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ASSOCIATIONS BETWEEN BIOLOGICAL ALCOHOL CONSUMPTION MARKERS, REPORTED ALCOHOL INTAKES, AND BIOLOGICAL HEALTH OUTCOMES IN AN AFRICAN POPULATION IN TRANSITION

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SUMMARY

BACKGROUND

Alcohol consumption probably plays an important role in the transition associated with urbanisation in developing countries. The World Health Organisation recently stated that alcohol consumption is the fifth leading cause of death worldwide and that intakes are increasing, especially in developing countries. A third of South Africans reported to drink, do so in excess (20 litres of absolute alcohol per drinker per year). The observed pattern of binge drinking is of concern. Binge drinking additionally results in an increased cardiovascular disease risk as well as micronutrient deficiencies, both showing high prevalences in the South African population. More importantly, there is a need to identify and assess with accuracy, high risk drinking in this population. Epidemiological evidence suggests a J or U shaped relationship between alcohol consumption and cardiovascular disease. The South African food based dietary guidelines advise "sensible" drinking, due to the possible cardiovascular protective effects associated with light to moderate alcohol consumption. Additionally, present recommendations for alcohol intake are based mainly on evidence of beneficial effects in populations of developed countries. It is, therefore, important to evaluate the cause and consequences of alcohol intake on both societal and health related issues in an African population, in order to readdress the South African food based dietary guidelines regarding alcohol consumption.

Identification and assessment of high risk drinking in a population may be problematic. Therefore, it could be more beneficial to use biological markers of alcohol consumption to verify reported intakes and to identify and assess high risk drinking with better accuracy. Percentage carbohydrate deficient transferrin (%CDT) and gamma glutamyl transferase (GGT) are sensitive to high alcohol consumption and are the most suitable biomarkers available for identifying alcohol abuse in most populations. Biomarkers are defined as indicators of actual or possible changes of systemic, organ, tissue, cellular and sub-cellular structure and functional integrity, which can be used singly or in batteries to monitor health and exposure to compounds in populations and individuals. Development

of validated and predictive biomarkers is an essential research objective in medical sciences. Biomarkers must be both biologically and methodologically valid and should reflect a future health outcome at a stage when dietary intervention will be effective.

AIMS AND OBJECTIVES

The main aim of this thesis is to examine aspects of the role that alcohol plays in the health transition amongst African volunteers in rural and urban areas of the North-West Province of South Africa. Specific objectives were to:

1. Review the literature on alcohol consumption and its consequences, with a focus on the South African situation.
2. Compare self reported alcohol consumption and its association with percentage carbohydrate deficient transferrin (%CDT) and gamma glutamyltransferase (GGT) in a random sample of rural and urban Africans in transition using samples from the *PURE study,* in an attempt to examine known biological markers for alcohol consumption in this population.
3. Examine the biological health outcomes of alcohol consumption in a random, apparently healthy sample of rural and urban Africans in transition, using the data from the *THUSA study.*

STUDY DESIGN

The THUSA study

In this cross-sectional, comparative, population-based study 1854 men and women, aged 15 years and older and from five levels of urbanisation (deep rural tribal areas, farms, informal housing areas or squatter camps, established urban townships and 'upper' urban areas) voluntarily participated. This Transition and Health during Urbanisation of South Africans study (THUSA) was conducted between 1996 and 1998. Thirty-seven randomly selected sites were investigated in rural and urban areas covering all districts of the North West Province of South

Africa. Pregnant and lactating women as well as subjects taking any form of chronic medication, with body temperatures above 37^0C and who were inebriated, were excluded.

The PURE study

This cross-sectional epidemiological survey was part of the North West Province, South African leg (NWPSA) of the 12-year Prospective Urban and Rural Epidemiology (PURE) study which investigates the health transition in urban and rural subjects. The main selection criterium was that there should be migration stability within the chosen rural and urban communities. The rural community (A) was identified 450 km west of Potchefstroom on the highway to Botswana. A deep rural community (B), 35 km east from A and only accessible by gravel road, was also included. Both communities are still under tribal law. The urban communities (C and D) were chosen near the North-West University (Potchefstroom Campus). Community C was selected from the established part of the Township next to Potchefstroom and D from the informal settlements surrounding community C. The baseline data for NWPSA were collected from October-December 2005. A total of 2010 apparently healthy African volunteers (35 years and older), with no reported chronic diseases of lifestyle, tuberculosis (TB) or known HIV were recruited from a sample of 6000 randomly selected households.

METHODS

A variety of quantitative and qualitative research techniques was used by a multi-disciplinary team to collect, analyse and interpret data generated from biological samples and questionnaires. Data were analysed using the Statistical Package for Social Sciences (SPSS), version 15 package. Means, medians, standard deviations and 95% confidence intervals were calculated. In the PURE study, data were not normally distributed and non-parametric tests were used to test for significant differences between groups. Wilcoxon signed ranks test and Mann-

Whitney/Wilcoxon rank sum tests were used to compare groups. Multivariate regression analysis, stepwise regression methods, Spearman rank-order and partial correlations were used to examine the associations between self-reported alcohol intake and biochemical markers (%CDT and GGT), whilst the latter was used for testing associations after adjustments of possible confounding factors.

As for the THUSA study, data that were not normally distributed were logarithmically transformed and non-parametric tests used to test for significant differences between groups and effects of urbanisation. Univariate analysis of variance (ANOVA), post hoc test of least significant differences (LSD), multivariate regression analysis, stepwise regression methods and Spearman rank-order correlations with adjustments for confounding factors were used to examine the relationships between alcohol consumption and biological (health) variables.

RESULTS

After an extensive in depth literature review on alcohol consumption with a focus on the South African situation, three review papers were generated discussing the role of alcohol consumption from a *molecular to a societal perspective*.

The THUSA study

In this study, 61.5% of the men and 25.2% of the women reported that they consumed alcoholic beverages. Mean alcohol intakes of men (30.2 +/- 47.8 g/day) exceeded the recommend value of 21g/day. The women had a mean intake of 11.4 +/- 18.8g/day, falling within the 12-15g/day recommendation. Older drinkers (>40 years) and those infected with HIV drank more. Levels of urbanisation had little effect on amounts consumed but sorghum beer was replaced by commercial beer in urban areas. Drinkers had significantly higher HDL-C, serum triglycerides, blood pressure and iron status variables than non-drinkers. When serum ferritin was used to classify subjects into those in negative iron balance (<12μg/L), "normal" balance (12-150μg/L) and positive iron balance (>150μg/L),

it became evident that alcohol intake almost doubled the proportion of subjects in positive iron balance (in men: from 25 to 46%; in women from 11 to 23%).

The PURE study

Of the 716 men and 1192 women, 64% and 33% respectively reported that they consumed alcohol. Mean habitual intakes of self-reported drinking men and women were 29.9 (+/-30.0) and 23.3 (+/-29.1) g of pure alcohol per day. A statistically significant correlation between the two dietary methods (QFFQ and 24 hour recall) was observed, higher than +0.45 in both men and women. Self-reported habitual intakes of the whole group correlated positively and significantly with both %CDT (R=0.32) and GGT (R=0.433). After controlling for confounding factors (body mass index and smoking), these relationships were R= 0.19 and 0.31 respectively. However, 19% (n=45) of the men and 26% (n=184) of the women non-drinkers had elevated GGT while 48% (n=113) and 38% (n=269) of the non-drinking men and women respectively had elevated %CDT levels.

DISCUSSION AND CONCLUSIONS

These results indicate that despite a significant correlation between reported alcohol intake and GGT and %CDT levels, other factors besides alcohol consumption influenced these two biological markers. Clearly, a more specific marker is needed.

The THUSA and PURE studies were done in the same areas of the North West Province from 1996-1998 (THUSA) and in 2005 (PURE). The amounts of alcohol consumption reported by the men drinkers were 30.2 and 29.9g/day, while the proportion of drinkers increased from 61.5% to 64.2% respectively. The women drinkers increased from 25.2% to 33% and the reported amounts shifted from 11.4 to 23.3g/day. These results suggest that the dietary questionnaire used in this population gave similar results for men and indicated a significant increase in alcohol intake amongst the women drinkers (11.4 vs 23.3g/day).

It is concluded that both GGT and %CDT could misclassify non-drinking subjects as drinkers in this African population and values of these two markers should be interpreted with care. Additionally, it may be necessary to revise the cut off values for a non drinking African population. Although the beneficial effect of alcohol consumption on HDL-C was observed, the effects on iron status and balance are of concern and should be researched in more detail.

KEYWORDS self-reported alcohol consumption, questionnaires, percentage carbohydrate deficient transferrin, gamma glutamyltransferase, Africans, transition, biological health outcomes, iron status, ferritin, PURE, THUSA.

OPSOMMING

AGTERGROND

Alkohol inname speel waarskynlik 'n belangrike rol in die voedingsoorgang wat geassosieer word met verwesteliking in ontwikkelende lande. Die Wêreld Gesondheidsorganisasie het onlangs verklaar dat alkoholinname wêreldwyd die vyfde grootste oorsaak van sterftes is en dat inname besig is om te verhoog veral in ontwikkelende lande. 'n Derde van Suid-Afrikaners wat drink drink oormatig (20 liter absolute alkohol per drinker per jaar). Hierdie waargeneemde drinkpatroon is kommerwekkend. Oormatige akute alkoholinname lei tot 'n verhoogde risiko vir kardiovaskulêre siektes sowel as mikronutriënttekorte, beide die toestande se voorkoms is hoog in die Suid Afrikaanse bevolking. Meer belangrik, is dat daar 'n behoefte in hierdie populasie bestaan om 'n metode te identifiseer wat met akkuraatheid hoë risiko drinkgewoontes kan assesseer. Epidemiologiese studies het 'n J- of U-vormige verhouding tussen alkoholinname en kardiovaskulêre siektes waargeneem. Die Suid-Afrikaanse voedselgebaseerde riglyne adviseer oordeelkundige alkohol inname, a.g.v. die moontlike kardiovaskulêre beskermende effekte geassosieer met lig tot matige alkoholinname. Die huidige aanbevelings aangaande alkoholinname is hoofsaaklik gebaseer op bewyse van voordelige effekte in populasies binne ontwikkelde lande. Dit is dus belangrik om die oorsaak en gevolge van alkohol inname op beide gemeenskaps- en gesondheidsverwante vlak te evalueer in 'n Afrikaanpopulasie in 'n ontwikkelende land om sodoende vas te stel of dit nie nodig is om die Suid-Afrikaanse voedselgebaseerde riglyne aangaande alkoholinname in heroorweging te neem nie.

Identifisering en beraming van hoë-risiko alkoholinnames in hierdie populasie is problematies. Daarom kan dit meer voordelig wees om biologiese merkers vir alkohol inname te gebruik om gerapporteerde innames te verifieer en om met meer akkuraatheid hoë risiko drinkgewoontes te identifiseer en te assesseer. Persentasie koolhidraattekort transferrien (%CDT) en gamma-glutamieltransferase (GGT) is sensitief vir alkohol inname en is die geskikste biomerkers beskikbaar om alkoholmisbruik te identifiseer in

die meeste populasies. Biomerkers word gedefiniëer as aanwysers vir werklike of moontlike veranderings van sisteme, organe, weefsels, selle of op sub-sellulêre vlak van struktuur en funksionele integriteit, wat alleen of gesamentlik gebruik kan word om gesondheid en blootstelling aan chemiese verbindings in populasies en individue te monitor. Biomerkers moet dus beide biologies en metodies geldig wees en moet die toekomstige gesondheidsuitkomste op 'n stadium aandui waartydens dieetintervensies nog effektief sal wees.

DOELWITTE EN OBJEKTIEWE

Die hoofdoelwit van die proefskrif is om die aspekte van die rol wat alkohol speel in die gesondheidsoorgang te ondersoek onder Afrikaan vrywilligers in 'n plattelandse en verstedelikte gebied van die Noordwes provinsie van Suid-Afrika. Spesifieke doelwitte, was om:

1. Om 'n oorsig te gee van die bestaande literatuur aangaande alkohol inname en die gevolge daarvan, met die fokus op die Suid-Afrikaanse situasie.
2. Self gerapporteerde alkoholinname en die assosiasie met vlakke van die %CDT en GGT in 'n gerandomiseerde steekproef van plattelandse en verstedelikte Afrikaanpopulasie in oorgang te vergelyk deur monsters te gebruik van die PURE studie, in 'n poging om bekende biologiese merkers vir alkoholinname in hierdie populasie te ondersoek.
3. Om biologiese gesondheidsuitkomste van alkoholinname in 'n gerandomiseerde steekproef ooglopend gesonde plattelandse en verstedelikte Afrikaanpopulasie in oorgang te ondersoek, deur van data uit die THUSA studie gebruik te maak.

STUDIE ONTWERP

Die THUSA studie

In hierdie dwarsdeursnit vergelykende populasie-gebaseerde studie het 1854 skynbaar gesonde mans en vrouens ouer as 15 jaar van vyf vlakke van verstedeliking, (diep plattelandse stam areas, plase, informele behuisingareas of plakkerskampe, gevestigde verstedelikte plakkerskamp en 'boonste' verstedelikte gebiede) vrywillig deelgeneem. Die oorgang en gesondheid gedurende verstedeliking van Suid

Afrikaners studie ('Transition and Health during Urbanisation of South Africans' - THUSA) was uitgevoer tussen 1996 en 1998. Sewe-en-dertig ewekansig geselekteerde gebiede is geöndersoek in verstedelikte en plattelandse areas van alle gebiede in die Noordwes provinsie van Suid-Afrika. Swanger en lakterende vroue, gebruikers van enige vorm van kroniese medikasie, individue met 'n liggaams temperatuur bo 37 ^{0}C en diegene wat bekonke was, was uitgesluit.

Die PURE studie

Die dwarsdeursnit epidemiologiese waarnemingstudie was deel van die Noordwes provinsie, Suid-Afrikaanse been van die 12 jaar prospektiewe verstedelikte en plattelandse epidemiologiese studie (PURE) wat die gesondheidsoorgang in verstedelikte en plattelandse persone ondersoek. Die hoof seleksiekriteria was dat daar migrasiestabiliteit binne die gekose plattelandse en verstedelikte gemeenskappe moes bestaan. Die plattelandse gemeenskap (A) was geïdentifiseer 450 km wes van Potchefstroom op die hoofweg na Botswana. 'n Diep plattelandse gemeenskap (B), 35 km oos van A wat slegs toeganglik is met 'n grondpad, was ook ingesluit. Beide gemeenskappe was nogsteeds onder stamwette. Die verstedelikte gemeenskappe (C en D) was naby die Noord wes -Universiteit (Potchefstroom kampus) geleë. Gemeenskap C was gekies uit die gevestigde deel van die plakkerskamp naby Potchefstrrom en D uit die informele nederstetting wat gemeenskap C omring. Die basislyndata van NWPSA was ingevorder vanaf Oktober tot Desember 2005. 'n Totaal van 2010 gesonde Afrikaanvrywilligers (35 jaar en ouer), met geen gerapporteerde kroniese siektes van lewenstyl, tuberkulose (TB) of bekende MIV-infeksies was gewerf uit 'n steekproef van 6000 ewekansig gekose huishoudings.

METODES

Verskeie kwantitatiewe en kwalitatiewe navorsingsmetodes was gebruik deur die multi-dissiplinêre span om data te versamel, te analiseer en om data te interpreteer vanaf biologiese monsters en vraelyste. Data was geanaliseer deur van die sagteware program SPSS ('Statistical Package for Social Sciences', weergawe 15) gebruik te

maak. Gemiddeldes, mediane, standaardafwykings en 95% verstrouensintervalle was bereken. In die PURE-studie was data nie normaal versprei nie en nie-parametriese teotse was gebruik om te toets vir betekenisvolle verskille tussen groepe. Wilcoxon gemerkte rang toetse en Mann-Whitney/Wilcoxon rangoptel toetse was gebruik om groepe met mekaar te vergelyk. Meerveranderlike regressie-analises, stapgewyse regressiemetodes, Spearman rangorde en parsiële korrelasies was gebruik om assosiasies tussen selfgerapporteerde alkoholinname en biochemiese merkers (%CDT en GGT) te bepaal, terwyl laasgenoemde gebruik was om assosiasies te toets wat geassosieer word na wysiging van moontlike faktore wat die resultate kan beïnvloed. In die THUSA-studie was data nie normaal versprei nie en was daar getoets vir betekenisvolle verskille tussen groepe en die effekte van verstedeliking. Eenveranderlike variansieanalise (ANOVA), post hoc toetse van die kleinste betekenisvolle verskille ('least significant differences LSD'), meerveranderlike regressieanalises, stapgewyse regressiemetodes en Spearman rang-ordekorrelasies met wysigings vir faktore wat die data kan beïinvloed was gebruik om die verwantskappe tussen alkoholinname en biologiese (gesondheids) veranderlikes te ondersoek.

RESULTATE

Na 'n omvattende in diepte literatuuroorsig aangaande alkoholinname met die fokus op die Suid-Afrikaanse populasie, was drie oorsig artikels geskryf wat die rol van alkoholinname vanaf 'n molekulêre tot op 'n gemeenskapsvlak beskryf.

Die THUSA studie

In die THUSA studie het 61.5% van die mans en 25.2% van die vrouens gerapporteer dat hulle alkoholiese drankies inneem. Gemiddelde alkoholinname van mans (30.2 +/- 47.8 g/dag) het die aanbevole waarde van 21g/dag oorskry. Die vroue het 'n gemiddelde inname van 11.4 +/- 18.8g/dag gehad waarvan die onderste grens binne die 12-15g/dag aanbeveling geval het. Ouer drinkers (> 40 jaar) en die MIV-geïnfekteerde proefpersone het meer gedrink. Vlakke van verstedeliking het 'n klein

effekgehad op die hoeveelhede wat ingeneem is, maar sorghumbier was vervang deur kommersiële bier in verstedelikte gebiede. Drinkers het betekenisvolle verhoogde HDL-C, serumtrigliseriedes, bloeddruk en ysterstatus as nie-drinkers gehad. Serum-ferritien was gebruik om persone te klassifiseer in groepe wat 'n negatiewe ysterbalans (< 12µg/L), 'n normale balans (12-150µg/L) of 'n positiewe yster balans (>150µg/L) gehad het en dit blyk dat alkoholinname onder die persone met 'n positiewe ysterbalans (in mans van 25 tot 46%; in vroue van 11 tot 23%) verbubbel het.

Die PURE studie

Van die 716 mans en 1192 vrouens, het 64% en 33% respektiewelik, alkoholinname gerapporteer. Gemiddelde gewoontelike innames van self-gerapporteerde drinkgewoontes onder mans en vroue was 29.9 (+/- 30.0) en 23.3 (+/- 29.1) g van suiwer alkohol per dag. 'n Statistiesbetekenisvolle korrelasie tussen die twee dieetgeskiedenis bepalingsmetodes (kwantitatiewe voedselfrekwensie vraelys en 24-uur-herroep) was gevind, hoër as +0.45 in beide mans en vrouens. Self-gerapporteerde gewoontelike innames van die hele groep het betekenisvol positief en betekenisvol met beide % CDT (r = 0.32) en GGT (r = 0.433) gekorreleed . Nadat gekontrolleer is vir faktore wat die resultate kon beïnvloed (liggaamsmassa-indeks en rookgewoontes), was hierdie verhoudings r = 0.19 en 0.31 respektiewelik. In die studie, het 19% van die mans en 26% van die vroue nie gedrink nie, maar verhoogde GGT gehad terwyl 48% en 38% van die nie-drinkende mans en vrouens respektiewelik, verhoogde %CDT vlakke gehad het wat aandui dat ander faktore anders as alkoholinname ook bydra tot vlakke van hierdie lewerensieme.

BESPREKING EN GEVOLGTREKKING

Hierdie resultate dui aan dat ten spyte van 'n betekenisvolle korrelasie tussen gerapporteerde alkoholinname en GGT en % CDT vlakke, ander faktore buiten alkohol inname hierdie twee biologiese merkers beïnvloed. Dit is duidelik dat 'n meer spesifieke merker benodig word.

Die THUSA-en die PURE-studies was uitgevoer in sekere areas van die Noordwes provinsie in 1996-1998 (THUSA) en in 2005 (PURE). Die hoeveelheid alkohol wat ingeneem was deur mans was 30.2 en 29.9g/dag, terwyl die aantal drinkers vermeerder het van 61.5% tot 64.2%, respektiewelik. Vroulike drinkers het vermeerder vanaf 25.2% tot 33% en die gerapporteerde hoeveelhede het verskuif van 11.4 tot 23.3g per dag. Dieetvraelyste het soortgelyke resultate gelewer vir mans en het 'n betekenisvolle toename in alkoholinname onder vroulike drinkers aangedui (11.4 vs. 23.3g/dag).
Die gevolgtrekking word gemaak dat beide GGT en %CDT proefpersone verkeerdelik kan klassifiseer as drinkers in hierdie Afrikaanpopulasie en waardes van hierdie twee merkers moetmet sorg geïnterpreteer moet word. Verder is dit noodsaaklik om die afsnywaardes vir 'n nie-drinkende Afrikaanpopulasie te hersien. Alhoewel die voordelige effekte van alkohol inname op HDL-C waargeneem is, is die effek op yster status en-balans kommerwekkend en moet dit in diepte nagevors word.

KERNWOORDE: self-gerapporteerde alkoholinname, vraelyste, persentasie koolhidraattekorttransferrien, gamma-glutamieltransferase, Afrikaanpopulasies, oorgang, biologiese gesondheiduitkomste, ysterstatus, ferritien, PURE, THUSA

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LIST OF ABBREVIATIONS

%CDT	Percentage carbohydrate deficient transferrin
µg/L	Micro grams per litre
ADH	Alcohol dehydrogenase
AIDS	Acquired immune deficiency syndrome
ALDH	Acetaldehyde dehydrogenase
AMP	Adenosine monophosphate
ANOVA	Analysis of variance
ARBDs	Alcohol-related birth defects
ARNDs	Alcohol-related neurodevelopmental disorders
AUDIT	Alcohol Use Disorders Identification Test
BMI	Body mass index
CAD	Coronary artery disease
CDT	Carbohydrate deficient transferrin
CETP	Cholesteryl ester transfer protein
CHD	Coronary heart disease
CI	Confidence interval
CV	Coefficient of variance
CVD	Cardiovascular disease
CYP2E1	Cytochrome P450 monoxygenases
DNA	Deoxyribonucleic acid
ECG	Electrocardiogram
EDTA	Ethylenediamine tetra acetic acid
FAEs	Foetal alcohol effects
FAS	Foetal alcohol syndrome
FASD	Foetal alcohol spectrum defects
g	Grams
g/day	Grams per day
g/dL	Grams per deciliter
g/ml	Grams per millilitre

GDP	Gross domestic product
GGT	Gamma glutamyltransferase
GTT	Glucose tolerance test
H_2O	Water
H_2O_2	Hydrogen peroxide
HDL-C	High-density lipoprotein-cholesterol
HEP G2	Human hepatoblastoma cell line
HIV	Human immunodeficiency virus
HPLC	High performance liquid chromatography
hr	Hour
HSC	Hepatic stellate cells
IL	Interleukins
kJ	Kilojoules
LDL	Low-density lipoprotein
Lp (a)	Lipoprotein (a)
LSD	Least significant differences
MAST	Michigan Alcohol Screening Test
Med	Median
MEOS	Microsomal ethanol oxidising system;
mm	Millimetre
MRC	Medical Research Council
n	Sample size (number)
NAD^+	Nicotinamide adenine dinucleotide
NADH	Reduced nicotinamide adenine dinucleotide
NADP	Nicotinamide adenine dinucleotide phosphate
NRF	National Research Foundation
NS	Not significant
NWPSA	North-West Province South Africa
NWPSA	North-West Province, South African leg
PAI-1	Plasminogen activator inhibitor type 1
pH	Potential hydrogen

PURE	Prospective Urban and Rural Epidemiology study
QFFQ	Quantitative food frequency questionnaire
ROS	Reactive oxygen species
rpm	Revolutions per minute
SADHS	South African Demographic and Health Survey
SD	Standard deviation
SMAC	Sequential multiple analyzer computer
SPSS	Statistical Package for Social Sciences
STI	Sexually transmitted infection
TB	Tuberculosis
TC	Total cholesterol
TG	Triglycerides
TGF β-1	Transforming growth factor beta-1
THUSA	Transition and Health during Urbanisation of South Africans study
TIBC	Total iron binding capacity
TNF	Tumour necrosis factor
tPA-Ag	Tissue type plasminogen activator antigen
UK	United Kingdom
USA	United States of America
VLDL	Very-low-density-lipoproteins
WE	Wernicke's encephalopathy
WHO	World Health Organisation

LIST OF SYMBOLS

^0C	Degrees Celcius
%	Percentage
μ	Micro
β	Beta
α	Alpha
r	Correlation
r_s	Spearman correlation coefficient
R	Partial Correlation
$\geq$	Greater than or equal to
>	Greater than
=	Equal
+/-	Plus minus
$\leq$	Smaller than or equal to
<	Less than

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INTRODUCTION

CHAPTER 1: INTRODUCTION

1.1 Background and motivation

Due to rapid urbanisation, the South African population is experiencing a health transition, often associated with the triple burden of disease (Vorster, 2002) because of the high prevalence of under nutrition-related infectious diseases, the emergence of risks of non-communicable chronic diseases, and the human immunodeficiency virus/ acquired immune deficiency syndrome (HIV/AIDS) pandemic. The use, misuse or abuse of alcohol probably plays an important role in this transition. The World Health Organisation (WHO) recently stated that alcohol consumption is the fifth leading cause of death worldwide and that intakes are increasing, especially in developing countries (WHO, 2000). Alcohol is one of the most consumed beverages in Africa (WHO, 2004). According to the WHO's database, fewer South Africans drink as compared to the individuals reported in the 44 other countries. However, one third of the South Africans reported to drink, do so in excess (20 litres of absolute alcohol per drinker per year) (Parry *et al.,* 2005). The same authors indicated that the observed pattern of binge drinking of about one third of all South African drinkers is of concern. Binge drinking is defined as a pattern of drinking that brings blood alcohol concentration to 0.08 gram percent or above. For the typical adult this pattern corresponds to consuming five or more drinks (male) or four or more drinks (female), in a period of about two hours (National Institute on Alcohol Abuse and Alcoholism, 2004). In this definition a drink refers to half an ounce of alcohol.

Alcohol misuse and abuse in South Africa is reported to be responsible for at least half of the 14 000 annual reported road deaths. It is also known that alcohol abuse is associated with the high crime, violence, sexual risk behaviour, family disruption and a host of individual and societal problems seen in this country (Parry *et al.,* 2005). Binge drinking additionally results in an increased cardiovascular disease (CVD) risk and is often associated with micronutrient deficiencies (McKee, 1999), both showing high prevalences in the South African population (Vorster, 2002). It is, therefore, important to evaluate the causes and consequences of alcohol intake in our population.

1.2 Biological health outcomes associated with alcohol consumption

There is agreement that amongst populations in the Western world, moderate alcohol consumption is associated with better cardiovascular health and longevity (De Gaetano *et al.,* 2003). This is also known as the "French Paradox": initially defined because the French, despite higher fat intakes, showed lower prevalence of coronary heart disease, an occurrence attributed to regular wine consumption. The proposed mechanisms for this protective effect of moderate wine consumption are (i) effects on plasma lipids, in particular an increase in high-density lipoprotein-cholesterol (HDL-C) (De Oliviera *et al.,* 2000; Sillanaukee *et al.,* 2000; Hannuksela & Savolainen, 2001); (ii) antithrombotic effects on platelet function (Hendriks & van der Gaag, 1998; Mennen *et al.,* 1999; Lacoste *et al.,* 2001); (iii) favourable changes in the coagulation and fibrinolysis balance (Djousse *et al.,* 2000; Mukamal *et al.,* 2001; van de Wiel *et al.,* 2001); (iv) improved endothelial function (Stein *et al.,* 1999) and (v) increased insulin sensitivity (Bell *et al.,* 2000; Flanagan *et al.,* 2000).

It is not clear what proportion of these effects may be attributed to the antioxidants in red wine or to ethanol and its metabolites *per se*. The non-alcoholic components of wine, especially the phenolic compounds, seem to play a significant role in cardioprotection (Puddey *et al.,* 1998; Van Golde *et al.,* 1999). However, scientific evidence has shown that the cardioprotective effects of alcohol consumption are not limited to one particular type of alcoholic drink, suggesting that ethanol reduces mortality risk independently, in addition to the contribution of other compounds such as polyphenols. Additionally, a J-shaped relationship between alcohol consumption and blood pressure has been suggested, with moderate drinkers generally having lower blood pressures (Gillman *et al.,* 1995; Beilin *et al.,* 1996), and epidemiological data clearly show higher mean blood pressures and/or hypertension with increasing alcohol consumption (Agarwal, 2002).

Reported effects of alcohol consumption on iron balance are also of concern. Alcohol consumption increases body iron stores (Whitfield *et al.,* 2001). The relationships between low or "safe" levels of alcohol use and indices of body iron stores, as well as factors that influence this alcohol-iron relationship, have not been fully characterised.

Ferritin is an iron-apoferritin complex, the major form of iron in tissues. Tissue and serum ferritin are in equilibrium. Serum ferritin increases in chronic alcoholism (Moirand *et al.,* 1995). The mechanisms for this effect remain unclear. Possible mechanisms offered to explain this effect are (i) increased absorption of iron due to increased secretion of hydrochloric acid and hence, increased iron solubility (Malenganisho *et al.,* 2007); and (ii) alcohol induction of ferritin expression as shown in a human hepatoblastoma cell line (HEP G2) (Moirand *et al.,* 1990).

The South African food based dietary guidelines advise sensible drinking due to the possible cardiovascular protective effects associated with moderate alcohol intake (Van Heerden & Parry, 2001). These putative beneficial effects are based almost entirely on evidence from populations of developed countries. Additionally, moderate alcohol consumption can only protect against CVD if the underlying risk is present i.e it will be difficult to detect any effect in a population where the level of risk is low. The problem, however, is that the South African population in transition is reported to have high levels of alcohol abuse (WHO, 2000), with its many adverse consequences (Parry *et al.,* 2005) and possibly little or none of the putative beneficial cardio-protective effects associated with moderate alcohol consumption. Parry *et al.* (2005) advised that a comprehensive strategy is required to address these high levels of risky drinking in South Africa. To develop a relevant, integrated and coherent strategy to address alcohol use, misuse or abuse, a much better understanding of the causes and consequences of binge drinking in South Africa is needed. However, before this can be accomplished, there is a need to identify and assess with accuracy, high risk drinking in this population.

1.3 Self reporting as a measuring tool for alcohol consumption

Identification and assessment of high risk drinking in a population can be problematic. Essential to such efforts are accurate measures of alcohol consumption. Verbal measures such as clinical interviews and questionnaire based instruments e.g. the Alcohol Use Disorders Identification Test (AUDIT), CAGE questions and the Michigan Alcohol Screening Test (MAST) are often used as tools for assessing problem drinking of individuals and populations (Reid *et al.,* 1999). Detailed validated quantitative food

frequency questionnaires (QFFQ) are an important source of intake information (MacIntyre *et al.,* 2000) and typically has low rate of false-positive responses, however, the primary weakness in using this methodology for alcohol intake assessments is that people may not report their alcohol intakes accurately (Midanik, 1988). Under-reporting has been shown to be common among alcohol dependents (Fuller *et al.,* 1988; Simpura *et al.*, 1987). Therefore, it could be more beneficial to use biological markers of alcohol consumption to verify reported intakes and to identify and assess high risk drinking with more accuracy.

1.4 Biomarkers of alcohol consumption

Alcohol biomarkers are considered valuable tools for objective identification, assessment and evaluation of high risk drinking in populations. Alcohol biomarkers could additionally be used clinically to evaluate treatment efforts and monitor abstinence and relapse in response to outpatient treatment (Helander, 2003). As a result, there is increasing interest in developing better methods to detect and monitor alcohol consumption. Alcohol biomarkers have been shown to provide information more objectively than self reporting (Helander, 2003). In a comprehensive systematic review by Salaspuro (1999), carbohydrate deficient transferrin (CDT) and gamma glutamyltransferase (GGT) were concluded to be the best biomarkers currently available for identifying alcohol abuse. GGT is a membrane-bound glycoprotein enzyme which catalyses the transfer of the gamma-glutamyl moiety of glutathione to various peptide acceptors (Niemela, 2007). Human transferrin occurs in isoforms with different levels of sialylation. There appear to be at least six such isoforms; penta-, tetra-, tri, di-, mono- and asialo transferrin (Wong, 1977). The asialo, monosialo and disialo isoforms are referred to as CDT.

Elevation of GGT in serum probably reflects its enhanced hepatic synthesis rate, increased transport to the liver plasma membranes, as well as liver injury (Teschke & Koch, 1986). The mechanisms responsible for the increase in serum CDT levels are still being investigated. One possibility is that alcohol consumption decreases the activity of glycoprotein glycosyltransferase enzymes, namely sialyltransferase,

galactosyltransferase, and N-acetylglucosamine transferase found predominately in hepatic Golgi complexes (Sadler, 1984). These are primarily responsible for addition of sialic acid and other carbohydrate moieties to the transferrin polypeptide chain via a process known as glycosylation (Jennet *et al.,* 1980). Alcohol consumption has also been thought to increase the activity of sialidase that is involved in the removal of carbohydrate moieties from transferrin (Sadler, 1984).

Additionally %CDT (measures the relative amount of CDT in proportion to total transferrin) has been shown to be a slightly better marker compared to the absolute value of CDT (Anttila *et al.*, 2003; Jeppsson *et al.*, 1993; Keating *et al.,* 1998; Kwoh-Gain *et al.*, 1990; Schellenberg *et al.*, 1989; Viitala *et al.,* 1998) and in situations where there are variations in transferrin concentrations as experienced during pregnancy, anemic and severe liver disease (Anton, 2001). An additional advantage of using %CDT is that gender-specific normal cut-off values are not necessary (Anton *et al.,* 2001). However, most of the data demonstrating a relationship between alcohol consumption and these biological markers come from non-African populations (Laatikainen *et al.,* 2002). Therefore, a continuous probing question is whether these two biomarkers (%CDT and GGT) are good indicators for detecting chronic alcohol abuse in an African population.

This study aims to show whether %CDT or GGT are good tools for verifying reported alcohol intakes and relationships between alcohol consumption and biological health outcomes in a South African population in transition.

1.5 Aims and objectives

The main aim of this thesis is to examine aspects of the role alcohol plays in the health transition amongst Africa volunteers in rural and urban areas of the North West Province of South Africa. Within this umbrella aim, specific projects, each with clearly defined objectives, were done.

- Firstly, an extensive literature survey on issues of alcohol use and abuse from a *molecular to a societal* perspective was conducted. A series of review papers were

written and submitted to the South African Journal of Clinical Nutrition. These are used as part of the literature study for this thesis. The titles for the three reviews are as follows:

1. Alcohol metabolism and health hazards associated with alcohol abuse in a South African context: a narrative review
2. The cardioprotective effects and putative mechanisms of light/moderate consumption of alcohol: a narrative review
3. Social causes and effects of alcohol misuse/ abuse in South Africa

• Secondly, the relationships of alcohol intake with biological health outcomes of Africans participating in the THUSA study were examined.

Specific objectives:

- To examine the mean daily alcohol intake of men and women
- To examine the mean daily alcohol intake of men and women drinkers at different levels of urbanisation
- To compare biochemical, physiological and dietary data of drinkers and non-drinkers
- To examine the relationship between alcohol intake and:
  - Blood pressure
  - Serum lipoproteins: HDL-C, total cholesterol (TC), triglycerides (TG)
  - GGT
  - Serum iron
- To compare low, normal and high ferritin groups of male drinkers and non-drinkers

• Thirdly, to examine the relationships between reported alcohol intake, %CDT and GGT in an African population in transition: the PURE study

Specific objectives:

- To examine the mean daily alcohol intake of men and women
- To compare self reported alcohol consumption by two different methods (24 hour recall and quantitative food frequency questionnaire) by gender

- To examine the associations between the above mentioned self reported alcohol intakes and the two alcohol biological consumption markers (%CDT and GGT)
- To compare biochemical, physiological and dietary data of drinkers and non-drinkers
- To examine the suitability of %CDT and GGT as proxy markers of alcohol consumption

The THUSA data set was reanalysed to explore the relationships between alcohol intake and health outcomes because a complete epidemiological data set was available and this had not been done previously. The PURE samples were used for examining biological markers of alcohol intake and not health outcomes because data on all the variables were not available.

1.6 Structure of the thesis

This thesis is presented in article format and consists of five manuscripts already submitted for publication (three reviews and two original experimental articles). Following this introductory chapter:

Chapter 2 comprises of three review papers (2.2 to 2.4) that will give a South African overview of alcohol use and abuse from a *molecular to a societal* perspective. These chapters will provide the background and literature necessary for the interpretation of the data from the two original experimental articles in this thesis;

Chapter 3 comprises of an original article which examines relationships of alcohol intake with biological health outcomes in an African population in transition;

Chapter 4 comprises of an original article which explores the relationships between reported alcohol intake, %CDT and GGT in an African population in transition;

Chapter 5 comprises of a general discussion, recommendations and conclusions. The relevant references are provided at the end of each chapter according to the authors instructions as specified by each journal to which the papers were submitted. The relevant references used in the unpublished chapters 1 and 5 are provided according to the requirements stipulated by the North-West University (Potchefstroom campus). The

technical style used in the unpublished chapters is uniform, but differs in other chapters according to the authors instructions of the specific journals. Addenda for both the THUSA and PURE studies close this thesis.

A conceptual framework that illustrates the areas examined in this thesis is given in Figure 1.1. The Figure shows that generation of more knowledge and quality information in the indicated areas should contribute to evidence-based recommendations on alcohol consumption.

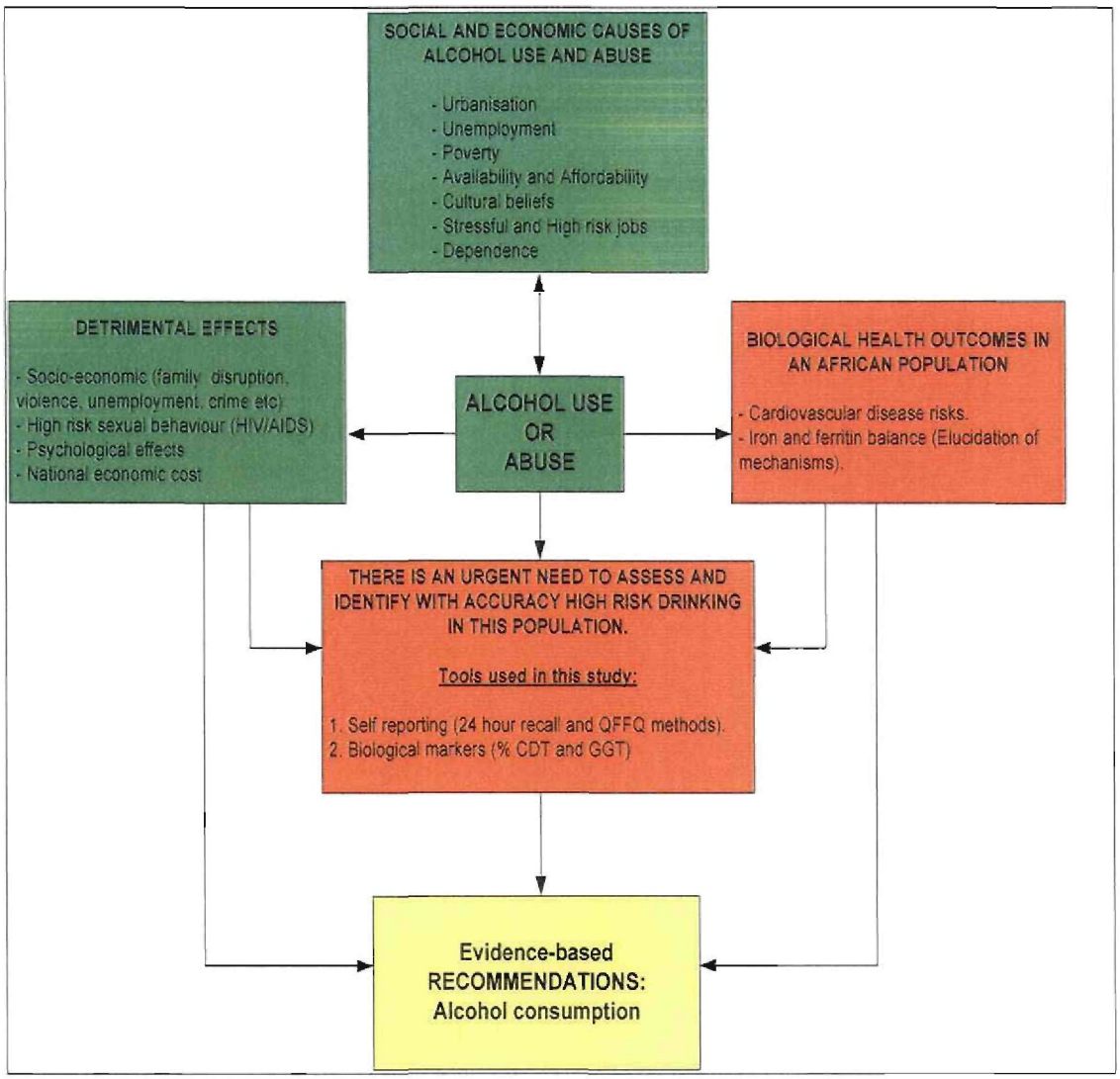

Figure. 1.1 Conceptual framework for areas examined in this thesis

1.7 Ethical considerations

This study forms part of the broader PURE and THUSA studies and the collection of information and, relevant biological samples from informed volunteers had the necessary ethical clearance from the Ethics Committee of the previous Potchefstroom University of Christian Higher Education (THUSA) and the Ethics Committee of the North-West University and North West Department of Health (PURE). The reference numbers for ethical approval are **4M5-95** (THUSA) and **04M10** (PURE).

1.8 Author's contributions to the separate papers in this thesis

The study reported in this thesis was planned and executed by a team of researchers and the contribution of each is listed in Table 1.1. A statement from the co-authors is also included, confirming their role in the study and giving their permission for the inclusion of the articles in this thesis. The statement is as follows:

"I declare that as co-author I have approved the above mentioned article, that my role in the study, as indicated above, is a representation of my actual contribution and that I hereby give consent that the manuscript may be used as part of the PhD thesis of Mr PT Pisa."

Table 1.1 List of research team and their contributions to this study

NAME	ROLE IN THE STUDY
Pedro Pisa (PhD candidate)	Writing and compilation of this thesis, blood sample analysis, all the statistical analyses in this thesis, interpretation of results and writing of publications, first author of 3 papers (Chapter 2.2., 2.3., & 4) and co-authored 2 papers (2.4., & 3) in this thesis.
Dr Du T, Loots Supervisor	Supervised this thesis and standardisation of %CDT assays, interpretation of results, co-authored 4 papers in this thesis (Chapter 2.2., 2.3., 2.4., & 4).
Prof HH Vorster Co-supervisor	Co-supervised this thesis, planning and coordinating the THUSA study, interpretation of results, co-authored 2 papers in this thesis (Chapter 3, 4)
Prof A Kruger	Planning and coordinating the PURE study, interpretation of results, co-authored 2 papers in this thesis (Chapter 3, 4)
Prof BM Margetts	Trained the PhD student (Pedro Pisa) on how to use the SPSS program, supervision of statistical analysis, interpretation of results, co-authored 2 papers in this thesis (Chapter 3, 4)
C Nienaber (PhD student)	Co-authored a paper in this thesis (Chapter 2.2)
RE Gopane (PhD student)	First author of a paper in this thesis (Chapter 3)
BM Setlalentoa (PhD student)	First author of a paper in this thesis (Chapter 2.4)
GN Thekisho (PhD student)	Co-authored a paper in this thesis (Chapter 2.4)
Dr EH Ryke	Supervised and co-authored writing of a paper in this thesis (Chapter 2.4)

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CHAPTER 2

LITERATURE BACKGROUND ON ALCOHOL

(from molecules to society)

CHAPTER 2: LITERATURE BACKGROUND ON ALCOHOL *(from molecules to society)**

2.1 Introduction

In this chapter, three review papers written collectively by the team from the North-West University examining the role of alcohol in the transition of Africans form the literature background of this thesis. The author (Pedro T Pisa) wrote the first two review papers and contributed intellectually and administratively to the third. This series of reviews were submitted for publication to the South Africa Journal of Clinical Nutrition in August 2008.

* This approach is in line with the philosophy of the Centre of Excellence for Nutrition at the North-West University, where a holistic but integrated trans-disciplinary approach is followed to examine nutrition-related health problems in South Africa, in both research and training (HH Vorster, personal communication).

2.2 ALCOHOL METABOLISM AND HEALTH HAZARDS ASSOCIATED WITH ALCOHOL ABUSE IN A SOUTH AFRICAN CONTEXT: A NARRATIVE REVIEW

(*Submitted for publication in the South African Journal of Clinical Nutrition*)

2.2 ALCOHOL METABOLISM AND HEALTH HAZARDS ASSOCIATED WITH ALCOHOL ABUSE IN A SOUTH AFRICAN CONTEXT: A NARRATIVE REVIEW

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Abstract

The World Health Organisation recently stated that alcohol consumption is the fifth leading cause of death worldwide and that intakes are increasing, especially in developing countries. Alcohol related effects are major threats to global public health. There is growing recognition of an association between alcohol abuse and a host of health and social problems in many parts of the world. In South Africa, a developing country with a rapidly growing economy, available evidence shows that alcohol is a leading risk factor for mortality and morbidity, hence a significant contributor to the burden of disease. The observed pattern of binge drinking of about a third of South African drinkers is of concern. In addition to physical dependence on alcohol, other psychological, genetic and social factors may contribute to development of alcoholic related diseases. To develop a relevant, integrated and coherent strategy to address alcohol use, misuse and abuse in South Africa, a much better understanding is needed of the metabolism of alcohol, and how the metabolic products and changes associated with alcohol abuse ultimately lead to biological health hazards. This review gives a broader understanding of the metabolism of alcohol and the biological health hazards associated with abuse. Levels of foetal alcohol syndrome in South Africa are the highest ever recorded, hence this review will separately address teratogenic effects associated with abuse.

Key words: alcohol metabolism, teratogenic effects, binge drinking, South Africa.

Introduction

Alcohol (ethanol) containing beverages are one of the most consumed beverages in Africa.[1] Ethanol is an ethyl alcohol with an energy value of 29.2 kilojoules/gram (7.1 kilocalories/gram),[2] and is made by fermenting and then distilling starch and sugar crops (maize, sorghum, potatoes, wheat, grapes, sugar-cane, even cornstalks, fruit and vegetable waste).

The absorption, distribution and elimination of alcohol have large individual variations.[3] Once absorbed, alcohol spreads throughout the body's water space (moves easily through cell membranes). The appearance of alcohol in the blood is not related only to the amount of alcohol consumed, but also to various factors affecting alcohol metabolism. These include gender, concentration of alcohol in the beverage, body composition, medication use, genetics, ethnic variations and the amount and type of food intake before alcohol consumption.[3] Most of the ingested alcohol is readily absorbed unchanged from the gastrointestinal tract and is one of the few substances readily absorbed from the stomach. Since alcohol is toxic in high amounts, the body attempts to get rid of it as quickly as possible by excretion of the unchanged ethanol, or its metabolites. Most of the ingested ethanol is metabolised in the liver.[4] However, a small amount is metabolised as it passes through the gut. Two major enzyme systems, namely the oxidative and non-oxidative pathways, mediate the initial phase of ethanol metabolism.[4,5]

The World Health Organisation (WHO)[1] estimated in 2004 that about two billion people worldwide consume alcoholic beverages and 76.3 million have diagnosable alcohol disorders. Thus the global burden of alcohol abuse both in terms of mortality and morbidity is considerable throughout the world.[1] South African drinkers are among the leading consumers of alcohol in the world. What is of more concern is that the majority of those reported to drink consume huge amounts of alcohol (20 litres of absolute alcohol per drinker per year),[6] characterising a condition termed binge drinking. The major adverse health effects associated with alcohol abuse are divided into biological health hazards (alcoholic liver disease, alcoholic pancreatitis, cancers, malnutrition, cardiac disorders, gastric complications and neurological disorders) and teratogenic effects.

This review discusses the metabolism of alcohol and the biological health hazards associated with alcohol abuse in a South African context.

Alcohol metabolism

Oxidative metabolism of alcohol

In the hepatocyte there are three oxidative pathways (Fig. 1) responsible for ethanol metabolism and these pathways are located in three different compartments: (1) alcohol dehydrogenase (ADH) and members of the cytochrome P450 system [predominately CYP2E1 (cytochrome P450 monoxygenases)] located in the cytosol,[5,7,8] (2) the microsomal ethanol oxidising system (MEOS) situated in the endoplasmic reticulum and (3) catalase located in the peroxisomes. Each of these systems metabolise ethanol to the highly reactive metabolite acetaldehyde. Due to the toxicity of this compound, the body quickly converts it to acetate in a second oxidation step by mitochondrial acetaldehyde dehydrogenase (ALDH). Finally, the acetate produced in the liver is released into the blood and is oxidised by peripheral tissues in the Krebs cycle to carbon dioxide, fatty acids and water.[9]

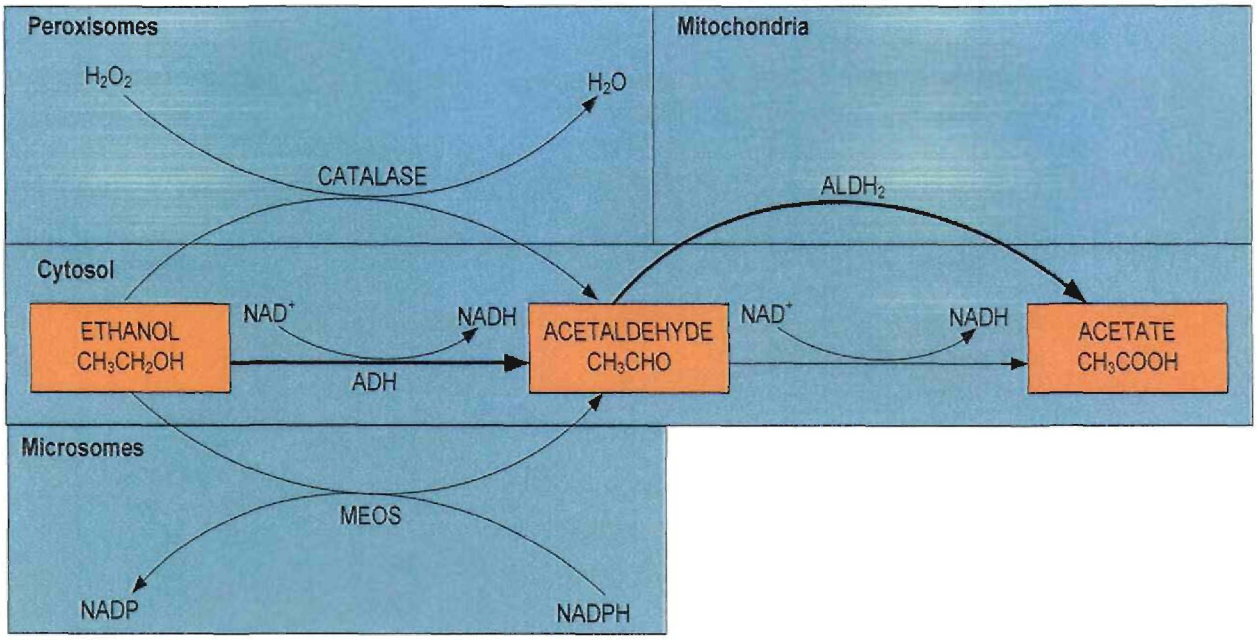

Fig. 1. Metabolism of ethanol
ADH = alcohol dehydrogenase; ALDH = acetaldehyde dehydrogenase; H_2O = water; H_2O_2 = hydrogen peroxide; MEOS = microsomal ethanol oxidising system; NAD^+ = nicotinamide adenine dinucleotide; NADH = reduced nicotinamide adenine dinucleotide; NADP = nicotinamide adenine dinucleotide phosphate

The alcohol dehydrogenase (ADH) system

Human ADH is a zinc containing enzyme located almost exclusively in the cytosol of cells. The highest ADH concentrations (approximately 80-90% of the total ADH activity in human tissue) have been found in the liver. ADH activity has also been detected in other tissues such as the

gut, kidneys and lungs. For the ADH-reaction, oxidised nicotinamide adenine dinucleotide (NAD^+) is needed and NADH (reduced form of NAD^+) is produced in the cytosol. This results in an increased NADH/NAD^+ ratio in the cytosol, with a marked shift in redox potential.[10] This redox imbalance is responsible for a series of metabolic alterations causing damage to various organs. Acidosis is increased by hyperlactacidemia and this reduces the capacity of the kidney to excrete uric acid, leading to hyperuricaemia (Fig. 2).

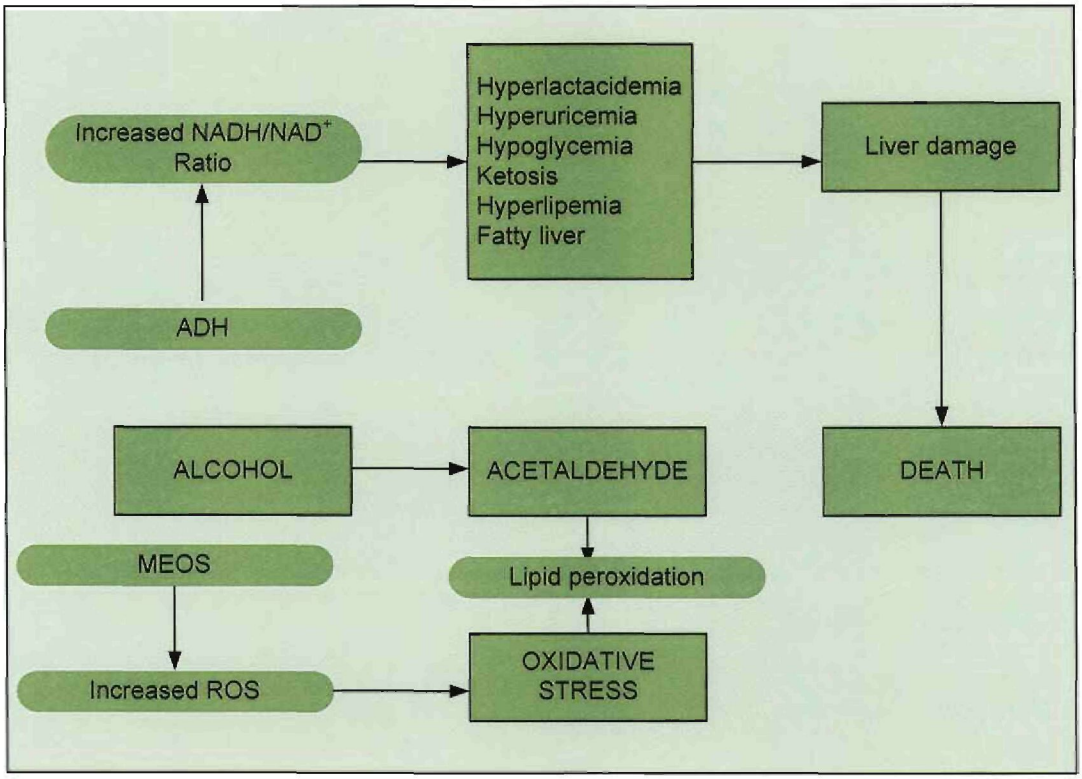

Fig. 2. Metabolic changes (hepatic) associated with alcohol metabolism
ADH = alcohol dehydrogenase; MEOS = microsomal ethanol oxidising system; NAD^+ = nicotinamide adenine dinucleotide; NADH = reduced nicotinamide adenine dinucleotide; ROS = reactive oxygen species

The increased ratio of NADH/NAD^+ additionally raises the α-glycerophosphate concentrations, which in turn favours the deposition of triglycerides in the liver. Additionally, excess NADH also favours fatty acid synthesis and accumulation in the liver in the form of triglycerides. The mechanisms by which this is thought to occur is by increased hepatic synthesis, decreased hepatic lipoprotein secretion, a greater mobilisation of fatty acids from adipose tissue favouring their hepatic uptake, and a decrease in fatty acid oxidation.[11] In individuals with depleted glycogen deposits or those who have pre-existing abnormalities in carbohydrate metabolism, alcohol

intoxification may cause severe hypoglycaemia due to a blockage of gluconeogenesis by the increase in the NADH/NAD^+ ratio.[11]

Microsomal ethanol oxidising system (MEOS)

The MEOS constitutes a second mechanism by which alcohol is oxidised. MEOS shares many properties with other microsomal metabolising components such as the cytochrome P-450, reduced nicotinamide adenine dinucleotide phosphate (NADPH) and oxygen. An increase in MEOS activity is usually due to chronic alcohol consumption and this in turn affects CYP2E1 which is the ethanol inducible fraction of the cytochrome P-450.[12] This phenomenon could be responsible for the metabolic tolerance of alcoholics to ethanol. Although CYP2E1 has a high capacity of metabolising ethanol, it also has the capacity for activating other hepatotoxic agents,[12] consequently contributing to liver damage. Additionally, the high redox potential of CYP2E1 for nicotinamide adenine dinucleotide phosphate (NADP) as a cofactor, leads to the formation of free oxygen radicals, oxidative stress and lipid peroxidation[13] as indicated in Fig. 2. Apart from the obvious consequences of oxidative stress on cardiovascular disease (CVD), atherosclerosis, diabetes, and cancers, it also activates Kupffer cells. Activation of these by oxidative stress, increase the expression of cytokines such as tumour necrosis factor (TNF) and interleukins (IL) which in turn lead to the activation of stellate cells with consequent increases in collagen synthesis favouring alcoholic liver disease.[14]

Catalase oxidative system

The third oxidative pathway to convert ethanol to acetaldehyde is by means of the enzyme catalase present in peroxisomes of the liver. Catalase, however, plays a very small role in alcohol metabolism.[5] *In vitro* catalase is capable of oxidising ethanol in the presence of a generating system of hydrogen peroxide, but physiologically the rate of alcohol metabolism by this system is reduced by addition of fatty acids and the β-oxidation of fatty acids is inhibited by the NADH generated during alcohol metabolism by ADH, thus inhibition of hydrogen peroxide production occurs leading to significantly diminished rates of peroxidation of alcohols *via* catalase.[15]

First pass metabolism

There is ample evidence that the stomach contributes in oxidative metabolism of ethanol. In the human stomach, the presence of class I, III and IV ADH isoenzymes for ethanol has been demonstrated.[16-18] Intravenous administration of a low dose of ethanol results in higher blood ethanol concentrations than oral intake of the same amount of ethanol. This has been well

demonstrated in human and rat studies and indicates that part of the ingested ethanol will be metabolised before reaching the peripheral blood, as absorption of ethanol from the gastrointestinal tract is virtually unprohibited. This is known as first pass metabolism and can theoretically occur in the liver, stomach or intestines.[19,20] Caballeria *et al.*[21] further describe evidence for first pass metabolism. They indicated ADH isoenzyme activity in the gastric mucosa and also showed that first pass metabolism disappears in patients' under-going gastrectomy, when gastric emptying is accelerated or when alcohol is administered to the duodenum.[21] Caballeria[22] later confirmed this observation, using gastrectomised patients. Blood ethanol concentrations were approximately the same after oral intake and after intravenous infusion of ethanol in these patients. He additionally showed that in healthy men, intraduodenal infusion of ethanol resulted in significantly higher blood ethanol concentrations than oral intake of ethanol, which also suggested that by-passing the stomach, first pass metabolism is diminished. Colonic bacteria (human flora) have been shown to contain high ADH activity and produce acetaldehyde after ethanol breakdown.[23] A bacteriocolonic pathway for alcohol metabolism has been suggested, with the acetaldehyde produced ultimately being broken down to acetate by bacterial ALDH.[24] Due to low activity of the ALDH in the colon, accumulation of acetaldehyde can occur during ethanol oxidation. This is one of the factors that contribute to pathogenesis of alcohol related gastrointestinal disease.[24]

Ethnic variations in gastric ADH have been reported and are implicated to contribute to the differences observed in ethnic alcohol tolerance and toxicity. Most Caucasians are reported to have α-ADH while most Asians have very low or undetectable activity, making the first pass metabolism highly reduced in the latter population group.[20] Frezza *et al.*[25] reported that the activity of stomach ADH is lower in women compared to men. However, this result is not consistent, as other studies have shown no significant differences between men and women[26] and below the age of 50.[27]

Non-oxidative metabolism of alcohol

A non-oxidative pathway for alcohol metabolism has been proposed, which is thought to form fatty acid ethyl esters from alcohol.[28] Evidence for this is seen in intoxicated subjects having significantly elevated concentrations of fatty acid ethyl esters in different organs such as the brain, liver and the heart, and are thought to result in the alcohol induced lesions in these organs.[3]

Alcohol elimination (excretion)

Most ethanol (90-98%) is eliminated from the body by oxidation *via* various enzyme systems to carbon dioxide and water as previously mentioned. The remaining ethanol is excreted by the lungs (1-5%) through expiration and 1-3% is excreted *via* other routes, such as urine (0.5-2.0%) and sweat (up to 0.5%).[29]

Increased tolerance to alcohol is displayed by chronic alcoholics. This is due to an increase in ethanol elimination rate or metabolic tolerance, and due to the adaptation of the central nervous system to alcohol.[30] The mechanisms of increased metabolic tolerance are attributed to increased ADH activity, increased mitochondrial reoxidation of NADH, a hypermetabolic state in the liver, increased microsomal oxidation and increased catalase activity.[24] Alcohol metabolism is also affected by the nutritional status of an individual, since malnutrition (undernutrition) diminishes ADH activity, similar to that which occurs during high alcohol consumption.[31]

Adverse effects associated with alcohol abuse

Metabolic changes associated with alcohol abuse ultimately lead to a number of biological health hazards. These have recently been summarised by Van Heerden and Parry[32] and are shown in Table I.

Table I. Summary of health hazards associated with alcohol abuse*

Nervous system	Acute intoxication: 'hangovers' and blackouts
	Persistent brain damage: Wernicke's encephalopathy (WE), Korsakoff's syndrome, cerebellar degeneration
Cerobrovascular disease	Strokes, particularly in young people
	Subarachnoid haemorrhage
	Subdural haematoma following cranial injury
	Withdrawal symptoms: tremor, hallucinations, fits
	Nerve and muscle damage: weakness, paralysis, 'burning' sensation in extremities
Liver	Fatty infiltration
	Alcoholic hepatitis
	Cirrhosis leading to liver failure
	Liver cancer

Gastro-intestinal system	Acid flux
	Tearing/rupture of oesophagus
	Cancer of the oesophagus
	Gastritis
	Aggravation and impaired absorption of food
	Chronic inflammation of the pancreas which may lead to diabetes and malabsorption of food
Nutrition	Malnutrition due to reduced food intake, toxic effects of alcohol on the gastrointestinal tract, impaired metabolism leading to weight loss, obesity, particularly in early stages of heavy drinking
Heart and circulation	Arrhythmias
	Hypertension
	Chronic damage to cardiac muscle leading to heart failure
Respiratory system	Pneumonia from inhalation of vomit
Endocrine system	Increased production of cortisol leading to obesity, acne, hirsutism, hypertension
	Condition mimicking hyperthyroidism with weight loss, anxiety, palpitations, sweating, tremor
	Severe hypoglycaemia resulting in coma
	Intense facial flushing in diabetes using chlorpropamide
Reproductive system	Men: loss of libido, impotence, testicular and penile shrinkage, loss of sexual hair
	Women: menstrual irregularities, shrinkage of breasts and external genitalia
Foetal development and teratogenic effects	Foetal alcohol effects, alcohol-related birth defects, alcohol-related neurodevelopmental disorders and foetal alcohol spectrum defects

*Adapted from Van Heerden and Parry.[32]

Alcohol affects the central nervous system of the body more than any other bodily function. Furthermore, ethanol acts as a central nervous system depressant.[33] Normal brain development in humans can be impaired by consuming large amounts of alcohol. An unusual complication of acute alcohol ingestion is Wernicke's encephalopathy (WE). It is a syndrome characterised by acute confusion, ataxia and eye movement abnormalities (opthalmoplegia and nystagmus).[34,35] It is caused by inadequate intake or absorption of thiamine causing lesions in the medial thalamic

nuclei, mammillary bodies, periaqueductal and periventricular brainstem nuclei and superior cerebellar vermis.[35] Failure to treat WE leads to an irreversible chronic form of the disease (Korsakoff psychosis), characterised by severe short-term memory loss.[35,36] Twenty–five percent and nearly half of chronic alcoholics may have peripheral neuropathy, including autonomic disorders[37] and myopathy respectively.[38]

A common after-effect of ethanol intoxication is the unpleasant sensation known as a hangover, which is partly due to the dehydrating effect of ethanol. Ethanol is known to mitigate the production of the antidiuretic hormone,[39] which is a hormone that acts on the kidney, favouring water reabsorption in the kidneys during filtration.

Alcohol affects many organs, most notably the liver causing both acute and chronic liver disease.[2,4] In the liver, ethanol can lead to three distinct pathological disorders, namely the fatty liver (alcohol-associated hepatic steatosis), alcoholic hepatitis and cirrhosis. Alcohol-associated hepatic steatosis is the most common form of liver injury and is reversible with abstinence.[40,41] Alcoholic hepatitis is characterised by inflammation of the liver, and cirrhosis by progressive hepatic fibrosis. These are the more serious forms of alcoholic liver disease.[42]

The fibrogenic effects of ethanol and its metabolites on hepatic stellate cells (HSC),[42,43] include changes of cellular activation such as increased collagen and DNA (deoxyribonucleic acid) synthesis,[44] increased expression of α- smooth muscle actin and depletion of retinyl palmitate.[45] These manifestations ultimately increase fibrosis. Ethanol and acetaldehyde additionally increase fibrosis by increasing autocrine transforming growth factor beta-1 (TGF β-1) expression in HSCs. In turn, TGF β-1 is able to upregulate type 1 collagen gene expression.[46-48]

Oxidative stress tends to increase in both chronic and acute ethanol administration.[49] Within the hepatocyte, ethanol induced oxidative stress occurs acutely through ethanol metabolism or chronically following the induction of CYP2E1.[2,50] CYP2E1 has been shown to generate reactive oxygen species (ROS) including the superoxide anion, hydrogen peroxide and hydroxyethyl free radicals.[2,51] Oxidative stress further activates HSC in alcoholic liver fibrogenesis, as human HSC collagen synthesis is induced by 4-hydroxynonenal, one of the common lipid peroxidation by-products.[52] The accumulation of NADH through ethanol metabolism promotes steatosis by stimulating the synthesis of fatty acids and opposing their oxidation. Through the reduction of pyruvate, elevated NADH also increases lactate, which stimulates collagen synthesis in

myofibroblasts.[2] The fatty liver is largely a result of the accumulation of acetyl CoA, which in turn favours fatty acid synthesis and inhibits the Krebs cycle.

Ethanol's energy per gram exceeds that of carbohydrates and proteins, and could account on average for half an alcoholic's (heavy drinker's) caloric intake.[2] Alcohol displaces nutrients like folate, thiamine and other vitamins causing malnutrition.[2] Inadequate intake and malabsorption due to gastrointestinal complications such as pancreatic insufficiency and impaired hepatic metabolism of nutrients causes secondary malnutrition.[2]

Alcohol is also known to have a carcinogenic effect and is classified as a Group 1 carcinogen by WHO.[53] Although some studies have failed to establish a direct connection between alcohol and its effect on cancer, there is strong indication that it may act as a carcinogen by enhancing the carcinogenic effects of other chemicals like tobacco. Garro and Lieber[54] indicated that alcohol enhances tobacco's ability to stimulate tumour formation in rats. In humans, the risk for mouth, tracheal and oesophageal cancer is 35 times greater for individuals who both smoke and drink than for people who neither smoke nor drink.[55]

Alcohol also has adverse effects on the human reproductive system. In males, alcohol causes atrophy of the semeninferous tubules, loss of sperm cells and increased production of abnormal sperm.[56] Additionally, alcohol has an adverse effect on testosterone synthesis, secretion[57,58] and is regarded as a testicular toxin.[59] Alcohol also reduces the sperm quality (deterioration of sperm concentration, output and motility).[60,61] In women, alcohol causes a variety of reproductive disorders from irregular menstrual cycles[64] to absence of ovulation and infertility.[62] Alcohol abuse is also associated with early menopause.[62] The mechanisms underlying alcohol's disruption of the female menstrual cycle and anovulation are temporary elevation of oestradiol,[62] testosterone,[63] decreased levels of insulin like growth factor 1 and reduced or absent pituitary luteinising hormone, respectively.[64]

Teratogenic effects

Alcohol is the most well known teratogen worldwide.[65] Of many substances of abuse (e.g., cocaine, heroin, marijuana), alcoholic beverages produce the most serious neurobehavioural effects in an unborn foetus.[65] This ultimately burdens the economy and the health sector as a whole. It is already well known that alcohol consumption by pregnant women increase their

chances of miscarriage or premature delivery,[32] low birth weight, congenital malformations[32,66,67] and foetal alcohol syndrome (FAS).[66,68]

Expression of FAS and the related disorders appears to be dependent on other component causes.[69] Burd *et al.*[68] describe FAS as a multi-element causal chain of interacting factors commonly including smoking, poor diet, poverty, low maternal education, heavy drinking, binge alcohol use, being unmarried, physical abuse and increased parity. The pattern and amount of alcohol consumed, timing of intake, developmental stage of the foetus at the time of exposure and socio-behavioural risk factors are pivotal determinants of birth outcome.[69] The full FAS phenotype manifests in children whose mothers had a history of chronic, daily, heavy alcohol use or frequent, heavy, intermittent alcohol use (binge drinking).[69]

FAS can develop at any stage of the pregnancy; however, it is during the first trimester that the foetus is most vulnerable to alcohol damage.[69] In some cases, alcohol-exposure during pregnancy does not always lead to a full manifestation of the syndrome. The related disorders which develop are described as foetal alcohol effects (FAEs), alcohol-related birth defects (ARBDs), alcohol-related neurodevelopmental disorders (ARNDs) or foetal alcohol spectrum defects (FASD).[66,70-72] These manifestations of the syndrome are widely variable and are six to eight times more prevalent than full-blown FAS.[70]

The mechanisms of ethanol's toxic effects to the developing foetus are becoming more clear.[73] Ethanol and acetaldehyde both cross readily through the placenta, depriving the developing foetal brain of both nutrients and oxygen. When ethanol crosses the placenta, foetal blood ethanol rises until it reaches equilibrium with maternal blood ethanol concentrations.[70] The harmful effects of alcohol in the foetus are, however, more pronounced than in the alcohol consuming mother, as the foetus is smaller in comparison to the blood alcohol levels and its detoxification system is not yet developed. Hence the ethanol remains longer in the foetal blood, prolonging the damage to its system.[73] Ethanol has additionally been shown to reduce neural cell progenation in the central nervous system of the developing foetus and escalate cell death by apoptosis.[70] Acetaldehyde is also highly toxic to the developing foetus. Acetaldehyde is implicated in impairing DNA methylation, resulting in intra-uterine growth retardation, hence lower birth weight and height, facial feature abnormalities, (underdeveloped maxillary region, small fissures between the lids of the eyes); neurodevelopmental abnormalities, such as microcephaly; congenital abnormalities of the joints and heart; and persistent mental retardation.[32]

Discussion and conclusion

Metabolic changes associated with alcohol abuse ultimately lead to a number of biological health hazards as mentioned. Ingestion of alcohol during pregnancy can have severe effects on the developing foetus. Over time, alcohol abuse has become a major public health concern, and an increasing awareness that alcohol-related problems constitute serious problems for not only individuals but families, communities and countries' economies. This pattern of irresponsible drinking in South Africa has increased public health and social problems, making the reduction of alcohol intake a priority for policy makers. Despite the urgent need to make a paradigm shift in regards to policies on alcohol use, a major problem that current policy markers face is how to quantify with accuracy whether drinking patterns in a particular community are comparatively heavy thus exacerbating health and psycho-socioeconomic problems and the question of how to curb or overcome dangerous drinking patterns arises. The WHO recently stated that alcohol consumption is one of the leading causes of death worldwide and that intakes are increasing, more importantly in developing countries.[6]

According to the WHO's database, fewer South Africans drink, compared to the individuals reported in 44 other countries. What is disturbing is the pattern of drinking; those reported to drink consume huge amounts of alcohol (20 litres of absolute alcohol per drinker per year). The observed pattern of binge drinking of about a third of South African drinkers is of concern.[74,75] Alcohol misuse and abuse in South Africa is responsible for at least half of the 14 000 annual reported road deaths. It is also known that this misuse is associated with crime,[76] violence, high sexual risk behaviour, family disruption and a host of individual and societal problems.[75] Binge drinking additionally results in a loss of the cardio-protective effects associated with alcohol and micronutrient deficiencies,[77] both occurrences showing high prevalence in the South African population.[78] The observed pattern of drinking amongst South Africans can also lead to alcohol dependency and addiction, further deepening this problem. South Africans are somewhat prone in terms of developing alcohol related problems, due to increasing economic hardships that usually accompany alcohol abuse.

The causal relationship between poverty and alcohol abuse can be synchronised with that of the egg and the chicken, the debate being which one comes first. In a study that investigated the short and long term effects of poverty and unemployment on alcohol abuse using structural equation modelling to better understand the observed conflicting relationships among them, it

was indicated that (a) increased poverty causes increased alcohol use and alcohol problems, and (b) recent unemployment decreases alcohol use while longer unemployment increases it. It is concluded that the effect of unemployment on alcohol abuse changes direction with time and, thus, both cross-sectional and longitudinal data are required to assess any meaningful relationship between them.[79] Thus unemployment and poverty could be leading causes of alcohol abuse in South Africa, since the two variables investigated remain high in this sub Saharan country.

Though the beneficial effects of moderate alcohol consumption remain stimulating, the levels of abuse among South African drinkers are of concern. Conclusively, more research is needed particularly for this African population to find out whether the French paradox is also applicable to this population before health promotion of moderate alcohol intake. The health hazards pertaining to this population also need to be weighed by policy makers so as to come with a comprehensive strategy to overcome abuse, dependency and still retain attributed health benefits from alcohol consumption.

The final guideline proposed by the Food Based Dietary Guidelines Work Group was "If you drink alcohol, drink sensibly", addresses the use of alcohol in South Africa.[32] However, considering current abuse of alcohol in South Africa, this guideline might need re-examining. Currently, total abstinence from alcohol may be the only solution for this country in crisis, but the applicability of such a goal could be far fetched and almost impossible to attain. Banning alcohol will surely lead users to turn to ingenious, exploitative and criminal methods of obtaining alcohol containing beverages[32] and will increase the number of people brewing home made alcohol concoctions. Therefore, the solution seems to be in educating the public to drink moderately or sensibly.

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2.3 THE CARDIOPROTECTIVE EFFECT AND PUTATIVE MECHANISMS OF LIGHT/MODERATE CONSUMPTION OF ALCOHOL: A NARRATIVE REVIEW

(*Submitted for publication in the South African Journal of Clinical Nutrition*)

2.3 THE CARDIOPROTECTIVE EFFECT AND PUTATIVE MECHANISMS OF LIGHT/MODERATE CONSUMPTION OF ALCOHOL: A NARRATIVE REVIEW

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Abstract

Objective. In this review we elucidate the possible mechanisms underlying the cardioprotective effects of light/moderate alcohol consumption and question whether ethanol *per se* or other ingredients in the various alcoholic beverages (e.g. polyphenols) are responsible for these effects.

Methods. A computerised search in seven databases Pub Med, Academic Search Premier, ERIC, Sports Discuss, Web of Science, Google and Science Direct was done, selecting intervention and epidemiological studies in which light/moderate consumption of alcoholic beverages of any kind had positive effects on cardiovascular risk factors and markers like lipid and lipoprotein profiles, haemostatic function, the cardiovascular system, insulin sensitivity, homocysteine and oestrogen levels. The hypothesised mechanisms underlying the cardioprotective effects of light/moderate alcohol consumption are discussed by taking the French paradox as the starting point.

Results. There is abundant scientific evidence showing positive cardioprotective effects of light/moderate alcohol consumption. Most of the beneficial effects of moderate alcohol consumption have been attributed to increased plasma high density lipoprotein, reduced fibrinogen concentrations, inhibition of platelet aggregation, increased insulin sensitivity and improved endothelial function. The non-alcoholic components of wine, especially phenolic compounds seem to play a significant role in cardioprotection. However, scientific evidence has shown that the cardioprotective effects of alcohol consumption are not limited to one particular type of alcoholic drink, suggesting that ethanol reduces mortality risk independently, in addition to the contribution of other compounds such as polyphenols.

Conclusion. Ethanol as well as the compounds specific to certain alcoholic beverages seem to play significant roles in the cardioprotection that is associated with light/moderate drinking. Presently there is not enough scientific evidence within the research domain that can allow or warrant public health promotion of alcohol consumption since much disparity and inconsistency is still present among researchers.

Key words: French paradox, Moderate alcohol consumption, Cardiovascular risk makers, Putative mechanisms.

Introduction

The "French paradox" is a phenomenon that was first noted by the Irish physician Samuel Black in 1819. It was the result of the observation of a low incidence of coronary heart disease (CHD) in France, despite a general dietary pattern high in saturated fats.[1] The low CHD mortality observed in France and Mediterranean populations has been attributed to an increased consumption of alcohol, particularly red wine. Since then, the debate of the effects of moderate/light alcohol intake reducing the risk of CHD has been ongoing for decades, with many suggesting this paradox to be an artefact of the way the French record their death statistics. However, the idea is now firmly set in the public research domain, and the hypothesis seems to be here to stay.

Alcohol consumption may be divided into three categories: light, moderate and heavy drinking. This is defined by the amount of alcohol consumed in alcoholic beverages in terms of pure ethanol per day.[2,3] "Light/moderate" alcohol intake is defined as an average consumption of 1 to 2 drinks per day and "heavy drinking by a consumption of $\geq$ 3 drinks per day of liquor or beer. In absolute terms, light/moderate drinking amounts to < 30g and heavy drinking amounts to > 30g of pure ethanol consumed daily.[4] There are numerous epidemiological and clinical studies illustrating that light/moderate drinking is associated with reduced risk of CHD, ischaemic stroke and total mortality in middle-aged and elderly men and women.[5-10]

Berger *et al.*[11] found that light/moderate alcohol consumption reduced the overall risk of stroke and ischaemic stroke in men. This benefit was seen with as little as one drink per week, and an increased consumption of up to one drink per day did not increase the observed benefit. In a Finnish study, Makela *et al.*[12] observed that among men aged 30-69 years of age, light/moderate drinking prevented some 400 CHD deaths each year. Rimm *et al.*[7] in their meta analysis, concluded that alcohol intake quantified as 30g of pure ethanol per day is causally associated with 24.7% risk reduction of CHD. Epidemiological evidence suggests a J- or U-shaped relationship between alcohol consumption and CHD, illustrating a higher risk when alcohol consumption is high, lower when alcohol consumption is low/moderate, and tends to go up again in individuals who never consume alcohol.[13,14] Such conclusions have been based on findings in epidemiological studies regarding the risks for CHD and death in individuals with low or moderate alcohol consumption, when compared with corresponding risks in individuals who do not consume alcohol at all.[7,15-17] Additionally, an argument exists that the J- shaped curve is due in part, to the presence of former heavy drinkers among current abstainers.

Although there is evidence suggesting the positive attributes of light/moderate consumption of alcohol, the mechanistic contribution of different alcoholic beverages remains debatable. Because alcohol is addictive, it is important to find out whether ethanol, auxiliary compounds, or metabolic end-products of ethanol contribute significantly and by what amount to this positive effect. In this review the possible mechanisms underlying the cardioprotective effects of light/moderate alcohol consumption and the question whether ethanol *per se* or other ingredients in the various alcoholic beverages (e.g. polyphenols) are responsible for these effects are elucidated. Because of rapid urbanisation, the South African population is experiencing a health transition. In Africa, alcohol (ethanol) containing beverages are one of the most consumed beverages.[18] The use, misuse or abuse of alcohol probably plays an important role in this transition. This population in transition experiences high levels of alcohol misuse and abuse with its many adverse consequences and possibly little or none of the putative beneficial cardio-protective effects associated with moderate alcohol consumption. To develop a relevant, integrated and coherent strategy to address alcohol use, misuse or abuse in South Africa, a much better understanding is needed of the causes and consequences of binge drinking, the mechanisms through which moderate intakes are cardio-protective, and therefore, why binge drinking possibly negates these protective effects.

Methods

A systematic computerised search in Pub Med, Academic Search Premier, ERIC, Sports Discuss, Web of Science, Google and Science direct was done, selecting intervention studies and epidemiological studies in which light/moderate consumption of alcoholic beverages of any kind had positive effects on cardiovascular risk factors and markers like lipid and lipoprotein profiles, haemostatic function, the cardiovascular system, insulin sensitivity, homocysteine and oestrogen levels and those that showed no positive effects were excluded. The selected articles that met this criteria where used to discuss the mechanistic effect to which light/moderate consumption of alcoholic beverages had on cardiovascular risk factors and markers. The two reviewers (PTP, DTL) independently screened papers for inclusion and from the above search, the final number of articles that were used was 82.

Putative biological mechanisms underlying cardioprotection by low/moderate alcohol consumption

As illustrated in Table I, several factors have been proposed to explain possible mechanisms by which alcohol could reduce CHD and atherosclerosis. [6,9,19,20] These include the effects of

low/moderate alcohol consumption on lipid and lipoprotein profiles, haemostatic function, the cardiovascular system, insulin sensitivity, homocysteine and oestrogen levels. The remainder of this review will focus in more detail on the proposed mechanisms by which alcohol may lower the risk for CHD and atherosclerosis.

Table I.	**Proposed biological mechanisms underlying cardioprotection by low/moderate alcohol consumption***
Variable	Cardioprotective effect of alcohol intake
Lipid and lipoprotein profile	Increases "good" HDL-cholesterol
	Reduces oxidation of harmful "bad" LDL-cholesterol
	Increases paraoxonase activity
Haemostatic function	Reduces platelet aggregation
	Reduces fibrinogen levels
	Increases fibrinolysis
Cardiovascular system	Increases coronary blood flow
	Reduces blood pressure
Hormones	Reduces blood insulin levels
	Increases blood insulin sensitivity
	Increases oestrogen
Other effects	Decreases plasma homocysteine levels

*Adapted from Agarwal.[4]

HDL= high-density lipoprotein; LDL= low-density lipoprotein.

Effects of moderate alcohol intake on lipid profiles

LDL is the main carrier of cholesterol and delivers cholesterol to various cells and tissues. HDL serves as an acceptor for cholesterol from various tissues and hence promotes the removal of cholesterol from the cell, and its secretion into the bile by the liver. To explain the terms to the general public, LDL-cholesterol is consequently designated "bad" cholesterol, as high levels are associated with increased deposition of cholesterol in arterial walls and an increased incidence of CHD. HDL-cholesterol on the other hand has been designated as "good" cholesterol. It should be noted that the best single indicator for the development of atherosclerotic heart disease is, therefore, not total cholesterol, but the ratio of plasma LDL-cholesterol to HDL-cholesterol (the lower the ratio, the lower the risk).

It has been established that the effect of alcohol consumption is primarily mediated by increasing HDL,[21-23] as recently indicated by Agarwal.[4] The 16,8% reduction of CHD proposed by Rimm *et al.*[7] was directly attributed to increased HDL, when consuming alcoholic beverages (beer, wine and spirits) constituting to 30g of ethanol per day. The proposed mechanism by which this may occur has been reviewed in detail by Agarwal,[4] as follows: The cholesteryl ester transfer protein (CETP) mediates transfer of cholesteryl esters from HDL into very low density lipoproteins (VLDL) and LDL, with a reciprocal exchange of triglycerides.[24] If the transfer rate is low, then it may reduce the reverse transport of cholesterol.[25] Reverse cholesterol transport can be enhanced by raising the HDL levels and thereby overcoming the negative effects associated with oxidized LDL on the atherogenic process. It was previously thought that alcohol consumption only increases HDL-3 alone. However, recent observations have shown that both classes, HDL-3 and HDL-2, contribute equally to the overall efficiency of reverse transport of cholesterol.[23] Thus, alcohol consumption may raise HDL levels either by altering the synthesis or by the effects of specific enzymes and proteins influencing HDL metabolism, and thereby positively affecting the HDL/LDL ratio.[4] Additionally, alcohol consumption is further associated with increases in plasma concentrations of apolipoprotein A1 and apolipoprotein A11, the principal components of HDL particles.[21]

It has been estimated in epidemiological studies that an individual consuming alcohol constituting to an average of 30g of ethanol per day shows an increment of 8mg/dl of plasma apolipoprotein A1, primarily due to increased synthesis in the liver,[7] which ultimately leads to increased HDL concentrations. In Agrawal's review,[4] it is opined that oxidation of LDL has also been shown to play an important role in the progression of atherosclerotic vascular disease.[26] The antioxidant capacity of red wine, due to its polyphenol content,[27,28] has been postulated to contribute to its stabilizing effects on LDL, by lowering oxidation of LDL and preventing atherosclerotic plaque formation.[29] An additional consideration to this process in light/moderate alcohol drinkers is the increase in human serum HDL-linked paraoxonase enzyme, which lowers risk of CHD.[30] This enzyme functions by limiting LDL peroxidation, preventing transformation of LDL into biologically active atherogenic particles,[4] hence providing protection against LDL oxidation, consequently reducing the risk of CHD.[31] Van de Gaag *et al.*[31] showed elevated fasting paraoxonase after the intake of wine, beer and spirits without significant variation when consuming the three alcoholic beverages, thus implicating ethanol to be the causal factor in this process.

Another consideration in evaluating the lipid risk factors for CHD, is elevated concentrations of lipoprotein (a) (Lp(a)).[32, 33] This molecule is similar in structure to LDL, except that it contains one additional large protein dubbed apolipoprotein A. The underlying mechanism by which Lp(a) functions is by inhibiting fibrinolysis by lowering of plasminogen levels.[34] Vasisht *et al.*[35] demonstrated that CHD patients have significantly higher levels of Lp(a) in comparison to those consuming alcohol. Similarly, a reduction in alcohol consumption is accompanied by significant increase in Lp(a) levels.[36] Furthermore, social drinking has been associated with lowered Lp(a) concentrations in middle-aged men. Considering this, lowered Lp(a) levels may be one of the factors explaining low mortality and retarded progression of CHD in social drinkers.[32]

Effects of moderate alcohol intake on haemostatic function and thrombosis

A wide range of factors have been identified in prospective epidemiological studies to affect blood thrombogenicity. There is increasing evidence of the relationship between the traditional cardiovascular risk factors such as diabetes mellitus, hypertension, hyperlipidemia and increased thrombogenicity, which in turn is characterised by hypercoagulability, hypofibrinolysis or increased platelet reactivity.[37] For this reason, much interest has recently been given to elevated blood coagulation in acute and chronic cardiovascular disturbances. Additionally, high fibrinogen concentrations have been implicated as a significant and independent risk factor for CHD.[38]

Agarwal's[4] review further establishes how moderate alcohol consumption (beer, wine, or liquor) has been shown to affect several haemostatic factors, including lowering fibrinogen concentrations[39-41] and increasing fibrinolytic factors such as tissue plasminogen activator and plasminogen activator inhibitor,[42-44] consequently reducing blood platelet aggregability.[45] The antiplatelet activity of wine is not only attributed to ethanol and its metabolites, but also to its polyphenol content. It seems that the polyphenols in red wine could significantly inhibit platelet aggregation and that this could explain, in addition to its ethanol content the protective effect of red wine against CHD.[4]

Effects of moderate alcohol intake on insulin resistance and insulin sensitivity

The inability of body tissues to utilise insulin is termed insulin resistance. High blood insulin levels that accompany insulin resistance are associated with a clustering of heart disease risk factors commonly termed Syndrome X and includes visceral obesity, glucose intolerance, high triglycerides, low HDL-cholesterol and high blood pressure. Insulin resistance is a strong predictor of CHD[46] and increased insulin sensitivity is considered to have beneficial effects on improving the atherosclerotic condition.[47] Moderate alcohol consumption is associated with

decreased insulin resistance and this partly explains the associated cardioprotective effects.[48,49] Insulin sensitivity in skeletal muscle has been shown to increase with moderate alcohol intake,[50] but the mechanism behind this remains obscure. The proposed mechanism that acetate in the peripheral tissues, derived from ethanol metabolism, generates sufficient levels of adenosine monophosphate (AMP) to temporarily stimulate the AMP-activated protein kinase, which in turn promotes the synthesis of long-lived proteins that boost insulin sensitivity is discussed by Agarwal.[4,51] Additionally, HDL cholesterol levels have been shown to increase as insulin sensitivity improves, and this is suggested as one of the mechanisms that alcohol has on HDL metabolism.[52]

Effects of moderate alcohol intake on hypertension

Hypertension is a strong CHD risk factor.[53] Epidemiological evidence has illustrated increased mean blood pressure and/or hypertension are associated with increasing alcohol intake.[6] In moderate drinkers it has been shown that a J-shaped relationship exists between alcohol intake and blood pressure, with the lowest levels in consumers of 1-3 drinks per day.[54,55]

Effects of moderate alcohol intake on oestrogen

Oestrogen not only lowers total cholesterol and LDL, but also raises HDL, which explains in part, why pre-menopausal women have less risk of developing CHD than men. After menopause, the cholesterol values and CHD risk in women become similar to those in men.[56] Alcohol consumption may increase blood oestrogen levels in postmenopausal women.[57] Agarwal[4] articulated how moderate alcohol consumption exerts influence not only on oestradiol and testosterone but also on the oestrogen-responsive pituitary hormones in normal post-menopausal women,[57] suggesting that moderate alcohol intake is an important factor for post-menopausal oestrogen status and may offer an explanation for the reported protective effect of moderate alcohol use with respect to post-menopausal CHD.

Effects of moderate alcohol intake on plasma homocysteine concentrations

High plasma homocysteine levels are also an independent risk factor for coronary, cerebral and peripheral arterial occlusive diseases.[58,59] The resulting endothelial dysfunction caused by elevated homocysteine levels is associated with atherogenesis and oxidative stress in humans.[4] Agarwal[4] additionally discussed how moderate alcohol intake has been shown to reduce homocysteine levels in observational studies.[60,61] Contrary to this, however, serum homocysteine levels increase even after moderate alcohol consumption, in social drinkers,[62] thus the

cardioprotective effect of moderate alcohol consumption in relation to homocysteine remains a debatable issue.

Discussion

Epidemiological studies suggest a J- or U- shaped relationship between alcohol intake and mortality, indicating that there are both beneficial and detrimental effects of alcohol consumption on health, depending on the dosage, with light/moderate consumption being associated with cardioprotection. The mechanisms proposed by which this may function include effects on lipid and lipoprotein profiles, haemostatic function, the cardiovascular system, insulin sensitivity, homocysteine and oestrogen levels.

Although there is substantial evidence showing the association between light/moderate alcohol consumption and reduced CHD risk, a pending question remains: "Is ethanol independently associated with the observed reduction of mortality rates, or are other substances, such as polyphenols in alcoholic beverages or the metabolic product acetate, responsible for the protective associations?" In prospective cohort studies an inverse association has been shown between wine,[63-65] beer, [65-68] and spirits[65,67,69,70,] consumption and CHD. This suggests that ethanol itself may play a vital role in the cardioprotective effects associated moderate alcoholic beverage consumption. This conclusion is also supported by Rimm *et al.*[71] who showed that an alcohol intake, quantified as 30g of pure ethanol per day, is causally associated with 24.7% risk reduction of CHD. In a population of 13000 men and women between the ages of 30-79 years of age, Gronbaek *et al.*[68] examined the association between the intake of different alcoholic drinks and mortality. In this population, the relative risk of death from CHD was reduced by the consumption of both wine and beer. Pellegrini *et al.*[72] evaluated the effect of moderate wine consumption on haemostatic variables, with the aim to elucidate the effects of ethanol and the non-alcoholic components in this beverage. The same group concluded that the beneficial effects (reduced fibrinogen levels) observed by their group were all attributed to the ethanol content and were unrelated to non-alcoholic components. However, the validity of this study was compromised as certain confounders such as diet and environmental factors were not controlled for. These studies indicate that ethanol itself may play a vital role in the cardioprotective effects associated moderate alcoholic beverage consumption.

In addition to ethanol's protective effect, the presence of polyphenolic antioxidants in alcoholic beverages, particularly in red wine, has also been shown to further increase this effect.[27,28] The

non-alcoholic component of wine, mainly made up of phenolic compounds, may be primarily responsible for the positive effects on lipids (inhibition of LDL oxidation and increase antioxidant capacity) and haemostatic factors. Researchers have shown that the polyphenols in red wine in the absence of ethanol play a vital role in cardioprotection. Stein *et al.*[73] showed an in *vivo* effect of purple grape juice on endothelial function and LDL oxidation. Their study recruited 15 patients suffering from angiographically documented coronary artery disease (CAD) and taking antioxidants and lipid lowering medications, supplemented with 7.7 ml/kg/d of purple grape juice for 14 days. The authors reported a significant improvement in endothelial function and reduced susceptibility of LDL to copper-induced oxidation in these patients. This study showed that flavonoids independent of alcohol may have cardioprotective effects. Further, in *vivo* experimentation using rats, showed either red or white wine and ethyl alcohol exerted comparable effects on haemostatic variables separately.[74] Wollny *et al.*[74] further examined whether the removal of ethanol from wine would decrease its beneficial effect and concluded that red wine regardless of alcohol content had substantial beneficial effects, suggesting the beneficial role of red wine to be attributed to its polyphenol content and not to ethanol. Keevil *et al.*[75] established in healthy humans inhibition of platelet activity after consumption of two cups of purple grape juice for one week, further elucidating the beneficial effects of polyphenols in cardioprotection.

A study comparing white and red wines, red wine polyphenols and a control alcoholic drink on LDL oxidation in humans showed no significant effects in the groups treated with various red wine polyphenols but a significant difference was seen between groups treated with white wine and the control drink.[76] This suggests that red wine consumption increases plasma polyphenols, thus enhancing antioxidative capacity that was shown by decreased plasma total peroxides and decreased lipid peroxides in the copper catalysed peroxidation of LDL–conjugated dienes. As for beer, the dealcoholised component, rich in vitamin B_6, vitamin B_2 and folate, may also play a part in the positive cardioprotective effects associated with beer. Vitamin B_6, vitamin B_2 and folate in beer may prevent alcohol-induced rise in serum homocysteine levels.[61,77]

From the above reported studies, both ethanol and polyphenols seem to have positive cardioprotective effects. Miyagi *et al.*[78] reported that only red wine consumption resulted in LDL resistance to oxidation in *vivo*. It was further postulated that alcohol increased the intestinal absorption of flavonoids.[78] Additionally, alcohol has been noted to be a natural stabiliser for polyphenols in red wine.[79,80]

Evidence from the existing literature suggests that both ethanol and polyphenols in red wine play a significant role in cardioprotection. It is not clear to what extent polyphenols in red wine or ethanol *per se* individually contribute to cardioprotective effects. This further reflects the complexity of mechanisms exhibited by both polyphenolic compounds and ethanol.

There is virtually no information on the possible contribution of the metabolites of ethanol (e.g acetate) to these putative cardioprotective effects. Two lines of evidence argue for a possible contribution of acetate production to cardioprotective effects: firstly the well-known "morning-after" effects of alcohol: alcohol intake is associated with an increase in tissue type plasminogen activator antigen (tPA-Ag) (i.e. antithrombotic) and plasminogen activator inhibitor type 1 (PAI-1) (i.e. thrombotic). The morning after alcohol consumption, tPA-Ag remains high while PAI-1 levels decrease, creating an antithrombotic, cardio-protective effect.[81] This suggests that the antithrombotic effects may be related to the metabolic products of alcohol. The second line of evidence comes from our own studies which showed that acetate, one of the metabolic products of alcohol, either given by capsule or produced from pectin in the large gut, had antithrombotic effects by changing the structure of fibrin networks.[82]

Conclusion

In conclusion the available literature illustrates that it's not a question of ethanol or other substances in alcoholic beverages constituting to the associated cardioprotective effects of alcohol, but that benefits exist from both the phenolic compounds of red wine and ethanol individually and combined. Both components have independently been shown to have cardioprotective effects, and to complement each other. It should still be noted that the health benefits observed might heavily be influenced by life-style, genetic and environmental factors. It is also well established that the cardioprotective effects of alcohol consumption depends on the drinker's age, sex, type of alcoholic beverage, nutritional status and the way the beverage is consumed (steady or binge).

From a public health perspective, one would wonder whether there is enough scientific evidence to warrant wide spread promotion and recommendation of moderate alcohol consumption, taking into account that abuse can also lead to addiction and dependency. Presently there is not enough scientific evidence within the research domain that can allow or warrant promotion of alcohol consumption since much disparity and inconsistency are still present among researchers and the

promotion of a little could also led to alcohol abuse (if a little is good, then more is better). Thus, for public health policy makers, the dilemma still exists whether to recommend alcohol intake or not, illustrating that further research is still required on the topic.

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2.4 THE SOCIAL ASPECTS OF ALCOHOL MISUSE/ABUSE IN SOUTH AFRICA: A REVIEW

(*Submitted for publication in the South African Journal of Clinical Nutrition*)

2.4 THE SOCIAL ASPECTS OF ALCOHOL MISUSE/ABUSE IN SOUTH AFRICA

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Abstract

Use of alcohol in Africa, particularly in South Africa, has a long history and is part of human life regardless of socio-economic background. Alcohol abuse has many negative health, economic and social consequences. The objective of this review is to present in brief the history of alcohol use and the social and economic causes and consequences of alcohol abuse in South Africa. The harmful socio-economic effects of alcohol abuse in South Africa are discussed by firstly emphasising that social and economic changes stemming from urbanisation account for new patterns of drinking among most Africans. Research has shown that socio-economic effects including unemployment, violence, crime, sexual risk behaviour, family disruption and work performance are associated with alcohol abuse. The South African legislation on alcohol is also incorporated to highlight the need to change or amend certain Acts in a bid to reduce alcohol abuse.

Key words: Social aspects, Psychological aspects, Alcohol abuse/misuse, South Africa.

Introduction

Alcohol has played a major role in the lives of many South Africans. Traditionally, in rural areas alcohol served many purposes. Not only was it used as a means of payment, and strengthening friendship, but beer was also associated with manhood and with the strengthening of the body.[1] Similarly in other African communities such as Kenya, alcohol was used to celebrate important occasions such as marriages and success in harvests. Drinking was moderated and subjected to certain guidelines as to when, how much, why and who should drink. Alcohol was mainly for domestic consumption.[2]

With the arrival of the European farmers (traders) in the 1800s there was a move by Africans to drink European liquor called "Cape Smoke". This was highly unacceptable to many farmers because they believed alcohol made Africans disobedient.[1] Apparently the disobedience was displayed when one was under the influence of liquor and would not take orders, absent oneself from work or even talk back, which was unacceptable. This led to many new laws in the 1900s which controlled drinking of mainly Africans. One of the controlling measures was the introduction of beer halls around 1908 which seemed to be based on the idea that it was wrong for the 'native' to have his beer hall.[1] This could, however, not stop the proliferation of illegal shebeens. One could argue that the prohibitions resulted in Africans wanting more and finding ways of acquiring more of both home brewed and European liquor (brandy). These are some of the traces that led to the misuse of alcohol, for one would have to consume more because there was no guarantee that one would get a drink again.

African beer was fermented from locally grown food such as sorghum and maize. This kind of beverage took about four to fourteen days to brew. In some other parts of Sub-Sahara Africa the alcoholic beverages available were fermented honey water, fermented fruits and juices, fermented sap of various species of palm and beers. The brewing of alcohol had economic spin offs for women who sold it as a way of supplementing the wages their husbands were earning. In order to meet the high demands, people tried different ways of brewing beer easily and quickly, often compromising quality. This is how "concoctions" started, most of which are brewed in less than a day.[3] It was a time during which South Africa as a country was entering an industrial age which accounted for a change in the traditional use of alcohol.

Also with the coming of Dutch Settlers and later the French Hugenots in the Cape as wine farmers from around 1652 onwards, African and Khoisan slaves mainly comprised the labour

force. In addition to their salary, the labourers were given wine. This system became known as the 'tot' or 'dop' system.[1,4,5] Through this system heavy drinking became entrenched in the lives of workers and their families for generations.[6] Alcohol was used by the colonisers as a mechanism to seize power – a form of political, economic and socio-cultural domination.[7] These were micro level practices that went unchecked. Since the problem is predominantly in the Western Cape the system has even managed to perpetuate racial stereotypes and inferences that the problem of over drinking is biologically determined and not socially constructed.[8] The 'dop' system was formally outlawed by the South African democratic government a decade ago though its effects still linger. In more recent years it has taken a variety of forms, including that of a 'gift' or supplement to remuneration, or as alcohol provided on credit.[9] Currently, there are still traces of the earlier problems. People are exposed to misuse and abuse that could be traced to drinking patterns of the 1600s. Parry and Bennets[8] in their study among South Africans found significant consumption differences by population group and gender with intake higher in urban than rural areas, individuals with ages between 35-44 and 45-54 years consumed more and there seemed to be a high rate of misuse over weekends. Similar trends were also observed in countries like Kenya.[10]

The most common factors leading to alcohol abuse in South Africa are urbanisation, stressful jobs, affordability and cultural beliefs. These factors are discussed below.

Modernisation and urbanisation

Rapid social and economic changes stemming from urbanisation account for new patterns of drinking in most African settings. The emerging patterns are often not built upon traditional drinking behaviours where there was social control. Instead these are influenced by factors such as easy access to alcohol which has a higher ethanol content as well as rigorous advertising in the media, which disregard traditional constraints on when alcohol may be consumed by whom and where.[8] Jernigan *et al.*[11] explains a pattern where people used to drink until the "beer ran out," but this is being radically replaced by a pattern of drinking "until the money runs out". As Willis[12] asserts, alcohol consumption is highly commoditized, and is no longer restricted to adults or to certain restricted occasions.

The traditional culture of drinking which seemed to have been obtained and determined by 'proper' drinking patterns appears to be eroded and replaced by multiple drinking cultures which vary from one community to the other. Most of these drinking cultures openly challenge earlier

ideas of temperance, age and gender restrictions. Migration has also contributed to this problem. Urbanisation appears to have impacted negatively on rural areas as some of the urban ways diffuse back to it. For instance traditional home beverages known for their nutritional value have been replaced by deadly concoctions which pose a health hazard.[12]

Stressful and high risk jobs

No field of occupation is exempted from the negative effects of alcohol abuse, yet the following are identified as some of the high risk and stressful jobs that predisposes workers to alcohol misuse: brewing and distilling industry, hoteliers and barmen/women, as well as those in the armed services – the police in particular.[13] The alcohol industry happens to be a major source of employment.[8] Risk is caused by availability of alcohol, high levels of responsibility and performance anxiety, alertness, as well as stress. With the South African Police stressors range from violence that is endemic in the country, high crime levels, emotional strain caused by organisational transformation, lack of resources, bureaucracy and family responsibilities.[14] Risky drinking in these high risk and stressful jobs is mainly to cope with social pressure and as an escape from reality, a form of 'letting off steam'.

Availability and affordability

One of the causes of alcohol abuse and misuse is its availability in terms of location, time and affordability. In 1997 in South Africa there were about 22 900 licensed outlets, including liquor stores, restaurants, taverns and supermarkets compared to about 20 000 informal liquor sectors, such as shebeens, which are mostly unregulated and operate outside the confines of the law. After nearly a decade these outlets have multiplied.[8] The South African Liquor Act of 2003[15] regulates times of operations for liquor trading. However, more outlets such as supermarkets and taverns follow different times of trade. Some of the unregulated outlets operate depending on demand. The age restriction is known to be 18 years and this information is displayed in bottle stores and supermarkets but there are no proper measures to ensure that this is adhered to. This makes alcohol easily and widely available and affordable to all races, genders, and ages – amidst restrictions.

Cultural beliefs

Traditionally it was not acceptable for native African women to drink alcohol. This view is supported by Mphi,[16] who asserts that women in Lesotho are not allowed to drink alcohol at all, despite the fact that most are brewers and traders of traditional beer. A woman who indulges in alcohol is subject to derision, condemnation and even divorce. In colonial Zimbabwe, male

members even fought against what they termed "joint drinking", that is, women and men drinking together at the municipal beer halls.[17] The danger of such practices is that it tends to subject women to private drinking that can produce public hazardous results. These inhibiting cultural practices are entrenched through socialisation in most South African communities. In the white culture such inhibitions appear to be absent. Both men and women from all socio-economic backgrounds are allowed to enjoy their alcohol intake in public places.[8] The young African women tend to emulate this behaviour presumably because of the influence of urbanisation and acculturation. Based on the findings of the Department of Health's South African Demographic and Health Survey (SADHS) conducted in 1998, the majority of risky weekend drinkers are African women (42.1%) and their age range is between 15-24years (30.1%).[18] Morojele *et al.*[19] in their study on 'Alcohol use and sexual behaviour among risky drinkers in Gauteng Province, South Africa' revealed gender differences in that men's drinking is traditionally and currently accepted as pleasure, recreational and sensation seeking. Their drinking is encouraged by their peers, and heavy drinking symbolises masculinity. Such behaviours perpetuate binge drinking.

Children living on the street

As pointed out by Maree,[20] children living on the street constitute one of the fastest growing problems in Africa. Children live on the streets due to varied reasons. Some would do so as an escape from reality or as a coping mechanism because of family disorganisation, divorce, poverty, loneliness, boredom, unemployment and crime. South Africa is equally plagued by this problem where children leave home to live on the streets.[21] Curiosity, delinquency and peer pressure also play a role. Because they live on the streets far from their parents, they have no boundaries that guide their behaviour. This is how they start sniffing glue, smoke dagga and other drugs and use and misuse alcohol.

Based on these causes people tend to be affected psychologically and socially.

Psychological effects

Alcohol misuse and abuse could lead to stress and anxiety. This could cause the individuals to increase their dosage in order to cope with their problematic situations, only to experience the same disillusionment when the effects wear off. People experience depression for various reasons. Bezuidenhout[22] states that some people may experience stress and anxiety because of alcohol abuse. It could be because of personal problems or failure to control their drinking. If not attended, he or she might commit suicide.[23] Findings of the research undertaken by the Medical

Research Council shows that one in four of those who killed themselves in South Africa were over the blood alcohol limit of 0.05g/100ml.[23] Chronic stress caused by alcohol abuse was also found to be related to youth suicide.[24] Some adolescents become aware of the adverse effects of alcohol and try to stop taking it but more often than not, they fail to do so especially without professional help and resort to committing suicide.

Social effects

Unemployment

South Africa is plagued by a high unemployment rate. Statistics South Africa in the September 2006 report,[25] indicated that 4 391 000 persons were unemployed, 12 815 000 were not economically active and 3 217 000 were discouraged work seekers (unemployed but had not taken steps to find work or start a business in the four weeks prior to the interview). Unemployed people may drink to escape reality and to cope with harsh situations they find themselves in. These views are supported by Ettner[26] whose results provided literature evidence that a recessionary environment or lay-offs resulting from harsh environmental regulation will increase alcohol abuse. Poverty as one of the end results of unemployment is high in South Africa. It is to be noted that communities living below the poverty datum line tend to spend the little bit of money they have on alcohol.[23]

Violence and crime

It is stated that alcohol is present in offenders and victims in many violent events. The results of Phase 3 of the 3-metros (Cape Town, Durban, and Gauteng) in South Africa Arrestees Study conducted during August/September 2000 continue to show a high level of drug usage including alcohol use among arrestees. Over all sites, 50% or more of persons arrested for the following crimes tested positive for at least one drug: drug and alcohol offences (75%), housebreaking (66%), motor vehicle theft (59%) and rape (50%).[27] Exposure to violence and alcohol is identified as one of the developmental factors that contribute to violence. Withdrawal symptoms can develop to aggressive behaviour towards family members, friends or members of the community. One of those violent behaviours often results into sexual assault.[28, 29]

Sexual risk behaviour

A study conducted by Morojele *et al.*[19] confirms that heavy alcohol consumption is a major health concern in South Africa and there is a link between alcohol consumption and sexual risk behaviour. The study also revealed that there were high levels of alcohol consumption and

unprotected sex among some members of the communities who engaged in casual relationships. Alcohol use is prevalent in South Africa and alcohol use may be associated with higher risk for human immunodeficiency virus (HIV) transmission. Olley *et al.*[30] argued that some HIV-infected individuals, despite knowledge of their status, continue to practice unsafe sex which places them and their partners at considerable risk. A partner who is under the influence of alcohol could be at risk because of such practices. According to the 2004 report by the Medical Research Council of South Africa, more than five million South Africans out of a total of forty-six million were HIV infected.[31] Kalichman *et al.*[32] confirmed in their study the association between alcohol use and HIV risk-related behaviour among 134 men and 92 women receiving sexually transmitted infection (STI) clinic services in Cape Town, South Africa. The study concluded that the association between alcohol use and sexual risk behaviours in a population at high-risk for HIV transmission demonstrates the need for integrating alcohol risk reduction counselling with HIV prevention counselling among STI clinic patients in South Africa.

The 2004 report by the Medical Research Council of South Africa further indicates that 37 000 children were infected with the HIV virus at or around birth (vertical transmission) and 26 000 were infected through breast feeding. A quarter to a third of the vertically infected children died before they reached one year of age.[31] Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) aggravates the already existing poverty especially when breadwinners lose their jobs because of ill health or death. In South Africa, there were approximately 3.3 million orphans as of 2004. Almost two thirds of children living in child-headed households were 13 years of age. Poverty, ill health, teenage pregnancy, delinquency, alcohol and drug abuse is a common occurrence in such homes.[31]

Family disruption

The function of a family as a system is to provide shelter, as well as emotional, economic and psychological support. But when one member abuses alcohol, the family becomes destabilised or the balance is affected. Alcohol abuse tends to retard the efforts of a family to maintain its balance. Money that should be used for the family is misused in alcohol and this could contribute to violence and poverty. Relationships are affected because the perpetrator is under the influence of alcohol and is not able to give love and care. A 1998 cross-sectional study on violence against women was undertaken in three South African provinces. This study showed how domestic violence was significantly (positively) associated with women drinking alcohol and conflict over the partner's drinking.[23] Lack of parental control due to the fact that parents do not provide clear

boundaries could lead to disarray in the family and alcohol abuse. It exposes children to anti-social behaviours since parents become negative role models.[22, 21]

Excessive intake of alcohol could also lead to divorce which can affect the partners who have to go through emotional traumatic experiences and adjustments which could be social, economic and sexual. Children may experience difficulty in dealing with divorce. They could be confronted with social, psychological, educational and economic adjustment.[22] Abuse of alcohol also affects social networks. A network can provide supportive environmental help as well as instrumental help. It provides sources for human relationships, recognition, affirmation and emotional support.[33] Social networks such as kin, friends, neighbours, extended family, work mates and acquaintances are affected by divorce as well. The divorced are at risk of social and/or emotional isolation and stigma. Social isolation is loneliness as a result of a distance they do not choose, or when they are without a social network. This could worsen the problem of alcohol abuse.

Work performance

Any working environment has certain expectations from its employees. They have to be productive in order to realise profits. Those employees who abuse alcohol are not likely to perform well. Some of the problems identified are absenteeism, low production (inability to meet deadlines, inability to follow procedures) and proneness to job related accidents. This could lead to dismissal that would affect the person and his family.[8] More employee assistance programmes should be introduced to deal with alcoholism that affects job performance. It was noted that enhanced production cannot be achieved if people have psycho-social problems because one cannot be separated from his/her environment.

The economic cost and injuries

The annual economic cost of alcohol misuse in South Africa could range between 0.5% and 1.9% of the gross domestic product (GDP). This is utilising a middle of the range estimate that considers costs associated with treatment, trauma, mortality and crime, which is about 1% of GDP. This translates to about R8.7 billion per year, an amount almost twice exceeding the one received in excise duties on alcoholic beverages in the period 2000/01.[34] Motor vehicles crashes in the country also account for approximately 11 deaths per 100 million kilometres travelled. Traffic crashes that involve pedestrians account for about 40% of annual mortality on the roads in South Africa. Alcohol abuse and poor roads are cited as the main contributory factors.[35]

Legislation on alcohol

The Department of Social Development is South Africa's leading government institution in combating alcohol and drug abuse. The vision of a society free from the abuse of alcohol and other forms of drugs is the driving force behind the introduction of various policies in the country. Some of these include: the Liquor Act of 2003, which covers all relevant aspects including production, distribution, and consumption of alcohol; the Prevention and Treatment of Drug Dependency Act of 1992, which provides for the establishment of a Central Drug Authority, the development of programmes and the establishment and management of treatment centres. The revised National Drug Master Plan 2005-2010 spells out strategic objectives to guide service providers in the provision of relevant and appropriate services. The strategies outlined in the policy include prevention, early intervention, treatment, aftercare and reintegration. In addition, the policies also include community-based intervention, capacity building, management of treatment practices and information management. International collaboration forms an integral part of the policies as South Africa sees the need to join the global fight against alcohol and drug abuse.[34] Gaps in the implementation and monitoring of these policies have been evident. However, concerted effort by all remains the obvious route to victory over the scourge of alcohol misuse and abuse.

The taxation of liquor also serves as a restrictive measure. A word of caution from Parry and Bennets[8] is that the taxes are not to be so huge as to promote a possibility of smuggling alcohol from neighbouring states or drive consumers to unhygienic concoctions. In terms of cultural intervention, religion seems to contribute to abstinence. A typical example is of people who follow Islam teachings which forbid alcohol intake. Most Africans are also socialised to reserve drinking of alcohol for adults.

Discussion and conclusion

Historically alcohol consumption contributed towards the strengthening of the socio-cultural fibre of African communities. Alcohol was regulated by social rules and used in moderation.[1] However, with time the pattern changed. The use of alcohol today poses a major threat to the quality of life of many South Africans, ultimately causing detrimental public health effects as well as negative socio-economic effects on the country. Alcohol abuse/misuse has become an everyday reality which directly or indirectly, impairs peoples' lives, not only individually, but also on a family, societal and national level.[8]

One of the most important public health and social issues facing South Africa is how to deal effectively and compassionately with persons and communities who are struggling due to alcohol abuse. Although significant achievements have been noted in the policy and legislative domain, the impact does not seem to match the extent of the disruption caused by alcohol abuse. There is an urgent need to re-address these policies and strategies to combat abuse. Moderate alcohol consumption has been shown to have significant health benefits[36] but, the disruption caused by alcohol abuse on different society levels, ranging from family breakdown to crime remains overwhelming. This presents policy-makers of South Africa with a dilemma whether to encourage moderate consumption of alcohol or promote total abstinence. The Food Based Dietary Guideline for South Africa does not clearly stipulate to the population how much alcohol it should consume so as to retain these attributed health benefits. There are indications that the African population is increasingly being prone to alcohol dependency, due to abuse. It seems necessary to define moderate drinking in no uncertain terms.

Besides the current policies put in place to curb alcohol abuse, a systematic program for monitoring and evaluating the impact of these policies should be established. Conclusively, there is need by policy makers to weigh the scientific findings that show health benefits due to light/moderate consumption of alcohol and the destructive effects of abuse before championing the way forward for this population. After such an exercise, the Food Based Dietary Guideline concerning alcohol use for South Africans might need to be revised.

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CHAPTER 3

RELATIONSHIPS OF ALCOHOL INTAKE WITH BIOLOGICAL HEALTH OUTCOMES IN AN AFRICAN POPULATION IN TRANSITION: THE THUSA STUDY

(*Submitted for publication in the South African Journal of Clinical Nutrition*)

CHAPTER 3: RELATIONSHIPS OF ALCOHOL INTAKE WITH BIOLOGICAL HEALTH OUTCOMES IN AN AFRICAN POPULATION IN TRANSITION: THE THUSA STUDY

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Abstract

Objective. Due to the fact that the present recommendations on alcohol intake are based mainly on evidence of beneficial effects in populations of developed countries, this study examines biological effects of alcohol consumption in an African population in transition.

Design. A cross sectional, comparative, population-based study.

Setting. Thirty-seven randomly selected sites in the North–West Province of South Africa, representing both rural and urban areas.

Subjects. This study included 1854 apparently healthy men and women older than 15 years who volunteered to participate. Pregnant and lactating women as well as subjects taking any form of chronic medication, with body temperatures above 37^0C and who were inebriated, were excluded.

Outcome measures. A validated, quantitative food frequency questionnaire was used to measure dietary intakes, including alcoholic beverages, expressed as absolute alcohol in grams per day. Anthropometric measurements and blood pressures were taken in triplicate using standardised equipment and procedures. Fasting blood samples were used to determine biochemical variables related to nutritional status and health. Serum gamma glutamyl transferase (GGT) was used to examine the reliability of reported alcohol intakes. The SPSS package was used to relate alcohol intake to blood pressure and biochemical variables, controlling for age, body mass index and blood glucose. Data from men and women, as well as drinkers and non-drinkers were analysed separately and compared.

Results. In this study, 61.5% of the men and 25.2% of women reported that they regularly consumed alcoholic beverages. Mean alcohol intakes of men (30.2 +/- 47.8 g/day) exceeded the recommend value of 21g/day. The women had a mean intake of 11.4 +/- 18.8g/day, which is within the 12-15g/day recommendation. Older drinkers (>40 years) and those infected with HIV drank more. Level of urbanisation had little effect on amounts consumed but sorghum beer was replaced by commercial beer in urban areas. Drinkers had significantly higher HDL-cholesterol, serum triglycerides, blood pressure and iron status variables than non-drinkers. When serum ferritin was used to classify subjects into those in negative iron balance (<12μg/L), "normal" balance (12-150μg/L) and positive iron balance (>150μg/L) it became evident that alcohol intake almost doubled the proportion of subjects in positive iron balance (in men: from 25 to 46%; in women from 11 to 23%).

Conclusion. Although the beneficial effect of alcohol consumption on HDL-cholesterol was seen in this population, the effects on iron status and balance are of concern and should be researched in more detail.

Key words: Alcohol, Africans, Nutrition Transition, Iron status, Ferritin.

Introduction

The food based dietary guidelines of many countries,[1] including South Africa,[2] recommend to the public that if alcohol is consumed, it should be in moderation, limited, or consumed sensibly.[1,2] This recommendation is based on the reality that there will always be alcohol consumers in any population and that moderate, limited or "sensible" consumption has been proven to have specific health benefits. The South African guideline, "If you drink alcohol, drink sensibly," is accompanied by an excellent support paper[2] which provides the evidence for both positive and negative social and physical health effects of alcohol consumption. This paper[2] and others[3] describe the patterns of alcohol consumption in South Africa, but the evidence of the physical health benefits of moderate consumption are based on studies done in other countries, due to the lack of South African data on possible beneficial effects. In addition to the well known cardio-protective effects of moderate consumption, primarily mediated through increased HDL-cholesterol and haemostasis[2], there are studies that additionally claim benefits on iron status.[4,5]

A recent publication[4] of the Dikgale study in the Limpopo Province of South Africa concluded that "traditional beer consumption seemed to prevent iron deficiency in those at risk, but appeared to induce iron overload in individuals at risk of developing iron overload". This potential "beneficial" effect of alcohol consumption on serum ferritin levels and thus iron status has also been observed in other African,[5] elderly,[6,7] Danish[8] and Australian populations.[9] However, the relationship between alcohol consumption and ferritin levels is also a known consequence of liver damage in chronic alcoholics.[10,11] The mechanisms through which this effect is mediated are unclear.[12-14] In this paper the THUSA data were analysed to examine the relationships between alcohol consumption and both "positive and negative" biological outcomes in an African population in transition to gain more information to either support or warn about the present alcohol guideline[2] to South African consumers.

Methods

Study design, subject selection and organisational procedures

The THUSA study (Transition and Health during Urbanisation of South Africans) was conducted from 1996-1998 in the North-West province of South Africa.[15] It was a cross-sectional comparative study in which a community based sample of 1854 apparently healthy African volunteers (15 years and older), were recruited from 37 randomly selected sites, using a statistical model that ensured a representative sample from 5 levels of urbanisation: deep rural, commercial farms, informal settlements, "middle class" urban and "upper" class urban. Pregnant and lactating

women, individuals taking chronic medication, those with oral temperatures above 37 ^{0}C and inebriated volunteers were excluded. Permission to conduct the study in specific areas with advice on recruitment procedures was obtained from the North West Department of Health, tribal chiefs, community leaders, headmasters of high schools, employees and mayors. The study was approved by the Ethics Committee of the University (**Ethics number: 4M5-95)** and all participating subjects signed an informed consent form. Subjects were fasted (10-12hours) prior to baseline blood sample collection and other biochemical measurements. They received lunch after completion of the glucose tolerance test. All subjects received feedback regarding blood pressure, fasting glucose levels and haemoglobin values. Where necessary, subjects were referred to their nearest health facility for further diagnosis and treatment. Subjects were remunerated for travelling expenses.

Questionnaires

The questionnaires were designed or adapted for this study population and were validated with appropriate methods.[15,16] Questionnaires were issued during individual interviews conducted by the researchers and specially trained African field workers in the language of the subjects' choice. The *demographic questionnaire* included questions on type of housing, access to electricity, water source, sanitation, personal and household income, health history (also of close family members), number and ages of people living in the house, ownership of property, education level, and smoking and drinking habits. Dietary intakes were measured using a *quantitative food frequency questionnaire* developed after a pilot study in which all foods consumed by this population were recorded and assessed. Nutrient intakes were analysed with a program based on the South African Food Composition Tables,[17] including grams of alcohol consumed per day.

Anthropometric measurements

An anthropometrist and trained postgraduate students measured height (stature), weight, seven skinfold thicknesses and body circumferences of all subjects in their underwear using calibrated instruments (Precision Health Scale, A & D Company, Japan; Invicta Stadiometer, IP 1465, UK; Holtain® unstretchable metal tape; John Bull® callipers). Measurements were taken in triplicate.

Clinical examinations

Two nursing sisters examined the subjects for signs of malnutrition. Oral temperatures were taken and blood pressure recorded in triplicate using a sphygmomanometer (Tycos®) with adjustable cuffs of different sizes.

Glucose tolerance test (GTT)

After a fasting blood sample was taken, a two-hour GTT commenced during which subjects took a 75g glucose load (Alpha® glucose powder, Allied Pharmaceuticals) dissolved in 250ml water.

Blood, serum, plasma, urine and cell samples

Blood was drawn from the *vena cephalica* using a sterile butterfly infusion set (Johnson & Johnson, 21G, 19mm) and syringes. For preparation of serum, 5ml blood was allowed to clot in glass in glass tubes, centrifuged at 3000rpm for 15minutes (Universal 16R^{TM}, Hettich, with cooling facilities), and transferred to 30 X 1ml Eppendorff tubes. Citrated blood was prepared by drawing 4.5ml of blood into a syringe containing 0.5ml 1 mol/L citrate (pH 4.5-4.8). Samples were centrifuged for 10min at 3000 rpm in plastic siliconised tubes and the plasma stored in 5 X 1ml Eppendorff tubes. Haematocrit (centrifuge method) and haemoglobin levels (Boehringer Mannheim) were measured in the field using ethylenediamine tetra acetic acid (EDTA) blood. All serum, plasma, and separated blood cells samples were immediately stored at -18 ^{0}C to -20 ^{0}C in the field for 2-4 days and afterwards at -84 ^{0}C in the laboratory.

Biochemical analyses

Serum proteins, minerals, electrolytes, glucose, lipids and enzymes were determined with the DAX system (discrete analyser Technicon DAX 48) in the Department of Chemical Pathology, University of Pretoria. Serum vitamin A and E as well as iron, ferritin, iron binding capacity and transferrin were determined in the Medical Research Council (MRC) laboratory of the National Research Programme for Nutrition Intervention at Tygerberg, using immunological, colorimetric, and high performance liquid chromatography (HPLC) methods. Fibrinogen was measured in citrated plasma with the method of Clauss using the ACL200 (Milan, Italy) system and the international fibrinogen standard {National Institute for Biological Standards and control (code 89/644), Hertfordshire, UK}

Statistical analyses

Data were analysed with the Statistical Package for Social Sciences (SPSS package) version 15. Means, medians, standard deviations, standard errors and 95% confidence intervals were calculated. Data that were not normally distributed were logarithmically transformed and non-parametric tests used to test for significant differences between groups and effects of urbanisation. Univariate analysis of variance (ANOVA), the post hoc test of least significant differences (LSD), multivariate regression analysis, stepwise regression methods and Spearman rank-order correlations with adjustments for confounding factors were used to examine the influence of alcohol consumption on biological (health) variables. For this paper, additional statistics were performed to explore the relationships of alcohol intake with variables known to

be influenced by alcohol. Drinkers and non-drinkers and men and women were analysed separately. To assess the relationship between alcohol and serum ferritin, men and women were grouped into those in negative iron balance (group1: serum ferritin below 12µg/L), "normal" iron balance (group 2: serum ferritin between 12 and 150µg/L) and positive iron balance (group 3: serum ferritin above 150µg/L).[18]

Data collection for the THUSA study was done in 1996 and 1998. To test if the two sets of data could be combined, total reported energy intakes of women in the 1996 and 1998 data sets were compared. The mean intake of the 1996 group was 7975 kJ and of the 1998 group 7997kJ, so the two sets of data were combined.

Results

The mean daily alcohol consumption of the THUSA participants are shown in Table I while mean intakes of subjects in different levels of urbanisation are shown in Table II. Proportionally, more men than women consumed alcohol (62 versus 25% respectively). Mean intakes of men were more than double that of women (30.2 versus 11.4g/day respectively). Men and women older than 40 years of age had higher mean intakes than those younger than 40 years of age.

Table I. Reported mean daily alcohol consumption of the THUSA-participants

Subject group	n (%)	Mean (g/day)*	SD
Men: drinkers	456 (61.5)	30.2	47.8
Men: non-drinkers	286 (38.5)	-	-
Women: drinkers	256(25.2)	11.4	18.8
Women: non-drinkers	759(74.8)	-	-
Men: drinkers < 40 years	255(55.9)	25.6	40.7
≥ 40 years	201(44.1)	36.0	55.1
Women: drinkers < 40 years	134(52.3)	10.8	20.7
≥ 40 years	122(47.7)	12.0	16.5

* Grams of absolute alcohol calculated from reported intake of alcoholic beverages using the South African Food Composition Tables[17]

SD = standard deviation

Men from the urban "middle class" level had the highest proportion of drinkers (73%) and also the highest mean intake of alcohol (33.7g/day). Women living on farms had the highest mean

intake (15.2g/day) but a larger proportion of women in informal housing areas reported that they consumed alcoholic beverages (35%).

Table II.	Mean daily alcohol intake of men and women drinkers at different levels of urbanisation			
Subject group	**n**	**%***	**Mean (g/day)**	**SD**
Men: drinkers (all ages)				
Rural	100	52	31.5	47.7
Farms	58	54	20.5	21.1
Informal settlements	88	69	30.8	49.8
Urban middle class	168	73	33.7	56.9
Urban upper class	42	49	25.0	24.6
Total	456	61	30.2	47.8
Women: drinkers (all ages)				
Rural	55	19	12.1	14.2
Farms	43	29	15.2	19.3
Informal settlements	61	35	10.9	20.8
Urban middle class	75	26	11.6	21.6
Urban upper class	22	21	2.8	6.2
Total	256	25	11.4	18.8

* Percentage of "drinkers" of total participants in each urbanisation group
SD = standard deviation

Previously, MacIntyre[16] compared the ten most consumed foods per person per day across the different urbanisation levels of this population. In women, sorghum beer was the fourth most consumed by rural women and those living on farms; second most consumed in those living in the informal housing areas and the eighth most consumed in the urban "middle" class population. No alcoholic beverage fell within the first top ten foods consumed by upper class urban women. As for men, sorghum beer was the third most consumed food by rural men and those living on farms and in informal housing areas. Commercial beer was the second most consumed by the urban "middle" class and most consumed by the urban "upper" class men.

In the total sample of drinkers and non-drinkers, 13% of men and 11.6% of women were HIV infected.[15] Table III shows that those subjects who consumed alcoholic beverages and who were HIV infected had slightly higher mean intakes than non-infected drinkers. The percentage of drinkers who were HIV infected was similar in men and women (13.5 and 13.7% respectively).

Table III.	Mean daily alcohol consumption of HIV-infected and non-infected self reported drinkers			
Subject group	**n**	**%***	**Mean (g/day)**	**SD**
Men: HIV- infected	62	13.5	36.2	67.7
Non-infected	396	86.5	29.1	43.8
Women: HIV- infected	35	13.7	13.0	15.3
Non-infected	221	86.3	11.1	19.3

* Percentage of drinkers
SD = standard deviation

Table IV compares the means of a number of health variables thought to be influenced by alcohol consumption between drinkers and non-drinkers by gender. The mean age of the male drinkers was significantly higher than that of male non-drinkers and, therefore, all correlations were adjusted for age. Both men and women drinkers showed increased mean serum HDL-cholesterol, serum triglycerides, blood pressure, serum iron (but not haemoglobin), and serum ferritin levels. Total iron binding capacity (TIBC) was significantly higher in non-drinking men and % saturation was significantly higher in drinkers for both men and women. Mean reported dietary intakes of iron did not differ significantly between drinkers and non-drinkers for both men and women.

Table IV.	Comparison of biochemical, physiological and dietary data of "drinkers" and non-drinkers							
Variable	**Men**				**Women**			
	Drinkers		**Non-drinkers**		**Drinkers**		**Non-drinkers**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (years)	39.2*	14.5	33.9	16.2	39.2	13.1	37.3	14.5
Body mass index (kg/m^2)	21.0	3.5	21.2	4.1	26.8	7.2	27.0	6.7
Total serum cholesterol (mmol/L)	4.04	1.02	3.91	0.94	4.24	1.00	4.24	1.11
HDL-cholesterol (mmol/L)	1.30*	0.44	1.07	0.30	1.23#	0.37	1.12	0.30
Serum triglycerides (mmol/L)	1.24*	0.88	1.10	0.61	1.40#	1.01	1.09	0.58
Blood pressure (mmHg)								
Systolic	128*	17	123	15	132#	25	126	20
Diastolic	78*	12	75	11	82#	15	77	13
Haemoglobin (g/dL)	13.5	2.2	13.5	2.0	12.4	2.1	12.1	2.1
Serum iron (mmol/L)	20.4*	9.1	16.5	7.4	16.6#	7.8	14.8	7.7
Serum TIBC (mmol/L)	64.1*	11.6	66.4	15.4	69.2	12.2	69.4	14.3
% Saturation	32.4*	14.6	26.0	13.0	24.8#	12.4	22.0	12.0
Serum ferritin (µg/L)	243*	345	141	252	115#	176	74	145
Dietary intakes of								
iron (mg)	9.3	4.4	9.0	4.4	8.9	4.2	8.4	4.1

* Significant difference between men drinkers and non-drinkers (ANOVA, $p \leq 0.02$)
# Significant difference between women drinkers and non-drinkers (ANOVA, $p \leq 0.02$)
SD = standard deviation
TIBC = total iron binding capacity

Table V shows that when controlling for age, body mass index and fasting blood glucose, the correlation between GGT and reported alcohol intake in men was not significant. In women the correlation was highly significant ($r = +0.233$, $p=0.0001$). The same table shows that when controlling for age and body mass index, HDL-cholesterol had a significant positive correlation with alcohol consumption in both men and women. In women there was an even higher correlation with serum triglycerides and also a significant correlation with total serum cholesterol. The correlation between alcohol consumption and blood pressure disappeared in both men and women after controlling for age and body mass index.

Table V.	Significant correlations between reported alcohol intakes and other variables in drinkers*			
Variable	**Men**		**Women**	
	r	**p**	**r**	**p**
Serum GGT[#]	-	NS	0.233	0.0001
Serum total cholesterol	-	NS	0.145	0.029
HDL-cholesterol	0.141	0.005	0.168	0.011
Triglycerides	-	NS	0.223	0.001
Haemoglobin (g/dL)	0.112	0.026		NS
Serum iron	0.110	0.030		NS
% Saturation	0.102	0.044		NS
Ferritin		NS	0.152	0.021

* Controlled for age and body mass index
[#] Controlled for age, body mass index and fasting blood glucose
GGT = gamma glutamyl transferase

The correlations between alcohol consumption and iron status variables are also shown in Table V. Serum ferritin, significantly higher in male and female drinkers (Table IV), showed a significant correlation in women only, while in men, haemoglobin, serum iron and % saturation had low but significant correlations.

Table VI compares the mean values of iron status variables in male drinkers and non- drinkers divided into three groups of "iron balance". For this purpose serum ferritin values of 12μg/L and 150μg/L were used to distinguish between those in negative (group 1) and positive (group 3) balance respectively.[18] As expected, the mean ages of those in positive balance were higher (significantly so in the drinkers).

Table VI.	Comparison of low, normal and high ferritin groups of male drinkers and non-drinkers					
Variable	**Drinkers**			**Non-drinkers**		
	1	**2**	**3***	**1**	**2**	**3***
Number	7	229	203	16	199	72
Proportion (Percentage)	2	52	46	6	69	25
Age (years) Mean	22.6	34.0	45.8[#]	25.8	31.0	44.4
SD	6.4	13.3	13.4	14.6	16.0	12.3
Alcohol intake Mean	6.6	26.8	34.8			
(g/day) SD	7.0	44.1	52.3			
Serum ferritin Mean	6	75	440[#]	6	64	384[•]
(µg/L) SD	3	37	429	3	38	415
Serum iron Mean	12.8	19.8	21.3	9.6	16.6	17.6[•]
(µg/L) SD	5.3	8.9	9.3	10.2	6.7	7.6
Haemoglobin Mean	12.8	13.7	13.3	11.5	13.6	13.4[•]
(g/dL) SD	1.4	2.4	1.9	2.5	1.9	2.0

* Group 1: Serum ferritin levels below 12 µg/L
Group 2: Serum ferritin levels between 12 and 150 µg/L
Group 3: Serum ferritin levels above 150 µg/L
[#] Significant differences within the drinkers groups (ANOVA, $p \leq 0.001$)
[•] Significant differences within the non-drinkers groups (ANOVA, $p \leq 0.001$)
SD = standard deviation

The mean alcohol intake of the male drinkers in negative balance (group 1) was 6.6g/day, compared to 26.8g/day of those in normal balance (group 2) and 34.8g/day was for those in positive balance (group 3). These striking differences were, however, only significant on a 10% level ($p \leq 0.094$). In the male drinkers, the significant differences between the three groups of serum iron and blood haemoglobin evident in the non-drinkers were not observed. In the non-drinkers, 6% of the men were, according to criteria used here, in "negative" iron balance and 25%

in positive balance (Table VI). In the drinkers, only 2% were in negative balance but 46% in positive balance.

Table VII shows similar data for women, which shows striking differences from the male data with regards to the lowest alcohol intake in women being observed in the group with normal iron balance.

Table VII.	**Comparison of low, normal and high ferritin groups of female drinkers and non-drinkers**					
Variable	**Drinkers**			**Non-drinkers**		
	1	**2**	**3***	**1**	**2**	**3***
Number	33	154	58	124	530	80
Proportion (Percentage)	14	63	23	17	72	11
Age (years) Mean	28.4	38.5	46.6[#]	31.2	37.1	48.3
SD	10.0	12.6	11.8	12.2	13.8	15.9
Alcohol intake Mean	12.3	7.7	20.1[#]			
(g/day) SD	20.4	11.7	28.8			
Serum ferritin Mean	6	6.4	384[#]	6	52	326[•]
(µg/L) SD	3	3.8	415	3	34	335
Serum iron Mean	12.4	16.8	18.6[#]	9.8	15.7	16.6[•]
(µg/L) SD	8.1	6.9	8.8	7.1	7.2	8.5
Haemoglobin Mean	11.3	12.5	12.6[#]	11.0	12.3	12.3[•]
(g/dL) SD	2.1	2.1	2.0	2.1	1.9	2.6

* Group 1: Serum ferritin levels below 12 µg/L
Group 2: Serum ferritin levels between 12 and 150 µg/L
Group 3: Serum ferritin levels above 150 µg/L
[#] Significant differences within the drinkers groups (ANOVA, $p \leq 0.001$)
[•] Significant differences within the non-drinkers groups (ANOVA, $p \leq 0.001$)
SD = standard deviation

Additionally, significant differences for serum iron and haemoglobin between the three groups were observed in both women drinkers and non-drinkers. In women drinkers, however, the proportion in negative iron balance was 14%, and in positive balance 23%, compared to the 17% and 11% in the non drinkers.

Discussion

Limitation of reported intakes

The first issue to address is the reliability of the reported alcohol intake data, because how much and what one drinks may be a sensitive question for many individuals. Intakes were assessed using two questionnaires: the health and lifestyle questionnaire to obtain an indication of drinking patterns and a validated quantitative food frequency questionnaire to measure habitual intakes of specific alcoholic beverages. The latter was used to calculate absolute alcohol intake per day. Gamma glutamyl transferase (GGT) is often used in epidemiological studies[19] as a proxy for alcohol intake. This liver enzyme detected in serum is, however, non-specific and may also be influenced by other factors such as diabetes. Although the population sample was recruited as apparently healthy, some subjects were diagnosed with diabetes[15] and therefore blood glucose as well as age and body mass index were controlled for in determining the relationship between reported alcohol intake and GGT. In women this relationship was highly significant but not in men, suggesting that women may have been more accurate and "honest" in their estimates of alcohol consumed. Nethertheless, the expected significant correlations between reported intake and variables known to be influenced by alcohol consumption[2] were observed in this study.

Amount of alcohol consumed

Most European, UK and North American country's food consumption guidelines recommend that daily alcohol intake should not exceed 5% of total energy intake, or 20g for men and 15g for women.[1,6,20] The male drinkers in the THUSA sample reported higher intakes (30.2g/day) while the women drinkers, with a mean intake of 11.4g/day, complied to this general guideline. However, the standard deviations were very large (47.8 and 18.8 respectively) illustrating a wide variety in intakes with many men and women having much higher intakes. Urbanisation had a small effect on amounts of alcohol consumed, however, a more pronounced effect on the type of alcoholic beverage taken by men with commercial beer replacing sorghum beer in urban areas. Because almost two thirds of the men reported intakes (61.5%) at mean levels above the recommended intake, it seems reasonable to conclude that alcohol may be a problem in the male population of this sample. In contrast, only 25% of women reported alcohol intake, and with

mean levels generally in the recommended range, the same conclusions cannot be drawn for women in this population. Therefore, a closer look at biological effects of alcohol consumption is necessary.

Biological effects of alcohol consumption

The beneficial effects of moderate alcohol consumption are related to increases in HDL-cholesterol, modified platelet clotting and fibrinolytic activities[2,21] as well as a lower risk for type 2 diabetes.[22] However, fibrinogen levels did not differ between drinkers and non-drinkers and the negative correlation of fibrinogen with alcohol intake in men ($r = -0.026$) was not significant ($p = 0.513$) results not shown here. The positive effect on HDL-cholesterol was significant in both men and women but was accompanied by increased triglyceride levels in the women. Mean levels of all serum lipids were, however, within normal ranges for both men and women.

A potential detrimental effect of alcohol intake on blood pressure disappeared when controlling for age and body mass index. It seems, therefore, that in balance, effects of alcohol on serum lipids and blood pressure (both cardiovascular risk factors) in this sample were small.

However, the effects on iron balance are of concern. Two studies, one in a rural population in Limpopo[4] and one from Tanzania,[5] interpreted the effects of alcohol on increases in serum ferritin as an improvement of iron status. The possible mechanisms offered to explain this effect are a contribution of micronutrients (including iron) by local, home brewed beverages[4,5] and an increased absorption of iron because of effects on gastric hydrochloric acid secretion and iron solubility.[5]

Ferritin is an iron-apoferritin complex, the major form of iron in tissues.[18] It sequesters iron in a readily available form. Serum ferritin is proportional to intracellular ferritin and, therefore, under normal circumstances, in equilibrium with body stores.[18] Serum ferritin levels greater than 150µg/L reflects stage 1 of positive iron balance. It is known that iron overload may be a problem in adult Africans,[23] in the aged[7,11] and because of excessive alcohol consumption.[11] Therefore, it is necessary to evaluate and weigh a potentially good effect of alcohol consumption on iron status in a population expected to be iron deficient[24] against a possible detrimental effect on iron overload or positive iron balance.

Tables VI and VII indicates that if levels of serum ferritin less than 12µg/L and more than 150µg/L are used to classify subjects as being in either a negative or positive iron balance, alcohol intake had a dramatic effect on the proportion of subjects in negative and positive iron balance. In men, 6% of non-drinkers were in negative balance and only 2% of drinkers. In women, the corresponding figures were 17 and 14%. However, the proportion of subjects in

positive balance almost doubled when evaluated by alcohol consumption: from 25% in the non-drinking men to 46% in drinking men and from 11 to 23% non-drinking and drinking women respectively. These changes in the proportion of subjects with increased serum ferritin levels may be interpreted as follows (i) alcohol intake increased body iron stores in a substantial number of men and women, or (ii) alcohol intake disrupted the equilibrium between the body and circulating ferritin levels. More research is needed before this question can be fully answered. Although haemochromatosis and its genetic determinants were not measured in the THUSA population, the above results indicate that alcohol intake may have detrimental effects on iron balance in an adult African population and should be examined further.

Conclusions

It is concluded that apparently healthy men participating in the THUSA study had mean reported intakes of alcohol that exceeded present recommendations of moderate intake while mean intakes of women were within the upper limit of these recommendations. Subjects who were HIV-infected drank more than uninfected subjects. The known beneficial effects of alcohol on HDL-cholesterol were apparent but non-drinkers also had mean HDL-cholesterol levels within the recommended range.[25] Alcohol intake was associated with an increased serum ferritin level and more drinkers than non-drinkers were in positive iron balance. It is suggested that this possible detrimental effect of alcohol on iron balance should be examined further in this population.

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CHAPTER 4

PERCENTAGE CARBOHYDRATE DEFICIENT TRANSFERRIN (%CDT) NOR GAMMA GLUTAMYLTRANSFERASE (GGT) ARE GOOD MARKERS FOR ALCOHOL CONSUMPTION IN AN AFRICAN POPULATION IN TRANSITION

(*Submitted for publication in the American Journal of Epidemiology*)

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Abstract

Alcohol consumption probably plays an important role in the health transition associated with urbanization in developing countries. However, before this interaction can be evaluated, a reliable measurement of alcohol intake is necessary for this population. The aim of this study was to compare values of two biological markers {percentage carbohydrate deficient transferrin (%CDT) and gamma-glutamyl transferase (GGT)} with reported alcohol intakes obtained by two dietary methods (24 hour recall and quantitative food frequency questionnaires) in urban and rural South African communities. Of the 716 men and 1192 women, 64% and 33% respectively reported to consume alcohol regularly. Mean habitual intakes of self-reported drinking men and women were 29.9 (+/-30.0) and 23.3 (+/-29.1) g of pure alcohol per day. Self-reported habitual intakes of the whole group correlated positively and significantly with both %CDT (R=0.32) and GGT (R=0.433). After controlling for confounding factors (body mass index and smoking), these relationships were R= 0.19 and 0.31 respectively. In this study, 19% of men and 26% of women non-drinkers had elevated GGT while 48% and 38% of the non-drinking men and women respectively had elevated %CDT levels, indicating that other factors besides alcohol consumption contributed to changes in these biological markers. It is concluded that GGT and %CDT values in this African population should be interpreted with care and that a more specific biological marker for alcohol consumption is needed.

Keywords: Self-reported alcohol consumption, questionnaires, percentage carbohydrate deficient transferrin, gamma glutamyltransferase, Africans, transition, PURE study.

Introduction

Due to rapid urbanization, South Africa is experiencing a health transition, associated with a triple burden of disease (1) characterized by a high prevalence of undernutrition-related infectious diseases, the emergence of non-communicable diseases, and the human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) pandemic. The use or abuse of alcohol probably plays an important role in this transition. The World Health Organization (WHO) recently stated that alcohol consumption is the fifth leading cause of death worldwide and that intakes are increasing, especially in developing countries (2). According to the WHO's database, fewer South Africans drink compared to individuals reported for the 44 other countries mentioned. What is, however, of concern, is that as much as one third of those South Africans reported to drink do so in excess (20 litres of absolute alcohol per drinker per year) (3). Alcohol misuse and abuse in South Africa is reported to be responsible for at least half of the 14 000 annual road deaths, high crime rates, violence, sexual risk behavior, family disruption and a host of individual and societal problems (3). Binge drinking additionally results in an increased cardiovascular disease (CVD) risk as well as micronutrient deficiencies (4), both having high prevalences in the South African population (1).

Epidemiological evidence suggests a J or U shaped relationship between alcohol consumption and CVD (5-7). The South African food based dietary guidelines advises "sensible" drinking, due to the possible cardiovascular protective effects associated with light to moderate alcohol consumption. The problem, however, is that this South African population in transition experiences high levels of alcohol misuse and abuse with its many adverse consequences, while little is known of the beneficial cardio-protective effects associated with light to moderate alcohol consumption. There is, therefore, a need to assess with accuracy, high risk drinking in this population and to relate alcohol intakes (exposure) to health outcomes.

Identification and assessment of high risk drinking in a population may be problematic. When self-reports of alcohol consumption are used as an indicator, there is usually under or over-reporting from the respondents. Although a detailed, validated quantitative food frequency questionnaire (QFFQ) is an important source of consumption information (8) and typically has low rates of false-positive responses, the primary weakness is that people may not report their alcohol intakes accurately (9). Under-reporting has been shown to be common in population surveys (10) mainly because of low participation by

alcoholics and heavy drinkers in these surveys. Also, there is the tendency of respondents, especially those that are alcohol dependent to under-report their consumption in questionnaires and interviews (11, 12). Therefore, it could be more beneficial to use biological markers of alcohol consumption to verify reported intakes and to identify and assess high risk drinking with better accuracy. Circulating carbohydrate deficient transferrin (CDT) and gamma glutamyl transferase (GGT) are sensitive to high alcohol consumption and are the most suitable biomarkers available for identifying alcohol abuse in most populations (13, 14). These biomarkers could be used in estimating or verifying reported alcohol consumption. %CDT, which measures the relative amount of CDT isoforms in proportion to total transferrin, has been shown to be a slightly better marker of alcohol abuse as compared to absolute CDT values (15-20) and in situations where there are variations in transferrin concentrations as experienced during pregnancy, anemic and severe liver disease (21). Additionally, there may not be a need for a gender-specific normal cut-off value when %CDT is used (22). Whether %CDT and GGT are good biological markers for detecting alcohol abuse in an African population still needs to be determined. Hence, in this paper self reported alcohol consumption and its association with %CDT and GGT in a random sample of rural and urban South Africans is compared and correlated.

Materials and methods

Study design and subjects

This cross-sectional epidemiological survey was part of the North West Province, (NWPSA) South African leg of the 12-year Prospective Urban and Rural Epidemiology study (PURE) which investigates the health transition in urban and rural subjects. The main selection criteria were that there should be migration stability within the chosen rural and urban communities. The baseline data for NWPSA were collected from October-December 2005. The rural community (A) was identified 450 km west of Potchefstroom on the highway to Botswana. A deep rural community (B), 35 km east from A and only accessible by gravel road, was also included. Both communities are still under tribal law. The urban communities (C and D) were chosen near the University in Potchefstroom. Community C was selected from the established part of the township next to Potchefstroom and D from the informal settlements surrounding community C. A total of 2010 apparently healthy African volunteers (35 years and older) were recruited from a sample of 6000 randomly selected households.

Selection of subjects. A household census of number of people, their ages and health profile was done on the 6000 households (1500 in each community) starting from a randomly selected address in the communities. The head of each household gave signed consent to fill out the questionnaire. If a person refused or was not at home, the next house randomly selected was taken and a non-complier questionnaire was filled out. From the data obtained, a selection of possible subjects older than 35 years of age with no reported chronic diseases of lifestyle, tuberculosis (TB) or known HIV was made (750 subjects from each community). These 3000 subjects were visited at home and after giving voluntary and informed consent, an extensive questionnaire regarding their physical and psychological health, socio-economic background, lifestyle practices and support systems available was completed.

Ethical considerations and organizational procedures. Permission to conduct the study in above mentioned communities with advice on recruitment procedures, were obtained from the North West Department of Health, tribal chiefs, community leaders, employers and mayors. The study was approved by the Ethics Committee of the North-West University, Potchefstroom, South Africa **(Ethics number: 04M10)**. All subjects were informed about the objectives and procedures of the study prior to participation. Subjects were asked to be in a fasted state for approximately 10 hours prior to sample collection. Trained (Setswana speaking) field workers assisted and were available to provide information in the participants' language of preference. Confidentiality and anonymity of all results were assured and all participants signed an informed consent form. Prior to the study an agreement with clinics and hospitals serving the communities from which the subjects were recruited was reached, and newly identified subjects with HIV, abnormal blood pressure, lung dysfunction, tuberculosis and abnormal electrocardiogram (ECG) were referred to them together with a standardised referral letter, without compromising the confidentiality of their health status. Participants received remuneration for all the travelling expenses to and from the clinics.

Questionnaires. A total of 2010 subjects were interviewed using structured, validated demographic, socio-economic, lifestyle and dietary questionnaires (QFFQ and 24 hour recall). Data on these 2010 subject's physical activity levels were also obtained in the same fashion. All questionnaires and home visits were done by 16 intensively trained fieldworkers recruited from the four different communities. The dietary questionnaire data (QFFQ and 24 hour recall) were coded by two dieticians and sent to the Medical Research Council of South Africa for computerisation, cleaning and nutrient analyses.

The questionnaires included two sets of questions regarding alcohol consumption: the quantity and frequency question from the food frequency questionnaire and another from the 24 hour recall. In both sets of questions, intakes of different beverages were assessed separately. Average alcohol intake was estimated by the amount of alcohol consumed per day and expressed as intake of pure alcohol (ethanol) in grams (g) per day. Calculations were based on the South African Food Composition Tables (23). Beer, home made brews, spirits and wine were considered to contain 3.6g, 3g, 36g and 9.4g of pure alcohol per 100g of beverage respectively. The QFFQ was used to distinguish drinkers and non-drinkers.

Blood pressure, ECG and anthropometry measurements. During the month of August until the end of November 2005, an appointment with each person who completed the questionnaires was made, and they were voluntarily taken by taxi to meet a team of expert researchers for the purpose of blood pressure (using the Omron automatic digital blood pressure monitor (Omron HEM-757), blood glucose (Vitros DT6011 Chemistry Analyzer, Ortho-Clinical Diagnostics, Rochester, New York, USA) and anthropometric measurements (height, weight, waist and hip circumference, mid upper arm circumference, triceps skinfold, calf circumference, calf skinfold, supra spinal skinfold, upper flexed arm circumference) using the guidelines adopted at the NIH sponsored Arlie Conference (24). The blood glucose measurements were used as a screening tool for diabetes. An ECG and lung function tests were done using spirometers.

HIV testing. All participants who gave informed consent for HIV testing were additionally given an option to know the outcome of the analysis. A rapid test was done according to the National Department of Health of South Africa's protocol. Everyone received pre-test counseling in groups of ten before the blood sample collection as well as individual post-test counseling for those participants who tested positive and opted to know the outcome of the test.

Blood samples. Blood was drawn from the ante-cubital vein in the subject's right arm, using a disposable needle. The blood collection tubes were filled (vacutainers) to capacity. This ensured optimal blood: anticoagulant ratios. Excessive use of tourniquets was avoided as this may lead to hemoconcentration and inaccuracies in analytical results. Contents of the tubes were mixed thoroughly by gently inverting each tube five times. Samples where labeled and immediately placed in ice boxes.

A new sterile transfer pipette was used to aliquot each individuals collected blood sample for analyses to follow. Blood was centrifuged within two hours of collection. Once the

blood was centrifuged and separated, it was stored at -70 °C until analysis. For the collection of serum, blood was allowed to clot (at room temperature for 30 minutes) and centrifuged at 2000g for 15 minutes at 10 °C. Collected serum was subsequently transferred to cryo tubes and stored at -70 °C until analysis. For plasma samples, blood was collected in ethylenediamine tetra acetic acid (EDTA) tubes and centrifuged at 2000g for 15 minutes at 4 °C. Plasma was transferred to cryo tubes and stored at -70 °C until analysis.

Biochemical analyses. The levels of GGT were measured by Sequential Multiple Analyzer Computer (SMAC), using the Konelab™ auto analyzer (Thermo Fisher Scientific Oy, Vantaa, Finland). The cut-off values were set at 80U/L and 50 U/L for men and women respectively. The same method (SMAC) was used for analysing total protein (T-protein), albumin, fasting blood glucose, serum high-density lipoprotein cholesterol (HDL-C) and iron. Serum %CDT analyses were performed by using an *in vitro* heterogeneous immunoassay with column separation followed by a turbidimetric measurement (Axis-Shield % CDT kit, Oslo, Norway). The measuring range of this test is 1.5 to 24 mg/L and cut-off values for %CDT were set at 2.6% following recommendations of the manufacturer. The coefficient of variance (CV) for all assays was <10%.

Statistical analysis

Data were analyzed using the SPSS (Statistical Package for Social Sciences, version 15) package. Means, medians, standard deviations and 95% confidence intervals were calculated. As data were not normally distributed, non-parametric tests were used to test for significant differences between groups. Wilcoxon signed rank tests and Mann-Whitney/Wilcoxon rank sum tests were used to compare groups. Multivariate regression analysis, stepwise regression methods, Spearman rank-order and partial correlations were used to examine the associations between self-reported alcohol consumption and biochemical markers (%CDT and GGT), whilst the latter was used for testing associations after adjustments of possible confounding factors. Drinkers and non-drinkers and men and women were analysed separately.

Results

Self reported mean consumption of pure alcohol in g/day by two different dietary methods (24 hour recall and QFFQ) for the PURE participants are shown in Table 1.

The estimated average alcohol intakes from the two dietary methods were significantly different. The QFFQ, which measures habitual alcohol intake, was higher than that for the 24 hour recall for both men and women. Self reported mean intakes of men were higher than that for women, using both dietary methods. As for self reported drinkers only, reported mean alcohol consumption from the QFFQ was more than double that as reported using 24 hour recall method for both men and women. A stepwise multiple regression method was used to determine the significant predictors for GGT and %CDT. Body mass index (BMI) and smoking emerged as valid confounders for this population. HIV infection and area of residence (rural or urban) were, however, not confounding factors.

Table 2 reports the associations between the biological markers and self reported intakes. A statistically significant correlation between the two different dietary methods was observed, higher than +0.45 in both women and men. In both men and women, GGT had a stronger correlation with reported alcohol consumption measures than %CDT. The same pattern was also shown amongst drinkers only. The correlation between %CDT and GGT was, however, low. After controlling for BMI and smoking, all correlations became weaker. The expected relationships of alcohol and biochemical and physiological variables known to be influenced by alcohol were also observed in this population. %CDT, GGT, albumin, iron and HDL-C were significantly higher in the drinkers in both men and women and BMI was significantly lower in drinkers (Table 3). Stratification of alcohol consumption into 4 groups (0, >0.01-15.99, 16.00-30.00, ≥30.01g/day of pure alcohol) from the QFFQ was done, based on recommendations that daily alcohol consumption should be approximately 20g for men and 15g for women (25, 26), and light to moderate alcohol intake being estimated to be <30g, and heavy drinking amounting to intakes >30g of absolute alcohol consumed daily (7). Mean %CDT and GGT for each group and percentage subjects with elevated values are shown in Table 4. A statistically significant percentage of the non-drinkers showed elevated GGT (18.9 and 25.6% men and women respectively) and %CDT (47.7 and 38.1% men and women respectively) levels.

Table 1. Comparison of means (SD) of self reported alcohol consumption by two different methods (24 hour recall and QFFQ) by gender and age group

Characteristic		24 hour recall method			QFFQ method			Test statistic (c)
	Age groups and Mean (SD) age (years)	N	Mean alcohol intake (SD) (g/day)	95% CI	N	Mean alcohol intake (SD) (g/day)	95% CI	Z-score
Total group								
Men	35-44	248	12.0(29.9)	8.3,15.8	245	20.7(31.9)	16.7,24.7	-5.194[b]*
	45-54	239	14.5(30.8)	10.6,18.4	238	19.1(24.3)	16.0,22.2	-3.808[b]*
	55-64	159	12.3(26.5)	8.1,16.4	156	19.7(27.8)	15.3,24.1	-3.729[b]*
	65-74	51	4.0(14.8)	-0.1,8.2	51	14.4(26.9)	6.8,22.0	-3.436[b]*
	>75	13	4.3(11.6)	-2.7,11.3	12	9.7(20.6)	-3.4,22.7	-0.135[b] (NS)
Total Men	49.8(10.3)	716	12.2(28.4)	10.1,14.3	708	19.2(28.0)	17.0,21.2	-8.000[a]*
Women	35-44	454	3.6(15.4)	2.1,5.0	450	7.7(18.6)	6.0,9.5	-6.850[b]*
	45-54	394	3.7(16.0)	2.1,5.3	388	7.7(20.1)	5.7,9.7	-6.336[b]*
	55-64	222	4.3(17.2)	2.0,6.5	220	8.8(23.8)	5.6,12.0	-4.467[b]*
	65-74	85	0.5(4.3)	-0.5,1.4	83	6.2(18.5)	2.2,10.3	-3.825[b]*
	>75	26	0.0(0.0)	0.0,0.0	26	3.1(15.7)	-3.2,9.5	-1.342[b] (NS)
Total Women	49.1(10.4)	1192	3.4(15.2)	2.5,4.3	1178	7.7(20.1)	6.5,8.9	-11.196[a]*
Self Reported Drinkers								
Men	49.5(9.5)	454	18.4(33.4)	15,21	454	29.9(30.0)	27,33	-8.378[b]*
Women	48.0(9.0)	392	9.9(25.0)	7,12	391	23.3(29.1)	20,26	-11.722[b]*

Abbreviation: CI, confidence interval, NS, Not significant; SD, Standard deviation; QFFQ, quantitative food frequency questionnaire; N, number of subjects.

[a] Based on negative ranks.

[b] Based on positive ranks.

[c] Wilcoxon Signed Ranks Test.

*Significant differences ($p \leq 0.05$) between 24 hour recall and QFFQ method.

Table 2. Correlations between gamma glutamyl transferase (GGT), percentage carbohydrate deficient transferrin (%CDT) and self reported alcohol consumption

Characteristic	%CDT r_s	GGT r_s	QFFQ method r_s	24 hr/recall method r_s	%CDT R	GGT R
Total sample						
QFFQ method	0.320**	0.433**	1.000	0.472**	0.193#	0.310#
24 hr/recall method	0.205**	0.321**	0.472**	1.000	0.165#	0.264#
%CDT	1.000	0.211**	0.320**	0.205**	1.000	0.110#
GGT	0.211**	1.000	0.433**	0.321**	0.110#	1.000
Gender						
Male:						
QFFQ method	0.333**	0.369**	1.000	0.458**	0.197#	0.291#
24 hr/recall method	0.222**	0.310**	0.458**	1.000	0.167#	0.301#
%CDT	1.000	0.253**	0.333**	0.222**	1.000	0.118#
GGT	0.253**	1.000	0.369**	0.310**	0.118#	1.000
Female:						
QFFQ method	0.198**	0.398**	1.000	0.411**	0.097#	0.314#
24 hr/recall method	0.088**	0.273**	0.411**	1.000	0.065	0.187#
%CDT	1.000	0.098**	0.198**	0.088**	1.000	0.072
GGT	0.098**	1.000**	0.398**	0.273**	0.072	1.000
Rural-Urban						
Rural:						
QFFQ method	0.350**	0.452**	1.000	0.454**	0.250#	0.331#
24 hr/recall method	0.189**	0.300**	0.454**	1.000	0.188#	0.267#
%CDT	1.000	0.209**	0.350**	0.189**	1.000	0.145#
GGT	0.209**	1.000	0.452**	0.300**	0.145#	1.000
Urban:						
QFFQ method	0.298**	0.387**	1.000	0.477**	0.088	0.259#
24 hr/recall method	0.220**	0.320**	0.477**	1.000	0.112#	0.241#
%CDT	1.000	0.217**	0.298**	0.220**	1.000	0.033
GGT	0.217**	1.000	0.387**	0.320**	0.033	1.000
Self reported drinkers						
Drinkers:						
QFFQ method	0.148**	0.275**	1.000	0.382	0.068	0.189#
24 hr/recall method	0.135**	0.270**	0.382**	1.000	0.101#	0.194#
%CDT	1.000	0.093*	0.148**	0.135**	1.000	0.009
GGT	0.093*	1.000	0.275**	0.270**	0.009	1.000

HIV status						
QFFQ method						
HIV non-infected	0.329**	0.431**	1.000	0.493**	0.191#	0.304#
HIV infected	0.263**	0.445**	1.000	0.387**	0.200#	0.371#
24 hr/recall method						
HIV non-infected	0.233**	0.332**	0.493**	1.000	0.189#	0.280#
HIV infected	0.059	0.266**	0.387**	1.000	0.061#	0.163#
%CDT						
HIV non-infected	1.000	0.223**	0.329**	0.233**	1.000	0.112#
HIV infected	1.000	0.126*	0.263**	0.059	1.000	0.089
GGT						
HIV non-infected	0.223**	1.000	0.431**	0.332**	0.112#	1.000
HIV infected	0.126**	1.000	0.445**	0.266**	0.089	1.000

Abbreviations: R, partial correlation after adjusting for BMI and smoking; r_s, spearman correlation coefficient; hr, hour.

**Correlation significant at the $p \leq 0.01$ level (2 tailed).

*Correlation significant at the $p \leq 0.05$ level (2 tailed).

#Partial Correlation significant at the $p \leq 0.05$ level (2 tailed).

Table 3. Comparison of means (SD) and medians of biochemical, physiological and dietary data of "drinkers" and non- drinkers

Variable	Men						Women					
	Drinkers			Non-drinkers			Drinkers			Non-drinkers		
	Mean (SD)	Med	95% CI	Mean (SD)	Med	95% CI	Mean (SD)	Med	95% CI	Mean SD	Med	95% CI
Age (years)	49.5 (9.5)	48.0	48.6,50.3	50.3 (11.6)	48.0	49.0,52.0	48.0 (9.0)	46.0	47.0,48.9	49.8 (11.0)	48.0	49.0,51.0
BMI (Kg/m^2)	20.2* (3.6)	19.5	19.9,20.6	21.9 (4.6)	20.9	21.4,23.0	25.4# (7.3)	25.4	24.7,26.2	27.5 (7.2)	26.7	27.0,28.0
Smoking	5.0* (4.9)	4.0	4.5,5.5	2.4 (4.1)	0.0	2.0,3.0	3.5# (3.6)	3.5	3.0,3.9	2.2 (3.4)	0.0	2.0,2.5
T-protein (g/L)	84.2 (15.8)	81.9	82.7,85.7	85.2 (17.5)	81.0	83.0,87.4	85 (17.9)	82.0	84.0,87.7	87.0 (18.2)	83.9	85.6,88.3
Albumin (g/L)	46.3* (13.7)	42.7	45.0,47.6	49.0 (13.0)	44.0	47.4,51.0	46.1# (13.3)	42.6	44.7,47.5	48.5 (12.5)	43.7	47.5,49.3
Serum iron (mmol/L)	23.4* (15.3)	18.7	21.9,24.8	20.5 (14.6)	16.2	18.7,22.4	21.6# (15.7)	17.3	20.0,23.3	16.2 (10.5)	13.8	15.4,17.0
%CDT	3.8* (1.7)	3.4	3.7,4.0	2.9 (1.4)	2.5	2.7,3.1	3.0# (1.3)	2.8	2.9,3.1	2.4 (1.0)	2.3	2.3,2.5
GGT (U/L)	152.5* (211.9)	81.9	132.3,172.8	91.0 (296.5)	43.9	54.0,128.4	131.5# (194.0)	67.1	111.6,151.4	50.7 (65.1)	33.7	46.0,55.4
HDL-C (mmol/L)	1.7* (0.7)	1.7	1.6,1.8	1.4 (0.6)	1.2	1.3,1.4	1.6# (0.7)	1.5	1.5,1.7	1.4 (0.5)	1.3	1.4,1.5
Fasting blood glucose (mmol/L)	5.3 (1.4)	5.2	5.1,5.4	5.4 (1.2)	5.3	5.2,6.0	5.6 (1.7)	5.5	5.3,5.7	5.7 (1.7)	5.4	5.5,5.8

Abbreviation: CI, confidence interval; Med, median, HDL-C, high-density lipoprotein cholesterol.
* Significant difference between men drinkers and non-drinkers (Mann-Whitney U, $p \leq 0.05$).
# Significant difference between women drinkers and non-drinkers (Mann-Whitney U, $p \leq 0.05$).

Table 4. Means (SD) of gamma glutamyl transferase (GGT), percentage carbohydrate deficient transferrin (%CDT) and percentages of elevated GGT and %CDT by reported alcohol consumption and gender

Gender	Alcohol consumption g/day[a]	N	GGT Mean (SD) (U/L)	95% CI	% with elevated GGT[b]	%CDT Mean (SD)	95% CI	% with elevated %CDT[c]
Men	0	236	91.0(296.5)	53.6,128.4	18.9	2.9(1.4)	2.7,3.1	47.7
	>0.01-15.99	177	129.7(250.0)	93.2,166.1	39.3	3.5(1.6)	3.3,3.8	66.8
	16.00-30.00	87	136.8(150.5)	105.0,168.5	50.6	4.1(1.7)	3.7,4.5	75.6
	≥30.01	150	188.7(187.0)	158.8,218.5	64.1	4.1(1.8)	3.8,4.3	81.3
Women	0	708	50.7(65.1)	45.9,55.4	25.6	2.5(1.0)	2.4,2.5	38.1
	>0.01-15.99	200	98.6(133.6)	80.4,116.8	51.9	3.0(1.3)	2.8,3.2	56.7
	16.00-30.00	57	136.0(195.5)	85.4,186.5	66.7	2.8(1.2)	2.4,3.1	55.2
	≥30.01	94	198.9(271.1)	144.5,253.2	77.3	3.1(1.3)	2.8,3.3	56.8

Abbreviation: CI, confidence interval; N, number of subjects.
[a]Quantitative food frequency questionnaire method.
[b]GGT: men ≥80U/L and women ≥ 50U/L.
[c]%CDT: for both men and women: ≥ 2.6%.

Discussion

Alcohol intake methodology. Guidelines from developed countries (Europe, UK and North America) recommend that daily alcohol consumption should not exceed 5% of total energy intake, or approximately 20g for men and 15g for women (25, 26). The QFFQ and the 24 hour recall methods used in this study are the most commonly used self-report methods for assessing alcohol consumption. Between the two reporting methods, the QFFQ seems to be the better method because it illustrates the habitual alcohol consumption whereas the 24 hour recall method reports intakes based on the previous 24 hours. Additionally, the pattern of alcohol consumption in this population tends to be heavy drinking at weekends, making the 24 hour recall generally a less reliable tool. In this study, 24 hour recall questionnaires were completed randomly throughout the households from Monday to Friday and hence were not influenced by the heavier drinking patterns on weekends. It is well known that both methods are prone to misreporting (under and over-estimation). African women may be more prone to underreporting alcohol intakes due to cultural and traditional norms of women being viewed with no respect if known to be alcohol consumers. African men may overestimate their intakes as drinking is associated with masculinity. The reliability of reported alcohol intakes remains debatable, but in this study there was no reason to under or over-report. The subjects were informed by well trained, sympathetic interviewers during individual interview sessions that all data in the study are confidential. The accuracy of using biological markers for assessing alcohol intake or abuse in this population is unknown. However, the symbiotic use of self reported alcohol intakes and biological markers may aid in identifying and assessing risky drinking patterns.

Alcohol intakes. Both men and women drinkers in this population reported high mean intakes of 29.9 and 23.3g/day respectively, which is far greater than the recommended general guidelines described above. High standard deviations (30.0 and 29.1) for both genders illustrate a wide range in intakes in these groups. Almost two thirds (64.2%) of the men in this sample reported to be drinkers compared to only a third of the women. Due to urbanization, this population is at present experiencing a health and dietary

transition (1). A cross sectional, comparative, population based study, the THUSA (Transition and Health during Urbanization of South Africans) study, conducted between 1996 and 1998 in the same localities as the present study, showed mean self-reported intakes for men and women drinkers of 30.2 and 11.4g/day respectively (27). Our results illustrate that mean alcohol intake amongst the women has doubled (23.3g/day) since then, suggesting women have either increased their consumption or are more honest in reporting their intakes. This may illustrate a reduced stigma surrounding alcohol consumption by women. Male drinkers in both studies (29.9 vs. 30.2g/day) had high intakes, but did not differ suggesting that their drinking patterns remained unchanged and/or their reporting maybe more honest and accurate.

Biological markers. Self reported men and women drinkers had GGT and %CDT values significantly higher than self reported non-drinkers. If the recommended cut-off values are used (GGT: men ≥80U/L and women ≥ 50U/L, %CDT: ≥ 2.6% for both men and women), both men and women drinkers had extremely high GGT and %CDT values indicating a chronic drinking pattern for both genders (Table 4).

Considering %CDT, other factors besides chronic intake of alcohol are known to be responsible for high %CDT values. Rare genetic D-variants of transferrin (28), inborn errors in glycoprotein metabolism (29) and liver diseases such as cirrhosis, primary biliary cirrhosis, chronic active hepatic and chronic viral hepatitis (30-33), may cause false positive results. Chronic iron deficiency and pregnancy may also influence the response of CDT (absolute measure) to heavy alcohol consumption (34, 35), though this has been thought not to influence %CDT (the relative measure). The possible contribution of liver diseases, though an apparently healthy non-pregnant population was included in this study, should also be considered. The men non-drinkers also showed mean elevated %CDT of 2.9, suggesting either the possibility of under-reporting of alcohol use by this group or other contributing factors.

Considering the GGT results similar conclusions can be made. Elevated mean GGT values in this sample suggest high alcohol consumption for both male and female drinkers. Male non-drinkers similarly had an elevated mean GGT value of 91U/L. Elevated GGT values are, however, also associated with other conditions such as

obesity, diabetes mellitus, hepatobiliary disorders, smoking and CVD (13, 36-39). Thus, the higher GGT among the drinkers may in part be explained by smoking, since drinkers (both male and female) significantly smoked more than their non-drinking counterparts.

Correlations. Both %CDT and GGT showed a relatively good and highly significant correlation with self-reported alcohol intakes, confirming that increased levels of %CDT and GGT values in this population are most likely due to high alcohol consumption. GGT showed better correlations with self reported intakes than %CDT. However, correlations between the two biological markers were low, suggesting that the responses of %CDT and GGT to alcohol consumption may occur via different mechanisms (40). These results correspond with those of other studies, using CDT, however (as opposed to %CDT), and correlating this to GGT (13). The combined use of CDT and GGT has been recommended as a better tool for identifying alcohol consumption and risky drinking patterns (14, 41, 42, 43). As previously mentioned, %CDT has been shown to be a better marker than CDT as it eliminates variations in transferrin. This is one of the first papers to our knowledge that reports correlations between %CDT and GGT, moreover in an African population.

Comparing the two dietary methods, the QFFQ showed stronger correlations with the biological markers than the 24 hour recall. A highly significant correlation was, however, obtained between the two different questionnaires assessing alcohol consumption, indicating that although the 24 hour recall method only measured daily intakes, these intakes correlated well to habitual intake. Correlations between biological markers and self reported intakes were not affected by HIV status and whether a participant stayed in a rural or urban area. After controlling for smoking and body mass index, all correlation coefficients decreased, illustrating a negative directional effect of the two confounders on the association between biological markers and self reported intakes.

Suitability of %CDT and GGT as proxy markers of alcohol intake in this African population. An important observation of this study is that in this population, the levels of both GGT and %CDT for the self reported non-drinkers were higher than the considered normal ranges based on studies done on other populations. However, GGT and %CDT levels increased progressively with increased intakes of reported alcohol consumption. Table 4 illustrates that 19% of non-drinking men and 26% of non-drinking women showed elevated GGT while 48% of non-drinking men and 38% non-drinking women had elevated %CDT. It was argued earlier that if alcohol consumption is currently stigmatized in South Africa, it would most probably be only in women. It is unlikely that men drinkers would report abstinence, although they may lie about absolute amounts consumed. Therefore, it seems reasonable to conclude that both GGT and %CDT could misclassify subjects as drinkers and the values of these two markers should be interpreted with care. Additionally, it may be necessary to revise the cut off values for an African population. It should be noted that in this study, HIV infection was not responsible for the observed elevations in GGT and %CDT in non-drinkers. The mean %CDT and GGT values between HIV-infected and non-infected participants were not significantly different amongst male and female non-drinkers. In conclusion, at this point in time, without a better biological alcohol consumption marker available, an in depth, qualitative interviewing of subjects, using a validated QFFQ may currently be the most accurate method for assessing alcohol consumption in an African population.

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CHAPTER 5

GENERAL SUMMARY, RECOMMENDATIONS, DISCUSSION AND CONCLUSIONS

CHAPTER 5: GENERAL SUMMARY, DISCUSSION, RECOMMENDATIONS AND CONCLUSIONS

5.1 Introduction

In this chapter a summary of the main findings from the two studies (PURE and THUSA) reported in this thesis will be given. The recommendations made in this thesis were based on these findings.

Additionally, the results from the two studies are integrated, discussed and interpreted, focusing on the compatibility of the main findings and the recommendations.

5.2 Main findings

The salient observations of the studies reported in this thesis were:

Alcohol consumption

In the PURE study, both men and women drinkers in this sample reported high mean alcohol intakes of 29.9 and 23.3g/day respectively, these intakes are higher than the guidelines from developed countries (Europe, UK and North America) which recommend that daily alcohol consumption should not exceed 5% of total energy intake, or approximately 20g for men and 15g for women (Walmsley *et al.,* 1998, WHO, 2003). In a similar, cross sectional, comparative, population based study (THUSA) conducted between 1996 and 1998 in the same localities as the PURE study, mean self-reported intakes for men and women drinkers of 30.2 and 11.4g/day respectively were recorded (Vorster *et al.,* 2000). From comparison of the data, it is clear that alcohol consumption in the men has remained at relatively the same high levels (29.9 vs. 30.2g/day) suggesting their intakes remained stable and/or reporting could be more accurate. Consumption amongst the women has, however, more than doubled (23.3g/day) since 1998. This may be due to two reasons: (i) women have either increased their consumption of alcoholic beverages or (ii) did not report their consumption honestly in 1996-1998, which in turn illustrates a reduced stigma around women's drinking habits.

Alcohol intake methodology

The QFFQ and the 24 hour recall methods are the most commonly used self-report methods for assessing dietary intakes and alcohol consumption. Comparison of the two reporting methods in the PURE study, confirmed the QFFQ to be the better method as it illustrates the habitual alcohol consumption, whereas the 24 hour recall method reports intakes based on the previous 24 hours only. Both methods are, however, prone to misreporting (under and over-estimation). The reliability of reported alcohol intakes remains debatable, but in this study there was no reason to under or over-report. However, the symbiotic use of self reported alcohol intakes, in combination with biological markers, may make identification and assessment of risky drinking more accurate.

Biological markers of alcohol consumption (PURE study)

Biomarkers are defined as indicators of actual or possible changes of systemic, organ, tissue, cellular and sub-cellular structure and functional integrity, which can be used singly or in batteries to monitor health and exposure to compounds in populations and individuals (Richardson *et al.,* 2003). Development of validated and predictive biomarkers is an essential research objective in medical sciences. Biomarkers must be both biologically and methodologically valid and should reflect a future health outcome at a stage when dietary intervention will be effective. A number of factors have been shown to influence the nature of the link between diet, health, and biomarkers. These factors include predisposition and susceptibility, predictivity and intervention/reversibility (Richardson *et al.,* 2003). By considering these factors, it may be possible to prioritise the specific diet/health issues and assess those markers that are used to confirm the link between a food/food component or beverage (exposure) and a physiological effect (outcome) (Branca *et al.,* 2001).

Biomarkers must be subject to evaluation taking into account intra-individual variation, the use of single measurements, timing of measurements and progression of disease, intake, absorption, metabolism and genetic influences. Within a study, the biomarker should change in a biologically relevant way and the change should be statistically significant for the target group (Richardson *et al.,* 2003). In the context of alcohol

consumption, biomarkers are somewhat different from that needed to obtain maximally valid self report information, where rapport, assurance of confidentiality, honesty and testing conditions are important. The accuracy of biomarkers information is rarely a function of sample collection but sample handling, storage and methods for quantifying and interpreting results. In this study, like in many other prospective cohort studies alcohol biomarkers are indications and confirm a link between habitual consumption of alcohol and the biomarker. GGT and %CDT are not hundred percent specific markers for alcohol consumption because their elevation is not only caused by alcohol alone but by other independent factors as described in previous chapters.

This study indicated that the self reported men and women drinkers had significantly higher GGT and %CDT values than self reported non-drinkers. Additionally, both the men and women drinkers mean GGT and %CDT values were significantly higher than the recommended normal ranges for these markers (GGT: men ≥80U/L and women ≥ 50U/L, %CDT: for men and women ≥ 2.6%). This may illustrate a chronic pattern of alcohol intake in both genders in this population. An important observation of this study is that in this population, levels of both GGT and %CDT were higher than normal ranges in self reported non-drinkers. However, GGT and %CDT levels increased progressively with increased intakes of reported alcohol consumption. In this study, 19% of non-drinking men and 26% of non-drinking women had elevated GGT while 48% and 38% had elevated %CDT. It should be noted that in this study, HIV infection was not responsible for the observed elevations in GGT and %CDT in non-drinkers. The mean %CDT and GGT values between HIV-infected and non-infected participants were not significantly different amongst male and female non-drinkers.

Both %CDT and GGT showed a relatively good and highly significant correlation with self-reported alcohol intakes, suggesting that the high levels of %CDT and GGT values of this population could be to some extent induced by alcohol consumption. GGT, however, showed higher correlations with self reported intakes than %CDT. Comparing with the THUSA study, GGT correlated significantly with reported alcohol consumption, but only in the men. The PURE study showed significant correlations

between GGT and alcohol consumption for both men and women. This probably suggests that the mechanism or circumstances in which alcohol induces high GGT levels could be different between men and women. Additionally, the BMI between men and women was significantly different for both studies with women having a higher BMI than the men.

When comparing the two methods of self reporting in the PURE study, the QFFQ showed stronger correlations with the biological markers than the 24 hour recall. A highly significant correlation was also shown between the two methods of self reporting, indicating that although the 24 hour recall method only measured intakes of the previous 24 hours, these intakes correlated with habitual intake. However, correlations between the two biological markers were low, suggesting that the responses of %CDT and GGT to alcohol consumption may occur through different mechanisms (Randell *et al.,* 1998). After controlling for smoking and body mass index, all correlation coefficients decreased, illustrating a negative directional effect of the two confounders on the association between biological markers and self reported intakes.

The major limitation of this study (prospective epidemiological study) is that there is limited ability to ascertain the actual amount of alcohol consumed in this population and additionally does not provide a sufficient basis for determining whether alcohol intake/biomarker association reflects a causal rather than a coincidental relationship. A dose response study design would be more appropriate. Additional factors to be considered would include consistency among various populations, magnitude of effect, strength of associations, specificity of effect and statistical significance.

Biological health outcomes of alcohol consumption (THUSA study)

The beneficial effects of moderate alcohol consumption are related to increases in HDL-C, modified platelet clotting and fibrinolytic activities (Van Heerden & Parry, 2001; De Groot & Zock, 1998) in addition to a lower risk for type 2 diabetes (Koppes *et al.,* 2005). In the THUSA study, platelet and fibrinolytic functions were not measured and risk of diabetes was not assessed. However, fibrinogen levels did not differ between drinkers and non-drinkers and the negative correlation of fibrinogen with alcohol intake

in men (r = -0.026) was not significant (p = 0.513). The positive effect on HDL-C was, however, significant in both men and women, but was unfortunately accompanied by an increase in triglyceride levels in the women. Mean levels of all serum lipids were, however, within normal ranges for both men and women. The potential detrimental effect of alcohol intake on blood pressure disappeared when controlling for age and body mass index. It seems that the effects of alcohol on serum lipids and blood pressure (both cardiovascular risk factors) in this sample were small.

The effects of alcohol consumption on iron balance are of concern. Serum ferritin is used as an indicator of iron status. Serum ferritin was used to classify subjects into those in negative iron balance (<12μg/L), "normal" balance (12-150μg/L) and positive iron balance (>150μg/L). In men, 6% of the non-drinkers were in negative balance and only 2% of drinkers. In women, the corresponding figures were 17 and 14% respectively. However, when comparing drinkers and non-drinkers, the proportion of subjects in positive iron balance almost doubled: from 25% in non-drinkers to 46% in drinking men and from 11 to 23% in women respectively. These changes in the proportion of subjects with increased serum ferritin levels may be interpreted by the following (i) that alcohol intake increased body iron stores in a substantial number of men and women, or (ii) that alcohol intake disrupted the equilibrium between the body and circulating ferritin levels. The possible mechanisms offered to explain this effect are a contribution from micronutrients (including iron) in local, home brewed beverages (Choma *et al.,* 2007; Malenganisho *et al.,* 2007) and an increased absorption of iron due to alcohol inducing gastric hydrochloric acid secretion which in turn increases iron solubility (Malenganisho *et al.,* 2007).

5.3 Recommendations and conclusions

Identification and assessment of risky drinking in this population (PURE). Although %CDT and GGT values significantly correlated to self reported intakes, after using normal cut-off values, it seems reasonable to conclude that both GGT and %CDT could misclassify subjects as drinkers and the values of these two markers should be interpreted with care. Considering this, new cut-off values for GGT and %CDT may be necessary for an African population. At this point in time, without a better biological

marker available, it is recommended that careful, in depth, qualitative interviewing of subjects, using a validated QFFQ, is currently the best method for assessing alcohol consumption in an African population.

Biological health outcomes of alcohol consumption (THUSA). In this study, the known beneficial effects of alcohol on HDL-C are confirmed; however, non-drinkers also had mean HDL-C levels within the European recommended range (De Backer *et al.,* 2003). Alcohol intake was associated with increased serum ferritin levels and more drinkers than non-drinkers were in positive iron balance. It is suggested that this possible detrimental/positive effect of alcohol on iron balance should be examined further in this population.

Alcohol consumption (THUSA and PURE). High intakes of alcohol are reported in both studies (PURE and THUSA). Even though alcohol consumption has been shown in the THUSA study to have beneficial effects on CVD through positive effects on HDL-C, the consumption of alcohol for cardioprotective purposes as a public health measure is discouraged, given the deleterious effects it might have on blood pressure and other physiological conditions. Considering the outcomes of these studies, the present food based dietary guideline for alcohol (which is currently based on evidence of beneficial effects of moderate alcohol consumption in populations of developed countries) may need to be revised for the African/South African population.

5.4 References

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ADDENDA

ADDENDA: THUSA study

ADDENDUM 1: Recruitment and informed consent form

ADDENDUM 1: Recruitment and informed consent form

THUSA PROJECT : PU FOR CHE

RECRUITMENT AND INFORMED CONSENT FORM

Title of the project: Nutritional and health status of Africans in transition

Name: ..... No.....

Address: .....

Tel no:.....

Age: .....

Are you pregnant? .....

Are you lactating? .....

Do you suffer from diabetes? hypertension? Other disease?.....

When did you have your last meal? .....

or anything but water to drink? .....

INFORMED CONSENT

I, the undersigned ..... (full names in print), have read the details of the project or, have listened to the oral explanation thereof, and declare that I understand it. I have had the opportunity to discuss relevant aspects with the researcher and declare that I voluntarily participate in the project. I hereby give consent to participate in the project.

.....

Signature of volunteer

Witnesses

....

Signed at ..... on .....

For subjects under the age of 21, signed consent of a parent or legal guardian is necessary.

1, ... (full names) the parent/legal guardian of the person named above, hereby consent that he/she may participate in the THUSA project.

Signature ..... Date .....

Relationship .....

ADDENDUM 2: Anthropometry form

ADDENDUM 2: Anthropometry form

THUSA PROJECT – SOUTH AFRICA 1998
ANTHROPOMETRY

Subject ID#

Gender (1 = M, 2 = F)

Projection box + constant

		.	

Skinfolds

Triceps			.				.				.		
Subscapular			.				.				.		
Illiac Crest			.				.				.		
Supraspinale			.				.				.		
Abdominal			.				.				.		
Front Thigh			.				.				.		
Medial Calf			.				.				.		

Girths

Arm - Relaxed			.				.				.		
Arm - Fully flexed/Tensed			.				.				.		
Forearm - Maximum			.				.				.		
Waist - Minimum			.				.				.		
Hip (Gluteal) - Maximum			.				.				.		
Thigh - 1cm below gluteal fold			.				.				.		
Thigh - Mid trio-tib lat			.				.				.		
Calf - Maximum			.				.				.		

Breadths

Humerus (cm)			.				.						
Wrist (cm)			.				.				.		
Femur (cm)			.				.				.		
Ankle (cm)			.				.				.		

Other

Mass (kg)				.	
Stature - Stretched (cm)				.	

ADDENDUM 3: Demographic questionnaire

ADDENDUM 3: Demographic questionnaire

Potchefstroomse Universiteit

vir Christelike Hoër Onderwys

Subject number			
Date	D	M	Y
Place			
Interviewer			

Home address _____

_____

_____

_____

Sex	Male	1
	Female	2

Age			
Date of birth	D	M	Y

First Language	Tswana	1
	Afr	2
	Eng	3
	Xhosa	4
	Zulu	5
	Other	6

Second Language	Tswana	1
	Afr	2
	Eng	3
	Xhosa	4
	Zulu	5

	Other	6

What is your marital status?	Never married	1
	Married	2
	Divorced	3
	Widowed	4

Do you suffer from:	High blood	Yes	1
		No	2
	Diabetes	Yes	1
		No	2
	CHD	Yes	1
		No	2
	Stroke	Yes	1
		No	2

Does anyone in your family suffer from:	High blood	Yes	1
		No	2
	Diabetes	Yes	1
		No	2
	CHD	Yes	1
		No	2
	Stroke	Yes	1
		No	2

Do you take medicine regularly?	Yes	1
	No	2
If yes - what do you take?		

Do you snuff?		Yes	1
		No	2
Do you smoke?		Yes	1
		No	2
If no - have you smoked regularly before?		Yes	1
		No	2
If yes - what do you smoke?		Cigarettes	1
		Tobacco/pipe	2
		Other	3
If other - describe			
How much do you smoke?	per day		
	per week		

For how long have you been smoking (years)	
Calculate pack years	

What is your highest qualification?	None	1
	< St.6	2
	St. 6-8	3
	St. 6-8 + trade	4
	St. 9-10	5
	St. 9-10 + trade	6
	St. 9-10 + academic	7

What is your occupation?	

Do you have a job at the moment?	Yes	1
	No	2

If yes - what kind of job?	

On which days of the week do you work?	Irregular (piece work)	1
	Part time (1-4 days)	2
	Full time (5-6 days)	3

How much money do you earn? Is it between:	R0-100	
	R101-500	
	R501-1000	
	R1000-2000	
	R2000-3000	
	R3000+	

What is the source of this income?	

Do you receive any additional pensions?	Yes	1
	No	2

How much pension do you receive per month?	

Interviewer - *Re-evaluate final income category*	R0-100	1
	R101-500	2
	R501-1000	3
	R1000-2000	4

	R2000-3000	5
	R3000+	6

Who else contributes money to your household? How much?

Yes	1
No	2

Who else contributes other resources eg. food, sharing work/chors to your household? - specify!

Yes	1
No	2

Does any member of your household have the right to use any property as his/her own?	Yes	1
	No	2

What type of property?	

How do you use it?	

Please name the members of your household

Member	Age	Education	Present job

What type of house do you live in?	Traditional	1
	Mokuku	2
	Brick house	3
	Other	4
Specify other		

Do you share a toilet with other households?	Yes	1

	No	2

What type of toilet do you have?	Communal	1
	None	2
	Bucket system	3
	Outside longdrop	4
	Outside chemical	5
	Outside water flush	6
	Inside water flush	7

Where do you get your drinking water from?	Fountain, river	1
	Communal tap	2
	Tap on premises	3
	Tap in house	4
	Other	5
If other specify		

Do you have access to electricity inside your house?	Yes	1
	No	2

What type of stove do you have?	None	1
	Coal/wood	2
	Gas or parrafin	3
	Electric	4

What type of fridge do you have?	None	1
	Parraffin	2
	Gas	3
	Electric	4

How long have you been living here? (years)	

Where did you live before coming here?	Rural area	1
	Farm	2
	Squatter camp	3
	Township	4

ADDENDUM 4: Quantitative food frequency questionnaire

ADDENDUM 4: Quantitative food frequency questionnaire

THUSA Quantitative Food Frequency Questionnaire

Subject ID **Subject Initials**

☐☐ ☐☐☐ ☐☐☐ ☐☐ ☐☐☐

Centre # **Community #** **Household #** **Subject #** **F**
M L

Today's date: ☐☐☐☐ ☐☐ ☐☐
year *month* *day*

1. Name: _____
_____

2. Not applicable in South Africa

3. National identity # or equivalent _____ **N/A** ☐

4. DOB: ☐☐☐☐ ☐☐ ☐☐ **OR** **Age** ☐☐ **years**

5. Sex: ☐ Female ☐ Male

Please think carefully about the food and drink you have consumed during the ***past month*** (four weeks). I will go through a list of foods and drinks with you and I would like you to tell me:

- If you eat the food
- How the food is prepared
- How much of the food you eat at a time
- How many times a day you eat it and if you do not eat it everyday, how many times a week or a month you eat it.

To help you to describe the amount of a food you eat, I will show you pictures of different amounts of the food. Please say which picture is the closest to the amount you eat, or if it is smaller, between the sizes or bigger than the pictures.

There are no right or wrong answers.

Everything you tell me is confidential. Only your subject number appears on the form.

Is there anything you want to ask now?

Are you willing to go on with the questions?

FOOD FREQUENCY QUESTIONNAIRE

INSTRUCTIONS: Circle the subject's answer. Fill in the amount and times eaten in the appropriate columns.

I shall now ask you about the type and the amount of food you have been eating in the last few months. Please tell if you eat the food, how much you eat and how often you eat it. We shall start with maize meal porridge.

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
PORRIDGE AND BREAKFAST CEREALS AND OTHER STARCH								
Maize-meal porridge	Stiff (pap)						3400	
Maize-meal porridge	Soft (slappap)						3399	
Maize-meal porridge	Crumbly (phutu)						3401	
Ting								
Mabella	Stiff						3437	
Mabella	Soft							
Oats							3239	
Other cooked porridge	Type: _____							
Breakfast cereals	Brand name of cereals at home now: _____ _____ _____ _____							

Do you pour milk on your porridge or cereal? Yes No

If yes, what type of milk (whole fresh, sour, 1%, fat free, milk blend, etc) _____

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
If yes, how much milk								
Do you put sugar on your porridge or cereal?		Yes	No					
If yes, how much sugar							3989	
							3989	
							3989	
Samp	Bought Self ground						3250	
Samp and beans	Give ratio of samp:beans						3402 (1:1)	
Samp and peanuts	Give ratio of samp:peanuts						3250 (samp)	
Rice	White						3247	
	Brown						3315	
	Maize Rice						3250	
Pasta	Macaroni Spaghetti Other specify: _____ _____						3262	
Pizza	Home made: Specify topping _____ _____						3353 (base+ch)	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Bought: Specify topping _____ _____						3353 (base+ch)	

You are being very helpful. Can I now ask you about meat?

CHICKEN, MEAT, FISH

How many times do you eat meat (beef, mutton, pork, chicken, fish) per week?

_____

Chicken (codes with skin)	Boiled						2926	
	Fried: in batter/crumbs Eg Kentucky						3018	
	Fried: Not coated							
	Bought: Chicken Licken						2925	
	Bought: Nando's							
	Roasted / Grilled						2925	
	Other: _____							
Do you eat chicken skin?	Always		Sometimes		Never			
Chicken bones stew								
Chicken feet							2997	
Chicken offal								
Red meat	How do you like meat? With fat Fat trimmed							
Red meat	Fried							
	Stewed							
	Mince with tomato and onion						2987	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other:							
Beef Offal	Intestines: boiled nothing added						3003	
	Stewed with vegetables							
	Liver						2920	
	Kidney						2923	
	Other: Specify _____ _____							
Goat meat	Boiled						4281	
	Stewed with vegetables							
	Grilled / Roasted						4281	
What type of vegetables is usually put into meat stews? _____								
Wors / Sausage							2931	
Bacon							2906	
Cold meats	Polony						2919	
	Ham						2967	
	Vienna						2936	
	Other: Specify _____ _____ _____							
Canned meat	Bully beef							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other: Specify _____ _____							
Meat pie	Beef						2939	
	Steak and kidney						2957	
	Cornish						2953	
	Chicken						2954	
	Other							
Hamburger	Bought							
Dried beans/peas/lentils	Soup						3145	
	Salad							
Soya products eg. Toppers	Brands at home now: _____ _____						3196 (Toppers)	
Pilchards in tomato/chilli/brine	Whole						3102	
	Mashed with fried onion							
Fried fish	With batter/crumbs							
	Without batter/crumbs							
Other canned fish	Tuna						3056 (oil)	
	Pickled fish							
	Other: Specify _____							
Fish cakes	Bought: Fried						3080	
	Home made with potato						3098	
Fish fingers	Bought						3081	
Eggs	Boiled/poached						2867	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Scrambled: milk + fat							
	Fried: Fat							

Now we come to vegetables and fruit

VEGETABLES AND FRUIT

Cabbage	How do you cook cabbage?							
	Boiled, nothing added						3756	
	Boiled with potato and onion and fat							
	Fried, nothing added Fried in							
	Boiled, then fried with potato, onion							
	Other:							
	Don't know							
Spinach/morogo/ beetroot leaves other green leafy	How do you cook spinach?							
	Boiled, nothing added						3913	
	Boiled with fat added Type of fat							
	With onion, tomato, potato							
	With peanuts							
	Other:							
	Don't know							
Tomato and onion gravy	Home made with fat Type of fat							
	Without fat						3925	
	Canned						4192	
Pumpkin (yellow)	How do you cook pumpkin?							
	Boiled, nothing added						4164	
	Cooked in fat and sugar Fat							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Boiled, little sugar and fat Fat							
	Other							
	Don't know							
Carrots	How do you cook carrots?							
	Boiled, nothing added						3757	
	Boiled, sugar and fat Fat							
	With potato and onion: Fat							
	Raw, salad						3709	
	Chakalaka							
	Other							
	Don't know							
Mealies/ Sweet corn	How do you eat mealies?							
	On cob – fat added Fat							
	On cob – no fat added						3725	
	Creamed sweet corn / canned						3726	
	Whole kernel/canned						3942	
Beetroot	Salad						3699	
	Boiled, nothing added						3698	
Potatoes	How do you cook potatoes?							
	Boiled/baked with skin						4155	
	Boiled/baked without skin						3737	
	Mashed							
	Roasted Fat							
	French fries (chips)						3740	
Sweet potatoes	How do you cook sweet potatoes?							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Boiled/baked with skin						3748	
	Boiled/baked without skin						3903	
	Mashed							
	Other: _____							
	Don't know							
Salad vegetables	Mixed salad: tomato, lettuce and cucumber						3921	
	Raw tomato						3750	
	Other salad vegetables: _____ _____							
Other vegetables, specify + preparation	_____ _____ _____							
Do you like fruit?		Yes		No				
Apples							3592	
Pears							3582	
Oranges							3560	
Naartjie							3558	
Grapes							3550	
Peaches	Fresh						3565	
	Canned						3567	
Apricots	Fresh						3534	
	Canned						3535	
Mangoes							3556	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Guavas	Fresh						3551	
	Canned						3553	
Avocado							3656	
Wild fruit/berries	Specify type: _____							
Dried fruit	Types: _____							
Other fruit	_____ _____							
If subject eats canned fruit: Do you have custard with the canned fruit?			Yes		2 No			
Custard	Home made: Milk							
	Commercial eg Ultramel						2716	
BREAD AND BREAD SPREADS								
Bread / Bread rolls	White						3210	
	Brown						3211	
	Whole wheat						3212	
Do you spread anything on the bread?			Always		Sometimes		Never	
Margarine	What brand do you have at home now?							
	Don't know _____							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Peanut butter							3485	
Jam/syrup/honey							3985	
Marmite / Fray bentos / Oxo							4058	
Fish/meat paste							3109	
Cheese	Type: _____ _____							
Achaar								
Other spreads	Specify: _____							
Dumpling								
Vetkoek	White flour						3257	
	Whole wheat flour						3324	
Provita, crackers, etc							3235	
Mayonnaise / salad dressing	Mayonnaise						3488	
	Other: Specify _____							
DRINKS								
Tea	English (normal)						4038	
	Rooibos						4054	
Coffee							4037	
Sugar/cup tea or coffee	Tea:						3989	
	Coffee:						3989	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Milk/cup tea or coffee	What type of milk do you use in tea and coffee?							
	Fresh/long life: whole/full						2718	
	Fresh/long life: 2%/low fat						2772	
	Fresh/long life: fat free						2775	
	Whole milk powder Brand: _____						2721 (powder)	
	Low fat milk powder Brand: _____						2825 (powder)	
	Skimmed milk powder Brand: _____						2825 (powder)	
	Milk blend Brand: _____						2770 (powder)	
	Whitener: type _____ _____							
	Condensed milk						2714	
	Evaporated milk						2715	
	None							
Milk as such	What type of milk do you drink milk as such?							
	Fresh/long life: whole/full						2718	
	Fresh/long life: 2%/low fat						2772	
	Fresh/long life: fat free						2775	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Condensed milk						2714	
	Sour/maas						2787	
	Other: _____ _____							
Milk drinks	Nestle: _____							
	Milo: _____							
	Flavoured milk: _____							
	Other:							
Yoghurt	Drinking yoghurt						2756	
	Thick yoghurt						2734	
	Low fat sweetened with fruit						2732	
Squash	Sweet O						4027	
	Six O							
	Oros/Lecol – with sugar						3982	
	- artificially sweetener						3990	
	KoolAid						4027	
	Other: _____ _____							
Fruit juice	Fresh/Liquifruit/Ceres						2866	
	Tropica (Dairy –fruit juice mix)						2791	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other: _____ _____ _____							
Fizzy drinks	Sweetened						3981	
Coke, fanta, etc	Diet							
Maueu/Motogo							4056	
Home brew								
Tlokwe							4039	
Beer							4031	
Spirits							4035	
Wine red							4033	
Wine White							4033	
Other specify	_____ _____ _____							
SNACKS AND SWEETS								
Potato crisps							3417	
Peanuts	Raw						4285	
	Roasted						3458	
Cheese curls, Niknaks, etc							3267	
Raisins							3552	
Peanuts and raisins								

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Chocolates	Name: _____ _____ _____							
Candies	Sugus, gums, hard sweets, etc						4000	
Sweets	Toffees, fudge, caramels						3991	
Biscuits/cookies	Type: _____ _____ _____							
Cakes and tarts	Type: _____ _____ _____							
Scones								
Rusks	Type: _____ _____							
Savouries	Sausage rolls						2939	
	Samoosas: Meat filling						3355	
	Samoosas: Vegetable filling						3414	
	Biscuits eg bacon kips							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other specify: _____							
Jelly							3983	
Baked pudding	Type: _____							
Instant pudding	Milk type: _____							
Ice cream							3483	
Sorbet							3491	
Other specify	_____ _____ _____							
SAUCES, GRAVIES AND CONDIMENTS								
Tomato sauce / Worcester sauce							3139	
Chutney							3168	
Pickles							3866	
Packet soups							3165	
Other:	_____ _____							
WILD BIRDS, ANIMALS OR INCECTS (hunted in rural areas or on farms)								

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Wild fruit								

MISCELLANEOUS: Please mention any other foods used more than once/two times a week which we have talked about:

INDIGENOUS/TRADITIONAL FOODS/PLANTS/ANIMALS

Please tell me if you use any indigenous plants OR other indigenous foods like mopani worms, locusts ect to eat

Specify								

Thank you very much for your cooperation and patience.

Good-bye!

ADDENDA

ADDENDA: PURE study

ADDENDUM 1: Appointment letter

ADDENDUM 1: Appointment letter

POTCHEFSTROOM CAMPUS: FACULTY OF HEALTH SCIENCES

PURE-SA Project (Prospective Urban and Rural Epidemiology)

APPOINTMENT LETTER

Dear Participant

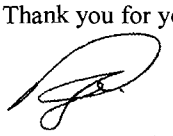
Thank you for being willing to help us in this very important project. We are sure that the project will contribute to improve health of all the people of the North West Province.

The aim of the project is to get enough information regarding the development of chronic diseases like Diabetes, Stroke, Lung disease and Heart disease with urbanisation to plan appropriate health and nutrition intervention strategies. At the time you receive this letter you would have been visited by a fieldworker and you already have filled out several questionnaires and signed consent to give a blood sample. This letter serves to inform you of the date and time the blood sample and other measurements will be done at the premises of the North-West University on the Potchefstroom Campus.

IMPORTANT INFORMATION

1. You will be picked up by a taxi accompanied by Ms Susan Legwete on ..... by 0....h00. Susan will tell you the place where you will be picked up.
2. You **MUST NOT EAT OR DRINK** anything after ten o'clock of the previous night (10 pm of the night before). This is necessary for the glucose test to be accurate.
3. You **MUST BRING YOUR ID DOCUMENT** with you
4. Your taxi fare will be paid by us and you will receive food after the blood sample is taken.
5. If you are employed, please show this letter to your employer.

Dear Employer
This serves to ask you to give one day's paid leave to..... in order to allow him/her to attend his appointment with the research team of the PURE-SA study at the North-West University.
Thank you for your cooperation. For any further information please contact Dr A Kruger at 082 7715778



A Kruger (project leader)

ADDENDUM 2: Recruitment and informed consent

ADDENDUM 2: Recruitment and informed consent

POTCHEFSTROOM CAMPUS

PURE-SA Project

INFORMED CONSENT FORM

Title of the project: PURE-Project (Prospective Urban and Rural Epidemiology)

INFORMED CONSENT (Phase 1)

I, the undersigned ..... (full names) understand that the only information that will asked from me is the family census and household questionnaires. I understand that a field worker from the PURE-study will ask me the questions and that all the information gained from me will kept confidential.

I indemnify the University, also any employee or student of the University, of any liability against myself, which may arise during the course of the project.

I will not submit any claims against the University regarding personal detrimental effects due to the project, due to negligence by the University, its employees or students, or any other subjects.

.....
(Signature of the subject)

Signed at .....on .....

Witnesses

1. .....

2. .....

Signed at ..... on .....

INFORMED CONSENT FORM

PURE-Project (Prospective Urban and Rural Epidemiology)

INFORMED CONSENT

I, the undersigned .....(full names)
read/listened to the information on the project in PART 1 and PART 2 of this document and I declare that I understand the information. I had the opportunity to discuss aspects of the project with the project leader and I declare that I participate in the project as a volunteer. I hereby give my consent to be a subject in this project.
I indemnify the University, also any employee or student of the University, of any liability against myself, which may arise during the course of the project.

I will not submit any claims against the University regarding personal detrimental effects due to the project, due to negligence by the University, its employees or students, or any other subjects.

I agree to be tested for HIV : YES NO

I want to know my HIV-status: YES NO

I agree to give a blood sample YES NO

(The HIV testing and other measurements will only be done during September-December 2005. You have the right to change your mind and at that time you will be asked to sign an inform consent again on HIV testing)

.....
(Signature of the subject)

Signed at .....on .....

Witnesses

1. .....

2. .....

Signed at ..... on .....

POTCHEFSTROOM CAMPUS

PURE-SA Project (Prospective Urban and Rural Epidemiology)

INFORMED CONSENT FORM (including the PRIMER-study)

I, the undersigned .....(full names)
read / listened to the information on the project in PART 1 and PART 2 of this document and I declare that I understand the information. I had the opportunity to discuss aspects of the project with the project leader and I declare that I participate in the project as a volunteer. I hereby give my consent to be a subject in this project.

I agree to be tested for HIV	Yes	No
I want to know my HIV-status	Yes	No
I agree to give a blood sample	Yes	No

I hereby also declare that I am aware that:

1. this blood sample will be used for the purpose of
    a. Isolating DNA to look at genetic factors that are currently associated with Type 2 Diabetes (i.e. the Calpain10, Adiponectin, Leptin and Leptin Receptor genes), or genetic factors that may be associated with Non Communicable diseases in the future. We give the assurance that all genetic tests and experiments will only focus on genotypes suspected to contribute to an increased risk of non communicable diseases of lifestyle.
    b. Testing for liver function by determining liver enzymes such as AST, GGT,
    c. Analyses of other than genetic parameters for Diabetes Mellitus such as HbA_1C, Blood glucose and Insulin
    d. Analyses of clotting factors and hypertension markers
    e. Analyses of bone health, iron and nutrition status
    f. And may be stored until such time as the above measurements/analyses will be done.
2. A two hour glucose tolerance test will be done
3. Body measurements such as height, weight, skinfold thicknesses, arm and leg circumferences will be taken
4. Electrocardiograph be taken
5. Blood pressure to be taken
6. Pulse wave velocity measurements will be made
7. A urine sample to be collected to analyse for the presence of heavy metals such as lead and mercury,
8. A Spirometer test to be performed to determine lung function
9. A handgrip test to be performed to test muscle strength
10. A hair sample to be taken to test for fumonisin mycotoxins.

.....
(Signature of the subject)
Signed at **... Potchefstroom / Ganyesa ...** (delete not applicable option) on **...../...../ 2005**

Witnesses

1. ..... **2.** .....

Signed at **... Potchefstroom / Ganyesa ...** (delete not applicable option) on **...../...../ 2005**

PART 1

1. **School/Institute:**
Faculty of Health Sciences, North-West University

2. **Title of project/trial:**
PURE: Prospective Urban and Rural Epidemiological study

3. **Full names, surname and qualifications of project leader:**
Dr. Annamarie Kruger, Ph.D. (Nutrition)

4. **Rank/position of project leader:**
Research Manager

5.. **Aim of this project**

PURE's aim is that understanding the different lifestyle and health transitions of individuals in response to societal changes will elucidate societal and individual adaptive strategies that could diminish the adverse health effects of industrialization and urbanization on health, while retaining its benefits.

6. **Explanation of the nature of all procedures, including identification of new procedures:**

Each participant will have to fill in a number of questionnaires (Adult questionnaire, Physical activity questionnaire, Food frequency questionnaire, Health questionnaire) with the help of field workers. A blood and urine sample will be taken. Physical measures will be performed, including anthropometric measures (such as weight, height, and waist circumference), blood pressure, lung capacity and lung volume and an ECG will be performed.

7. **Description of the nature of discomfort or hazards of probable permanent consequences for the subjects which may be associated with the project: (Including possible side-effects of and interactions between drugs or radio-active isotopes which may be used.)**

It will take each participant quite a while (about two hours) to complete all the tests and discomfort may be experienced with the taking of blood samples. No measures will have permanent damage or consequences for the participants.

8. **Precautions taken to protect the subjects:**

The research nurse will be present at all times, and will be responsible for the blood sampling. She is very experienced and has performed these procedures numerous times in previous studies.

9. **Description of the benefits which may be expected from this project:**

When measures with immediate results are taken, such as blood glucose levels or blood pressure, the information will be communicated to the individual to seek professional help. Since this study is a longitudinal study, subjects that are high at risk will be identified from the dataset and personal feedback will be given.

10. Alternative procedures which may be beneficial to the subjects:

There will be tested for HIV/AIDS, therefore pre-test counselling will be given. If the subject wants to know his/her status and he/her tests positive, post counselling will also be given.

PART 2

To the subject signing the consent:
You are invited to participate in a research project. It is important that you read/listen to and understand the following general principles, which apply to all participants in our research project:

1. **Participation in this project is voluntary.**
2. **It is possible that you personally will not derive any benefit from participation in this project, although the knowledge obtained from the results may be beneficial to other people.**
3. **You will be free to withdraw from the project at any stage without having to explain the reasons for your withdrawal. However, we would like to request that you would rather not withdraw without a thorough consideration of your decision, since it may have an effect on the statistical reliability of the results of the project.**
4. **The nature of the project, possible risk factors, factors which may cause discomfort, the expected benefits to the subjects and the known and the most probable permanent consequences which may follow from your participation in this project, are discussed in Part 1 of this document.**
5. **We encourage you to ask questions at any stage about the project and procedures to the project leader or the personnel, who will readily give more information. They will discuss all procedures with you.**
6. **The University staff will use standardised procedures and take all possible precaution to protect the subject from risks.**
7. **All information will be kept CONFIDENTIAL and no personal information will be published without my consent.**

Dr ANNAMARIE KRUGER
Contact details: 082 771 5778 / 018 299 4037(Office)

Potchefstroom Campus

The PURE project
Information to communities

Dear Participant

Thank you for being willing to help us in this very important project. We are sure that the project will contribute to improve health of all the people of the North West Province.

The aim of the project is to get enough information regarding the development of chronic diseases like Diabetes, Stroke, Lung disease and heart disease with urbanisation to plan appropriate health and nutrition intervention strategies.

For this study we need 2 000 subjects whom we can follow for 12 years. The baseline survey will be done from April 2005 to November 2005. The subjects must be from rural as well as urban communities. Therefore, 500 subjects from 4 different levels of urbanisation will be needed. Ganyesa and Tlakgameng were chosen for the rural and semi-rural areas because they are still under tribal law with a good infra structure and stability. We also spoke to Chief M. Letlhogile and the mayor Mr E. Tladinyane and both gentlemen gave us permission to do the research in these two communities. Ikageng and the informal Ikageng were chosen as it is convenient and near the University. Cllr GG Megalanyane and Cllr Mahesh Roopa are informed about the study.

All the questionnaires will be filled out at your houses by trained research field workers who are from your communities. After a household survey and a family census on most of the households in your community to give us an overview of the total community, 250 men and 250 women from all four sites (Ganyesa, Tlakgameng, Ikageng, and the Informal Ikageng) will be asked to proceed with the study. These subjects should be

- Older than 35 years
- Healthy – which means that they must not be aware of any disease and do not take any chronic medication

These 2 000 subjects will be asked to fill out the adult questionnaire, the food frequency questionnaire, the health questionnaire and the physical activity questionnaire. We will also make an appointment with each subject to take some measurements such as weight, height, skinfold thicknesses, ECG (test for heart abnormalities), lung functions, blood pressure, blood glucose, blood samples and a urine sample.

It is very important that we gather quality data and knowledge. Because HIV/AIDS is such a devastating illness and affects almost all aspects of health, it is necessary to know if HIV is absent before we analyse the data. Therefore we will ask questions about your HIV status which you are allow not to answer.

It is also very important to us that you feel free to participate in this study and that you understand what the study is all about. The fieldworker will ask you to sign this form after you have read and understood it.

Kind regards

Dr ANNAMARIE KRUGER
Contact details: 082 7715778 / 018 2994037(W) / 018 2907024(H)

ADDENDUM 3: Referral letter

ADDENDUM 3: Referral letter

POTCHEFSTROOM CAMPUS: FACULTY OF HEALTH SCIENCES

PURE-SA Project (Prospective Urban and Rural Epidemiology)

REFERRAL LETTER

To whom it may concern

Dear Doctor/Sister
Mr/Ms .....participated in a project of our research group on .....

His/her fasted/random blood glucose was .....mmol/L

His/her resting blood pressure was .....mmHg

Will you please be so kind to attend to this patient?
Thank you and warm regards

.....
Dr A Kruger (project leader)
Contact details: 082 7715778

ADDENDUM 4: Quantitative food frequency questionnaire

ADDENDUM 4: Quantitative food frequency questionnaire

PURE Quantitative Food Frequency Questionnaire

Subject ID **Subject Initials**

☐☐ ☐☐☐ ☐☐☐ ☐☐ ☐☐☐

Centre # **Community #** **Household #** **Subject #** **F**
M L

Today's date: ☐☐☐☐ ☐☐ ☐☐
year *month* *day*

1. Name: _____
_____

2. Not applicable in South Africa

3. National identity # or equivalent _____ **N/A** ☐

4. DOB: ☐☐☐☐ ☐☐ ☐☐ **OR** **Age** ☐☐ **years**

5. Sex: ☐ Female ☐ Male

Please think carefully about the food and drink you have consumed during the ***past month*** (four weeks). I will go through a list of foods and drinks with you and I would like you to tell me:

- If you eat the food
- How the food is prepared
- How much of the food you eat at a time
- How many times a day you eat it and if you do not eat it everyday, how many times a week or a month you eat it.

To help you to describe the amount of a food you eat, I will show you pictures of different amounts of the food. Please say which picture is the closest to the amount you eat, or if it is smaller, between the sizes or bigger than the pictures.

There are no right or wrong answers.

Everything you tell me is confidential. Only your subject number appears on the form.

Is there anything you want to ask now?

Are you willing to go on with the questions?

FOOD FREQUENCY QUESTIONNAIRE

INSTRUCTIONS: Circle the subject's answer. Fill in the amount and times eaten in the appropriate columns.

I shall now ask you about the type and the amount of food you have been eating in the last few months. Please tell if you eat the food, how much you eat and how often you eat it. We shall start with maize meal porridge.

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
PORRIDGE AND BREAKFAST CEREALS AND OTHER STARCH								
Maize-meal porridge	Stiff (pap)						3400	
Maize-meal porridge	Soft (slappap)						3399	
Maize-meal porridge	Crumbly (phutu)						3401	
Ting								
Mabella	Stiff						3437	
Mabella	Soft							
Oats							3239	
Other cooked porridge	Type: _____							
Breakfast cereals	Brand name of cereals at home now: _____ _____ _____ _____							

Do you pour milk on your porridge or cereal? Yes No

If yes, what type of milk (whole fresh, sour, 1%, fat free, milk blend, etc) _____

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
If yes, how much milk								
Do you put sugar on your porridge or cereal?		Yes		No				
If yes, how much sugar							3989	
							3989	
							3989	
Samp	Bought Self ground						3250	
Samp and beans	Give ratio of samp:beans						3402 (1:1)	
Samp and peanuts	Give ratio of samp:peanuts						3250 (samp)	
Rice	White						3247	
	Brown						3315	
	Maize Rice						3250	
Pasta	Macaroni Spaghetti Other specify: _____ _____						3262	
Pizza	Home made: Specify topping _____ _____						3353 (base+ch)	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Bought: Specify topping _____ _____						3353 (base+ch)	

You are being very helpful. Can I now ask you about meat?

CHICKEN, MEAT, FISH

How many times do you eat meat (beef, mutton, pork, chicken, fish) per week?

_____

Chicken (codes with skin)	Boiled						2926	
	Fried: in batter/crumbs Eg Kentucky						3018	
	Fried: Not coated							
	Bought: Chicken Licken						2925	
	Bought: Nando's							
	Roasted / Grilled						2925	
	Other: _____							
Do you eat chicken skin?	Always		Sometimes		Never			
Chicken bones stew								
Chicken feet							2997	
Chicken offal								
Red meat	How do you like meat? With fat Fat trimmed							
Red meat	Fried							
	Stewed							
	Mince with tomato and onion						2987	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other:							
Beef Offal	*Intestines: boiled nothing added*						3003	
	Stewed with vegetables							
	Liver						2920	
	Kidney						2923	
	Other: Specify _____ _____							
Goat meat	Boiled						4281	
	Stewed with vegetables							
	Grilled / Roasted						4281	
What type of vegetables is usually put into meat stews? _____								
Wors / Sausage							2931	
Bacon							2906	
Cold meats	Polony						2919	
	Ham						2967	
	Vienna						2936	
	Other: Specify _____ _____ _____							
Canned meat	Bully beef							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other: Specify _____ _____							
Meat pie	Beef						2939	
	Steak and kidney						2957	
	Cornish						2953	
	Chicken						2954	
	Other							
Hamburger	Bought							
Dried beans/peas/lentils	Soup						3145	
	Salad							
Soya products eg. Toppers	Brands at home now: _____ _____						3196 (Toppers)	
Pilchards in tomato/chilli/brine	Whole						3102	
	Mashed with fried onion							
Fried fish	With batter/crumbs							
	Without batter/crumbs							
Other canned fish	Tuna						3056 (oil)	
	Pickled fish							
	Other: Specify _____							
Fish cakes	Bought: Fried						3080	
	Home made with potato						3098	
Fish fingers	Bought						3081	
Eggs	Boiled/poached						2867	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Scrambled: milk + fat							
	Fried: Fat							

Now we come to vegetables and fruit

VEGETABLES AND FRUIT

Cabbage	How do you cook cabbage?							
	Boiled, nothing added						3756	
	Boiled with potato and onion and fat							
	Fried, nothing added Fried in							
	Boiled, then fried with potato, onion							
	Other:							
	Don't know							
Spinach/morogo/ beetroot leaves other green leafy	How do you cook spinach?							
	Boiled, nothing added						3913	
	Boiled with fat added Type of fat							
	With onion, tomato, potato							
	With peanuts							
	Other:							
	Don't know							
Tomato and onion gravy	Home made with fat Type of fat							
	Without fat						3925	
	Canned						4192	
Pumpkin (yellow)	How do you cook pumpkin?							
	Boiled, nothing added						4164	
	Cooked in fat and sugar Fat							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Boiled, little sugar and fat Fat							
	Other							
	Don't know							
Carrots	How do you cook carrots?							
	Boiled, nothing added						3757	
	Boiled, sugar and fat Fat							
	With potato and onion: Fat							
	Raw, salad						3709	
	Chakalaka							
	Other							
	Don't know							
Mealies/ Sweet corn	How do you eat mealies?							
	On cob – fat added Fat							
	On cob – no fat added						3725	
	Creamed sweet corn / canned						3726	
	Whole kernel/canned						3942	
Beetroot	Salad						3699	
	Boiled, nothing added						3698	
Potatoes	How do you cook potatoes?							
	Boiled/baked with skin						4155	
	Boiled/baked without skin						3737	
	Mashed							
	Roasted Fat							
	French fries (chips)						3740	
Sweet potatoes	How do you cook sweet potatoes?							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Boiled/baked with skin						3748	
	Boiled/baked without skin						3903	
	Mashed							
	Other: _____							
	Don't know							
Salad vegetables	Mixed salad: tomato, lettuce and cucumber						3921	
	Raw tomato						3750	
	Other salad vegetables: _____ _____							
Other vegetables, specify + preparation	_____ _____ _____							
Do you like fruit?		Yes		No				
Apples							3592	
Pears							3582	
Oranges							3560	
Naartjie							3558	
Grapes							3550	
Peaches	Fresh						3565	
	Canned						3567	
Apricots	Fresh						3534	
	Canned						3535	
Mangoes							3556	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Guavas	Fresh						3551	
	Canned						3553	
Avocado							3656	
Wild fruit/berries	Specify type: _____							
Dried fruit	Types: _____							
Other fruit	_____							
If subject eats canned fruit: Do you have custard with the canned fruit?			Yes	2 No				
Custard	Home made: Milk							
	Commercial eg Ultramel						2716	

BREAD AND BREAD SPREADS

Bread / Bread rolls	White						3210	
	Brown						3211	
	Whole wheat						3212	
Do you spread anything on the bread?			Always	Sometimes	Never			
Margarine	What brand do you have at home now?							
	Don't know _____							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Peanut butter							3485	
Jam/syrup/honey							3985	
Marmite / Fray bentos / Oxo							4058	
Fish/meat paste							3109	
Cheese	Type: _____ _____							
Achaar								
Other spreads	Specify: _____							
Dumpling								
Vetkoek	White flour						3257	
	Whole wheat flour						3324	
Provita, crackers, etc							3235	
Mayonnaise / salad dressing	Mayonnaise						3488	
	Other: Specify _____							
DRINKS								
Tea	English (normal)						4038	
	Rooibos						4054	
Coffee							4037	
Sugar/cup tea or coffee	Tea:						3989	
	Coffee:						3989	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Milk/cup tea or coffee	What type of milk do you use in tea and coffee?							
	Fresh/long life: whole/full						2718	
	Fresh/long life: 2%/low fat						2772	
	Fresh/long life: fat free						2775	
	Whole milk powder Brand: _____						2721 (powder)	
	Low fat milk powder Brand: _____						2825 (powder)	
	Skimmed milk powder Brand: _____						2825 (powder)	
	Milk blend Brand: _____						2770 (powder)	
	Whitener: type _____ _____							
	Condensed milk						2714	
	Evaporated milk						2715	
	None							
Milk as such	What type of milk do you drink milk as such?							
	Fresh/long life: whole/full						2718	
	Fresh/long life: 2%/low fat						2772	
	Fresh/long life: fat free						2775	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Condensed milk						2714	
	Sour/maas						2787	
	Other: _____ _____							
Milk drinks	Nestle: _____							
	Milo: _____							
	Flavoured milk: _____							
	Other:							
Yoghurt	Drinking yoghurt						2756	
	Thick yoghurt						2734	
	Low fat sweetened with fruit						2732	
Squash	Sweet O						4027	
	Six O							
	Oros/Lecol – with sugar						3982	
	- artificially sweetener						3990	
	KoolAid						4027	
	Other: _____ _____							
Fruit juice	Fresh/Liquifruit/Ceres						2866	
	Tropica (Dairy –fruit juice mix)						2791	

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other: _____ _____ _____							
Fizzy drinks	Sweetened						3981	
Coke, fanta, etc	Diet							
Maueu/Motogo							4056	
Home brew								
Tlokwe							4039	
Beer							4031	
Spirits							4035	
Wine red							4033	
Wine White							4033	
Other specify	_____ _____ _____							
SNACKS AND SWEETS								
Potato crisps							3417	
Peanuts	Raw						4285	
	Roasted						3458	
Cheese curls, Niknaks, etc							3267	
Raisins							3552	
Peanuts and raisins								

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Chocolates	Name: _____ _____ _____							
Candies	Sugus, gums, hard sweets, etc						4000	
Sweets	Toffees, fudge, caramels						3991	
Biscuits/cookies	Type: _____ _____ _____							
Cakes and tarts	Type: _____ _____ _____							
Scones								
Rusks	Type: _____ _____							
Savouries	Sausage rolls						2939	
	Samoosas: Meat filling						3355	
	Samoosas: Vegetable filling						3414	
	Biscuits eg bacon kips							

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
	Other specify: _____							
Jelly							3983	
Baked pudding	Type: _____							
Instant pudding	Milk type: _____							
Ice cream							3483	
Sorbet							3491	
Other specify	_____ _____ _____							
SAUCES, GRAVIES AND CONDIMENTS								
Tomato sauce / Worcester sauce							3139	
Chutney							3168	
Pickles							3866	
Packet soups							3165	
Other:	_____ _____							
WILD BIRDS, ANIMALS OR INCECTS (hunted in rural areas or on farms)								

FOOD	DESCRIPTION	AMOUNT	TIMES EATEN				CODE	AMOUNT / DAY
			Per day	Per week	Per month	Seldom / Never		
Wild fruit								
MISCELLANEOUS: Please mention any other foods used more than once/two times a week which we have talked about:								

INDIGENOUS/TRADITIONAL FOODS/PLANTS/ANIMALS

Please tell me if you use any indigenous plants OR other indigenous foods like mopani worms, locusts ect to eat

Specify								

Thank you very much for your cooperation and patience.

Good-bye!

ADDENDUM 5: Pure 24 hour recall dietary intake

ADDENDUM 5: Pure 24 hour recall dietary intake

PURE 24-hour recall dietary intake

Subject ID **Subject Initials**

☐☐ ☐☐☐ ☐☐☐ ☐☐ ☐☐☐

Centre # **Community #** **Household #** **Subject #** **F**
M L

Today's date: ☐☐☐☐ ☐☐ ☐☐
year *month* *day*

1. Name: _____
_____

2. Not applicable in South Africa

3. National identity # or equivalent _____ **N/A** ☐

4. DOB: ☐☐☐☐ ☐☐ ☐☐ **OR** **Age** ☐☐ **years**

5. Sex: ☐ Female ☐ Male

6. What day was yesterday? (tick correct one)

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

7. Would you describe the food that you ate yesterday as typical of your usual food intake?

Yes	1	No	2

Greetings!

Thank you for giving up your time to participate in this study. I hope you are enjoying it so far. Here we want to find out what people living in this are eat and drink. This information is important to know as it will tell us if people are eating enough and if they are healthy.

There are no right or wrong answers.

Everything you tell me is confidential. Only your subject number appears on the form.

Is there anything you want to ask now?

Are you willing to go on with the questions?

I want to first ask you a few general questions about your food intake, the preparation of food and the type of food that you use in your home.

Instruction
Circle the subject's answer.

8. What type of pot do you usually use to prepare food in? (may answer more than one)

Iron pot ..... ☐
1

Stainless steel pot ..... ☐ **2**

Aluminium pot ..... ☐
3

Glass ware ..... ☐ **4**

Other (specify) ..... ☐
5

9. Do you eat maize meal porridge? Yes **1** No **2**

If YES, what type do you have at home now?

Brand name:

_____

Don't know: _____ **2**

Grind self: _____ **3**

If brand name is given, do you usually use this brand? Yes **1** No **2** Don't know **3**

Where do you get your maize meal from? (may answer more than one)

Shop ..... ☐
1

Employer ..... ☐
2

Harvest and grind self ..... ☐
3

☐

Other (specify) .....
4

Don't know ..... ☐ ...
5

10. Do you eat fat/margarine or use it in the preparation of food? Yes **1** No **2**

If YES, what type do you have at home now?

Brand name:

_____

Don't know: _____ **2**

If brand name is given, do you usually use this brand? Yes **1** No **2** Don't know **3**

11. Do you use oil in the preparation of food? Yes No
2

If YES, what type do you have at home now?

Brand name:

_____

Don't know: _____ **2**

If brand name is given, do you usually use this brand? Yes **1** No **2** Don't know **3**

What type of oil do you buy for deep frying?

Brand name:

_____

Do you use the same oil more than once? Yes **1** No **2**

If yes, how many times will you use the same oil?

_____

12. What type of salt do you use?

Give brand names

_____

Do you add salt to food while it is being cooked?

Always 1	Sometimes 2	Never 3	Don't know 4

Do you add salt to your food after it has been cooked?

Always 1	Sometimes 2	Never 3

Do you like salty foods eg salted peanuts, crisps, chips, fritos, biltong, dried sausage, etc

Very much 1	Like it 2	Not at all 3

13. Do you use any of the following:

	Name of product	**Amount per day**
Vitamins/vitamins and minerals		
Tonics		
Health foods		
Body building preparations		
Dietary fibre supplement		
Other: Specify _____ _____ _____		

I want to find out about everything you ate or drank yesterday, including water or food you pick from the veld. Please tell me everything you ate from the time you woke up yesterday up to the time you went to sleep. I will also ask you where you ate the food and how much you ate.

To help you to describe the amount of a food you eat, I will show you pictures and examples of different amounts of the food. Please say which picture or example is the closest to the amount you eat, or if it is smaller, between the sizes or bigger than the pictures.

Time	Place	Description of food and preparation method	Amount	Amount in gram	Code (office use)