Challenges For Dedicated Smoking Cessation Services In Developing Countries

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Declaration

I, GY Tadzimirwa, declare that research is based on my own independent work done under supervision. Neither the whole work nor a part, is being, or will be submitted for any other degree to any other university. The work was not reported or published prior to registration for the abovementioned degree.

Signed by candidate

Abstract

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Background

South Africa, the country ranked as the 'second most stressful country to live in' has an estimated 7 million smokers. A dedicated smoking cessation clinic established at Groote Schuur Hospital, Cape Town, provides the only clinical service and training centre in the country.

Objectives

To evaluate the smokers attending the clinic, in order to better understand the requirements of smoking cessation services in resource-limited settings.

Methods

Demographic and smoking-related data was collected prospectively from all clinic attendees since its inception. Nicotine dependence, depression scores and exhaled carbon monoxide levels were formally evaluated. Consent was provided to review the collected data.

Results

Ninety-seven smokers were evaluated. Their mean(standard deviation)age 50.9(10.9)years, and 59% (57/97) were male. The median age of smoking initiation was 16(interquartile range(IQR) 8 - 28) with a current median daily consumption of 12(IQR 7-20). Overall men smoked more than women, with a median of 20(cigarettes per day(IQR 10 - 20) v 12(IQR 5 - 20) respectively (p=0.001). The median Fagerström nicotine dependence score was 5(IQR 3 - 7), with scores of 6(IQR 4 - 8) for men and 5(IQR 2 - 7) for women (p=0.06); 50% of smokers had a Fagerström score <6(low to above-average dependence) and 22% a score of ≥8 (extreme dependence). The median Patient Health Questionnaire-9(PHQ-9) depression score was 8(IQR 4 - 11), and 49% of smokers had symptoms of at least minor depression (score ≥10). The clinic could not provide pharmacotherapy. The self-reported quit rate was 28% at median follow up of 22 months(IQR 14 -39).

Conclusions

In smokers attempting to quit, moderate levels of nicotine dependence coexist with significant depression and anxiety symptoms. These data inform resource allocation and public health strategies, suggesting that in resource-limited smoking cessation services, psychological/behavioural support focusing on depressive symptoms may be a greater priority than simple pharmacotherapy.

Acknowledgements and Contributions

I am immensely grateful to Professor Richard van Zyl-Smit for his incredible generosity in instructing, mentoring and supervising me at every step of the research process. He constructed the smoking cessation clinic and conceived the idea of an evaluation of this clinic in a resource constrained environment. He remained a supportive supervisor, involved in every step from the first protocol draft to the final published manuscript which was reviewed by each co-author.

Monika Kamkuemah provided insight through her statistical analyses of the data. Cascia Day and Christine Cooper were essential in the data collection in the smoking cessation clinic. Dr Ali Esmail and Professor Dheda provided a critical review at various stages of analysis and interpretation of the results.

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Abbreviations

CHEC-CCT: Cape Higher Education Consortium- City of Cape Town

CI: Confidence Interval

CO: Carbon monoxide

COPD: Chronic Obstructive Airways Disease

FEV_1: Forced Expiratory Volume in 1 second

GSH: Groote Schuur Hospital

HIV: Human Immunodeficiency Virus

IQR: Interquartile Range

LMIC: Low- And Middle-Income Countries

SEM: Standard Error of Mean

NRT: Nicotine Replacement Therapy

PHQ-9: Patient Health Questionnnaire-9

PPM: Parts Per Million

SA: South Africa

SADHS: South Africa Demographic and Health Survey

SD: Standard Deviation

TB: Tuberculosis

UK: United Kingdom

USA: United States of America

WHO: World Health Organisation

Chapter 1: Introduction

Background

Smoking has been identified as a risk factor for multiple poor health outcomes of which lung cancer was the first to be identified.[1] The impact of smoking on declining population health has been apparent since the early 1900s when a relationship between increased prevalence of smoking and increased incidence of lung cancer, previously uncommon, was identified [1, 2]. Since then multiple meta-analyses have highlighted relationships between smoking and non-communicable diseases including cardiorespiratory disease, auto-immune disease, subfertility, malignancy, cerebrovascular disease and poor feto-maternal outcomes. [2-6]

South Africa's first burden of disease report in 2000 highlighted the quadruple burden of disease the country faces and the need for a multifaceted approach to improving health which includes managing modifiable risk factors, particularly smoking [7]. 8.5% of all deaths (and 13 % of deaths in adults) are attributable to smoking and resulted in 3.7 to 4.3% of deaths and disability adjusted life years due to lung and other cancers, cardiovascular disease, COPD, TB and other medical conditions in South Africa in 2000.[8] 18.1% of the population was living with HIV in 2007 where there is a high incidence of TB for which smoking is a risk factor and is likely a factor in driving the syndemic of HIV and TB. In addition, both smoking and TB increase the risk of COPD. [9-12] In South Africa smokers have an increase in all-cause mortality and in a country with a burden of TB and HIV [12]; with TB risk increased by smoking it is imperative that smoking cessation is central to health care.

All-cause mortality has been shown to be 2 to 4 times higher in smokers compared to those who have never smoked. However, those who quit smoking successfully lower their risk with every year of cessation. Furthermore, those who manage to quit smoking prior to the age of 45 have the same life expectancy as those who have never smoked. [13]

Impact of mass smoking cessation efforts

The prevalence of smoking in different regions varies and is influenced by culture, levels of education, income and the presence of tobacco control policies.[14, 15] In sub- Saharan Africa the prevalence of smoking ranges from 1.8% in Zambia to 25.8 % in Sierra Leone and a prevalence of 22% in South Africa.[15] Sub-Saharan Africa has been described as being in stage 1 of the smoking epidemic where western countries have shown a decline in smoking prevalence and Sub-Saharan Africa, on the contrary, has illustrated a significant rise. However, amongst Sub-Saharan countries who are signatories to the WHO Framework Convention on Tobacco Control and have implemented some of the measures necessary under this convention the smoking prevalence seems lower in those who implemented the Convention earlier. [15]

The first South Africa Demographic and Health Survey (SADHS) in 1998 reported a decline in smoking prevalence from following implementation of Tobacco control measures in 1990, however the second SADHS in 2009 reflected that although the proportion of men smoking had declined, there was a persistently high smoking prevalence amongst women and young adults.[16] This was also reflected in a cross sectional study among black urban dwellers between 2008 and 2009.[17]

The South African government has made efforts to minimise poor outcomes due to smoking with legislature restricting tobacco use, advertising and trade following the WHO MPOWER strategy.

The financial benefits of smoking cessation are marked and the associated personal and societal benefits of smoking cessation outweigh any benefit from smoking.[18]

Individual smoking cessation strategies

In populations with TB the SCIDOTS project showed that in addition to improved and sustained smoking cessation rates among patients who receive intervention there is the added benefit of reduced rates of defaulting treatment compared to those without intervention. [19] People who stop smoking and those who have never smoked have an improved life expectancy and slower rate of deterioration of FEV_1 compared to those who continue smoking.[20, 21]

However, it is difficult to simply quit and many people will relapse and still face a negative impact on their health.

Smoking cessation approaches encompass both pharmacologic and non-pharmacologic interventions which include motivational interviewing, counselling during routine doctor's visits, mass advertising and use of nicotine replacement therapies which are all better than placebo in improving the chances of smoking cessation. Community based programs that support people in their efforts to quit further improve chances of success. [18]

The pharmacological therapies central to smoking cessation are varenicline; most likely to assist in cessation, with bupropion as an alternative which tends to be more suitable to a broader patient profile including those with organ dysfunction (such as renal failure). Pharmacological intervention has been shown to be effective and strategies that combine both these approaches have been shown to be superior to those that employ only one or the other but there is little evidence for efficacy of population targeted strategies. The South African guidelines for smoking cessation reflect these findings[22], however, a limiting factor is that pharmacological interventions are only available at individuals' expense.

Effective smoking cessation strategies are imperative to the long-term outcomes for a variety of patient groups. The smoking cessation clinic that runs at Groote Schuur Hospital is the only one of its kind in South Africa and offers a source for investigation into effective strategies of smoking cessation in a resource-limited setting.

Identifying factors which support successful quitting, and those that act as barriers, is imperative to the development of a successful service. This study is aimed at assessing the socio-demographic and dependency profile of the patients who attend this clinic and the factors that may improve successful cessation.

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Chapter 2: Article in Publication Ready Format

Challenges for dedicated smoking cessation services in developing countries

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ABSTRACT

Background.

South Africa, ranked as the world's second most stressful country to live in, has an estimated 7 million smokers. A dedicated smoking cessation clinic established at Groote Schuur Hospital, Cape Town, provides the only clinical service and training centre in the country.

Objectives.

To evaluate the smokers attending the clinic, in order to better understand the requirements of smoking cessation services in resource-limited settings.

Methods.

Demographic and smoking-related data were collected prospectively from all clinic attendees since its inception. Nicotine dependence, depression scores and exhaled carbon monoxide levels were formally evaluated. Consent was provided to review the data collected.

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Ninety-seven smokers were evaluated. Their mean (standard deviation) age was 50.9 (10.7) years, and 59% (57/97) were male. The median age of smoking initiation was 16 years (interquartile range (IQR) 8 - 28), with a current median daily consumption of 12 cigarettes (IQR 7 - 20). Overall men smoked more than women, with a median of 20 cigarettes per day (IQR 10 - 20) v. 12 (IQR 5 - 20), respectively (p=0.001). The median Fagerström nicotine dependence score was 5 (IQR 3 - 7), with scores of 6 (IQR 4 - 8) for men and 5 (2 - 7) for women (p=0.06); 50% of smokers had a Fagerström score of <6 (low to above-average dependence) and 22% a score of ≥8 (extreme dependence). The median Patient Health Questionnnaire-9 (PHQ-9) depression score was 8 (IQR 4 - 11), and 49% of smokers had symptoms of at least minor depression (score ≥10). The clinic could not provide pharmacotherapy. The self-reported quit rate was 28% at median follow-up of 22 months (IQR 14 - 39).

Conclusions

In smokers attempting to quit, moderate levels of nicotine dependence coexist with significant depression and anxiety symptoms. These data inform resource allocation and public health strategies, suggesting that in resource-limited smoking cessation services, psychological/behavioural support focusing on depressive symptoms may be a greater priority than simple pharmacotherapy.

INTRODUCTION

The detrimental effect of smoking on population health has been apparent since the early 1900s when a relationship between increased prevalence of smoking and increased incidence of lung cancer, previously uncommon, was identified.[1,2] Since then, numerous studies have highlighted the relationships between smoking and non-communicable diseases including cardiorespiratory disease, autoimmune disease, subfertility, malignancy, cerebrovascular disease and poor fetomaternal outcomes.[2-6]

South Africa (SA)'s first burden of disease report in 2000 highlighted the quadruple burden of disease the country faces and the need for a multifaceted approach to improving health that includes managing modifiable risk factors, particularly smoking.[7] It was reported that in SA in 2000, smoking accounted for 8.5% of all deaths (and 13% of deaths in adults aged >35 years) and 3.7 - 4.3% of disability-adjusted life-years due to lung and other cancers, cardiovascular disease, chronic obstructive pulmonary disease (COPD), tuberculosis and other medical conditions.[8] South Africa has an estimated 7.2 million adults living with HIV; 60% of which are co-infected with TB, with 61% of adults on antiretroviral therapy.[9] In addition, both smoking and TB increase the risk of COPD. [10-13] However, individuals who quit smoking successfully lower their risk with every year after cessation. Furthermore, those who manage to quit before the age of 45 have the same life expectancy as those who have never smoked.[14]

Many low- and middle-income countries (LMICs) have made significant efforts to minimise adverse health outcomes due to smoking, with legislature restricting tobacco use, advertising and trade following the World Health Organization (WHO) MPOWER strategy.[15] Formal cessation programmes mainly exist in high-income countries, which equate to ~15% of the world's population able to access cessation support.[16] Very few data exist on formal cessation programmes provided in low-income settings or on how applicable cessation strategies developed in high-income settings are to low-income countries.[16,17] Furthermore, smoking cessation pharmacotherapy such as nicotine replacement therapy (NRT), although on the WHO essential medicine list, is not always available to smokers.[18,19] This is particularly true in SA, where, although it is classed as a middle-income country, no smoking cessation pharmacotherapy is available to smokers accessing public health services.

A combination of behavioural therapy and pharmacological support is regarded as the interventional strategy with the highest odds of long-term cessation. There are, however, no data to indicate who will be unsuccessful if pharmacotherapy is not added to behavioural interventions.

OBJECTIVES

A dedicated smoking cessation clinic established at Groote Schuur Hospital (GSH) in Cape Town is the only one of its kind in SA. Our objectives were to assess the sociodemographic and dependency profiles of the smokers who attended this clinic and their short- and long-term outcomes. By understanding the characteristics and needs of smokers in this setting, we hoped to provide relevant data to help guide locally applicable smoking cessation services applicable in LMICs. Identifying factors that support successful quitting, and those that act as barriers, are imperative in understanding the requirements for psychological and pharmacological support in such services.

METHODS

Establishing the clinic

The first SA smoking cessation clinical practice guidelines were published in 2013.[19] Prior to this date and the establishment of the GSH clinic in December 2012, no formal smoking cessation services existed in the public sector. No pharmacotherapy was available for smoking cessation in the government hospitals, and availability of nicotine patches was very limited owing to available products being withdrawn from SA. With permission from the Head of the Division of Pulmonology, a specialised clinic was introduced to offer evaluation of and smoking cessation support to any smoker wishing to quit. The clinic was established within the respiratory outpatient services for convenience, as the trained staff were from the Division of Pulmonology and the clinic was physically near to the cardiology outpatients and transplant services. The doctors had received limited smoking cessation training at a variety of local workshops, and a nursing sister was trained to provide additional counselling. No specialist psychological/psychiatric support or pharmacotherapy was available in the clinic.

The study reviewed data collected from all smokers attending GSH's smoking cessation clinic since its inception. New patient data collection commenced at the clinic inception in 2012 and was truncated in September 2016. A pre-formed data capturing sheet to guide the consultation and to assimilate the required smoking cessation-specific information was used. Self-reported scales (Fagerström, Patient Health Questionnnaire-9 (PHQ-9), etc.) were completed by the individual person, with the remaining evaluation completed by the attending doctor. Information captured included age, motivation to quit, tobacco smoking history, medical history, Fagerström score, Wisconsin withdrawal score, PHQ-9 depression score and perceived medication affordability. Carbon monoxide (CO) levels were tested using a piCO Smokerlyzer (Bedfont, UK)) at each visit.

Interventions

After completing the prespecified questionnaires, all attendees were seen by a doctor (a pulmonologist or medical registrar). Basic smoking history was confirmed, and level of motivation and reasons for wishing to quit were evaluated. Counselling was performed by the doctor, as there were limited alternative counselling personnel. Counselling included evaluation of previous attempts to quit and reasons for relapse or failure. Information on nicotine dependence was provided, as well as on the importance of behavioural change and pharmacotherapy if needed. Interviews were conducted in a motivational interviewing style directed towards behavioural change with a specific focus on self-motivation, problem solving and strategies for coping with withdrawal symptoms.

Ethical considerations

Ethics approval to perform this clinical patient database review was granted by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee and GSH administration (HREC REF:667/205) At the time of their first visit, all patients provided written informed consent to have their data relevant to the smoking cessation clinic collected as part of the standard evaluation of all patients at the clinic. Participants also provided contact details to allow for telephonic contact to provide support and evaluate outcomes.

Statistical analysis

Data were entered onto an electronic database and independently reviewed for accuracy. Analysis was conducted using Graphpad prism 5.0 for Mac OSX (GraphPad Software, USA) and Stata 13 (StataCorp, USA). Continuous data were expressed as means (standard deviations (SDs)) or medians with interquartile ranges (IQRs). For categorical data, the χ^2 test or Fisher's exact test was used. The Mann-Whitney test or Student's *t*-test was used to test the association between continuous and categorical variables. A *p*-value of 0.05 was used to determine statistical significance.

RESULTS

Participants

The weekly smoking cessation clinic received the majority of its referrals from cardiology, respiratory and other tertiary clinics (organ transplant, infertility) at GSH. A few attendees were 'healthy smokers' from outside the hospital. During the audit review, 98 smokers attended for at least one visit. Only 1 attendee did not complete the requisite forms and was not included in any of the analyses.

Detailed characteristics of the patients attending the clinic are reported in Table 1. There was a predominance of male smokers (60%, 58/97). The mean (SD) age of attendees was 51.1 (10.9) years. There was no difference in the age of men compared with women, and the median age of smoking initiation was similar at 16 years (IQR 8 - 28). On average, men smoked more cigarettes per day than women (median 20 (IQR 10 - 20) v. 12 (IQR 5 - 20), respectively; *p*=0.001), resulting in higher cumulative total pack-years of smoking at the time of the first visit (33 (IQR 20 - 45) v. 21 (IQR 7 - 33); *p*=0.001). However, at the time of the first visit the majority of attendees were smoking 12 cigarettes per day on average. The most frequent motive noted for quitting was, not unexpectedly, health reasons (Table 2).

The majority of attendees had previously tried to quit: 91% had made at least one attempt within the past year, with 48% making more than four attempts in the past 12 months. Only 8% reported having previously used pharmacotherapy in a quit attempt. Of the attendees, 68% lived with other smokers in the house. One-third (32%) indicated at the initial visit that they could potentially afford to purchase medication privately to assist with the quit attempt (Table 2).

Nicotine dependence was evaluated using the Fagerström Test.[20] The median score was 6 (IQR 3 - 7). Women had slightly lower scores than men (median 5 (IQR 2 - 7) v. 6 (IQR 4 - 8), respectively; *p*=0.06), as shown in Table 2. However, 50% of smokers had a score of 4 - 5, indicating 'above-average' dependence, and 23% had a score >8, indicating 'extreme dependence' (Fig. 1). Exhaled CO levels were similar in men and women, with a mean (SD) score of 15.9 (9.1) parts per million. Exhaled CO correlated positively with current tobacco consumption (Spearman's *r*=0.52 (95% confidence interval (CI) 0.28 - 0.70); *p*<0.001)) and with Fagerström scores, although less strongly (*r*=0.41 (95% CI 0.15 - 0.62); *p*=0.02). Current number of cigarettes per day correlated strongly with the Fagerström score (*r*=0.74 (95% CI 0.62 - 0.82); *p*<0.001) (Fig. 2). Motivation to quit was reported as high, and there was no difference in in that regard between men and women.

Depressive symptoms were prospectively evaluated, and complete scores were evaluable in 55 attendees at the first visit using the PHQ-9 depression test. Nearly two-thirds (63%) of smokers reported at least minor symptoms of depression when screened at the first visit, and 38% (21/55) expressed symptoms of at least moderately severe depression (score ≥15) (Fig. 3); 18% (10/55) would be classified as severely depressed based on the PHQ-9 score. Evaluating the individual specified

subcategories making up the Wisconsin Withdrawal Scale at the initial visit (when the participants were still smoking), patients had on average high (>2/4) subscores for anger, anxiety and sadness (Table 2).

Smokers who had attended the clinic were contacted by telephone in 2016/17. Using the contact numbers provided at the first visit, only 46 (47%) of the 97 attendees were contactable. The median time to follow-up was 22.5 months (IQR 14 - 39) after the first clinic visit. Based on self-reported smoking status, 13 attendees (28%) had successfully quit, 33 (72%) were still smoking, and 2 were stated to have died (cause not reported). Although the review was not specifically powered to evaluate predictors of outcome, individuals who had successfully quit had lower mean (SD) PHQ-9 depression scores than those who had been unsuccessful (3.9 (1.9) v. 7.1 (1.0), respectively; *p*=0.046). In univariate analysis this translated into a trend towards successful quitting with a lower depression score (odds Ratio 0.86 (95% CI: 0.76;1.00; *p*=0.056). There was no difference in the number of clinic visits attended in those who quit successfully v. those who did not, nor in duration of follow-up when contacted. Time to first cigarette in the morning was not predictive of success, and no difference was seen between quitters and non-quitters with regard to baseline nicotine dependence scores (Fagerström score 4 v. 5; *p*=0.34) (Fig. 4, A and B).

DISCUSSION

Access to formal smoking cessation services is very limited in LMICs.[16] In this cohort of smokers from a low- to middle-income population group in SA attending a dedicated smoking cessation service, high levels of depressive symptoms were common, with accompanying moderate nicotine dependence. Currently no pharmacotherapy is provided by the government to assist smokers in quitting. Given the high level of depressive symptoms and stressors with relatively low nicotine dependence reported by the attendees, psychological and behaviour support for smokers should be a priority. The role for pharmacological support, given its poor availability and high cost, needs to be prospectively determined. Despite the lack of pharmacotherapy or specialised psychological support to assist in smoking cessation, some patients were successful in quitting smoking.

Global smoking cessation guidelines, including the SA guidelines, recommend a combination of behavioural support/counselling and pharmacotherapy to support smoking cessation attempts.[19,21,22] The WHO has placed NRT on the essential medication list, but access to pharmacotherapy is severely limited and costly in resource-constrained settings, even in a high- to middle-income country such as SA.

To date there have been very limited data published on smoking cessation clinics in LMICs. The majority of reports are on integrated/opportunistic brief interventions alongside healthcare services.[16,17] Opportunities such as tuberculosis and or HIV treatment programmes have shown promise as an opportunity to address tobacco smoking in conjunction with treating infectious diseases.[23,24] In many developed-world settings, in-hospital smoking cessation strategies have been an opportunity to commence interventions.[25] What is clear, however, is that if patients are not followed up or continued on treatment on discharge, all gains during the hospital stay with regard to quitting smoking are essentially for naught.

SA has been characterised as the world's second most stressful country to live in, although these data do not include much of Africa.[26] If one compares the level of stressors in SA to other countries

globally, however, Egypt (for example) is ranked 15th, Brazil 17th, China 29th, the UK 56th and Australia 70th. During counselling of the smokers in our study, common reported stressors included personal safety, financial insecurity, health concerns, community safety and anxieties regarding the country's future. These concerns may be intensified by a hospitalisation or acute medical illness, especially if an additional financial strain and burden is precipitated by lack of income and family support.[27] Unexpected hospital admissions may therefore not be the best opportunities to intervene, given the accompanying heightened stress.

Smokers in our outpatient cohort showed significant levels of background depressive symptoms, both on the formal PHQ-9 depression scoring and also when we evaluated the subscore of the Wisconsin Withdrawal Scale (while the attendees were still smoking). In active smokers, a balance exists between tobacco/nicotine dependence and the psychological/ behavioural habit of smoking (although these aspects are not always clearly separable). There is strong evidence that counselling and pharmacotherapy go hand in hand, with a combination generally better than either alone.[21] What is not clear, and has no literature to support it, is how to estimate whether an individual will be able to quit without the addition of medication. There is a strong correlation between Fagerström score and long-term cessation success,[28] and specifically time to first cigarette in the morning has been shown to be a simple measure to use.[28] Additionally, underlying depression and poor outcomes are correlated in reports from smoking cessation services.[29] In our cohort, no significant correlation was found between dependence indices and outcome, although the audit was not primarily powered to evaluate predictors of outcome owing to the nature of the study. Despite the lack of pharmacotherapy the long-term quit rates were encouraging, although an estimation of true success was not possible owing to the excessive loss to follow-up and inability to confirm smoking status chemically. What was evident in this cohort of low-income smokers was the low to moderate level of nicotine dependence and moderate to high level of depressive symptoms. This finding raises the question whether resources should preferably be spent on skilled counselling when establishing dedicated smoking cessation centres in low-income settings, or on the provision of NRT/varenicline/bupropion to aid in the quit attempts for all patients.

Study limitations

The study has several limitations. Referral to the service was encouraged for smokers motivated to quit. The service did not have on-site specialised counselling for depression or anxiety, but relied on referral to such services. The level of depressive symptoms may be different in individuals who are not willing to quit, but the characteristics of the attendees presented were of those wanting help to stop smoking. It was not possible to evaluate whether outcomes would be different if the patients had had access to pharmacotherapy. There is therefore uncertainty whether to prioritise counselling or medication, but the high level of depressive symptoms requires attention irrespective of smoking status. Follow-up was incomplete, as many of the contact telephone numbers that were provided did not work. Prespecified powered outcome calculations were not possible, but patient data collection is ongoing.

Recommendations

The questions facing the clinician with limited access to pharmacotherapy to assist smoking cessation are who should receive it, and whether it is possible to predict who will not be successful without the provision of medication. An approach could be to initiate an intensive behaviour motivation intervention irrespective of dependence scores, and to provide NRT at the second attempt for those who fail due to withdrawal symptoms. The strategy in our clinic was to provide a support service that

did not previously exist in an attempt to help smokers quit, and to gather the necessary data to motivate for locally relevant psychological and/or pharmacological interventions. Based on the data from this cohort, attending to the social, financial and emotional upheaval described by the majority of smokers seen may be of far more importance than pharmacotherapy in achieving long-term freedom from tobacco dependence. Poverty alleviation, sustainable income and mental health are not issues than can simply be solved by a nicotine patch or gum. Providing behavioural tools to assist with coping with life stressors, counselling and appropriate referral to social services is a starting point to explore in low-income settings where the behavioural aspects of tobacco dependence as a coping mechanism may outweigh the pure chemical addiction.

As with all interventions in medicine, the certainty with which outcomes/response to therapy can be predicted enhances our decision-making and ability to motivate to funders to support treatment strategies. In low-resourced areas, the clinician is bound to equitable resource allocation and often provides interventions for those who will 'benefit' the most. If we could reasonably identify those who will inevitably fail without pharmacotherapy, we could motivate for such targeted interventions. Extrapolating from the nicotine dependence scores in this cohort, ~25% had very high dependence and should by any major guideline strategy have been receiving pharmacological support. The PHQ-9 scores indicative of major depression in ~1 in 5 smokers would warrant appropriate referral to competent psychiatric services before any quit attempt is made. Depending on the skills of the service providers (doctor v. psychologist), these services could be interlinked.

CONCLUSIONS

Smoking cessation should be a priority in all healthcare services, especially in low-income settings where smoking results in a significant health burden, drives mortality rates and consumes substantial disposable income in those who can least afford it. High levels of depression and social stressors existed in our cohort of smokers, suggesting that interventions targeting the behavioural aspects of tobacco dependence should be emphasised and potentially balanced with the provision of NRT for those with very high dependence. Prospective, scalable and cost-effective interventions for tobacco dependence are needed to address this major modifiable risk factor for communicable and non-communicable diseases in low-income settings.

DECLARATION

None

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To the E16 Staff who assisted with establishing the clinic

AUTHOR CONTRIBUTIONS

RvZS established the audit, AE,CD,RVZS,CC collected the data, MK, RVZS, GT analysed the data, All authors reviewed the manuscript prior to publication.

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CONFLICTS OF INTEREST

Rvzs honoraria from Pfizer for smoking cessation related academic presentations.

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LIST OF FIGURES

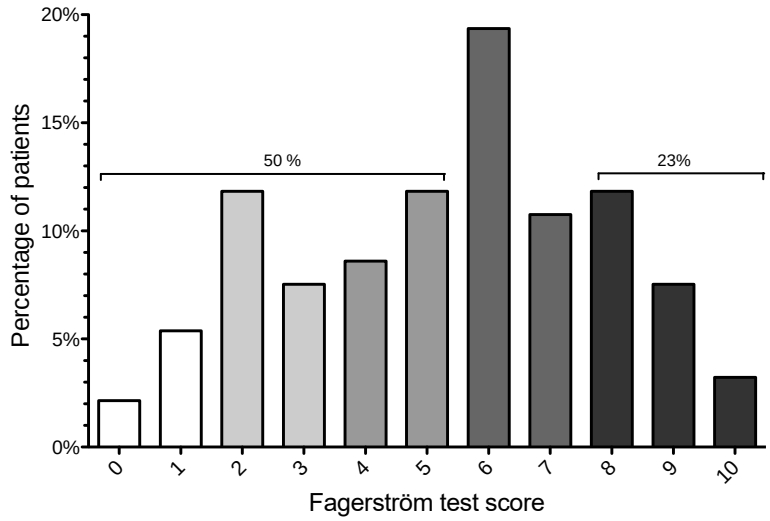

Fig. 1. Fagerström scores for nicotine dependence. (Interpretation of dependence scores: 0 - 1 low, 2 - 3 average, 4 - 5 above average, 6 - 7 high, 8 - 10 extreme nicotine dependence.)

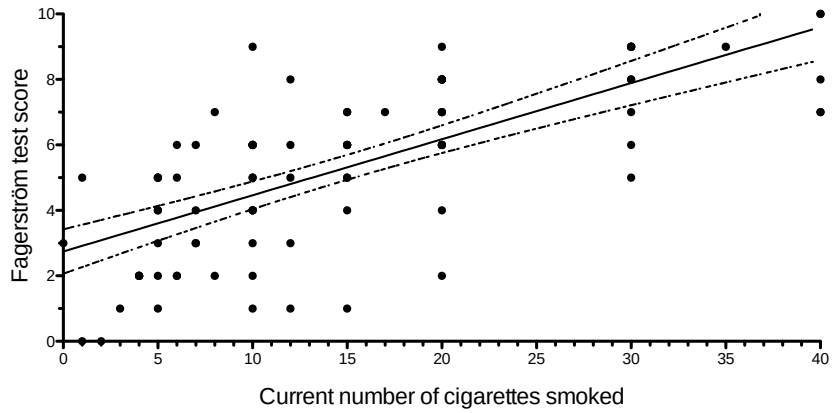

Fig. 2. Correlation between current daily number of cigarettes smoked and Fagerström score for nicotine dependence. Solid line: regression line with 95% CI Spearman's r=0.74 (95% CI 0.62 - 8.82); p<0.0001. (CI = confidence interval.)

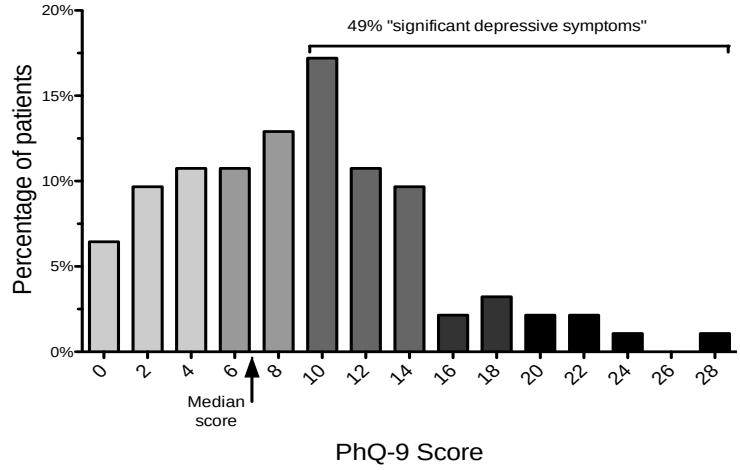

Fig. 3. PHQ-9 depression scores. (Interpretation of PHQ-9 score: 0 - 4 no symptoms, 5 - 9 minimal symptoms, 10 - 14 minor depression/major depression mild, 15 - 19 major depression moderately severe, >20 major depression severe; PHQ-9 = Patient Health Questionnnaire-9.)

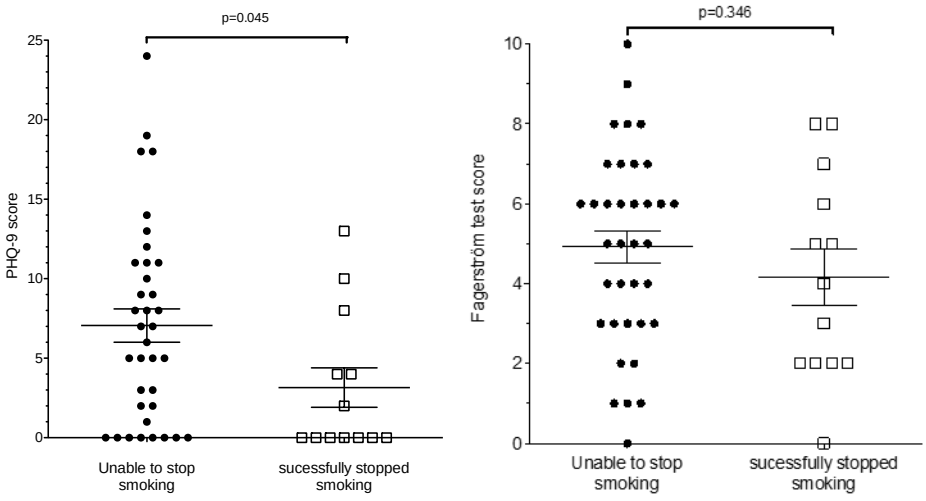

Fig. 4. Characteristics of patients with known outcomes at 2 year median follow up: (A) PHQ-9 depression score by outcome, (B) Fagerström nicotine dependence score by outcome. (Mean ±SEM)

TABLES

Table 1. Attendee characteristics			
Characteristics	**Female (*N*=39, 40%)**	**Male (*N*=58, 60%)**	**Total (*N*=97)**
Current age (years), mean (SD)	48.5 (9.5)	52.4 (11.3)	50.9 (10.7)
Age at smoking initiation (years), median (IQR)	16 (15 - 19)	16 (14 - 18)	16 (14.5 - 18)
Total years smoked, mean (SD)	31.7 (10.1)	34.7 (11.9)	33.5 (11.3)
Average number per day smoked, median (IQR)	12 (5 - 20)*	20 (10 - 20)*	20 (10 - 20)
Current number per day smoked, median (IQR)	11 (8 - 17)	15 (6 - 25)	12 (7 - 20)
Total pack-years smoked, median (IQR)	21 (7 - 33)*	33 (20 - 45)*	29.5 (12.5 - 40)
Previous attempt to quit smoking, *n* (%)	32 (82)	43 (75)	75 (78)
Quit attempts in the past year, *n* (%)			
None	3 (8)	6 (11)	9 (9)
1 - 4	18 (46)	23 (40)	41 (43)
>4	18 (46)	28 (49)	46 (48)
Lives with smoker in house, *n* (%)	28 (72)	37 (65)	65 (68)
Number of smokers in house, *n* (%)			
0	11 (28)	20 (35)	31 (32)
1 - 2	17 (44)	21 (37)	38 (40)
>2	11 (28)	16 (28)	27 (28)
SD = standard deviation; IQR = interquartile range. *$p<0.05$.			

Table 2. Dependence and barriers to quitting smoking

Variable	**Female**	**Male**	**Total**
Fagerström dependency score (*n*=90), median (IQR)	5 (2 - 7)*	6 (4 - 8)*	6 (3 - 7)
Exhaled CO (ppm), median (IQR)	15 (9 - 23)	14 (9 - 20)	14.5 (9 - 20)
Motivation score (1 - 10), median (IQR)	10 (8 - 10)	10 (6 - 10)	10 (8 - 10)
Reasons for quitting smoking, *n* (%) (n=98)			
Personal health	21 (54)	22 (39)	43 (44)
Financial reasons	3 (8)	1 (2)	4 (4)
Family	1 (3)	3 (5)	4 (4)
Fertility	0	1 (2)	1 (1)
PHQ-9 depression score (*n*=55), median (IQR)	8 (4 - 11)	8 (5 - 11)	8 (4 - 11)
PHQ-9 total score, *n* (%) (n=55)			
0 - 4	9 (41)	6 (18)	15 (27)
5 - 9	8 (36)	11 (33)	19 (35)
10 - 15	2 (9)	9 (27)	11 (20)
>15	3 (14)	7 (21)	10 (18)
Wisconsin Withdrawal Scale subscore, median (IQR)			
Anger (*n*=87)	2.33 (1.3 - 3)	2 (1.33 - 3.3)	2 (1.3 - 3)
Anxiety (*n*=90)	2.5 (1.8 - 3)	2.25 (1.3 - 2.8)	2.25 (1.25 - 3)
Sadness (*n*=89)	2 (1.3 - 2.6)	1.75 (1 - 2.5)	2 (1.25 - 2.5)
Patient could potentially afford to purchase medication (*N*=87), *n* (%)	10 (28)	18 (35)	28 (32)

IQR = interquartile range; CO = carbon monoxide; ppm = parts per million; PHQ-9 = PHQ-9 = Patient Health Questionnnaire-9.
*$p<0.05$.

Chapter 3: Appendices

Protocol

INTRODUCTION

Smoking has been identified as a risk factor for multiple poor health outcomes of which lung cancer was the first to be identified.(1) In South Africa smokers have an increase in all-cause mortality and in a country with a burden of TB and HIV (2); with TB risk increased by smoking it is imperative that smoking cessation is central to health care. However, it is difficult to simply quit and many people will relapse and still face a negative impact on their health. There are multiple interventions available for those who are motivated to quit which include motivational interviewing, nicotine replacement therapy, antidepressants and nicotine receptor agonists. The smoking cessation clinic that runs at Groote Schuur Hospital is the only one of its kind in South Africa and offers a source for investigation into effective strategies of smoking cessation in a resource-limited setting.

Identifying factors which support successful quitting, and those that act as barriers, is imperative to the development of a successful service. This study is aimed at assessing the demographic and dependency profile of the patients who attend this clinic and their short and long term outcomes as it relates to their success or failure in quitting. We hope to evaluate the success of a smoking cessation service in this setting and this may assist in administrative support for specific services for smoking cessation.

BACKGROUND

The impact of smoking on declining population health has been apparent since the early 1900s when a relationship between increased prevalence of smoking and increased incidence of lung cancer, previously uncommon, was identified (1, 3). Since then multiple meta-analyses have highlighted relationships between smoking and non-communicable diseases including cardiorespiratory disease, auto-immune disease, subfertility, malignancy, cerebrovascular disease and poor feto-maternal outcomes.

South Africa's first burden of disease report in 2000 highlighted the quadruple burden of disease the country faces and the need for a multifaceted approach to improving health which includes managing modifiable risk factors, particularly smoking (4). 8.5% of all deaths (and 13 % of deaths in adults) are attributable to smoking and resulted in 3.7 to 4.3% of deaths and disability adjusted life years due to lung and other cancers, cardiovascular disease, COPD, TB and other medical conditions in South Africa in 2000.(5) 18.1% of the population was living with HIV in 2007 where there is a high incidence of TB

for which smoking is a risk factor and is likely a factor in driving the syndemic of HIV and TB. In addition, both smoking and TB increase the risk of COPD. (2, 6-8)

All-cause mortality has been shown to be 2 to 4 times higher in smokers compared to those who have never smoked. However, those who quit smoking successfully lower their risk with every year of cessation. Furthermore, those who manage to quit smoking prior to the age of 45 have the same life expectancy as those who have never smoked. (9)

The financial benefits of smoking cessation are marked and the associated personal and societal benefits of smoking cessation outweigh any benefit from smoking.(10) In populations with TB , in addition to improved and sustained smoking cessation rates among patients who receive intervention there is the added benefit of reduced rates of defaulting treatment compared to those without intervention. (11) People who stop smoking and those who have never smoked have an improved life expectancy and slower rate of deterioration of forced expiratory volume in 1 second(FEV_1) compared to those who continue smoking.(12, 13)

The South African government has made efforts to minimise poor outcomes due to smoking with legislature restricting tobacco use, advertising and trade since 1994 in the form of the Tobacco Products Control Act but multiple clinical smoking cessation strategies have been identified.

Motivational interviewing has been shown to be more effective than brief discussion during primary care.(14) Pharmacological intervention has also been shown to be effective and strategies that combine both these approaches have been shown to be superior to those that employ only one or the other but there is little evidence for efficacy of population targeted strategies. The South African guidelines for smoking cessation reflect these findings(15), however, a limiting factor is that pharmacological interventions are only available at individuals' expense.

Effective smoking cessation strategies are imperative to the long term outcomes for a variety of patient groups. Evaluating the only dedicated public sector smoking cessation clinic in the country is central to identifying strengths and weaknesses of the current efforts at assisting patients in quitting. It is important to identify trends in the patients who present to the clinic, those who are successful and what factors influence their outcome. Investigating the characteristics of the patients in this resource constrained clinic will be helpful in identifying whether or not intervention strategies can be successful without facilities that would be available in a more resource-replete setting. This will guide hospital administrators in determining the need for funding of smoking cessation services with regards to adequate support staff and access to pharmacological intervention.

RESEARCH QUESTION

What is the impact of a dedicated smoking cessation clinic, in a tertiary hospital with limited access to internationally accepted essential support services, in evaluating and assisting motivated patients to stop smoking?

HYPOTHESIS

Lack of access to extended counselling services and pharmacological therapy will impact significantly on even highly motivated patients' ability to quit smoking regardless of their level of dependency.

STUDY AIMS AND OBJECTIVES

To characterize the demographic backgrounds of patients who present to the Groote Schuur Hospital smoking cessation clinic

To determine the level of nicotine dependence among the patients attending the smoking cessation clinic

To evaluate the need for smoking cessation medication to support quit attempts

To determine if there is a relationship between the level of dependence and success

To determine the proportion of participants who manage to quit smoking at the time of folder review: at least 3 months after first visit to the smoking cessation clinic.

METHODOLOGY

Study Design

This is a cohort study of patients collected prospectively attending the Groote Schuur Hospital smoking cessation clinic

Study Population and Sample

1. The study population will consist of all adults, over the age of 18, attending the smoking cessation clinic at Groote Schuur Hospital from January 2013 to May 2016.
2. The data will be collected from patient smoking cessation clinic records and electronic data records at Groote Schuur Hospital and the Lung Clinical Research Institute at University of Cape Town for the period January 2013 to May 2016 and is expected to include over 90 patients.
3. Inclusion Criteria: Adults who smoke and attend the smoking cessation clinic

CONSENT

Ethical approval to perform this clinical study database review was granted by the UCT HREC (667/2015) and Groote Schuur Hospital administration. All patients at time of first visit signed consent

to have their data relevant to the smoking cessation clinic collected as part of the standard evaluation of all patients at the clinic. Participants also provided contact details to allow for telephonic contact to provide support and evaluated successful outcomes.

CONFIDENTIALITY

All patient records are stored in a secure access restricted storage location within the E16 respiratory clinic. No persons not directly involved in the Clinic have access to the clinical notes. Electronic databases to allow for statistical analysis will be password restricted and all personal identifiers will be removed from such data sets to ensure confidentiality.

VARIABLES AND MEASUREMENTS

Data collection sheets and electronic databases will be used to collect the following information

Variable	Numerical	Categorical Ordinal	Categorical Nominal	Possible values
Age	X			18-80
Gender			X	M, F
Pack years	X			0-150
Level of motivation	X			0-10
Previous attempts			X	Y,N
Exhaled CO	X			0-30
Fagerstrom test		X		0-10
Wisconsin withdrawal scale -Anger -Anxiety -Concentration -Craving -Hunger -Sadness -Sleep		X		0-4
Personal Health Questionnaire (PHQ-9)		X		0-11
Smoker's emotional index		X		
Use of drugs			X	Y,N
Use of Nicotine replacement therapy			X	Y,N
Success			X	Y,N
Method used to quit			X	P,G,C,Z,E,N,S,
Long term quitting			X	Y,N

DATA ANALYSIS PLAN

The data will be extracted from the UCT lung institute database and stored in excel spreadsheets. Upon cleaning the data using Microsoft excel pivot tables, it will be exported to STATA 14 (Stata Corp, College Station, Texas) for analysis. Statistical tests will be performed according to whether the variable is continuous or categorical. Continuous data will be expressed as mean values ± SD or median values (IQR) depending on the normality of data. For categorical data the χ^2 test or Fisher exact test and the Z test will be used to test for a statistical difference between variables and proportions, respectively. The Mann – Whitney, and Student t-test will be used to test the association between continuous and categorical variables.

The age, age when started smoking, number of smoking pack.years and level of motivation will be reported as mean or median depending on the normality of the data and it will be analysed for men and women and then for the entire population. Gender will be reported as the number of males and females as a proportion of the study sample. The fagerstrom scores will be reported as a frequency

with which each of the scores occurs. The t-test (or mann-whitney u test if data is non-parametric) will be used to analyse the correlation between age when started smoking and fagerstrom scores; Wisconsin withdrawal scores and pack years of smoking; fagerstrom scores and exhaled carbon monoxide. The chi squared test will be used to analyse correlation between gender and motivation to quit as well as gender and previous attempts to quit.

SAMPLE SIZE CALCULATION

The study will evaluate the whole population of patients attending the smoking cessation clinic up to 01 June 2016. The start date will be from clinic onset date and new patient data collection will be truncated as at 01 June 2016.

STRENGTHS AND LIMITATIONS

The study is the first of its kind in South Africa. It will give insight into the disadvantages and advantages of a smoking cessation program without the easy access to pharmacologic intervention. Another strength of the study is the fact that it will provide data about the demographics of patients who are being referred for assistance with smoking cessation and this may, in future, guide smoking cessation efforts at community level, primary and secondary care levels.

The patients attending the clinic are referred with the express intention of quitting smoking (as per clinic requirements) and will not be representative of general smokers within the community. Although not restricted to tertiary service patients, most patients are referred from specialist services such as transplant, coronary care unit and infertility clinics. This might bias the results to highly motivated patients and those with complex medical co-morbidities. Access to pharmacological support is limited strictly to patients who can afford to purchase medication themselves and thus will impact outcomes. Changed patient details over time may result in loss to follow up and therefore limit data collection.

IMPLICATIONS

Smoking is a well described cause of multiple causes of morbidity and mortality. It remains a leading cause of death in South Africa and the need for successful smoking cessation programs would have massive implications from a public health perspective. This research is important as it evaluates the only dedicated public service smoking cessation clinic in South Africa and would identify whether or not it is successful and why. Meta analyses have shown that more interventions are better than any single intervention and that the availability of medication to support cessation attempts in combination with counselling is more effective that counselling alone. This research will define both the socio-economic characteristics but also smoking patterns and dependency of a cohort of smokers

motivated to quit smoking. It will provide important data to hospital administrators on the need for cessation services, and support in the form of cessation counselling and medication. This would support applications for funding of drugs in the public health system to allow success for more people and subsequently reduce the burden of disease due to smoking.

BUDGET

Currently there is no additional cost to carry out this research: the electronic database has already been set up and maintained but the Lung Clinical Research Institute at the University of Cape Town. Funding will be sought to allow for presentation of data at a local conference and for publication in a peer review journal.

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Ethics Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
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17 July 2018

HREC REF: 667/2015

A/Prof R van Zyl-Smit
Division of Pulmonology
E-16 Respiratory Clinic
c/o Sr Christin Cooper
NGSH

Dear A/Prof van Zyl-Smit

PROJECT TITLE: E16 RESPIRATORY CLINIC SMOKING CESSATION SERVICE-PRACTICE AUDIT

Thank you for your study staff amendment form submitted to the Faculty of Health Science Human Research Ethics Committee.

The HREC approves the addition of Dr Gamuchirai Tadzimirwa to the study for degree purposes of MMed in Medicine. The HREC acknowledges that Dr Tadzimirwa is part of the above-mentioned study.

Please quote the HREC reference number in all your correspondence.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Clinic Questionnaire

.

E16 Respiratory Clinic smoking cessation clinic

(For GSH folder)

The following patient is attending the smoking cessation programme at E16

Hospital sticker

Date started on cessation programme:

Target Quit date:

Medication:

Side effects or complications:

Successful quit date:

Smoking cessation clinic

Clinic pt. number

Hospital sticker

Clinic: E16/ UCTLI/ UCT Private

Date of first visit

Name		Folder number	
Surname		Date of Birth	
Gender		Current age	

Tel. number

What is your motivation to quit?

On a scale of 1- 10 how motivate are you to quit? 1=don't want to quit 10 = desperate to stop

Smoking history

Age when started smoking		Pack years :
Total number of years smoked		
Average number smoked since started		
Average number over past year		
Current number per day		

Have you previous tried to quit (Y/N)		**What methods have you used?**	
When was your last attempt		patch	
Longest period of abstinence		gum	
No. of quit attempts in past year		champix	
		zyban	
		other	

Do you live with a smoker? (Y/N)	
How many smokers are in the house	

Do you have any Medical conditions? Y / N

Hypertension		**Current medication**
Angina		
Cardiac arrhythmias		
Diabetes		
Depression		
Asthma		
COPD		

Do you consent to having your data anonymously stored electronically on a secure computer for audit and research purposes to determine the effectiveness of the smoking program?

Signed _____

Date _____

Dr. reviewing patient _____

Clinic pt. number	Hospital sticker	Folder number	Date
Surname			

Weight (kg)		BP		Exhaled CO	
Height (m)		Pulse		Pregnancy test	
BMI (wt/htxht)					

Fagerström test (visit one)

Please answer each question...

1. How soon after you wake up do you smoke your first cigarette?

	score
After 60 minutes	0
31-60 minutes	1
6-30 minutes	2
Within 5 minutes	3

2. Do you find it difficult to refrain from smoking in places where it is forbidden?

No	0
Yes	1

3. Which cigarette would you hate most to give up?

The first in the morning	1
Any other	0

4. How many cigarettes per day do you smoke?

10 or less	0
11 to 20	1
21 to 30	2
31 or more	3

5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?

No	0
Yes	1

6. Do you smoke even if you are so ill that you are in bed most of the day?

No	0
Yes	1
TOTAL SCORE	

0-2 Very low dependence **5 Medium dependence** **8-10 Very high dependence**

3-4 Low dependence **6-7 High dependence**

Scores under 5: "Your level of nicotine dependence is still low. You should act now before your level of dependence increases."

Score of 5: "Your level of nicotine dependence is moderate. If you don't quit soon, your level of dependence on nicotine will increase until you may be seriously addicted. Act now to end your dependence on nicotine."

Score over 7: "Your level of dependence is high. You aren't in control of your smoking – it is in control of you! When you make the decision to quit, you may want to talk with your doctor about nicotine replacement therapy or other medications to help you break your addiction."

Clinic pt. number	Hospital sticker	Folder number		date	
Surname					

Wisconsin withdrawal scale

Please answer each question

	Strongly disagree	Disagree	Feel Neutral	Agree	Strongly agree	Score
1. Food is not particularly appealing to me.	0	1	2	3	4	
2. I am getting restful sleep.	0	1	2	3	4	
3. I have been tense or anxious	0	1	2	3	4	
4. My level of concentration is excellent	0	1	2	3	4	
5. I awaken from sleep frequently during the night	0	1	2	3	4	
6. I have felt impatient	0	1	2	3	4	
7. I have felt upbeat and optimistic	0	1	2	3	4	
8. I have found myself worrying about my problems	0	1	2	3	4	
9. I have had frequent urges to smoke	0	1	2	3	4	
10. I have felt calm lately	0	1	2	3	4	
11. I have been bothered by the desire to smoke a cigarette.	0	1	2	3	4	
12. I have felt sad or depressed	0	1	2	3	4	
13. I have been irritable, easily angered.	0	1	2	3	4	
14. I want to nibble on snacks or sweets.	0	1	2	3	4	
15. I have been bothered by negative moods such as anger, frustration, and irritability	0	1	2	3	4	
16. I have been eating a lot.	0	1	2	3	4	
17. I am satisfied with my sleep.	0	1	2	3	4	
18. I have felt frustrated	0	1	2	3	4	
19. I have felt hopeless or discouraged	0	1	2	3	4	
20. I have thought about smoking a lot	0	1	2	3	4	
21. I have felt hungry	0	1	2	3	4	
22. I feel that I am getting enough sleep	0	1	2	3	4	
23. It's hard to pay attention to things.	0	1	2	3	4	
24. I have felt happy and content	0	1	2	3	4	
25. My sleep has been troubled	0	1	2	3	4	
26. I have trouble getting cigarettes off my mind	0	1	2	3	4	
27. It had been difficult to think clearly	0	1	2	3	4	
28. I think about food a lot.	0	1	2	3	4	

Nicotine use inventory

Have you smoked any cigarettes since last visit (Y/N)	
Have you used any other tobacco product (pipe, cigars chew)? (Y/N)	
Have you smoked any cigarettes (even a puff) in last 7 days (Y/N)	
Have you used any nicotine containing products (patch, gum in last 7 days) (Y/N)	
If you have started smoking again when did you start?	

Hospital sticker

Clinic pt. number _____ **Folder number** _____ **Date**

Surname _____

Patient Health Questionnaire (PHQ-9)

Over the past 2 weeks? (Please answer each question)

	not at all	Several days	more than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down. Depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself or that you area failure or have let your self or your family down	0	1	2	3
7. Trouble concentration on things such as reading the newspaper or watching TV	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or hurting yourself in some way	0	1	2	3
	add columns		+	+
	Total score			

10. If you have checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

not difficult at all _____
Somewhat difficult _____
Very Difficult _____
Extremely difficult _____

Hospital sticker

Clinic pt. number _____ Folder number _____ Date _____

Surname _____

The Smoker's Emotional Index. (circle your answer)

1. If cigarettes were a person for you, they would be:
   a. an acquaintance
   b. a friend
   c. a good friend
   d. a sibling / brother or sister

2. If cigarettes were an object for you, they would be:
   a. a table
   b. a chair
   c. a cane/ walking stick
   d. a finger

3. Imagine that you dreamed of looking at yourself in a mirror. The picture you saw was:
   a. smiling
   b. serious
   c. sad
   d. crying

4. Think about how you have faced the problems that come up in your life. In this regard you:
   a. are satisfied
   b. are not happy
   c. sometimes feel useless
   d. feel like a failure

5. Regarding your personal relationships you:
   a. have great friends or relatives who understand you
   b. have at least one person to look at in difficult times
   c. only have superficial relationships
   d. are always alone

6. You feel that you are a person who is:
   a. calm
   b. preoccupied
   c. distressed
   d. extremely distressed

Reference:
Baddini-Martinez J, de Padua AI. Can an index of smokers' emotional status predict the chances of success *in* attempts to quit smoking? Med Hypotheses. 2013; 80:722-5.

Hospital sticker

Clinic pt. number _____ Folder number _____ Date _____

Surname _____

Clinical history (visit one)

Specific (medical and psychiatric history present?)

Sleep

GI symptoms currently

Anxiety/ depression

Examination

Gen

ENT

Resp

CVS

Abdo

Clinic pt. number _____ Hospital sticker Folder number _____ Date _____

Surname _____

Management plan

Are medical risk factors present?

Level of dependence (fagerstrom)

Current smoking No./day

Level of motivation

Counseling notes:

GI s/e, sleep disturbances

Mood changes and contacting site

Can patient afford to buy medication?

Prescription

Varenicline

Buproprion

Nicotine gum

Target quit date set

Date of next visit

Summary of scores for first visit

Fagerström score: _____

PHQ-9 score_____

Wisconsin:_____

Anger_____

Anxiety_____

Concentration_____

Craving_____

Hunger_____

Sadness_____

Sleep_____

Follow up visits

Hospital sticker

Clinic pt. number _____ Folder number _____ Date _____

Surname _____

Quit date

Visit No.	Day 1 Quit		2 wks post quit		6 wks post quit			11 wks post quit		
Did patient have phone call?		1wk post quit		4 wks post quit		8 wks post quit	10 wks post quit		6 months	1 year

Weight _____ BP _____ Pulse _____ Exhaled CO _____

PLEASE answer each question

Wisconsin withdrawal scale	Strongly disagree	Disagree	Feel Neutral	Agree	Strongly agree	Score
1. Food is not particularly appealing to me.	0	1	2	3	4	
2. I am getting restful sleep.	0	1	2	3	4	
3. I have been tense or anxious	0	1	2	3	4	
4. My level of concentration is excellent	0	1	2	3	4	
5. I awaken from sleep frequently during the night	0	1	2	3	4	
6. I have felt impatient	0	1	2	3	4	
7. I have felt upbeat and optimistic	0	1	2	3	4	
8. I have found myself worrying about my problems	0	1	2	3	4	
9. I have had frequent urges to smoke	0	1	2	3	4	
10. I have felt calm lately	0	1	2	3	4	
11. I have been bothered by the desire to smoke a cigarette.	0	1	2	3	4	
12. I have felt sad or depressed	0	1	2	3	4	
13. I have been irritable, easily angered.	0	1	2	3	4	
14. I want to nibble on snacks or sweets.	0	1	2	3	4	
15. I have been bothered by negative moods such as anger, frustration, and irritability	0	1	2	3	4	
16. I have been eating a lot.	0	1	2	3	4	
17. I am satisfied with my sleep.	0	1	2	3	4	
18. I have felt frustrated	0	1	2	3	4	
19. I have felt hopeless or discouraged	0	1	2	3	4	
20. I have thought about smoking a lot	0	1	2	3	4	
21. I have felt hungry	0	1	2	3	4	
22. I feel that I am getting enough sleep	0	1	2	3	4	
23. It's hard to pay attention to things.	0	1	2	3	4	
24. I have felt happy and content	0	1	2	3	4	
25. My sleep has been troubled	0	1	2	3	4	
26. I have trouble getting cigarettes off my mind	0	1	2	3	4	
27. It had been difficult to think clearly	0	1	2	3	4	
28. I think about food a lot.	0	1	2	3	4	

Nicotine use inventory

Have you smoked any cigarettes since last visit (Y/N)	
Have you used any other tobacco product (pipe, cigars chew)? (Y/N)	
Have you smoked any cigarettes (even a puff) in last 7 days (Y/N)	
Have you used any nicotine containing products (patch, gum in last 7 days) (Y/N)	
If you have started smoking again when did you start?	

Please answer each question

Over the past 2 weeks?	not at all	Several days	more than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down. Depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself or that you area failure or have let your self or your family down	0	1	2	3
7. Trouble concentration on things such as reading the newspaper or watching TV	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or hurting yourself in some way	0	1	2	3
	add columns Total score		+	+

10. If you have checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

not difficult at all _____
Somewhat difficult _____
Very Difficult _____
Extremely difficult _____

Clinic pt. number	Hospital sticker	**Folder number**		**Date**	
Surname				**Quit date**	
				Visit No.	

Follow up notes

Has the patient quit?

Any relapses?

GI side effects ?

Sleep and dreams?

Anxiety/ depression?

Other medication side effects?

Examination (if needed)

Wisconsin score	
Exhaled CO	
Weight gain/loss	
Medical complications	
Psychiatric risk?	

Management plan for next period:

Instructions for authors (South African Medical Journal)-abbreviated

Full instructions available at the following url:

http://www.samj.org.za/index.php/samj/about/submissions

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, which will delay publication.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).

- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAMJ is a generalist medical journal, therefore for articles covering genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.

- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

**NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'

- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Published Article

SAMJ RESEARCH

Challenges for dedicated smoking cessation services in developing countries

G Y Tadzimirwa,[1] MB ChB; **C Day**,[1] MB BCh, Dip HIV Man (SA), MMed (Medicine); **A Esmail**,[1] MD, FCP (SA), Cert Pulmonology (SA); **C Cooper**,[2] Dip Nurs; **M Kamkuemah**,[3] MPH; **K Dheda**,[1,4] MB BCh, FCP (SA), FCCP, FRCP, PhD; **R N van Zyl-Smit**,[1,4] MB ChB, MRCP (UK), Dip HIV Man SA, FCP (SA) MMed, Cert Pulm (SA), PhD

[1] *Division of Pulmonology, Department of Medicine, Faculty of Health Sciences, University of Cape Town, South Africa*
[2] *Division of Nursing, E16 Respiratory Clinic, Groote Schuur Hospital, Cape Town, South Africa*
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Corresponding author: *R N van Zyl-Smit (richard.vanzyl-smit@uct.ac.za)*

Background. South Africa, ranked as the world's second most stressful country to live in, has an estimated 7 million smokers. A dedicated smoking cessation clinic established at Groote Schuur Hospital, Cape Town, provides the only clinical service and training centre in the country.
Objectives. To evaluate the smokers attending the clinic, in order to better understand the requirements of smoking cessation services in resource-limited settings.
Methods. Demographic and smoking-related data were collected prospectively from all clinic attendees since its inception. Nicotine dependence, depression scores and exhaled carbon monoxide levels were formally evaluated. Consent was provided to review the data collected.
Results. Ninety-seven smokers were evaluated. Their mean (standard deviation) age was 50.9 (10.7) years, and 59% (57/97) were male. The median age of smoking initiation was 16 years (interquartile range (IQR) 8 - 28), with a current median daily consumption of 12 cigarettes (IQR 7 - 20). Overall, men smoked more than women, with a median of 20 cigarettes per day (IQR 10 - 20) v. 12 (IQR 5 - 20), respectively (p=0.001). The median Fagerström nicotine dependence score was 5 (IQR 3 - 7), with scores of 6 (IQR 4 - 8) for men and 5 (2 - 7) for women (p=0.06); 50% of smokers had a Fagerström score <6 (low to above-average dependence) and 22% a score ≥8 (extreme dependence). The median Patient Health Questionnnaire-9 (PHQ-9) depression score was 8 (IQR 4 - 11), and 49% of smokers had symptoms of at least minor depression (score ≥10). The clinic could not provide pharmacotherapy. The self-reported quit rate was 28% at median follow-up of 22 months (IQR 14 - 39).
Conclusions. In smokers attempting to quit, moderate levels of nicotine dependence coexist with significant depression and anxiety symptoms. These data inform resource allocation and public health strategies, suggesting that in resource-limited smoking cessation services, psychological/behavioural support focusing on depressive symptoms may be a greater priority than simple pharmacotherapy.

S Afr Med J 2019;109(6):431-436. DOI:10.7196/SAMJ.2019.v109i6.13631

The detrimental effect of smoking on population health has been apparent since the early 1900s, when a relationship between increased prevalence of smoking and increased incidence of lung cancer, previously uncommon, was identified.[1,2] Since then, numerous studies have highlighted the relationships between smoking and non-communicable diseases including cardiorespiratory disease, autoimmune disease, subfertility, malignancy, cerebrovascular disease and poor fetomaternal outcomes.[2-6]

South Africa (SA)'s first burden of disease report in 2000 highlighted the quadruple burden of disease the country faces and the need for a multifaceted approach to improving health that includes managing modifiable risk factors, particularly smoking.[7] It was reported that in SA in 2000, smoking accounted for 8.5% of all deaths (and 13% of deaths in adults aged >35 years) and 3.7 - 4.3% of disability-adjusted life-years due to lung and other cancers, cardiovascular disease, chronic obstructive pulmonary disease (COPD), tuberculosis and other medical conditions.[8] South Africa has an estimated 7.2 million adults living with HIV, 60% of whom are co-infected with TB, with 61% of adults on antiretroviral therapy.[9] In addition, both smoking and TB increase the risk of COPD.[10-13] However, individuals who quit smoking successfully lower their risk with every year after cessation. Furthermore, those who manage to quit before the age of 45 have the same life expectancy as those who have never smoked.[14]

Many low- and middle-income countries (LMICs) have made significant efforts to minimise adverse health outcomes due to smoking, with legislation restricting tobacco use, advertising and trade following the World Health Organization (WHO) MPOWER strategy.[15] Formal cessation programmes mainly exist in high-income countries, which equate to ~15% of the world's population able to access cessation support.[16] Very few data exist on formal cessation programmes provided in low-income settings or on how applicable cessation strategies developed in high-income settings are to low-income countries.[16,17] Furthermore, smoking cessation pharmacotherapy such as nicotine replacement therapy (NRT), although on the WHO essential medicine list, is not always available to smokers.[18,19] This is particularly true in SA, where, although it is classed as a middle-income country, no smoking cessation pharmacotherapy is available to smokers accessing public health services.

A combination of behavioural therapy and pharmacological support is regarded as the interventional strategy with the highest

odds of long-term cessation. There are, however, no data to indicate who will be unsuccessful if pharmacotherapy is not added to behavioural interventions.

Objectives

A dedicated smoking cessation clinic established at Groote Schuur Hospital (GSH) in Cape Town is the only one of its kind in SA. Our objectives were to to assess the sociodemographic and dependency profiles of the smokers who attended this clinic and their short- and long-term outcomes. By understanding the characteristics and needs of smokers in this setting, we hoped to provide relevant data to help guide locally applicable smoking cessation services applicable in LMICs. Identifying factors that support successful quitting, and those that act as barriers, is imperative in understanding the requirements for psychological and pharmacological support in such services.

Methods

Establishing the clinic

The first SA smoking cessation clinical practice guidelines were published in 2013.[19] Prior to this date and the establishment of the GSH clinic in December 2012, no formal smoking cessation services existed in the public sector. No pharmacotherapy was available for smoking cessation in government hospitals, and availability of nicotine patches was very limited owing to available products being withdrawn from SA. With permission from the Head of the Division of Pulmonology at GSH, a specialised clinic was introduced to offer evaluation of and smoking cessation support to any smoker wishing to quit. The clinic was established within the respiratory outpatient services for convenience, as the trained staff were from the Division of Pulmonology and the clinic was physically near the cardiology outpatients and transplant services. The doctors had received limited smoking cessation training at a variety of local workshops, and a nursing sister was trained to provide additional counselling. No specialist psychological/psychiatric support or pharmacotherapy was available in the clinic.

The study reviewed data collected from all smokers attending GSH's smoking cessation clinic since its inception. New patient data collection commenced when the clinic opened in 2012 and was truncated in September 2016. A pre-formed data capturing sheet to guide the consultation and to assimilate the required smoking cessation-specific information was used. Self-reported scales (Fagerström, Patient Health Questionnnaire-9 (PHQ-9), etc.) were completed by the individual person, with the remaining evaluation completed by the attending doctor. Information captured included age, motivation to quit, tobacco smoking history, medical history, Fagerström score, Wisconsin withdrawal score, PHQ-9 depression score and perceived medication affordability. Carbon monoxide (CO) levels were tested using a piCO Smokerlyzer (Bedfont, UK) at each visit.

Interventions

After completing the prespecified questionnaires, all attendees were seen by a doctor (pulmonologist or medical registrar). Basic smoking history was confirmed, and level of motivation and reasons for wishing to quit were evaluated. Counselling was performed by the doctor, as there were limited alternative counselling personnel. Counselling included evaluation of previous attempts to quit and reasons for relapse or failure. Information on nicotine dependence was provided, as well as on the importance of behavioural change and pharmacotherapy if needed. Interviews were conducted in a motivational interviewing style directed towards behavioural change with a specific focus on self-motivation, problem solving and strategies for coping with withdrawal symptoms.

Ethical considerations

Ethics approval to perform this clinical patient database review was granted by the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (ref. no. 667/205) and GSH administration. At the time of their first visit, all patients provided written informed consent to have their data relevant to the smoking cessation clinic collected as part of the standard evaluation of all patients at the clinic. Participants also provided contact details to allow for telephonic contact to provide support and evaluate outcomes.

Statistical analysis

Data were entered onto an electronic database and independently reviewed for accuracy. Analysis was conducted using Graphpad prism 5.0 for Mac OSX (GraphPad Software, USA) and Stata 13 (StataCorp, USA). Continuous data were expressed as means (standard deviations (SDs)) or medians with interquartile ranges (IQRs). For categorical data, the χ^2 test or Fisher's exact test was used. The Mann-Whitney test or Student's *t*-test was used to test the association between continuous and categorical variables. A *p*-value of 0.05 was used to determine statistical significance.

Results

Participants

The weekly smoking cessation clinic received the majority of its referrals from cardiology, respiratory and other tertiary clinics (organ transplant, infertility) at GSH. A few attendees were 'healthy smokers' from outside the hospital. During the audit review, 98 smokers attended for at least one visit. Only 1 attendee did not complete the requisite forms and was not included in any of the analyses.

Detailed characteristics of the patients attending the clinic are reported in Table 1. There was a predominance of male smokers (60%, 58/97). The mean (SD) age of attendees was 51.1 (10.9) years. There was no difference in the age of men compared with women, and the median age of smoking initiation was similar at 16 years (IQR 8 - 28). On average, men smoked more cigarettes per day than women (median 20 (IQR 10 - 20) v. 12 (IQR 5 - 20), respectively; p=0.001), resulting in higher cumulative total pack-years of smoking at the time of the first visit (33 (IQR 20 - 45) v. 21 (IQR 7 - 33); p=0.001). However, at the time of the first visit the majority of attendees were smoking 12 cigarettes per day on average. The most frequent motive noted for quitting was, not unexpectedly, health reasons (Table 2).

The majority of attendees had previously tried to quit: 91% had made at least one attempt within the past year, with 48% making more than four attempts in the past 12 months. Only 8% reported having previously used pharmacotherapy in a quit attempt. Of the attendees, 68% lived with other smokers in the house. One-third (32%) indicated at the initial visit that they could potentially afford to purchase medication privately to assist with the quit attempt (Table 2).

Nicotine dependence was evaluated using the Fagerström Test.[20] The median score was 6 (IQR 3 - 7). Women had slightly lower scores than men (median 5 (IQR 2 - 7) v. 6 (IQR 4 - 8), respectively; p=0.06), as shown in Table 2. However, 50% of smokers had a score of 4 - 5, indicating 'above-average' dependence, and 23% had a score >8, indicating 'extreme dependence' (Fig. 1). Exhaled CO levels were similar in men and women, with a mean (SD) score of 15.9 (9.1) parts per million. Exhaled CO correlated positively with current tobacco consumption (Spearman's r=0.52 (95% confidence interval (CI) 0.28 - 0.70); p<0.001)) and with Fagerström scores, although

Table 1. Attendee characteristics

Characteristics	Female (*N*=39, 40%)	Male (*N*=58, 60%)	Total (*N*=97)
Current age (years), mean (SD)	48.5 (9.5)	52.4 (11.3)	50.9 (10.7)
Age at smoking initiation (years), median (IQR)	16 (15 - 19)	16 (14 - 18)	16 (14.5 - 18)
Total years smoked, mean (SD)	31.7 (10.1)	34.7 (11.9)	33.5 (11.3)
Average number per day smoked, median (IQR)	12 (5 - 20)*	20 (10 - 20)*	20 (10 - 20)
Current number per day smoked, median (IQR)	11 (8 - 17)	15 (6 - 25)	12 (7 - 20)
Total pack-years smoked, median (IQR)	21 (7 - 33)*	33 (20 - 45)*	29.5 (12.5 - 40)
Previous attempt to quit smoking, *n* (%)	32 (82)	43 (75)	75 (78)
Quit attempts in the past year, *n* (%)			
None	3 (8)	6 (11)	9 (9)
1 - 4	18 (46)	23 (40)	41 (43)
>4	18 (46)	28 (49)	46 (48)
Lives with smoker in house, *n* (%)	28 (72)	37 (65)	65 (68)
Number of smokers in house, *n* (%)			
0	11 (28)	20 (35)	31 (32)
1 - 2	17 (44)	21 (37)	38 (40)
>2	11 (28)	16 (28)	27 (28)

SD = standard deviation; IQR = interquartile range.
*$p<0.05$.

Table 2. Dependence and barriers to quitting smoking

Variable	Female	Male	Total
Fagerström dependence score (*N*=90), median (IQR)	5 (2 - 7)*	6 (4 - 8)*	6 (3 - 7)
Exhaled CO (ppm), median (IQR)	15 (9 - 23)	14 (9 - 20)	14.5 (9 - 20)
Motivation score (1 - 10), median (IQR)	10 (8 - 10)	10 (6 - 10)	10 (8 - 10)
Reasons for quitting smoking (*N*=98), *n* (%)			
Personal health	21 (54)	22 (39)	43 (44)
Financial reasons	3 (8)	1 (2)	4 (4)
Family	1 (3)	3 (5)	4 (4)
Fertility	0	1 (2)	1 (1)
PHQ-9 depression score (*N*=55), median (IQR)	8 (4 - 11)	8 (5 - 11)	8 (4 - 11)
PHQ-9 total score (*N*=55), *n* (%)			
0 - 4	9 (41)	6 (18)	15 (27)
5 - 9	8 (36)	11 (33)	19 (35)
10 - 15	2 (9)	9 (27)	11 (20)
>15	3 (14)	7 (21)	10 (18)
Wisconsin Withdrawal Scale subscore, median (IQR)			
Anger (*N*=87)	2.33 (1.3 - 3)	2 (1.33 - 3.3)	2 (1.3 - 3)
Anxiety (*N*=90)	2.5 (1.8 - 3)	2.25 (1.3 - 2.8)	2.25 (1.25 - 3)
Sadness (*N*=89)	2 (1.3 - 2.6)	1.75 (1 - 2.5)	2 (1.25 - 2.5)
Patient could potentially afford to purchase medication (*N*=87), *n* (%)	10 (28)	18 (35)	28 (32)

IQR = interquartile range; CO = carbon monoxide; ppm = parts per million; PHQ-9 = PHQ-9 = Patient Health Questionnaire-9.
*$p<0.05$.

less strongly (r=0.41 (95% CI 0.15 - 0.62); p=0.02). Current number of cigarettes per day correlated strongly with the Fagerström score (r=0.74 (95% CI 0.62 - 0.82); $p<0.001$) (Fig. 2). Motivation to quit was reported as high, and there was no difference in in that regard between men and women.

Depressive symptoms were prospectively evaluated, and complete scores were evaluable for 55 attendees at the first visit using the PHQ-9 depression test. Nearly two-thirds (63%) of smokers reported at least minor symptoms of depression when screened at the first visit, and 38% (21/55) expressed symptoms of at least moderately severe depression (score ≥15) (Fig. 3); 18% (10/55) would be classified as severely depressed based on the PHQ-9 score. Evaluating the individual specified subcategories making up the Wisconsin Withdrawal Scale at the initial visit (when the participants were still smoking), patients had on average high (>2/4) subscores for anger, anxiety and sadness (Table 2).

Smokers who had attended the clinic were contacted by telephone in 2016/17. Using the contact numbers provided at the first visit, only 46 (47%) of the 97 attendees were contactable. The median time to follow-up was 22.5 months (IQR 14 - 39) after the first clinic visit. Based on self-reported smoking status, 13 attendees (28%) had successfully quit, 33 (72%) were still smoking, and 2 were stated to have died (cause not reported). Although the review was not specifically powered to evaluate predictors of outcome, individuals who had successfully quit had lower mean (SD) PHQ-9 depression scores than those who had been unsuccessful (3.9 (1.9) v. 7.1 (1.0),

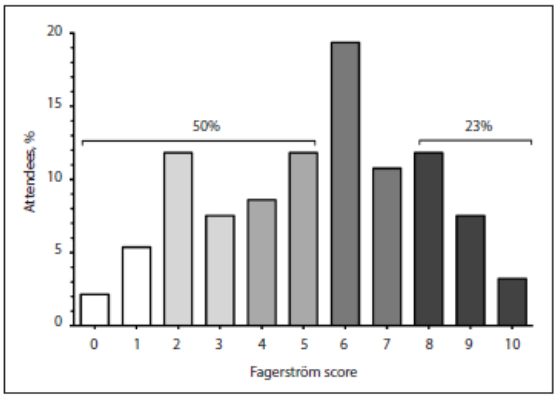

Fig. 1. Fagerström scores for nicotine dependence. (Interpretation of dependence scores: 0 - 1 low, 2 - 3 average, 4 - 5 above average, 6 - 7 high, 8 - 10 extreme nicotine dependence.)

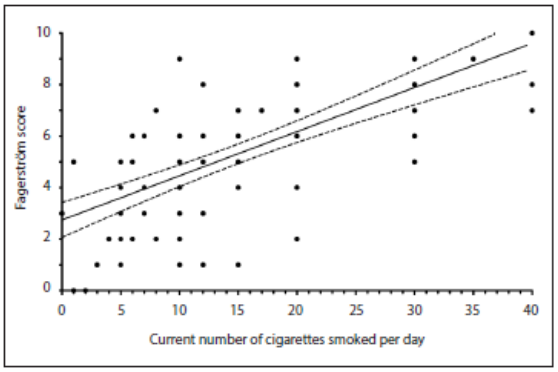

Fig. 2. Correlation between current daily number of cigarettes smoked and Fagerström score for nicotine dependence. Solid line: regression line with 95% CI, Spearman's r=0.74 (95% CI 0.62 - 8.82); p<0.0001. (CI = confidence interval.)

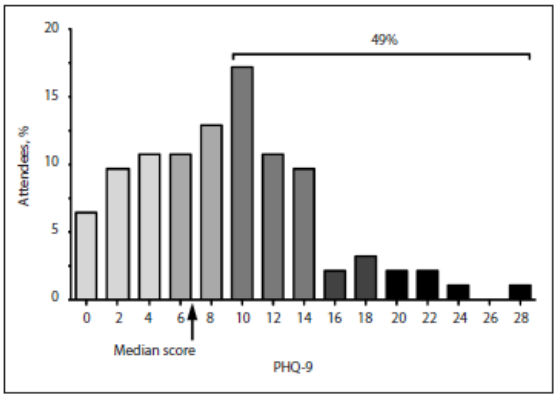

Fig. 3. PHQ-9 depression scores. (Interpretation of PHQ-9 score: 0 - 4 no symptoms, 5 - 9 minimal symptoms, 10 - 14 minor depression/major depression mild, 15 - 19 major depression moderately severe, >20 major depression severe; PHQ-9 = Patient Health Questionnnaire-9.)

respectively; p=0.046). In univariate analysis this translated into a trend towards successful quitting with a lower depression score (odds ratio 0.86 (95% CI 0.76 - 1.00); p=0.056). There was no difference in the number of clinic visits attended by those who quit successfully v. those who did not, or in duration of follow-up when contacted. Time to first cigarette in the morning was not predictive of success, and no difference was seen between quitters and non-quitters with regard to baseline nicotine dependence scores (Fagerström score 4 v. 5; p=0.34) (Fig. 4, A and B).

Discussion

Access to formal smoking cessation services is very limited in LMICs.[16] In this cohort of smokers from a low- to middle-income population group in SA attending a dedicated smoking cessation service, high levels of depressive symptoms were common, with accompanying moderate nicotine dependence. Currently no pharmacotherapy is provided by the government to assist smokers in quitting. Given the high level of depressive symptoms and stressors with relatively low nicotine dependence reported by the attendees, psychological and behaviour support for smokers should be a priority. The role for pharmacological support, given its poor availability and high cost, needs to be prospectively determined. Despite the lack of pharmacotherapy or specialised psychological support to assist in smoking cessation, some patients were successful in quitting smoking.

Global smoking cessation guidelines, including the SA guidelines, recommend a combination of behavioural support/counselling and pharmacotherapy to support smoking cessation attempts.[19,21,22] The WHO has placed NRT on the essential medication list, but access to pharmacotherapy is severely limited and costly in resource-constrained settings, even in a middle-income country such as SA.

To date there have been very limited data published on smoking cessation clinics in LMICs. The majority of reports are on integrated/opportunistic brief interventions alongside healthcare services.[16,17] Opportunities such as tuberculosis and HIV treatment programmes have shown promise as a chance to address tobacco smoking in conjunction with treating infectious diseases.[23,24] In many developed-world settings, in-hospital smoking cessation strategies have been an opportunity to commence interventions.[25] What is clear, however, is that if patients are not followed up or continued on treatment on discharge, all gains during the hospital stay with regard to quitting smoking are essentially for naught.

SA has been characterised as the world's second most stressful country to live in, although these data do not include much of Africa.[26] If one compares the level of stressors in SA with other countries globally, however, Egypt (for example) is ranked 15th, Brazil 17th, China 29th, the UK 56th and Australia 70th. During counselling of the smokers in our study, common reported stressors included personal safety, financial insecurity, health concerns, community safety and anxieties regarding the country's future. These concerns may be intensified by a hospitalisation or acute medical illness, especially if an additional financial strain and burden is precipitated by lack of income and family support.[27] Unexpected hospital admissions may therefore not be the best opportunities to intervene, given the accompanying heightened stress.

Smokers in our outpatient cohort showed significant levels of background depressive symptoms, both on the formal PHQ-9 depression scoring and also when we evaluated the subscore of the Wisconsin Withdrawal Scale (while the attendees were still smoking). In active smokers, a balance exists between tobacco/nicotine dependence and the psychological/ behavioural habit of smoking (although these aspects are not always clearly separable). There is strong evidence that counselling and pharmacotherapy go hand in hand, with a combination generally better than either alone.[21] What

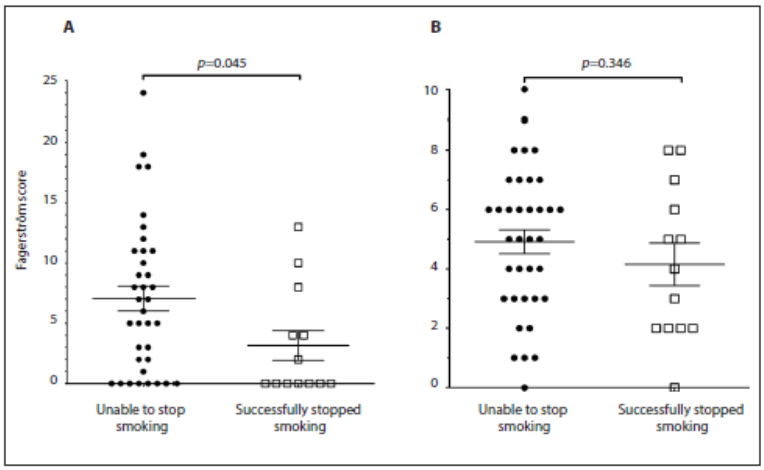

Fig. 4. Characteristics of patients with known outcomes at 2-year median follow up: (A) PHQ-9 depression score by outcome; (B) Fagerström nicotine dependence score by outcome (mean (SD)). (PHQ-9 = Patient Health Questionnaire-9; SD = standard deviation.)

is not clear, and has no literature to support it, is how to estimate whether an individual will be able to quit without the addition of medication. There is a strong correlation between Fagerström score and long-term cessation success,[28] and specifically time to first cigarette in the morning has been shown to be a simple measure to use.[28] Additionally, underlying depression and poor outcomes are correlated in reports from smoking cessation services.[29] In our cohort, no significant correlation was found between dependence indices and outcome, although the audit was not primarily powered to evaluate predictors of outcome owing to the nature of the study. Despite the lack of pharmacotherapy long-term quit rates were encouraging, although an estimation of true success was not possible owing to the excessive loss to follow-up and inability to confirm smoking status chemically. What was evident in this cohort of low-income smokers was the low to moderate level of nicotine dependence and moderate to high level of depressive symptoms. This finding raises the question whether it is preferable to spend resources on skilled counselling when establishing dedicated smoking cessation centres in low-income settings, or on the provision of NRT/varenicline/bupropion to aid in quit attempts for all patients.

Study limitations

The study has several limitations. Referral to the service was encouraged for smokers motivated to quit. The service did not have on-site specialised counselling for depression or anxiety, but relied on referral to such services. The level of depressive symptoms may be different in individuals who are not willing to quit, but the characteristics of the attendees presented were of those wanting help to stop smoking. It was not possible to evaluate whether outcomes would have been different if the patients had had access to pharmacotherapy. There is therefore uncertainty whether to prioritise counselling or medication, but the high level of depressive symptoms requires attention irrespective of smoking status. Follow-up was incomplete, as many of the contact telephone numbers that were provided did not work. Prespecified powered outcome calculations were not possible, but patient data collection is ongoing.

Recommendations

The questions facing the clinician with limited access to pharmacotherapy to assist smoking cessation are who should receive it, and whether it is possible to predict who will not be successful without the provision of medication. An approach could be to initiate an intensive behaviour motivation intervention irrespective of dependence scores, and to provide NRT at the second attempt for those who fail due to withdrawal symptoms. The strategy in our clinic was to provide a support service that did not previously exist in an attempt to help smokers quit, and to gather the necessary data to motivate for locally relevant psychological and/or pharmacological interventions. Based on the data from this cohort, attending to the social, financial and emotional upheaval described by the majority of smokers seen may be of far more importance than pharmacotherapy in achieving long-term freedom from tobacco dependence. Poverty alleviation, sustainable income and mental health are not issues that can simply be solved by a nicotine patch or gum. Providing behavioural tools to assist with coping with life stressors, counselling and appropriate referral to social services is a starting point to explore in low-income settings where the behavioural aspects of tobacco dependence as a coping mechanism may outweigh the pure chemical addiction.

As with all interventions in medicine, the certainty with which outcomes/response to therapy can be predicted enhances our decision-making and ability to motivate to funders to support treatment strategies. In low-resourced areas, the clinician is bound to equitable resource allocation and often provides interventions for those who will 'benefit' the most. If we could reasonably identify those who will inevitably fail without pharmacotherapy, we could motivate for such targeted interventions. Extrapolating from the nicotine dependence scores in this cohort, ~25% had very high dependence and should by any major guideline strategy have been receiving pharmacological support. The PHQ-9 scores indicative of major depression in ~1 in 5 smokers would warrant appropriate referral to competent psychiatric services before any quit attempt is made. Depending on the skills of the service providers (doctor v. psychologist), these services could be interlinked.

Conclusions

Smoking cessation should be a priority in all healthcare services, especially in low-income settings where smoking results in a significant health burden, drives mortality rates and consumes substantial disposable income among those who can least afford it. High levels of depression and social stressors existed in our cohort of smokers, suggesting that interventions targeting the behavioural aspects of tobacco dependence should be emphasised and potentially balanced with the provision of NRT for those with very high dependence. Prospective, scalable and cost-effective interventions for tobacco dependence are needed to address this major modifiable risk factor for communicable and non-communicable diseases in low-income settings.

Declaration. None.

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Author contributions. RNvZS established the audit, AE, CD, RNvZS and CC collected the

data, MK, RNvZS and GYT analysed the data, and all authors reviewed the manuscript prior to publication.

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Conflicts of interest. RNvZS received honoraria from Pfizer for smoking cessation-related academic presentations.

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Reviewer Comments

Date: Sep 18, 2018
To: "Richard van Zyl-Smit" richard.vanzyl-smit@uct.ac.za
From: "SAMJ" submissions@hmpg.co.za
Subject: Decision on your Submission to SAMJ

Ref.: SAMJ13631
Challenges for dedicated smoking cessation services in developing countries
South African Medical Journal

Dear Professor van Zyl-Smit,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript.

For your guidance, reviewers' comments are appended below.

If you are prepared to undertake the work required, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript.

Your revision is due by Oct 16, 2018. Please let us know if you require additional time.

To submit a revision, go to https://samj.editorialmanager.com/ and log in as an Author. You will see a menu item called Submission Needing Revision.

Best wishes

Bridget Farham, PhD
Editor
South African Medical Journal

Reviewers' comments:

Reviewer's Responses to Questions

Please comment on your General impression of this manuscript - bear the following in mind:

Is the article relevant?

Does it offer anything new?

Are there similar studies in our region/outside the region?

Does it add to the existing medical body of knowledge?

On first glance, are the methods, results and conclusions reasonable?

Do the conclusions actually draw on the results?

Does the article have a clear message?

Will it help SAMJ readers make better clinical decisions and, if so, how?

Is a general medical journal the right place for it?

Reviewer #1: The article has a clear message and is well presented. It is new data. Also see below overall comments

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Please comment on the Methods and analysis presented in this manuscript

Study design

Is the research question and planned outcomes clearly defined?

Was the sample adequate and sufficiently described?

Are the methods adequately described and appropriate to the study objectives?

Statistical considerations

Are simple statistical methods applied appropriately?

Reviewer #1: There are no problems with this aspect except for the large drop out numbers

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Please comment on the Results, Discussion and Conclusions presented in this manuscript

Results

Is the population/sample adequately described?

Are the results clearly presented?

Are they credible and do they answer the research question?

Are tables clear and useful, not simply mirroring data discussed in the Results text?

Reviewer #1: It is well written but has flaws- see overall comments

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Discussion

Are the results well discussed in light of previous evidence and the literature?

Are the limitations of the study sufficiently discussed?/ Are the strengths and weakness discussed?

Is the meaning and relevance of the study discussed?

Reviewer #1: As above

Conclusion

Are the implications of the research summarised?

Do the authors make relevant recommendations for future research or application?

Reviewer #1: As above

Reviewer #1: Challenges for dedicated smoking cessation services in developing countries: SAMJ13631
This is a well written paper that describes a successful smoking cessation clinic that functions without access to pharmacotherapy. A quit rate of 28% is as high as that described for many of the more expensive medications but It is a pity however that only about half were contactable after the follow up period- As such it is possible that only 12-14% actually quit if all the patients that were not traceable still smoked. I am also concerned that it was self-reported smoking status that was used as this is notoriously unreliable as the subjects are reluctant to admit failure and to disappoint their doctor. As such the discussion which states that acceptable outcomes were achievable is only probably true as previous studies have shown benefit of supportive therapy as a means of quitting.
To me the greatest value of the study would be to describe the setting up of the clinic and to describe the interventions that were employed, eg how much counselling was provided, was there a psychologist in attendance, was there a dedicated help line, how many visits did each patient make, wht interval were the visits, what were the 3 month success rates and were these checked by CO measurements. Were those that were not contactable patients who dropped out of the programme early etc etc - these data are not provided
It is interesting that there is a relationship to depression as quitting per se enhances depression and can be associated with suicidal ideation. However antidepressants generally ae not effective other than Zyban and as such correction of the depression alone has not been shown to be successful.

As is noted Sa is a stressful place to live in- It is somewhat "pie in the sky" to suggest that job opportunities would help- Whether or not one is unemployed is not usually an important determinant of smoking status. What is more important is level of education and if this were to be achievable it would also help with employment.
There are a few specific points:
1. Line 49: Background: "programmes... equate"
2. line 17 page 2 background ...imperative to the understand the requirements...
3. line 37 methods: ...were completed by the individual, with the remaining evaluations completed...
4. Results line 38: were 'healthy smokers"
5. Page 2 discussion Line 10: What is unclear and there is no literature to support it, is the....
If some of these questions are addressed I think that this paper is publishable and could provide guidance on how to set up and manage a clinic in a LMIC.

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