Descriptive epidemiological study of head and neck cancers at a single institution in Southern Africa.

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Abstract

Head and Neck Cancers (HNCs) constitute a major public health concern worldwide. The incidence is approximately two times more in less-developed regions as compared to more developed regions. The estimated incidence in sub-Saharan Africa is 27593 per 100000 with a cumulative risk of 0.66. We evaluated patient demographics, risk factors, tumours characteristics, prognostic factors, disease stage, treatment intent and treatment modality in a cohort of patients with HNC in Cape Town, SA.

Records of all HNC patients that presented to Tygerberg Hospital oncology department between 1 January 2015 and 31 December 2017 were reviewed. The following variables were described: patient demographics, which include age, sex, HIV status, and socio-economic status as well as tumour characteristics, risk factors, treatment intent and treatment modalities.

Data was collected from 854 patients seen between 2015 and 2017. There were 603 (71%) male and 251 (29%) female. The male to female ratio was 2.4:1. The age range was 10-89 years (median age 58 years). Smoking was a risk factor in 737 (86.3%) and alcohol in 634 (74.2%) of patients. Of the 167 patients with oropharyngeal primaries, 16 (9.58%) patients had p16 positive, 78 (46.70%) were p16 negative and the p16 status was unknown in 73 (43.7%). The most common site was the oral cavity (n=320) and the most common sub-site was the anterior tongue (n=137). Eleven patients had two separate primaries at the time of diagnosis. In total, 466 patients (53.87%) presented with locally advanced, stage IVA disease.

The median age of diagnosis, the most predominate primary site; histological subtype and stage at presentation were consistent with that reported in the literature. We have demonstrated that the majority of patients present at a late stage, with locally advanced disease. This together with the predominate risk factors of smoking and alcohol consumption is a potential target for health campaigns and awareness programmes. This cohort will be followed up for treatment outcomes and survival rates.

Opsomming

Kop- en-nek kankers (KNK's) is 'n groot probleem vir die openbare gesondheid sektor. Die voorkoms van KNK's is ongeveer twee keer meer in minder gegoede areas in vergelyking met meer ontwikkelde streke. Die geraamde voorkoms in sub-Sahara Afrika is 27 593 per 100 000 individue met 'n kummulatiewe risiko van 0,66. Ons het die pasiënt kenmerke , risiko faktore, gewas kenmerke, prognostiese faktore, siekte stadium,en behandelings doelwitte asook die behandelings modaliteit in 'n groep pasiënte wat met KNK's gediagnostiseer was geëvalueer.

Kliniese verslae van alle KNK's-pasiënte wat vanaf 1 Januarie 2015 tot 31 Desember 2017 by Tygerberg-hospitaal se onkologie-afdeling gepresenteer het, is nagegaan. Die volgende veranderlikes is beskryf: pasiënt kenmerke, ouderdom, geslag, MIV- en sosio-ekonomiese status, sowel as die kanker gewas-karaktertrekke, risiko faktore, behandelings-doelwitte en modaliteit is geëvalueer.

Kliniese inligting van 854 pasiënte, is nagegaan. Daar was 71% manlike en 29% vroulike pasiënte. Die verhouding tussen mans en vroue was 2.4:1. Die groep se ouderdom verspreiding was 10-89 jaar, met 'n gemiddelde ouderdom van 58 jaar. Rook was 'n risiko faktor in 86,3% en alkohol in 74,2% van die pasiënte.

In 167 pasiënte met primêre orofaryngeale kanker, was 9,58% pasiënte p16 positief, 46,70% was p16 negatief en in 43,7% van die pasiënte was die p16-status onbekend. Die oorwegende aangetasde area was die mondholte (n = 320) met die algemeenste sub-lokasie die anterior gedeelte van die tong (n = 137). Elf pasiënte het by hul aanvanklike presentasie, gepresenteer met twee afsonderlike primêre kankers. In totaal het 53,87% pasiënte gepresenteer met lokaal gevorderde stadium IVA-siekte.

Die gemidelde ouderdom by diagnose, die oorheersende primêre area; histologiese subtipe en stadium tydens aanvanklike presentasie was in ooreenstemming met wat in die Internationale literatuur gemeld word. Ons het ook getoon dat die meerderheid van pasiënte presenteer met lokaal gevorderde siekte en met die risiko faktore van rook en alkohol misbruik is dit 'n potensiële teiken vir gesondheids veldtogte en bewusmakings programme. Hierdie groep word ook nog tans opgevolg vir behandelings uitkomste en oorlewing syfers.

Descriptive epidemiological study of head and neck cancers at a single institution in Southern Africa.

Table of contents

Descriptive epidemiological study of head and neck cancers at a single institution in Southern Africa.

Introduction.

Head and Neck Cancers (HNCs) constitute a major public health concern worldwide. There has been a significant increase in the global incidence of HNCs, which is increasing sharply in developing countries. The incidence is approximately two times more in less-developed regions as compared to more developed regions [(2)].

The worldwide incidence is greater than 550000 cases with approximately 350000 deaths per annum [(2)]. In 2017, about 63030 new cases of oral cavity, pharyngeal and laryngeal cancer will occur in the USA (about 3.7% of all new cases). An estimated 13360 deaths from HNCs will occur during the same period [(2)].

The estimated incidence in sub-Saharan Africa is 27593 per 100000 with a cumulative risk of 0.66 [(1)] . According to the 2014 South African National Cancer Registry, the age-standardised ratios were 2.01, 1.71, 1.56, 2.64, 0.36 and 0.13 per 100000 per year for males, for mouth, tongue, nasopharynx, larynx, lip and gum respectively and 0.80, 0.46, 0.42, 0.2, 0.15 and 0.09 for females [(3)].

The most common histological type is squamous cell carcinoma and its variants, which accounts for about 90% of all head and neck malignancies. Other histologic types include adenocarcinoma, NOS (Not Otherwise Specified), adenoid cystic carcinoma, mucoepidermoid carcinoma, melanoma and small cell neuroendrocrine carcinoma.

Over 50% of HNCs occur in men [(4)]. The male to female ratio is different for each sub site. The male to female ratio is 3:1 for oral cavity and pharyngeal cancers. Males are also more likely to have HPV-associated cancers [(4)].

The incidence of HNCs increases with age, with most patients being between the ages of 50-70. [(4)]. Younger patients can also develop HNCs. The younger patients are more likely to be of female gender with no known risk factors[(4)]. Younger patients often present with more advanced disease, which may be due to more aggressive nature of the disease or delay in diagnosis, and as a result have a poorer prognosis.

Approximately 30% of patients present with localised disease, 47% with regional disease and 18% with distant or metastatic disease [2]. The survival decreases with increasing stage of disease. The 5-year overall survival is 83% for localised disease, 63% for regional disease and 38% for distant disease [2].

Predictors of overall survival include older age, higher tumour stage and high alcohol consumption [8].

There are numerous, well-established risk factors for the development of HNCs. These include tobacco, alcohol, high-risk human papilloma virus (HR-HPV) exposure, Epstein Barr virus (EBV) infection, dental factors such as poor oral health, dietary deficiencies and betel leaf chewing. HR-HPV status is an important risk factor and prognostic factor in oropharyngeal lesions. Other factors, increasing the risk, include occupational exposure (wood dust and nickel exposure), sun exposure (for lip squamous cell carcinoma), smokeless tobacco, cigars and marijuana [4]. Chronic exposure of the aero-digestive tract to these factors can result in the development of pre-malignant lesions of the mucosa, which can ultimately lead to invasive malignancy.

Currently there is limited data regarding epidemiological trends of HNCs in Southern Africa. The aim of the current study was to evaluate and describe patient demographics, risk factors, tumours characteristics, prognostic factors, disease stage, treatment intent and treatment modality, at a single institution in Southern Africa. This information could be used to promote awareness of HNCs and support disease prevention programmes.

Methods and materials

This retrospective cross-sectional study was conducted at Tygerberg Hospital (TBH) oncology department, Western Cape, South Africa. Ethics approval was obtained from the University of Stellenbosch Health Research Ethics Committee (S18/08/172) as well as Tygerberg Hospital.

Records of all patients that presented between 1 January 2015 and 31 December 2017 were reviewed. Variables analysed were age, sex, HIV status, the Eastern Cooperative Oncology group (ECOG) performance status and socio-economic status.

The uniform patient fee schedule (UPFS) was used as a surrogate for socioeconomic status. This allocated category depends on the individual's/household's income per annum (in South African rands/Euros), as shown in appendix 1. Tumours were classified according to anatomical site. Staging was done according to the American Joint Committee on Cancer (AJCC) TNM 7th edition.

Treatment intent was described as radical or palliative. Radical treatment modalities consisted of surgery, chemotherapy or radiation therapy alone or in combination. Palliative treatment modalities consisted of chemotherapy, radiotherapy and/or best supportive care. Surgery is seldom used as a treatment modality in patients with palliative intent.

Data was collected from routine patient files, and entered into a customised data collection sheet. Data from the data collection sheets was entered into Microsoft Excel 2013. Statistical analysis was performed using Microsoft Excel.

Results

Data was collected from 854 patients seen between 2015 and 2017, with 865 tumours being reported. There were 603 (71%) males and 251 (29%) females. The male to female ratio was 2.4:1. The age range was 10-89 years (median age 58 years). Table 1 shows the distribution of patients for each age group.

Table 1. Age distribution of head and neck cancer patients

Age group	Number of patients (%)
≤ 30	15 (1.76)
31-40	20 (2.34)
41-50	140 (16.39)
51-60	331 (38.76)
61-70	246 (28.81)
71-80	82 (9.60)
>80	20 (2.34)

Smoking was a risk factor in 737 (86.3%), alcohol in 634 (74.2%) and both in 620 (72.6%) of patients. Fifty-six (9%) were HIV positive, 721 (84%) were negative and 77 (7%) had unknown HIV status.

The ECOG performance status was recorded as 0 in 5 (0.59%), one in 460 (53.86%), two in 232 (27.17%), three in 128 (14.89%), four in 27 (3.16%) and unknown in two (0.23%) patients.

Table 2 shows uniform patient fees schedule (UPFS), which is a surrogate for the socio-economic status of patients. The vast majority of patients had no reported income.

Table 2. Socio-economic status of head and neck cancer patients.

UPFS	Number of patients (%)
0	339 (39.70)
1	403 (47.19)
2	45 (5.27)
3	20 (2.34)
Medical aid	24 (2.81)
Unknown	23 (2.69)

The most common site was the oral cavity (n=320) followed by the larynx (n= 188) and the oropharynx (n=167). The most common sub-site was the anterior tongue (n=137) followed by the supraglottic larynx (n=98). Eleven patients had two separate primaries at the time of diagnosis. Appendix 2 shows the distribution of disease according to anatomical site.

The most predominate histological type was squamous cell carcinoma (SCC), which accounted for 791 (92.6%) of all cases. In patients who had two synchronous primaries, both primaries were found to be SCCs.

There were 174 (20.37%) grade I or well differentiated SCCs, 409 (47.90%) grade II or moderately differentiated SCCs, 58 (6.79%) grade III or poorly differentiated SCCs and 150 (17.56%) SCCs with unknown histological grade.

Of the 167 patients with oropharyngeal primaries, 16 (9.58%) patients had p16 positive SCCs (p16 antibody showing nuclear and cytoplasmic positivity in more than 70% of the tumour cells), 78 (46.70%) were p16 negative and the p16 status was unknown in 73 (43.7%). Three (18.75%) of the p16 positive oropharyngeal lesions were HPV-DNA positive using Polymerase Chain Reaction (PCR).

The majority of patients presented with locally advanced disease, 466 (53.87%) had stage IVA disease at presentation. Eight patients had two primaries at the time of diagnosis and both of these were stage IVA. Patients with two primaries had each primary staged separately. Distant metastases were diagnosed in 53 patients, of which 35 had lung metastasis, 10 had multiple sites, two presented with bone metastasis and six patients had other sites for distant disease. Table 3 shows the sub-site distribution according to the TNM stage grouping.

Table 3. The sub-site distribution according to the TNM stage grouping. Number of patients n=854. Number of tumours n=865.

Stage grouping	Anatomical site	Number of tumours (%)
I	Oral cavity	34 (3.93)
	Larynx	23 (2.66)
	Other	5 (0.58)
II	Oral cavity	24 (2.81)
	Larynx	13 (1.52)
	Oropharynx	8 (0.94)
	Other	8 (0.94)
III	Larynx	33 (3.86)
	Oral cavity	20 (2.34)
	Oropharynx	18 (2.10)
	Nasopharynx	8 (0.94)
	Other	13 (1.52)
IVA	Oral cavity	207 (24.24)
	Oropharynx	97 (11.36)
	Larynx	93 (10.89)
	Hypopharynx	27 (3.16)
	Salivary gland	14 (1.64)
	Sinuses	14 (1.64)
	Other	22 (2.58)

IVB	Oropharynx	28 (3.28)
	Oral cavity	25 (2.92)
	Hypopharynx	16 (1.87)
	Larynx	11 (1.29)
	Sinuses	10 (1.17)
	Other	22 (2.58)
IVC	Larynx	14 (1.64)
	Oropharynx	11 (1.29)
	Unknown primary	8 (0.94)
	Hypopharynx	6 (0.70)
	Oral cavity	5 (0.58)
	Other	9 (1.05)
IV	Sinuses	3 (0.35)
	Base of tongue	1 (0.12)
	Other	3 (0.35)
Unstaged	Oral cavity	5 (0.58)
	Oropharynx	3 (0.35)
	Other	4 (0.47)

Four hundred and forty nine (52.58%) patients were treated with radical/curative intent and 405 (47.42%) received palliative treatment. Radical treatment modalities consisted of surgery, radiotherapy and chemotherapy, alone or in combination. Palliative treatment consisted of surgery, radiotherapy, chemotherapy, combined radiotherapy and chemotherapy or best supportive care alone. The radical treatment group one patient had surgery followed by definitive chemoradiation and one patient only received induction chemotherapy. Four of the 11 patients with second primaries were treated with palliative intent. Table 4 shows the distribution of various treatment modalities, according to treatment intent.

Table 4. Treatment modalities

Treatment intent	Treatment modality	Number of patients (%)
Radical	Surgery	325 (38.06)
	Radiotherapy	32 (3.75)
	Adjuvant radiotherapy	140 (16.39)
	Adjuvant chemoradiation	56 (6.56)
	Definitive chemoradiation	93 (10.89)
	Neoadjuvant/induction chemotherapy	31 (3.63)
Palliative	Surgery	1 (0.12)
	Radiotherapy	310 (36.30)
	Chemotherapy	11 (1.29)
	Chemotherapy and radiotherapy	4 (0.47)
	Best supportive care	87 (10.19)

Discussion

HNCs constitute a major public health concern worldwide. There has been a significant increase in the global incidence of HNCs, which is increasing sharply in developing countries [(1)]. Studies from South America and West Africa have shown a similar burden of disease [(11, 27, 28)]. Currently there is limited data regarding epidemiological trends of HNCs in Southern Africa. The aim of the current study was to evaluate and describe patient demographics, risk factors, tumours characteristics, prognostic factors, disease stage, treatment intent and treatment modality at a single institution in Southern Africa, and compare them to reported international trends. This information could be used to promote awareness of HNCs and support disease prevention programmes.

Eight hundred and fifty four patients were diagnosed with HNCs between 2015 and 2017, 12.7% of all patients seen at the Radiation Oncology Department at Tygerberg Hospital during this period.

The median age in this cohort was 58 years, with most patients being between the ages of 51 and 70 years, similar to the data reported in literature [4]. Over 70% of patients were males, consistent with the existing reports that men are two to three times more likely to develop HNC [4]. The male: female ratio was 2.4:1; globally this ratio varies between 2:1 to 4:1. [18]

Smoking was a risk factor in 737 of the subjects (86.3%), and alcohol in 634 (74.2%). Both smoking and alcohol were co-risk factors in 620 (72.6%) of the patients. Eleven (50%) of the patients with HPV positive tumours also had both smoking and alcohol as risk factors. Tobacco smoking and alcohol consumption are well-established major risk factors for HNCs and a synergistic effect of these two factors has been consistently reported [19].

Fifty-six (9%) patients were HIV positive, 721 (84%) were HIV negative and 77 (7%) had unknown HIV status. The HIV prevalence in the Western Cape was 12.6% in 2017. The South African National HIV Prevalence, Incidence and Behaviour Survey in 2012 reported an HIV prevalence of 7.6% in individuals over 50 years of age [29]. The prevalence of HIV in our patient group, with a median age of 58, is similar that of the nationwide prevalence in over 50 year olds. HIV infection increases susceptibility to opportunistic infections and virus-induced cancers, however, the exact mechanism of HIV promoted carcinogenesis is not known [20].

According to the 2011 South African census, low-income households are classified as those with a combined annual household income of below R19200. In this study, 56% of the patients fall into the low-income category. Studies have shown an increased risk of HNCs in individuals of lower socioeconomic status, even after controlling for other risk factors such as smoking and alcohol consumption [21, 22]. In addition due to the structure of health care in South Africa the number of patients with low-income will be higher in this centre.

The most common anatomical site in this study was the oral cavity (320, 37%), followed by the larynx (188, 21.73%) and then the oropharynx (167, 19.31%). The most common sub-site was the anterior tongue, accounting for 15.84% (137) of the cases, followed by supraglottis 11.33% (98) and the glottis 10.40% (90), in descending order of frequency. The Surveillance, Epidemiology, and End Results [SEER] Programme reports that the commonest site for HNC is the oral tongue followed by the larynx [14].

Field cancerization describes the presence of premalignant fields surrounding the primary tumour and has been related to the high rate of local recurrence in HNCs as well as the development of synchronous primaries [23]. Synchronous cancer is defined as two or more neoplasms identified simultaneously in the same patient. It is estimated that one to six percent of patients diagnosed with SCC of head and neck will have a synchronous primary in the head and neck region [24]. In this study eleven (1.3%) presented with a synchronous primary in the head and neck region.

Amongst HNCs diagnosed, the most predominate histological type was SCC, which accounted for 791 (92.6%) of all cases. This is consistent with the incidence of SCC in the head and neck region, reported in the literature.

ICON-S was a multicentre cohort study conducted in Europe and North America; they found 73.26% of patients had HPV-positive oropharyngeal SCC [25]. In this study, sixteen (9.58%) of oropharyngeal lesions were HPV-positive. Due to the large number of oropharyngeal primaries with unknown HPV status, we are unable to draw conclusions regarding the overall incidence. The large percentage of oropharyngeal lesions with unknown p16 status is due to the fact that p16 has only become a routine test in recent years. The incidence of oropharyngeal cancer in males younger than 60 years of age is increasing, whereas cancers of the oral cavity and SCC of the lung are declining in incidence. This contrast suggests an aetiology other than tobacco smoking in this patient group. In females, all three cancers are increasing in incidence, which indicates smoking as the major etiological factor [26].

According to the Surveillance, Epidemiology, and End Results (SEER) database, in the United States 42-62% of patients with HNCs presented with locally advanced disease and 16-27% with distant metastases[2]. An epidemiological review of head and neck patients at a university hospital in Brazil reported that 47.8% of patients had T3/T4 disease and 31.9% had node positive disease [11]. In the current study, a significant number of patients presented with locally advanced disease, 466 (53.87%), consistent with the data from the SEER database. The incidence of distant metastases was 6.21%, which is lower than that of patients presenting in the United States.

The treatment intent and modality offered to patients depends on multiple factors, i.e. stage at presentation, performance status, co-morbidities, social circumstances as well as patient's wishes. In our patient group, 449 (52.6%) patients had treatment with radical intent and 405 (47.4%) with palliative intent. The majority of patients in the radical intent group had surgery

(72.4%) and approximately the same proportion of patients received radiotherapy as part of their treatment. Two hundred and twenty six patients (50.3%) received combined modality, including surgery, chemotherapy and radiotherapy.

Of the patients that received palliative intent, 76.5% received radiotherapy and 21.5% were not fit for any treatment and received medical palliation and best supportive care. Just less than half of the patients were for palliative intent; this could be due to the late stage at presentation. The latter could be attributed to poor socio-economic status, lack of knowledge and understanding, problems accessing the health services and possible other unknown factors i.e. genetic factors in this patient population.

Conclusion

In conclusion, the epidemiological factors described in this study of HNC patients in a tertiary hospital in Southern Africa (median age of diagnosis, the most predominate primary site, histological type and stage at presentation) were consistent with those reported in the. We have demonstrated that the majority of patients present at a late stage, with locally advanced disease. This together with the predominate risk factors of smoking and alcohol consumption is a potential target for health campaigns and awareness programmes. This cohort will be followed up for treatment outcomes and survival rates.

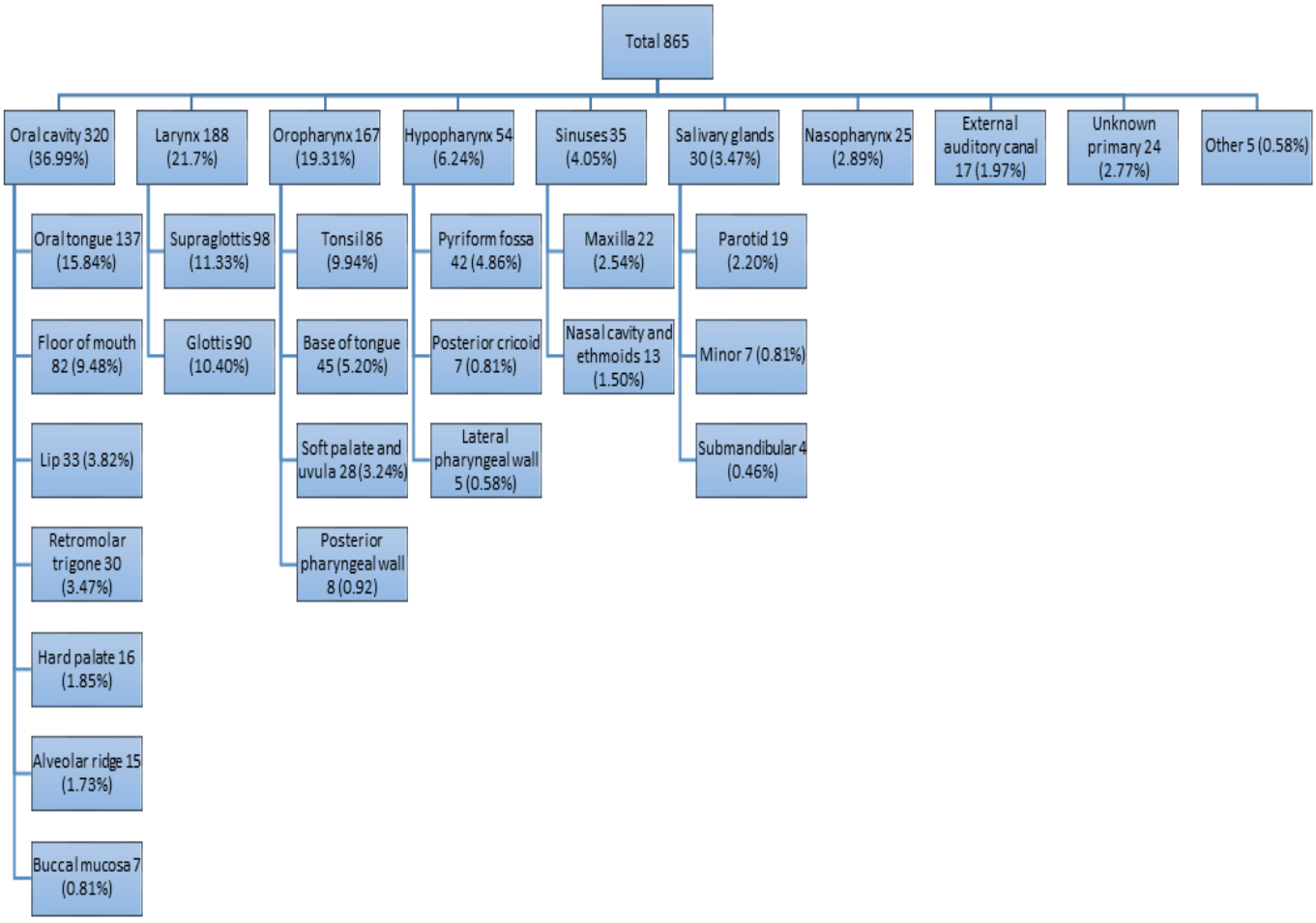
Appendix 1.

Uniform patient fee schedule

Tariff category	Household gross income per annum (01/02/2001-31/03/2017)	Household gross income per annum (from 01/04/2017)	Single without dependents gross income per annum (01/02/2001-31/03/2017)	Single without dependents gross income per annum (from 01/04/2017)
H0- patients under the age of 18, pensioners and the unemployed				
H1	Less than R50 000(€3200)	Less than R100000 (€6400)	Less than R36000 (€2200)	Less than R70000 (€4450)
H2	More than or equal to R50000 (€3200) but less than R100000 (€6400)	More than or equal to R100000 (€6400) but less than R350000 (€22300)	More than or equal to R36000 (€2200) but less than R72000 (€4600)	More than or equal to R70000 (€4450) but less than R250000 (€16000)
H3	More than or equal to R100000 (€6400)	More than or equal to R350000 (€22300)	More than or equal to R72000 (€4600)	More than R250000 (€16000)

Appendix 2

Distribution of disease according to anatomical site.



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