BOYS ONLY:	
How old were you when your voice broke?	
Have you ever made someone pregnant?	Yes Don't know No
BOYS AND GIRLS:	
Have you ever had sex?	Yes No
Have you ever had sex without using a condom?	Yes No
Do you think it is important to use a condom when you have sex?	Yes No
Do you use any form of contraception?	1. None 2. Condom 3. Pill 4. Injection 5. Morning-after pill 6. Other (specify):
Are you waiting to have sex until you are older?	Yes No
Have you ever had any kind of sexual contact with anyone?	Yes No
Did you have sex before your 15th birthday?	Yes No
Have you ever been forced or pressured into having sex when you didn't want to?	Yes No
Have you ever been high on drugs or alcohol when you had sex with someone?	Yes No
During the last 12 months, have you had a discharge from, or sores on your private parts?	Yes No
Have you ever had sex with someone you know or suspect has HIV or AIDS?	Yes No
Have you ever been tested for HIV?	Yes No
When were you last tested for HIV and what were the results?	Date: Result: Positive Negative
Have you had sex with two or more people in the past 3 months?	Yes No
Have you ever had anal sex (this means the penis enters the anus)?	Yes No
Did you use a condom the last time you had sex?	Yes No
When you have sex, do you talk to your partner about using a condom?	Yes No
Have you ever been sexually involved with someone who is more than 5 years older than you?	Yes No
Have you ever had sex with someone who is the same gender as you?	Yes No
Have you ever had sex with someone who has sex with both males and females?	Yes No
Have any of your closest friends had sex?	Yes No

PAR – PARENT INTERVIEW (CLINICIAN ADMINISTERED or SELF-REPORT)

PARENT INFORMATION:

Full name:	
Relationship to child:	1. Mother 2. Father 3. Grandmother 4. Grandfather 5. Guardian 6. Other (specify):

Contact numbers:	Home:	Work:	Cell:

Marital status:	1. married 2. co-habiting 3. widowed 4. divorced & living apart 5. divorced & living together 6. separated 7. remarried 8. other (specify):

Combined household income (before tax deductions) **PER YEAR**	1. Less than R10 000 2. R10 000 – 20 000 3. R20 000 – 40 000 4. R40 000 – 60 000 5. R60 000 – R100 000 6. More than R100 000

PARENTAL EMPLOYMENT:

What do you do for a living? (e.g. teacher, professor, unemployed, student)	
What does your child's other parent / caregiver do for a living?	

DEVELOPMENTAL MILESTONES (CHILD)

How old was your child when they did the following tasks for the first time?		
sitting	5 – 8 months	older than 9 months
crawling	7 – 9 months	older than 10 months
walking	11 – 15 months	older than 16 months
first words spoken	10 – 15 months	older than 16 months
speaking in short sentences	18 – 24 months	older than 2 years
speaking in full sentences	3 – 4 years	older than 4 years

PARENTAL EDUCATION:

Highest level of education reached?	Mother	Father	Guardian
Mark one response for each person as follows:			
1. 0 years (No Grades / Standards) = No formal education (never went to school)	1.	1.	1.
2. 1-6 years (Grades 1-6 / Sub A-Std 4) = Less than primary education (didn't complete primary school)	2.	2.	2.
3. 7 years (Grade 7 / Std 5) = Primary education (completed primary school)	3.	3.	3.
4. 8-11 years (Grades 8-11 / Stds 6-9) = Some secondary education (didn't complete high school)	4.	4.	4.
5. 12 years (Grade 12 / Std 10) = Secondary education (completed senior school)	5.	5.	5.
6. 13+ years = Tertiary education (completed university / technikon / college)	6.	6.	6.
7. Don't know	7.	7.	7.

ALCOHOL USE: Time-Line Follow Back Data	**Study #**		**Test Age**	......y ......m

Drinking Status: 1. Non-Drinker   2. Occasional/Light Drinker   3. Alcohol Abuse (DSM-IV) 4. Alcohol Dependence (DSM-IV)

Information for **OCCASIONAL** and **NON-DRINKERS** only		Information for **ALCOHOL USE DISORDERS** only	
Drinking onset age (first incidence)	1. never drank 2. ...... years	**Drinking onset age** (first incidence)	...... years
Lifetime dosage (total units consumed)		**Regular drinking onset age**	...... y ...... m
Age of first intoxication	...... y ...... m	**Age of first intoxication**	...... y ...... m
Alcohol type	1. beer 2. wine 3. liquor	**Lifetime dosage** (total units consumed)	*f

AUD'S: phases of regular drinking (including phases of cessation/sobriety)	**1**	**2**	**3**	**4**	**Total/ Ave**
age range (younger to older)	......y ......m to ......y ......m	......y ......m to ......y ......m	......y ......m to ......y ......m	......y ......m to ......y ......m	
duration (months)	*f	*f	*f	*f	*f
frequency (days per month)					
average quantity (per day)					
maximum quantity (per day)					
Drinking style: 1. Non-drinker 2. Occasional (<15 days per month 3. Weekends only 4. Binge (+3 consecutive days) 5. Frequent (>15 days per month)	1. 2. 3. 4. 5.	1. 2. 3. 4. 5.	1. 2. 3. 4. 5.	1. 2. 3. 4. 5.	
Alcohol type: 1. beer 2. wine 3. liquor	1. 2. 3.	1. 2. 3.	1. 2. 3.	1. 2. 3.	
Associated life **event**(s)/change(s) [**+** or **-**]: (e.g. 8+) 1. family 2. work 3. school 4. medical 5. residence 6. legal 7. financial 8. peer group 9. drug use 10. treatment 11. death 12. emotional					
Context % (per typical drinking day)	alone ....% with others ....%	alone ....% with others ....%	alone ....% with others ....%	alone ....% with others ....%	
Time % (per typical drinking day)	morning ......% afternoon ......% evening ...... %	morning ......% afternoon ......% evening ...... %	morning ......% afternoon ......% evening ...... %	morning ......% afternoon ......% evening ...... %	

TOBACCO USE: Time-Line Follow Back Data	Study #		Test Age	......y ......m

1. NON-SMOKERS (never smoked) or 2. OCCASIONAL/LIGHT SMOKERS (<100 cigarettes in lifetime)		**2. REGULAR SMOKERS (>100 lifetime dose)**	
Smoking onset age (first incidence of smoking)	1. never smoked 2. ...... years	**Smoking onset age** (first incidence of smoking)	...... years
Lifetime dosage (total cigarettes smoked)		**Regular smoking onset age** (1 cigarette per day)	...... y ...... m
Tobacco type	1. cigarette 2. cigar 3. pipe 4. chew	**Lifetime dosage** (total cigarettes smoked)	*f

REGULAR SMOKERS: phases of regular smoking (including phases of cessation)	1	2	3	4	Total/ Ave
age range (younger to older)	......y ......m to ......y ......m	......y ......m to ......y ......m	......y ......m to ......y ......m	......y ......m to ......y ......m	
duration (months)	*f	*f	*f	*f	*f
frequency (days per month)					
average quantity (per day)					
maximum quantity (per day)					
Tobacco type: 1. cigarette 2. cigar 3. pipe 4. chew tobacco	1. 2. 3. 4.	1. 2. 3. 4.	1. 2. 3. 4.	1. 2. 3. 4.	
Associated life **event**(s)/change(s) [+ or -]: (e.g. 8+) 1. family 2. work 3. school 4. medical 5. residence 6. legal 7. financial 8. peer group 9. drug use 10. treatment 11. death 12. emotional					
Context % (per typical smoking day)	alone ....% with others ....%	alone ....% with others ....%	alone ....% with others ....%	alone ....% with others ....%	
Time % (per typical smoking day)	morning ......% afternoon ...... % evening ...... %	morning ......% afternoon ...... % evening ...... %	morning ......% afternoon ...... % evening ...... %	morning ......% afternoon ...... % evening ...... %	

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| **DRUG USE: Time-Line Follow Back** | **Study #** | | **Test Age** | ......y ......m |

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1. CANNABIS
a) Never Used   b) Occasional/Light User

Onset age (first incidence of cannabis use)	1. never used 2. ...... years
Lifetime dosage (total)	

2. METHAMPHETAMINE
a) Never Used   b) Occasional/Light User

Onset age (first incidence of methamphetamine use)	1. never used 2. ...... years
Lifetime dosage (total)	

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3. OTHER DRUGS (specify.......................................)
a) Never Used   b) Occasional/Light User

Onset age (first incidence)	1. never used 2. ...... years
Lifetime dosage (total)	

4. OTHER DRUGS (specify.......................................)
a) Never Used   b) Occasional/Light User

Onset age (first incidence)	1. never used 2. ...... years
Lifetime dosage (total)	

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5. OTHER DRUGS (specify.......................................)
a) Never Used   b) Occasional/Light User

Onset age (first incidence)	1. never used 2. ...... years
Lifetime dosage (total)	

6. OTHER DRUGS (specify.......................................)
a) Never Used   b) Occasional/Light User

Onset age (first incidence)	1. never used 2. ...... years
Lifetime dosage (total)	

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7. OTHER DRUGS (specify.......................................)
a) Never Used   b) Occasional/Light User

Onset age (first incidence)	1. never used 2. ...... years
Lifetime dosage (total)	

8. OTHER DRUGS (specify.......................................)
a) Never Used   b) Occasional/Light User

Onset age (first incidence)	1. never used 2. ...... years
Lifetime dosage (total)	

Dietary Intake: 24-HOUR RECALL QUESTIONNAIRE

Researcher:………………………………………   Contact no:………………..

Subject code:……………………………………….   Date of this report:…………………………

Food Item and Description	Household Measure	Gram	Code

PHYSICAL ACTIVITY / INACTIVITY

Researcher:………………………………………

Contact no:………………..

Subject code:……………………………………….

Date of this report:…………………………

PHYSICAL ACTIVITY RELATED INFORMATION			
Do you participate in organized sport (school or club)? 1. Yes 2. No			
If yes, which sport, how often and duration per occasion			
Sport	Times/week (A)	Duration/ occasion (B)	Total duration AxB
Rugby			
Soccer			
Netball			
Hockey			
Other			
Do you participate in recreational sport e.g. playing soccer, running around, netball, games with friends after school? 1. Yes 2. No			
If yes:			
Times/week (A)		Duration/ occasion (B)	Total duration A x B

Do you watch **television** regularly? 1. Yes 2. No		
If yes, how often and duration per occasion		
Times/week (A)	Duration/ occasion (B)	Total duration AxB
Do you play **computer** games or use a computer regularly? 1. Yes 2. No		
If yes, how often and duration per occasion		
Times/week (A)	Duration/ occasion (B)	Total duration A x B

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Dietary Intake: INDICATOR FOODS

Researcher:………………………………………… Contact no:………………..

Subject code:……………………………………. Date of this report:…………………………

Instructions to Interviewer:
Go through the list of food items on the next two pages and mark those foods that are eaten by the interviewee **more often than once a month**. If the food item is eaten (marked *YES*), fill in how many **times per week OR** how many **times per month** it is usually eaten.
Please note: Fill in the times per week **OR** times per month column, **not both**.
If the food item is eaten every day, fill in a "7" in the times per week column.

Food Item	No	Yes	Times per week	OR Times per month
Meats, red				
Meats, processed				
Meats, tinned				
Chicken, with skin				
Fish, tinned or smoked				
Fish, fresh				
Eggs				
Milk/sour milk, yoghurt				
Cheese, yellow				
Legumes (kidney beans, lentils)				
Bread, white				
Bread, brown				
Breakfast cereals (ready to use)				
Breakfast cereals/porridge, to be cooked				
Rice, pap, pasta, samp, potato (mash/ boiled)				
Oranges and naartjies				
Apples, bananas, pears				
Orange or yellow vegetables (sweet potato, pumpkin, butternut, carrots)				
Green vegetables (spinach, peas, beans broccoli)				
Mixed vegetables				
Cabbage, cauliflower, lettuce				
Tomato (raw or cooked)				
Margarine/butter				
Peanut butter/ peanuts				
Fried foods, potato chips				
Fried foods, other (fat cakes, fish, chicken)				
Pies, sausage rolls, samoosas				
Meats, organ (liver, kidneys)				
Sugar				
Chocolate				
Sweets (boiled, jelly, lollipops)				
Cake, biscuits, doughnuts				
Juice, fruit				
Juice, other (carbonated, concentrate mixed with water)				
Crisps (potato-based, maize-based, wheat-based)				
Take outs (e.g. KFC, McDonalds)				
Jam, syrup, honey				

Dietary Intake: FRUIT and VEGETABLES; MEAL PATTERNS

Researcher:…………………………………………

Contact no:………………..

Subject code:…………………………………….

Date of this report:…………………………

FRUIT and VEGETABLES

Instructions to Interviewer: After all 24HR questionnaires have been completed, look at the fruit and vegetable intake over the 3 recalls.

If no fruit intake was reported on one or more of the three 24-hour recall days, ask the following question (only select the single most important reason):

1.	Why do you not eat fruit more than once per day?		
1.1	Not available at home	Yes	No
1.2	Not for sale in the area	Yes	No
1.3	Too expensive	Yes	No
1.4	Do not like fruit	Yes	No
1.5	Other, specify…	Yes	No
1.6	Not applicable, does eat fruit more than once per day	Yes	No

If no vegetable intake was reported on one or more of the three 24-hour recall days, ask the following question (only select the single most important reason):

2.	Why do you not eat any vegetables more than once per day?		
2.1	Not available at home	Yes	No
2.2	Not for sale in the area	Yes	No
2.3	Too expensive	Yes	No
2.4	Do not like vegetables	Yes	No
2.5	Other, specify …	Yes	No
2.6	Not applicable, does eat vegetables more than once per day	Yes	No

MEAL PATTERNS

3. When are meals usually eaten and when are snacks usually eaten on school days?			
3.1	Snack at home before breakfast	Yes	No
3.2	Meal at breakfast at home	Yes	No
3.3	Snack before school	Yes	No
3.4	Snack at first break	Yes	No
3.4	Snack at second break	Yes	No
3.5	Snack on the way home, after school	Yes	No
3.6	Meal at lunch time (home, after care, friend)	Yes	No
3.7	Snack during early afternoon	Yes	No
3.8	Snack during late afternoon	Yes	No
3.9	Meal at supper at home/friend	Yes	No
3.10	Snack after supper	Yes	No

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