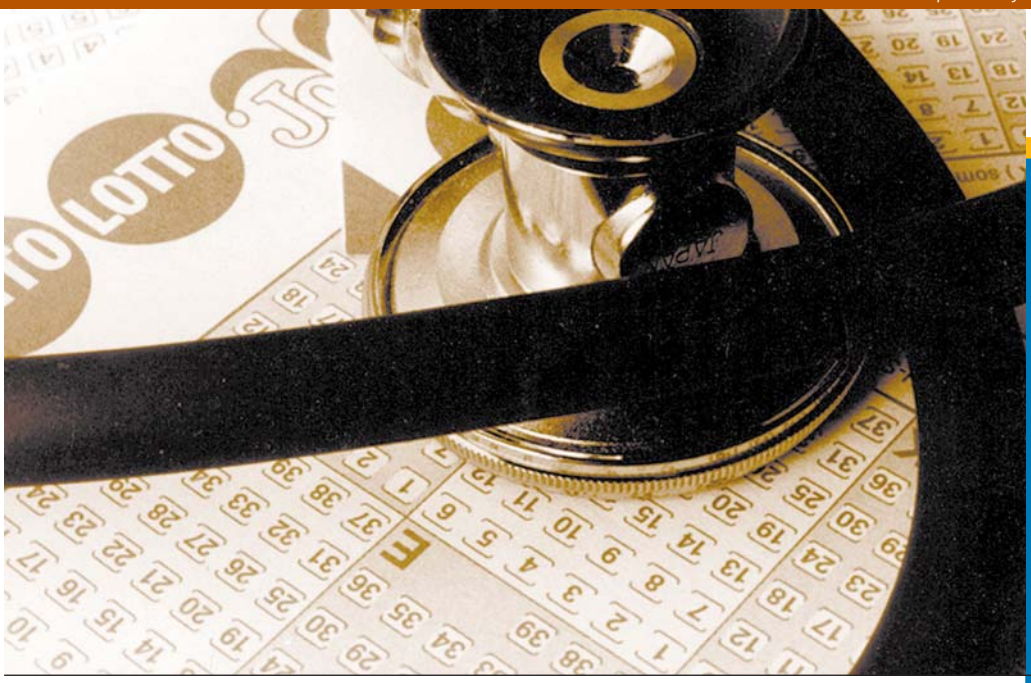

Samuli Saarni

Health-Related Quality of Life and Mental Disorders in Finland

Publications of the National Public Health Institute A 9/2008

Department of Mental Health and Alcohol Research
National Public Health Institute, Helsinki
and
Department of Psychiatry
University of Helsinki

Helsinki, Finland 2008

Samuli Saarni

Health-Related Quality of Life and Mental Disorders in Finland

Academic Dissertation

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Mannerheimintie 166
FIN-00300 Helsinki, Finland
puh. (09) 4744 1, fax (09) 4744 08

Folkhälsoinstitutet
Mannerheimvägen 166
FIN-00300 Helsingfors, Finland
tel. (09) 4744 1, fax (09) 4744 08

National Public Health Institute (NPHI)
Mannerheimintie 166
FIN-00300 Helsinki, Finland
tel. +358-9-4744 1, fax +358-9-4744 08

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Supervised by

Professor Jouko Lönnqvist, MD, PhD
Department of Mental Health and Alcohol Research
National Public Health Institute, Helsinki, Finland

Professor Harri Sintonen, PhD
Department of Public Health
University of Helsinki, Finland

Docent Jaana Suvisaari, MD, PhD
Department of Mental Health and Alcohol Research
National Public Health Institute, Helsinki, Finland

Reviewed by

Docent Jyrki Korkeila, MD, PhD
Department of Psychiatry
University of Helsinki, Finland

and

Professor Unto Häkkinen, PhD
Centre for Health Economics (CHESS)
National Research and Development Centre for
Welfare and Health (STAKES), Helsinki, Finland

Opponent

Professor Raimo K.R. Salokangas, MD, PhD
Department of Psychiatry
University of Turku, Finland

If, then, there is some end of the things we do, which we desire for its own sake (everything else being desired for the sake of this), and if we do not choose everything for the sake of something else (for at that rate the process would go on to infinity, so that our desire would be empty and vain), clearly this must be the good and the chief good. Will not the knowledge of it, then, have a great influence on life? Shall we not, like archers who have a mark to aim at, be more likely to hit upon what is right? If so, we must try, in outline at least, to determine what it is, and of which of the sciences or capacities it is the object.

Aristotle, Nikomachean Ethics. Translation W.D.Ross

CONTENTS

Samuli Saarni, Health-related quality of life and mental disorders in Finland.
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Abstract

Quality of life (QoL) is becoming one of the key outcomes of health care. This is due to increased respect for the subjective valuations and well-being of patients and an increasing part of the ageing population living with chronic, non-fatal conditions. Health-related quality of life (HRQoL) aims to capture the aspects of QoL that health and health care can influence. Preference-based generic HRQoL measures enable estimation of health utility, the quality component needed for calculating quality-adjusted life years (QALYs). These combine morbidity and mortality into a single index, allowing direct comparisons across different treatments and conditions, and can thus be very useful for rational rationing, evidence-based medicine and other health policy decisions.

Ideally, the HRQoL associated with different conditions is estimated using a representative general population sample, reliable diagnostics and preference-based HRQoL measures. However, studies like this are lacking, as mental disorders can not be reliably diagnosed utilizing simple self-report measures used in most surveys. HRQoL studies using proxy-measures for mental disorders, and studies using other methods for estimating the burden of disease, have suggested that mental disorders may be comparable in severity to the most serious somatic conditions, and that they may be the single largest cause of non-fatal disease burden in the developed world.

This study aimed to compare the individual severity (in decreased HRQoL) and public health burden (in QALYs lost to morbidity) of major chronic conditions in Finland, including and focusing on reliably diagnosed psychiatric conditions. The relationship between HRQoL and different age-groups, different classes of anxiety and depressive disorders and different alcohol consumption patterns was investigated separately.

The study is based on the Health 2000 survey, a representative general population survey of 8028 Finns aged 30 and over. Sociodemographic information, alcohol consumption and self-reported somatic conditions (if diagnosed by a physician) were asked for with interviews. Depressive, anxiety and alcohol use disorders were diagnosed with the Composite International Diagnostic Interview (M-CIDI). HRQoL was measured with two preference-based questionnaire measures, the 15D and the EQ-5D, with 83% of the sample completing at least one of the instruments.

This study found that people with psychiatric disorders had the lowest 15D HRQoL scores at all ages, in comparison to other main groups of chronic conditions. Considering 29 individual conditions, three of the four most severe (on 15D) were psychiatric disorders; the most severe was Parkinson's disease. Of the psychiatric disorders, chronic conditions that have sometimes been considered relatively mild - dysthymia, agoraphobia, generalized anxiety disorder and social phobia - were found to be the most severe, as measured with HRQoL. This was explained both by the severity of the impact of these disorders on mental health domains of HRQoL, and also by the fact that decreases were widespread on most dimensions of HRQoL.

Considering the public health burden of conditions, musculoskeletal disorders were associated with the largest burden, followed by psychiatric disorders. These were associated with 23% and 12% of the total QALYs lost due to morbidity on 15D, respectively, as identified in this study. Psychiatric disorders were associated with the largest burden at younger ages, accounting for 37% of the disease burden at ages 30-45 years. Of individual conditions, the largest burden found was for depressive disorders, followed by urinary incontinence and arthrosis of the hip and knee. The public health burden increased greatly with age, so the ageing of the Finnish population will mean that the disease burden caused by chronic conditions will increase by a quarter up to year 2040, if morbidity patterns do not change.

Investigating alcohol consumption and HRQoL revealed that although abstainers had poorer HRQoL than moderate drinkers, this was mainly due to many abstainers being former drinkers and having the poorest HRQoL. Moderate drinkers did not have significantly better HRQoL than abstainers who were not former drinkers. Also heavy drinkers had lower HRQoL than abstainers who were not former drinkers, but this was statistically significant only for the most heavily drinking 5-10% (women drinking on average 24 drinks and men 52 drinks per week).

In conclusion, this study showed that psychiatric disorders are associated with a large part of the non-fatal disease burden in Finland. In particular anxiety disorders appear to be more severe and have a larger public health burden than previously thought. More generally, this study showed that measuring HRQoL at population level can be feasible and it can provide important and useful information regarding the well-being of the population.

Keywords: Mental disorders, health-related quality of life, quality of life, 15D, EQ-5D, Finland, survey

Samuli Saarni, Terveyteen liittyvä elämänlaatu ja mielenterveyden häiriöt Suomessa.
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Tiivistelmä

Elämänlaadun merkitys terveydenhuollon päämääränä on korostumassa. Tämä johtuu potilaiden omien arvostusten painoarvon kasvusta sekä väestön ikääntymisestä seuraavasta kroonisten sairauksien suhteellisesta yleistymisestä. "Terveyteen liittyvä elämänlaatu" pyrkii tavoittamaan ne elämänlaadun osat, joihin terveys ja terveydenhuolto voivat vaikuttaa. Preferenssipohjaisten, taudeista riippumattomien terveyteen liittyvän elämänlaadun mittareiden käyttö mahdollistaa ns. terveysutiliteettien arvioinnin; nämä muodostavat laatupainotteisten elinvuosien (Quality-adjusted life years, QALY) laatutekijän. Laatupainotteiset elinvuodet yhdistävät sairastavuuden ja kuolleisuuden yhdeksi summapistemääräksi, mikä mahdollistaa erilaisten hoitojen ja sairauksien vaikutusten suoran vertailun. Tämä voi hyödyttää terveydenhuollon resurssien rationaalista jakoa, näyttöön perustuvaa lääketiedettä ja muuta terveyspoliittista päätöksentekoa.

Eri tautien elämänlaatuvaikutusten mittaus edellyttää kattavan väestöaineiston sekä luotettavan diagnostiikan. Tämänkaltaisia, preferenssipohjaisia terveyteen liittyvän elämänlaadun mittareita käyttäviä tutkimuksia ei kuitenkaan juuri ole. Mielenterveyden häiriöitä ei voi luotettavasti diagnosoida yksinkertaisilla kyselyillä, joita useimmissa väestötutkimuksissa käytetään. Olemassa olevat mielenterveyttä sivuavat, terveyteen liittyvää elämänlaatua tai muita väestön tautikuormaa mittaavia menetelmiä käyttävät tutkimukset kuitenkin viittaavat siihen, että mielenterveyden häiriöt voivat olla yhtä vakavia kuin vakavimmat yleiset somaattiset sairaudet, ja ne voivat olla suurin yksittäinen tautitaakkaa aiheuttava sairausryhmä länsimaissa.

Tämän tutkimuksen tavoitteena oli vertailla keskeisten kroonisten sairauksien vaikutusta sekä yksilöiden terveyteen liittyvään elämänlaatuun että kansanterveyteen arvioimalla sairastamiseen liittyviä laatupainotteisten elinvuosien menetyksiä. Tutkimus keskittyy erityisesti mielenterveyden häiriöihin. Iän, eri ahdistuneisuus- ja masennushäiriöiden sekä alkoholinkäytön yhteys terveyteen liittyvään elämänlaatuun tutkittiin erikseen.

Tutkimus pohjautuu Terveys 2000 - tutkimukseen, joka on kattava väestöotos sisältäen 8028 vähintään 30-vuotiasta suomalaisista. Sosiodemografiset perustiedot, alkoholinkäyttötavat ja lääkärin toteamat somaattiset sairaudet selvitettiin haastattelulla. Masennus-, ahdistus- ja alkoholihäiriöt diagnosoitiin strukturoidulla mielenterveyshaastattelulla

(M-CIDI). Terveyteen liittyvää elämänlaatua mitattiin 15D ja EQ-5D kyselyillä, joista jompaankumpaan 83% vastasi hyväksyttävästi.

Tutkimuksessa todettiin, että mielenterveyden häiriöistä kärsivillä on matalin terveyteen liittyvä elämänlaatu (15D) kaikissa ikäluokissa, muihin sairausryhmiin verrattuna. Tutkittaessa 29 sairautta erikseen 15D:llä, vakavimmaksi yksilötasolla osoittautui Parkinsonin tauti, mutta seuraavat kolme olivat mielenterveyden häiriöitä. Tutkittaessa mielenterveyden häiriöitä tarkemmin, vakavimmiksi osoittautuivat pitkäaikainen masennus (dystymia), julkisten paikkojen pelko (agorafobia), yleistynyt ahdistuneisuushäiriö ja sosiaalisten tilanteiden pelko. Tämä johtui toisaalta useilla terveyteen liittyvän elämänlaadun osa-alueilla todetusta heikentymisestä, toisaalta mielenterveyteen liittyvien osa-alueiden heikentymisen voimakkuudesta.

Tutkittaessa häiriöiden vaikutuksia kansanterveyteen sairastamiseen liittyvien laatupainotteisten elinvuosien menetyksinä, tuki- ja liikuntaelinsairaudet sekä mielenterveyden häiriöt aiheuttivat suurimman sairauskuorman. Ensin mainittuihin liittyi 23% ja jälkimmäisiin 12% tässä tutkimuksessa 15D:llä todetuista laatupainotteisten elinvuosien menetyksistä. Mielenterveyden häiriöihin liittyi kuitenkin 37% tautitaakasta nuorimmassa, 30-45 vuotiaiden ikäryhmässä. Yksittäisistä sairauksista suurimman tautikuorman aiheuttivat masennus, virtsainkontinenssi ja polven tai lonkan nivelrikko. Koska sairastavuus lisääntyi jyrkästi iän myötä, koko väestön ikääntyminen lisää kroonisten sairauksien aiheuttamaa tautikuormaa noin neljänneksellä vuoteen 2040 mennessä, mikäli sairastavuus pysyy nykyisellään.

Tutkittaessa alkoholinkäyttöä ja terveyteen liittyvää elämänlaatua todettiin, että absolutisteilla oli huonompi terveyteen liittyvä elämänlaatu kuin kohtuukäyttäjillä. Tämä johtui kuitenkin pääosin siitä, että merkittävä osa absolutisteista oli entisiä alkoholinkäyttäjiä, joiden terveyteen liittyvä elämänlaatu oli erityisen huono. Verrattuna absolutisteihin, jotka eivät olleet entisiä alkoholinkäyttäjiä, kohtuukäyttäjien terveyteen liittyvä elämänlaatu oli yhtä hyvä, mutta eniten alkoholia käyttävän 5-10%:n selkeästi huonompi. Selkein terveyteen liittyvän elämänlaadun lasku koski naisia, jotka juovat yli 24 annosta ja miehiä, jotka juovat yli 52 annosta alkoholia viikossa.

Yhteenvetona tutkimus osoitti, että suuri osa kroonisiin sairauksiin yhdistettävästä terveyteen liittyvän elämänlaadun menetyksestä liittyy mielenterveyden häiriöihin. Erityisesti ahdistuneisuushäiriöiden vaikutukset osoittautuivat vakavammiksi kuin aiemmin on ajateltu, sekä yksilön että kansanterveyden tasolla. Terveyteen liittyvän elämänlaadun mittaus väestötasolla on toteutettavissa, ja se voi tuottaa hyödyllistä tietoa väestön terveydestä ja hyvinvoinnista.

Avansanat: Mielenterveyden häiriö; terveyteen liittyvä elämänlaatu; elämänlaatu; 15D, EQ-5D, Suomi, väestötutkimus

Abbreviations

15D	The 15D health-related quality of life instrument
AQoL	Assessment of Quality of Life
COPD	Chronic obstructive pulmonary disease
CLAD	Censored least absolute deviations
CVD	Cardiovascular disease
DALY	Disability-adjusted life year
DSM-IV/III-R	Diagnostic and Statistical Manual of Mental Disorders, 4^{th} edition / 3^{rd} edition, revised
EBM	Evidence-based medicine
EQ-5D	The EuroQoL health-related quality of life instrument
GAD	Generalized anxiety disorder
GHQ-12	General Health Questionnaire, 12 question version
HUI	Health Utilities Index
HRQoL	Health-related quality of life
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10^{th} revision
LS	Life satisfaction
M-CIDI	Munich - version of the Composite international diagnostic interview
MCID	Minimally clinically important difference
MDD	Major depressive disorder
OECD	Organisation for Economic Co-operation and Development
OLS	Ordinary least squares
QALY	Quality-adjusted life year
QWB	Quality of Well-being Index
QoL	Quality of life
PD	Panic disorder
SE	Standard error
SF-36 / SF-6D	Medical Outcomes Study Short-form HRQoL instruments
SG	Standard gamble
SES	Socio-economic status
SP	Social phobia
SRH	Self-rated health
TTO	Time trade-off
VAS	Visual analogue scale
WHO	World Health Organization
WTP	Willingness to pay
YLD	Years lived with disability

List of original publications

This thesis is based on the following original articles referred to in the text by their Roman numerals:

I Samuli I Saarni, Tommi Härkänen, Harri Sintonen, Jaana Suvisaari, Seppo Koskinen, Arpo Aromaa, Jouko Lönnqvist: The impact of 29 chronic conditions on health-related quality of life: A general population survey in Finland using 15D and EQ-5D. Quality of Life Research 2006(8):1403-14. doi: 10.1007/s11136-006-0020-1

II Samuli I Saarni, Jaana Suvisaari, Harri Sintonen, Seppo Koskinen, Tommi Härkänen, Jouko Lönnqvist: The health-related quality-of-life impact of chronic conditions varied with age in general population. Journal of Clinical Epidemiology 2007(60): 1288-1297. doi: 10.1016/j.jclinepi.2007.03.004

III Samuli I Saarni, Jaana Suvisaari, Harri Sintonen, Sami Pirkola, Seppo Koskinen, Arpo Aromaa and Jouko Lönnqvist: Impact of psychiatric disorders on health-related quality of life: a general population survey. British Journal of Psychiatry 2007(190):326-32. doi: 10.1192/bjp.bp.106.025106

IV Samuli I Saarni, Kaisla Joutsenniemi, Seppo Koskinen, Jaana Suvisaari, Sami Pirkola, Harri Sintonen, Kari Poikolainen and Jouko Lönnqvist: Alcohol consumption, abstaining, health utility and quality of life – a general population survey. Alcohol and Alcoholism 2008:1-13. doi:10.1093/alcalc/agn003

1. Introduction

A profound change towards individualism has taken place in Western societies during the last century. This manifests in health care as a shift from paternalism to increased respect of the autonomy of the patient: the physician can not be the sole judge of success or failure of health care interventions, but the opinions, values and views of patients must be taken into account. Health for individuals is not just absence of disease or infirmity but can, as the WHO put it, be seen as a state of complete physical, psychological and social well-being and not merely the absence of disease or infirmity (WHO 1946). Furthermore, diseases do not limit themselves to individuals, but may also seriously affect the well-being of other people (Sales 2003).

This shift in health care ethics has been made a necessity by the rapid change in demographics and disease burden in developed countries: the population has become older, the relative burden of acutely fatal diseases has decreased and the burden of chronic conditions has increased. Thus the relative importance for measuring mortality as an outcome of health care has decreased and, conversely, the importance of evaluating how people manage with several chronic conditions and disabilities has increased. In other words, medicine has been moving from a biomedical model of curing disease towards a more functional and resource-oriented model of improving functional capacity, health and well-being due to both practical and ideological reasons (Nussbaum and Sen 1993; Katschnig, Freeman et al. 2006).

A third, and the most recent driving force behind the interest in quality of life (QoL) and health-related quality of life (HRQoL), is the rise of health economics and the evidence-based medicine (EBM) movement. EBM emphasises the importance of using measured, inductive evidence to justify health care decisions, instead of relying on expert opinions or deduction from biological or other theories. EBM has increased the importance and quality of outcome measurement in health care. Health economics on the other hand, like Aristotle above, requires a generic, global, single-dimensional outcome measure in order to directly compare the costs and benefits of different health care interventions. Preference-based health-related quality of life measurement aims to meet all these demands with quality-adjusted life years (QALYs) - a generic metric that combines morbidity and mortality into a single index.

Sixty years after the WHO definition of health, the interest in quality of life research in health care has started to gain momentum and is increasing rather exponentially. Medline finds around 1400 citations for "quality of life" before 1980, 6500 citations from the eighties, 28000 citations from the nineties and 62000 citations from years 2000 to 2007. The promise to deliver humane, patient-centred knowledge on the effects of diseases and health care interventions on quality of life (that would then be used to justly maximise public well-being) is great and tempting. Several obstacles, however, still stand in the way. The future will show whether these promises will be fulfilled. In any case, comprehensive knowledge of the QoL impact of different conditions and disorders is a necessary prerequisite for any attempt to rationally improve the QoL of patients.

2. Review of the literature

2.1 Researching quality of life

2.1.1 Quality of life and values

Defining and operationalising quality of life has been neither easy nor very successful. This is unsurprising because, from the philosophical point of view, the question of the definition of the QoL approaches the fundamental question of ethics: the definition of a good life or the meaning of life (Nussbaum and Sen 1993). In practice, there are hundreds of measurement instruments for QoL, most of which have been used only sporadically (Garratt, Schmidt et al. 2002). This, in connection with the *a priori* fact that there can not be a direct way of observing what true QoL is, has left the field without a gold standard. A popular way of overcoming these difficulties is to use a multi-dimensional definition of QoL including many, if not all, things that can be beneficial for well-being, for example 1) subjective satisfaction or happiness, 2) ability to function (physical, mental and social) and 3) availability of necessary resources (material standard of living, social support) (Katschnig, Freeman et al. 2006). A more philosophically oriented approach would be to separate three kinds of theories of the good life: 1) hedonist theories, emphasising some form of (positive) conscious emotion or feeling, 2) preference satisfaction theories, emphasising the fulfilment of personal preferences or desires and 3) ideal theories, concentrating on fulfilment of other normative ideals than those aforementioned (Brock 1993).

Developing quality of life measures is in reflexive relation to our own view of QoL: our ideals about what constitutes a good quality life guides the beginning of the development process, but the practical issues inherent in all measure-development then start to influence the measures. Further, the most popular measures may eventually start to influence our understanding of the original construct. Developing quality of life measures is thus a fundamentally value-laden, normative process (Chisholm, Healey et al. 1997; Murray, Salomon et al. 2000).

2.1.2 Health-related quality of life and health state preferences

It is obvious that health is only one, although important, determinant of quality of life (Bowling 1996). Health-related quality of life (HRQoL) is a more narrow concept than QoL; HRQoL tries to capture the aspects of QoL that health, and ideally also health care, can influence. Of the three components of QoL mentioned above, HRQoL instruments generally concentrate on functional capacity. Thus HRQoL is in theory a more practical way of measuring the impact of different diseases than QoL.

Quality-adjusted life year (QALY) is a metric that combines mortality and morbidity into a single index score. This is important for comparisons between different diseases and treatments. Preference-based generic HRQoL measures, such as the 15D and the EQ-5D used in this study, form the quality-component of QALYs. In practice they are multi-attribute utility scales, which means that they consist of several dimensions that can be combined into a single summary score using preferences of real people for certain health states (Dolan 2000). The preferences are anchored at death (HRQoL=0) and full health (HRQoL=1) in order to allow combination with mortality. The most favoured methods for preference elicitations are time trade-off (TTO) and standard gamble (SG). They require the respondents to estimate how many life years they would give up (TTO) or how large a risk of sudden death they would accept (SG) in order to be in full health in comparison to another health state. The resulting preference score is commonly referred to as health utility. Preferences can also be elicited using visual analogue scale (VAS) by, for example, anchoring the scale at "best possible QoL" and "worst possible QoL". Furthermore, the willingness to pay (WTP) method investigates how much people would be willing to pay for certain health outcomes. This incorporates monetary values directly into the process of health state valuation (Fayers and Machin 2007). Preferences can be elicited from people who are in health states to be valued or have at least sometimes experienced them, or from healthy people who have to imagine being in the health states to be valued. There is no gold standard for how and from whom the valuations should be elicited. Both 15D and EQ-5D use health preferences elicited from the general population. This assumes that preferences do not vary between different groups of people; especially between patients and healthy people, or people at different ages.

There is also no gold standard for HRQoL measurement, nor for preference elicitation. Hundreds of HRQoL measures with different properties are in use (Garratt, Schmidt et al. 2002), and even those with preference-based scoring systems often produce conflicting results (Tengs and Wallace 2000; Hawthorne, Richardson et al. 2001; Kopec and Willison 2003). The major HRQoL measures based on multi-attribute utility theory are listed in the appendix.

There are also competing approaches to measuring quality-adjusted survival (i.e. combining morbidity and mortality). The most popular alternative is disability-adjusted life years (DALY), made famous by the Global Burden of Disease (GBD) studies (Murray and Lopez 1996) and then used in several local settings (Peterson, Backlund et al. 1998; Mathers, Vos et al. 1999; Melse, Essink-Bot et al. 2000). The DALY method combines separately collected prevalence data and disability weights for different diseases. The weights are generally collected from experts who value different diseases, and generally assumed to be constant (i.e. all states of a disease are taken to be equally severe). This contrasts with the QALY approach that measures prevalence and health states simultaneously, allowing for the true variation in disease severities, and uses population preferences for health states.

Obviously, the best method for summarising population health depends on the purpose of the measurement and the data available; all methods make fundamental assumptions that can be contested, and all datasets are imperfect. DALYs were originally used to describe the burden of disease globally with a very heterogeneous database. From the health economic perspective however, the key interest lies in investigating the marginal benefits of health interventions and health care systems. This information is highly policy-relevant, as it could be used for optimizing the functioning of health care - for example via rationing decisions and health technology assessment. The QALY approach, starting with people and not with disease, appears more suitable for health economic analysis, and could even be used at individual level - for example, as an outcome in a pay-for-performance system. Furthermore, QALYs can also be used for describing burden of disease if the data are available (Williams 1999; Mooney and Wiseman 2000; Murray and Lopez 2000; Williams 2000).

2.2 Surveys measuring HRQoL and chronic conditions

In order to compare the burden of different diseases and conditions using health utilities or QALYs, a representative population sample, utility-based health measurement and reliable diagnostics are needed. As very few studies fulfil all three - especially when it comes to psychiatric disorders - the literature review is limited to studies fulfilling the first two criteria. Studies identified are presented in Table 1. Comparing different studies still requires caution, as different HRQoL measures may yield different results despite being utility-based (Tengs and Wallace 2000). Also, the surveys have different samples, response rates, statistical methods and diagnostic procedures.

Table 1. General population surveys estimating health utility losses of chronic conditions.

Reference	N (response rate) age, country	HRQoL measurement	Somatic diagnostics, included conditions	Psychiatric diagnostics, included conditions	Results	Comment
Burström 2001b (Burström, Johannesson et al. 2001)	Sample = 4 950 (resp. rate 63%) 20-88 years Sweden	EQ-5D (UK TTO)	Self-reported by questionnaire: Diabetes as diagnosed by physician ("diabetes"), "asthma", use of antihypertensive medications ("hypertension"), chest pain during activity within last 12 months ("angina pectoris"), "neck/shoulder pain" or "low back pain" (if pain more than twice a week during last 6 months)	"Mental distress" (defined as 2/12 or more problems GHQ-12, prevalence 21%)	Diabetes -0.060 Mental distres -0.125 Hypertension -0.022 Angina pectoris -0.045 Asthma -0.021 Neck/shoulder pain -0.081 Low back pain -0.115	Results adjusted with linear regression for age, gender, SES, other conditions
Lubetkin 2005 (Lubetkin, Jia et al. 2005)	13200 respondents (resp. rate ~56%) 18+ years USA	EQ-5D (USA TTO)	Self-reported by interview: Diabetes, asthma, high blood pressure, emphysema, stroke or TIA ("stroke") or "heart disease" (including coronary heart disease, angina, heart attack or other heart condition)	-	Diabetes -0.041 Hypertension -0.046 Heart disease -0.059 Asthma -0.038 Stroke -0.056 Emphysema -0.076	Results adjusted with linear regression for age, gender, race, SES, other conditions
Barton 2007 (Barton, Sach et al. 2007)	Sample = 2770 (resp. rate 63%) 45+ years UK	EQ-5D (UK TTO)	Self-reported by questionnaire: back pain, hip pain, knee pain (on most days of the last month), diagnosed with heart disease, stroke, asthma, cancer, diabetes, rheumatoid arthritis or osteoarthritis)	-	Back pain -0.155 Hip pain -0.110 Knee pain -0.111 Heart disease -0.052 Stroke -0.074 Asthma -0.032 Cancer -0.024 Diabetes -0.058 Rheumatoid arthritis -0.102 Osteo-arthritis -0.079	Results adjusted with linear regression for age, gender, race, education, BMI, smoking, other conditions
Johnson 2000 (Johnson and Pickard 2000)	Sample = 4200 (resp. rate 37%) 18+ years Canada	EQ-5D (UK TTO)	Self-reported by questionnaire: Arthritis/rheumatism, asthma, cancer, emphysema/bronchitis, diabetes, glaucoma, ulcers, high blood pressure, heart disease, epilepsy.	"depressive feelings": Defined by question 'how often in the past four weeks have you felt depressed?' with 5 response options, 'none' to 'all of the time', categorized at 3/5. Prevalence 18.6%		Only raw scores reported

Reference	N (response rate) age, country	HRQoL measurement	Somatic diagnostics, included conditions	Psychiatric diagnostics, included conditions	Results	Comment
Sullivan 2005 (Sullivan, Lawrence et al. 2005)	Sample = 93380 (resp. rate 41%) 18+ years USA	EQ-5D (USA TTO)	Self-reported in interview, open question. Over 100 classes of chronic conditions (lasting over 1 year) included.	Self-reported in interview, including, for example: "Alcohol-related mental disorders" (0.19 %) "Affective disorders" (1.04 %) "Anxiety, somatoform, dissociative, and personality disorders" (6.36 %)	Examples: Senility and organic mental disorders -0.175 Parkinson's -0.111 Rheumatoid arthritis -0.085 Affective disorders -0.074 Osteoarthritis -0.061 Congestive heart failure -0.055 Anxiety, somatoform, dissociative, personality disorders -0.042 Alcohol-related disorders -0.002 (n.s.)	Adjusted with CLAD regression for age, gender, race, ethnicity, income, education, number of chronic conditions
Fryback 1993 (Fryback, Dasbach et al. 1993)	Sample = 1700 (Resp rate 80%) Age 45-89 Beaver Dam, WI, USA	Quality of Well-being Index (QWB), TTO	28 conditions, asked separately in interview, included if bothered in last 12 months.	"depression" (12 month prevalence 4,6%) "anxiety" (4.0%) "sleep disorder" (10.0%)	Congestive heart failure -0.10 Myocardial infarction -0.09 Depression -0.08 Angina pectoris -0.07 Anxiety -0.05 Sleep disorder -0.05	QWB scores age-adjusted with linear regression to sample mean of 64 years
Mittmann, N 1999 (Mittmann, Trakas et al. 1999)	Sample = 17 626 (Resp. rate n.a.) 12+ years Canada	Health utilities index (HUI) mark III	Interview, 22 chronic conditions asked separately (if diagnosed by a professional).	-		No age-adjusted results reposted
Schultz 2003 (Schultz and Kopec 2003)	Sample = 73 402 (Resp. rate 79%) 12+ years	HUI, mark III	Interview, 21 chronic conditions were asked separetely (if diagnosed by a professional)	-	Alzheimers disease -0.34 Stroke -0.17 Urinary incontinence -0.13 Arthritis/ rheumatism -0.09 Chronic bronchitis/ emphysema -0.08 Cataract -0.08 Back problems -0.06 Heart disease -0.06 Diabetes -0.06	Results adjusted with linear regression for age, gender and other chronic conditions

Reference	N (response rate) age, country	HRQoL measurement	Somatic diagnostics, included conditions	Psychiatric diagnostics, included conditions	Results	Comment
Manuel 2002 (Manuel, Schultz et al. 2002)	Sample = 48 770 (Resp. rate 73%) 18+ years Ontario, Canada	HUI, mark III	Telephone interview, 20 chronic conditions asked separately + open question, categorized in 11 groups	"Mental disorder" as diagnosed with CIDI DSM-III-R 12-month depression prevalence questions. Prevalence ~4%	Age-adjusted HUI scores: (female/male) Injuries 0.76/0.79 Mental disorder 0.85/0.85 Musculoskeletal disorders 0.88/0.90 Heart disease 0.90/0.90 Respiratory disorders 0.93/0.93	Population mean scores n.a.
Isacson 2005(Isacson, Bingefors et al. 2005)	Respondents = 3986, (resp. rate 60%) 20-64 years Sweden	TTO	Mail questionnaire, separately mentioned: headache, backache/ache in legs, arms, shoulders, asthma, diabetes, angina, hypertension, dermatological problems, problems in the urinary tract, gastrointestinal problems	"Depression" (if feeling depressed on the day filling the questionnaire, prevalence of 3.8%) "anxiety" (prevalence 12.5%) "sleeping disorder" (prevalence 18.4%)	Depression -0.090 Diabetes -0.047 Anxiety -0.045 Sleeping disorder -0.034 Hypertension -0.033 Gastrointesti-nal problems -0.026	Results adjusted with linear regression for age, gender and other conditions
Wells 1999 (Wells and Sherbourne 1999)	Sample = 33 932 (Resp. rate 52%) 18+ years Managed primary care patients with mental health insurance, USA (not a general population survey)	TTO, SG	Self-report current conditions, asked separately: asthma, diabetes, hypertension, arthritis, migraine, chronic lung problems, neurological, heart, gastrointestinal tract, vision or back problems.	"12-month MDD" (prevalence 19.8%), "12-month double depression" (5.3%), "12 month dysthymia" (0.9%), "lifetime bipolar disorder" (1.9%), 1-month depressive symptoms (5.6%): self-report by questionnaire, containing 5 questions from CIDI depression	Depression -0.079/-0.036 (TTO/SG) Neurological problems -0.047/-0.035 GI tract problems -0.040/n.s. Diabetes -0.022/-0.033 Arthritis -0.016/-0.012 Migraine -0.014/-0.015	Results adjusted with linear regression for age, gender, education, ethnicity, other conditions.

2.2.1 Comparing the severity of different conditions

Few comprehensive surveys have compared the relative HRQoL impact of several chronic conditions using multi-attribute utility-based HRQoL measures (EQ-5D, Quality of Well-being Index, QWB, Health Utilities Index, HUI, Assessment of Quality of Life AQoL, SF-6D, Rosser-Kind Index) or using direct valuation methods (TTO or SG) (Fryback, Dasbach et al. 1993; Johnson and Coons 1998; Mittmann, Trakas et al. 1999; Johnson and Pickard 2000; Burström, Johannesson et al. 2001; Burström, Johannesson et al. 2001; Manuel, Schultz et al. 2002; Schultz and Kopec 2003; Lubetkin, Jia et al. 2005).

Measured with EQ-5D, a Swedish study investigating seven conditions found that the largest decreases in HRQoL were associated with mental distress, low back pain and neck/shoulder pain (Burström, Johannesson et al. 2001). A UK study including ten conditions (five of which were musculoskeletal) found the most severe conditions to be back, knee and hip pain and rheumatoid arthritis (Barton, Sach et al. 2007). A US study containing six conditions ranked emphysema, heart disease and stroke as having the greatest age-adjusted HRQoL impact (Lubetkin, Jia et al. 2005). Another larger US study considering over 100 conditions ranked mental retardation, senility and organic mental disorders, spinal cord injury, multiple sclerosis and paralysis as the most severe. Considering conditions included in our study, the most severe were Parkinson's disease, rheumatoid arthritis, affective disorders, osteoarthritis and congestive heart failure (Sullivan, Lawrence et al. 2005).

A Canadian study using the HUI found that the greatest losses of HRQoL were associated with Alzheimer's disease, stroke and urinary incontinence (Schultz and Kopec 2003). Another Canadian study using wider diagnostic groupings found that the lowest age-adjusted HUI scores were associated with injuries, depression and musculoskeletal disorders (Manuel, Schultz et al. 2002).

Using Quality of Well-being Index in a US sample, the largest losses of HRQoL were observed in persons reporting heart failure, myocardial infarction and depression (Fryback, Dasbach et al. 1993).

In addition to using multi-attribute utility instruments like 15D, EQ-5D and HUI, health utility losses associated with different conditions can also be estimated using different direct valuation techniques, for example the standard gamble (SG) or time trade-off (TTO) (Dolan 2000). A Swedish postal survey (Isacson, Bingefors et al. 2005) using a TTO exercise and self-reported conditions found that feeling depressed on the current day was clearly the most severe of the included 12 conditions, followed by self-reported anxiety. Similar results were found by a large US study of managed primary care patients (Wells and Sherbourne 1999) that used both SG and TTO exercises, self-reported somatic conditions and 12-month depression diagnosis based on selected CIDI questions. It found that depression was associated with clearly the largest loss of health utility, in comparison to the 11 included somatic conditions.

2.2.2 Age and the impact of conditions

Whether the severity of conditions varies by age has theoretical and practical importance. Although it is not very important for QALY approach used in this study, it is essential for the other popular method of estimating the burden of diseases, the disability-adjusted life years (DALY) method (Gold, Stevenson et al. 2002). The DALY method combines separately collected prevalence data and disability weights, whereas the QALY approach uses specific population studies. In practice, the disability weights are usually assumed to be constant, i.e. all instances of a disease are considered to be equally disabling. In theory, the disability weights could be stratified by the same covariates (such as age, sex, severity of the condition) that the prevalence can be stratified. However, as this is burdensome, it is important to know for which conditions age-stratified disability weights and prevalence information are actually needed - i.e. whether the severity of conditions varies significantly by age.

None of the surveys reviewed in Table 1 focus on the issue of whether the health utility impacts of conditions vary by age. Only two of the surveys reported the HRQoL losses separately for different ages. The first of these (Fryback, Dasbach et al. 1993) using the Quality of Well-being Index in USA reported age-stratified scores for some chronic conditions, but the authors did not comment on the age-related differences. No statistical testing was reported, and no clear age-related trends in QWB scores were observed in comparison to controls. The latter study (a Canadian study using the HUI) (Schultz and Kopec 2003) concluded that the impact of chronic conditions on HRQoL is not the same at all ages, and the authors noted that conditions such as bowel problems or chronic bronchitis seem to have a greater effect on older individuals' quality of life. The severity of stroke, migraine and stomach/intestinal ulcers also seemed to increase with age, but no statistical testing was reported.

A study using direct TTO exercise and 12 self-reported conditions (Isacson, Bingefors et al. 2005) estimated the relative impact of depression in comparison to the other conditions, stratified by age. In their study, depression accounted for 11% of the health utilities lost due to disability identified. The proportion of all health utilities lost associated with depression decreased from 15% at ages 35-44 (prevalence 4.6%, difference in mean utilities between depressed and non-depressed -0.16) to 5% at ages 55-64 (prevalence 3%, difference of 0.07), suggesting both possible causes for the decreasing burden of depression by age: decreased prevalence and decreased severity (absolutely and/or relative to increased utilities lost due to other conditions).

2.2.3 Mental disorders and health-related quality of life

The only survey from Table 1 that included several psychiatric conditions and HRQoL instrument (Sullivan, Lawrence et al. 2005) found that self-reported "affective disorders" were associated with larger health utility loss (loss of -0.07 on EQ-5D) than "anxiety, somatoform, dissociative or personality disorders" (-0.04). "Alcohol-related disorders" did not associate with a statistically significant impact on the EQ-5D.

Two studies using direct valuation method came to almost identical conclusions: The Swedish postal survey (Isacson, Bingefors et al. 2005) using a TTO exercise estimated 0.09 lost utilities for depression, and -0.045 for anxiety. Diagnoses were based on self-report, and controlled for other somatic and psychiatric conditions (depression, anxiety, sleep disorder). A large US study of managed care patients (Wells and Sherbourne 1999) using both SG and TTO exercises found probable 12-month MDD to be associated with loss of 0.08 health utilities on TTO and 0.04 on SG. The study diagnostics was based on seven self-reported CIDI depression and mania questions, and the authors made provisional diagnoses of other 12-month affective disorders as well. This showed that double depression (MDD and dysthymia) was the most severe condition (-0.13 and -0.07 utilities on TTO and SG, respectively), in comparison to dysthymia only (-0.08/n.s.) or MDD only (-0.05/-0.02). This study did not include, and thus did not control for, other psychiatric disorders.

2.2.4 Surveys investigating alcohol consumption, HRQoL and other measures of well-being

2.2.4.1 Mortality, J-curve and HRQoL

There are several studies investigating the association between mortality and alcohol consumption. For example, a recent meta-analysis found robust evidence of reduced risk of mortality associated with moderate alcohol consumption and increased risk associated with heavy consumption and abstaining (Di Castelnuovo, Costanzo et al. 2006). This is commonly referred to as the J-curve between alcohol consumption and mortality. However, it is unclear whether this J-curve applies to HRQoL as well.

The meta-analysis (Di Castelnuovo, Costanzo et al. 2006) also investigated the subgroup of studies that had tried to separate former drinkers or very light drinkers from abstainers, and found that this significantly reduced - but did not eliminate - the benefits of moderate alcohol consumption. However, one meta-analysis using very strict inclusion criteria did not find this (Fillmore, Kerr et al. 2006; Fillmore, Stockwell et al. 2007). This study concluded that only seven of the 54 studies included were not misclassifying former drinkers or very low drinkers as abstainers. Beneficial effects of moderate alcohol consumption on mortality were observed only in those studies including some kind of classification error. The seven studies using most rigorous classification of abstainers

found no statistically significant benefits of moderate alcohol consumption. However, as this meta-analysis was very strict and excluded most of the studies conducted on the topic, the results are difficult to interpret and some uncertainty remains over the health benefits of alcohol (Eigenbrodt, Fuchs et al. 2006). Generally, there appears to be a consensus, based on epidemiological and biological data, that moderate alcohol consumption decreases the risk of coronary heart disease (Rimm and Moats 2007). However, whether this reduction is associated with clinically important improvement of HRQoL or other aspects of QoL is unclear. Studies on the topic are complicated by the fact that former drinkers have higher risk of mortality, morbidity, low socioeconomic status and poor health behaviours in comparison to other abstainers. Thus pooling all abstainers as one group is likely to exaggerate the benefits of moderate alcohol consumption in comparison to abstaining (Fillmore, Golding et al. 1998; Gmel, Gutjahr et al. 2003).

General population surveys have not examined the benefit or harm of alcohol consumption using utility-based HRQoL measures. Considering surveys using HRQoL measures other than utility-based, a US study using SF-36 found that "non-current" drinkers reported poorest mental and physical health, although the difference compared to lifetime abstainers was small and not statistically significant (Stranges, Notaro et al. 2006). The US study did not find consistent differences between lifetime abstainers and current drinkers. In contrast, a Dutch study similarly using the SF-36 found that former drinkers had in general intermediate scores between other abstainers and drinkers (van Dijk, Toet et al. 2004). On mental health, former drinkers actually scored best, but otherwise the best scores were observed for light and moderate drinkers. However, even excessive drinkers (men drinking over 42 drinks and women over 28 drinks per week) had better health than abstainers. No explicit questions about quitting drinking or past alcohol problems were asked. A Japanese study on healthy male workers using five SF-36 subscales and explicitly asking about former drinking status found former drinkers to have general health scores below, and current drinkers to have vitality scores above, those of long-term abstainers (Saito, Okamura et al. 2005). No other subscales were statistically significant when background variables were controlled for. There was no trend for worse scores for heavy drinkers (>483g/week) on any of the SF-36 subscales. However, the study is problematic as it is limited to healthy workers, meaning that people with largest alcohol-related and other problems are excluded. In sum abstainers, especially those who are former drinkers, appear to have problems on some domains of HRQoL in comparison to moderate drinkers. Surprisingly however, none of the previous surveys found negative association of heavy alcohol consumption and HRQoL.

2.2.4.2 Other domains of well-being

A recent review of the literature on moderate drinking, health and well-being identified several studies with widely varying categorizations of drinkers and explanatory variables (El-Guebaly 2007). The review identified five surveys investigating self-rated health and moderate alcohol consumption, with four finding a J-curve and one finding the health benefits of alcohol extend to heavy alcohol use. It also identified three studies

concerning general mental health, each finding moderate alcohol users to have the best general mental health. Some studies have examined "Life satisfaction" (LS). A pioneering survey in USA examined satisfaction with several areas of life but, after accounting for confounding socioeconomic variables, almost no associations between alcohol consumption and LS were found (Hingson, Scotch et al. 1981). A previous Finnish survey noted a J-formed relationship between LS and alcohol consumption, but this was before any adjustments (Koivumaa-Honkanen, Honkanen et al. 2000). A British study using several psychological measures found that GHQ scores (controlling for age, social class and smoking) were best for light drinking men, in comparison to abstainers and heavy drinkers, but this was not found for women (Roberts, Brunner et al. 1995). In sum, moderate drinking seems to be associated with improved well-being, at least if socioeconomic factors and former drinking are not controlled for.

Regarding self-rated health (SRH), a Dutch study found that abstainers and heavy drinkers had worse SRH than light or moderate drinkers (San Jose, van de Mheen et al. 1999). According to Australian data on the number of alcoholic drinks per day, those with no drinks or with over three daily drinks had worse SRH than light or moderate drinkers (Wang, Smith et al. 2006). A Spanish study found that all drinking groups (up to over 7 drinks / day) had better SRH than abstainers (Guallar-Castillon, Rodriguez-Artalejo et al. 2001). These studies however, did not differentiate between different groups of abstainers. A British study that tried to address the former drinker-problem found that light and moderate drinkers (0-20 drinks per week for women and 0-35 drinks for men) had better self-rated health and less psychological distress than heavy drinkers and abstainers at the age of 33. There were no differences between models including and excluding problem drinkers, but results for problem drinkers were not reported separately and no adjustments for socioeconomic factors were made (Power, Rodgers et al. 1998). A previous Finnish general population survey examining the odds of good self-reported health did not find ex-drinkers to differ from lifetime abstainers, but those who had deliberately decreased their alcohol intake had poorer health (Poikolainen, Vartiainen et al. 1996). Improved SRH was best at consumptions between 40-99g (3-8 drinks) per week, and SRH was decreased at consumptions exceeding 300g (25 drinks) per week (adjusting for sociodemographic factors). A similar large US survey (French and Zavala 2007) found that moderate drinking men (4-14 drinks per week) had increased odds of good SRH in comparison to abstainers, as had women who had drank more than 12 drinks in the last year. Moderate drinking women had best SRH. Former drinkers did not differ from other abstainers, but former drinkers included anyone who had drunk over 12 drinks per year but abstained for the last year. A previous Finnish study found that the labour market underperformance of male abstainers was almost entirely due to some abstainers being former drinkers (Johansson, Alho et al. 2006). These results support the view that those abstainers who have quit drinking are doing more poorly than other abstainers on a very broad range of measures.

3. Aims of the study

This study aimed to measure the utility-based HRQoL losses associated with common chronic somatic conditions, reliably diagnosed psychiatric conditions and different alcohol consumption patterns in Finland, using two established HRQoL measures.

The study consists of four original publications, the aims of which were:

I To investigate the individual-level HRQoL impact of 29 chronic conditions, including reliably diagnosed psychiatric disorders in the Finnish general population and to estimate the public health impact of these 29 chronic conditions, using QALYs lost due to morbidity.

II To estimate how the individual severity (HRQoL) and public health impact (QALYs lost to morbidity) of these conditions varies at different ages, and to predict how the ageing of the Finnish population affects the QALYs lost due to morbidity.

III To investigate the HRQoL and QALY losses associated with depressive and anxiety disorders and alcohol dependence, and to examine which domains of HRQoL are lost in these psychiatric disorders.

IV To investigate how the amount of alcohol consumed relates to HRQoL, and to test, whether those abstaining from alcohol consist of two different groups in relation to HRQoL: those who have quit using alcohol for some reason, and others.

4. Subjects and methods

4.1 The Health 2000 survey

4.1.1 The sampling and data gathering

This study is based on the Health 2000 survey, a comprehensive health interview and examination survey that was carried out in Finland from autumn 2000 to spring 2001. The National Public Health Institute had the main responsibility for the survey, with other Finnish social and health care organisations participating. The main aim of the Health 2000 survey was to obtain information on the most important public health problems in the country, their causes and treatment as well as on the population's functional and working capacity (Aromaa and Koskinen 2004). The methods of the survey and baseline reports have been published and are available on the internet at www.ktl.fi/terveys2000.

The survey is based on two-stage stratified cluster sampling design, consisting of 8028 people aged 30 years and over and living in mainland Finland. The sampling frame was first regionally stratified to five university hospital regions. From each of these regions, 16 health care districts were sampled as clusters, yielding altogether 80 health care districts in the whole country. The 15 largest health centre districts were included in the sample, and the remaining 65 health centre districts were selected by systematic probability proportional to size sampling. From each of these 80 health centre districts, persons were selected by systematic sampling. Persons aged 80 years and over were oversampled by doubling the sampling fraction. For the 15 largest health centre districts that were all included, the sample sizes were proportional to population size. In the remaining 65 health care districts the sample sizes were equal within each university hospital region, so that the total number of persons drawn from a university hospital region was proportional to the corresponding population size (Aromaa and Koskinen 2004). The study was approved by the ethics committee of the National Public Health Institute and the Hospital District of Helsinki and Uusimaa.

The survey consisted of the following parts:

1. Interview at home (or institution),
2. Health examination at the local health centre,
3. Several self-report questionnaires,
4. Interview and a health examination of non-respondents at home (or institution),
5. Telephone interview and/or a mail questionnaire of remaining non-respondents and,
6. Gathering of register information on the whole sample.

The interview was used to gather, among other things, basic background and sociodemographic information, information about health and illnesses as well as use of medicines, use of health services and health-related behaviour. The interviewers left a questionnaire (questionnaire 1) that participants were asked to bring with them to the health examination. The health examination included a thorough health and dental examination and several laboratory tests. It also contained a computer assisted mental health interview, the Munich version of the Composite International Diagnostic Interview (M-CIDI) (Wittchen and Pfister 1997; Wittchen, Lachner et al. 1998). After the health examination, the participants received further questionnaires (questionnaires 2 and 3) to be filled in directly or later and mailed to the National Public Health Institute. Reminders were sent to non-respondents. All questionnaires and the interviews are available at www.ktl.fi/terveys2000 and the methods are described in detail in Heistaro 2005.

4.1.2 Sociodemographic factors

The age and gender were available for all 8028 people sampled from register data. In the analyses, age was classified into six groups, 30-44, 45-54, 55-64, 65-74, 75-84 and 85 years and over, as there is no reason to presume the relationship between HRQoL and age to be linear. Other sociodemographic information was obtained at the home interview. Education was classified as basic, secondary or higher. Those who had completed vocational school, or who had passed the matriculation examination were classified as having secondary education. Degrees from higher vocational institutions, polytechnics and universities were classified as higher education. Self-reported family income was adjusted for family size using the OECD formula (OECD 1982) in which the first adult of a family is weighted as 1.0, other adults as 0.7, and children less than 18 years old as 0.5. Marital status was classified to those married or cohabiting, and others.

4.1.3 Somatic conditions

Participants were asked in the home interview whether they had ever been diagnosed by a physician with any of 43 specified diseases and conditions. If they answered yes, additional questions about time of diagnosis, treatments, visits to a physician and condition-specific issues were asked. Twenty-five somatic conditions were included in this study, based on their public health importance, chronic nature and the reliability of self-report diagnostic classification. The disorders included and their prevalence is reported in Table 2. Problems with back or neck and disturbing allergy were considered only if the participant had visited a doctor for this condition during the past 12 months. Only unoperated cataract was considered. For Study II, the conditions were categorised to nine clinically relevant and mostly ICD-10 based categories (Table 2.)

Table 2. Categorisation of conditions included in the study, their prevalence, proportion of women and mean age[1].

Groups of conditions (Study II)	Conditions (Study I)	Prevalence, %	Proportion women, %	Age, mean
Cardiovascular disorders	Coronary heart disease	8.3	47	70
	Heart failure	4.5	63	73
	Hypertension	30.9	53	59
Musculoskeletal disorders	Arthrosis of hip or knee	12.6	60	64
	Back problems	7.5	54	52
	Neck problems	5.1	67	53
	Other arthrosis	8.9	60	60
	Rheumatoid arthritis	3.2	66	65
Neurological disorders	Migraine	7.6	76	51
	Parkinson's disease	0.5	46	72
	Stroke	2.8	48	70
Problems of hearing	Loss of hearing	16.0	41	61
	Tinnitus	12.0	43	60
Psychiatric disorders	Alcohol use disorders	4.2	18	45
	Anxiety disorders	4.2	59	49
	Depressive disorders	6.5	66	49
	Psychosis	1.3	61	51
Pulmonary disorders	Chronic obstructive pulmonary disease	5.9	51	60
	Asthma	8.8	62	57
Problems of vision	Cataract	3.3	73	72
	Glaucoma	3.1	74	69
	Macular degeneration	3.3	66	71
Other disorders	Cancer	4.9	70	66
	Diabetes	5.9	53	64
	Inflammatory bowel disease	2.2	64	58
	Psoriasis	2.3	42	54
	Urinary incontinence	13.0	77	64
	Disturbing allergy	5.1	65	49
Disability caused by accident	Disability caused by accident	13.5	36	57

[1] Prevalence, age and proportion women are weighted to represent the Finnish population aged 30 and over

4.1.4 Psychiatric diagnostics

At the health examination the participants attended a structured mental health interview, which used the Finnish translation of the German computerised version of the Composite International Diagnostic Interview (M-CIDI) (Wittchen and Pfister 1997; Wittchen, Lachner et al. 1998). It was used to assess 12-month prevalence of depressive, anxiety or alcohol use disorders and lifetime prevalence of alcohol dependence (Pirkola, Isometsä et al. 2005) using DSM-IV (1994) criteria. This study includes depressive disorders (major depressive disorder (MDD), dysthymia) alcohol dependence and abuse, and anxiety disorders (agoraphobia, generalized anxiety disorder (GAD), panic disorder (PD) and social phobia (SP)). Psychosis was diagnosed, if the participant self-reported suffering from psychosis or the physician conducting the health examination considered the participant had a probable psychotic disorder.

4.1.5 Alcohol consumption

Alcohol use was measured in questionnaire 1 with questions in which the participants were asked to report their average weekly consumption of 1) beer, cider and long drinks, 2) spirits and 3) wine during the past month. The results were converted into grams of alcohol per week. The intention was to group participants into equally sized deciles based on their alcohol use. However, as there were more than 10% of abstainers and the scale was not fully continuous in the lowest end, it was impossible to achieve 10 equally sized groups. As women belonging to the highestdrinking decile still drank relatively little (mean 214 g/week, little over 2 drinks / day) the highest decile was divided in two groups. In addition, the participants were asked whether they a) have been teetotal for their entire life (or tasted alcohol maximum ten times) b) have used alcohol earlier, but then quit, or c) use alcohol currently. The frequency of drinking during the last year was assessed.

Abstainers, i.e. those who had not drunk during the past month, were first classified into two groups: "former drinkers", including abstainers who said they have used alcohol earlier but since quit and those who received a lifetime diagnosis of an alcohol use disorder. The rest were classified as "other abstainers". In order to investigate the effect of the length of the abstaining period, former drinkers and other abstainers were categorized into six groups with regards to a) alcohol-related diagnoses and b) having drank alcohol during the last year, but not the last month.

Study IV excluded people aged 65 or over, as alcohol can be assumed to affect the elderly and working aged populations differently. Furthermore, due to mortality and the common decline in alcohol consumption with age, old people become a rather selected group especially regarding heavy alcohol consumption and health. Pregnant women (N=31) were also excluded.

4.1.6 Health-related quality of life: The 15D and the EQ-5D

The 15D measure includes 15 questions, tapping 15 dimensions of HRQoL: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity (Sintonen 1994; Sintonen 1995; Sintonen 2001). Each dimension has five grades of severity, and so the 15D defines a vast number of health states. The 15D can be used as a single index score measure or as a profile. In this study, to calculate the 15D utility index, we have used valuations elicited from the Finnish population using the multi-attribute utility method (Sintonen 1995). The 15D values range between 1 (full health) and 0 (dead). Changes of over 0.02 - 0.03 points on the 15D scale are considered minimally clinically important (Sintonen 1994; Sintonen 2001), as people are likely to consider themselves feeling better or worse after changes of this magnitude. Study III also included a 15D profile, which shows how individual dimensions of HRQoL are affected. In calculating the profile, the above mentioned preference-based scoring system was used to scale all dimensions between 0 and 1, thus making the losses on different domains comparable. The 15D compares favourably with similar instruments in most of the important properties (Sintonen 1994; Sintonen 1995; Hawthorne, Richardson et al. 2001; Sintonen 2001; Stavem, Bjornaes et al. 2001). The 15D was included in questionnaire 3. Subjects with 12 or more completed 15D dimensions were included, and missing values were predicted with linear regression analysis using the other 15D dimensions, with age and gender as independent variables, as recommended by the author of the measure (Sintonen 1994). Six percent of respondents had 1-3 dimensions imputed; of these, 85% had only one dimension missing. The most common missing dimension was sexual functioning.

The EuroQoL EQ-5D measure (1990; Brooks 1996; Rabin and de Charro 2001) includes five questions, tapping five dimensions of HRQoL: mobility, self-care, usual activities, pain or discomfort and anxiety or depression. Each dimension is divided into three categories of severity: no, moderate or extreme problems. Thus the EQ-5D defines 243 different health states. It too can be converted into a single index score representing health utilities. This study used the most commonly used tariff, the UK time-trade-off (TTO) values to generate the EQ-5D utility index (Dolan, Gudex et al. 1996; Dolan 1997; Kind, Hardman et al. 1999). The EQ-5D TTO-index values range from 1 (full health) to -0.59 (0=being dead). There is no unequivocally agreed threshold for minimally clinically important change on the EQ-5D, but thresholds averaging 0.07 points have been observed (Walters and Brazier 2005). The EQ-5D is among the most evaluated of HRQoL measures (Garratt, Schmidt et al. 2002). The EQ-5D and the 15D have been compared in a few studies, and demonstrated good test-retest reliability and construct validity (Hawthorne, Richardson et al. 2001; Stavem, Bjornaes et al. 2001). The EQ-5D was included in questionnaire 1, and only respondents fully completing the instrument were included in the analysis; there is no established way to reliably impute missing EQ-5D values.

4.1.7 Subjective quality of life, health and mental well-being

Study IV also included measurements of global, subjective quality of life, self-rated health (SRH) and mental well-being. Subjective QoL was measured by asking the respondents to rate their current quality of life as a whole, for the last 30 days, on a scale from 0 (worst possible quality of life) to 10 (best possible quality of life). Self-rated general health was measured similarly, asking the participants about their current health status with a 10-point Likert scale anchored at worst possible health (0) and best possible health (10). Mental well-being was measured with the 12-question version of the General Health Questionnaire (GHQ-12)(Goldberg 1972; Goldberg, Gater et al. 1997). The scale has a range between 0 and 12, with higher points indicating higher mental distress. GHQ is also widely used as a screening instrument for mental disorders. Ideal cut-off points for identifying mental disorders vary between populations, but generally fall between >1 and >3 positive answers (Goldberg, Gater et al. 1997; Schmitz, Kruse et al. 1999; Holi, Marttunen et al. 2003). Subjects with 9 or more completed GHQ-12 questions were included in the analysis, and the GHQ sum score was calculated weighted to number of missing responses.

4.2 Response rates

The original sample comprised 8028 persons, of whom 7977 were alive at the beginning of the study. 6986 (88%) people were interviewed in their home or in an institution, and 6770 (85%) participated in either the health examination proper, or the home health examination. 6681 (83%) of participants completed either the 15D or EQ-5D. 77% completed the 15D and 77% completed the EQ-5D. Non-respondents were significantly older (average 58.8 years) than those who responded to either of the HRQoL questionnaires (average 52.3 years for EQ-5D, 52.5 years for 15D, $P<0.001$). GHQ-12 was available for 84.8%, SRH for 85.1% and QoL for 85.1% of the sample.

4.3 Statistical methods

All statistical analyses have been conducted using STATA 8 for Windows statistical software (StataCorp 2003). Analyses used the survey procedures of STATA and took into account the two-stage sampling design, oversampling of old people and non-response using weights calibrated in Statistics Finland (Heistaro 2005). This was done to ensure the prevalence of conditions and other rates given in this study match the true prevalence of disorders in the Finnish population as closely as possible. Similarly, the regression analyses included as many participants as possible. In practice this means that the prevalence of disorders presented in the tables of this study can not always be directly calculated from the number of cases presented. Also, as the different analyses included in this study use data from slightly different combinations of instruments, the number of participants in different analyses varies slightly.

4.3.1 HRQoL, censoring and corner solutions

This study aimed to estimate the HRQoL losses associated with common chronic somatic conditions, psychiatric disorders and alcohol consumption patterns. In addition to presenting unadjusted data and background characteristics, regression modelling was used to take into account sociodemographic factors and chronic conditions, as considered appropriate in each study. Studies I and II adjusted for age, gender, education, income, marital status and chronic conditions, as the aim was to estimate the individual contribution of each condition or disorder. Due to the large number of conditions included, interactions between variables were not explored. Study III included four different regression models that added somatic and psychiatric conditions stepwise, in order to investigate the importance of somatic and psychiatric comorbidity to the HRQoL impact of psychiatric conditions. Study IV did not adjust for somatic conditions, as it was hypothesised that there is a complex interaction between alcohol consumption, abstaining, age and somatic and psychiatric disorders (alcohol consumption causes illness, and illness influences alcohol consumption). Furthermore, Study IV investigated gender separately using different categories of alcohol consumption, as the patterns of consumption and effects of alcohol vary between genders.

All utility-based HRQoL measures are anchored to death (0) and perfect health (1). However, the measures differ greatly in the actual distribution of the scores. In general population studies, most HRQoL instruments have a large proportion of respondents reporting perfect health, commonly interpreted as right-censored data. In Health 2000 data, this rate is 15% for 15D and 47% for EQ-5D. Thus we have used a Tobit regression model for the regression analyses of HRQoL data (Tobin 1958; Austin, Escobar et al. 2000). EQ-5D TTO index is statistically far more problematic than the 15D, as in addition to the high rate of censoring the scale is not continuous but includes a gap between 1 and 0.88

However, this choice is not entirely unproblematic. The rate of people receiving perfect scores (1) on HRQoL is commonly seen as censoring rate, i.e. it is assumed that there is true variation of HRQoL above 1 but this is not captured by the measures. This is theoretically acceptable on the one hand, because it is unlikely that the health of a large group would be exactly similar, and that the health of this population could not be improved. On the other hand however, it is also possible that people will at a certain point simply stop trading length of life or possibility of death for improved health; this would be more appropriately called a "corner solution" rather than "censoring" (Wooldridge 2002). In both cases, however, a further problem is that Tobit regression, like ordinary linear regression, is based on normal distribution of residuals.

Another alternative proposed for censored data is the censored least absolute deviations (CLAD) model (Powell 1984; Austin 2002). CLAD models, incorporating weights and clustering, can be estimated in STATA using a user-written macro. The question whether to use Tobit or CLAD models cannot be answered purely on statistical grounds, however, because the models estimate different things (Wooldridge 2002). The Tobit (and ordinary

least squares) models estimate the changes of the mean, whereas CLAD estimates changes of the median. This presents a problem, when trying to estimate QALYs, because they should reflect the strength of each individual's preferences. It can be argued (Dolan 2000; Clarke, Gray et al. 2002), but we have assumed that the use of the mean is more appropriate in the QALY context.

Equally important is to decide which marginal effects one is interested in. Four different marginal effects can be estimated for the Tobit model. The beta coefficient of the Tobit describes the changes of the latent (unobserved) variable (e.g. the true HRQoL which expands over 1). Other possible estimates are changes on the unconditional expected value of the dependent variable (e.g. the expected changes on the measured HRQoL scores, as done in this study), changes on probability of being uncensored and changes in the conditional expected value of the dependent variable (McDonald and Moffitt 1980; Cong 2000).

In practise, many surveys still use ordinary least squares (OLS) regression even with EQ-5D (Burström, Johannesson et al. 2001; Burström, Johannesson et al. 2001; Lubetkin, Jia et al. 2005). With the high censoring rates of EQ-5D, this can cause significant bias (Austin, Escobar et al. 2000). In Study I CLAD and Tobit models were compared for analysing HRQoL data. It was concluded that marginal effects after Tobit models can be used when QALY estimates are needed for both 15D and EQ-5D, but that the 15D estimates are likely to be more reliable than the EQ-5D estimates. Thus marginal effects after Tobit regression have been used in Studies II-IV, emphasising 15D results.

5. Results

5.1 The individual-level HRQoL impact of major chronic conditions

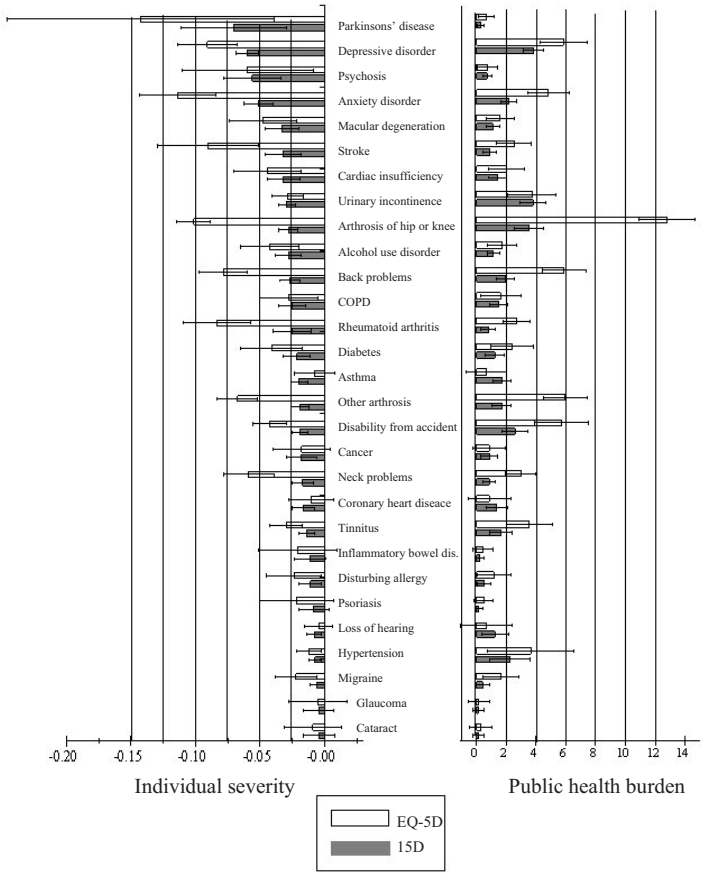
This study investigated how 29 common chronic conditions associated with individual-level HRQoL losses. This was done separately for each condition (Study I), and by diagnostic categories and age-groups (Study II).

Chronic conditions were found to be common: 76% of participants had at least one of the conditions included in the study, and 55% had two or more conditions. Number of conditions increased with age from average of 1.1 conditions at ages between 30 and 45 years to an average 4.0 conditions at ages 75 or over. Prevalence of individual conditions is reported in Table 2 and for groups of conditions in Table 3. The only group of conditions that did not increase in prevalence by age was psychiatric conditions.

Considering the unadjusted HRQoL scores reported, people with Parkinson's disease, heart failure, macular degeneration and stroke reported the lowest scores on both 15D and EQ-5D. When disorders were grouped and investigated by age-groups, people diagnosed with psychiatric disorders had the lowest HRQoL scores in all age-groups as measured by 15D. On EQ-5D, people with vision problems, psychiatric problems and musculoskeletal problems had the lowest EQ-5D scores at younger ages, whereas those with neurological disorders had the lowest scores in the oldest age-group.

Figure 1 shows the HRQoL loss associated with each condition on both measures, sorted by condition severity on 15D, when all background variables and other chronic conditions were adjusted for. In the fully controlled models, Parkinson's disease was still the most disabling condition on both measures. On 15D, depressive disorders, psychosis and anxiety disorders were the most severe conditions after Parkinson's. On EQ-5D, these were anxiety disorders, arthrosis of the hip and knee and depressive disorders. Only four of the 29 chronic conditions did not have a statistically significant ($p<0.05$) association with HRQoL on either 15D or EQ-5D.

Figure 1. Severity (HRQoL losses associated with chronic conditions, left) and public health burden (annual QALY losses associated with morbidity, per 1000 people, right). Adjusted for age, gender, education, income, marital status and other conditions, with 9



When investigating the conditions in groups (Study II) adjusting for background variables and other groups of conditions, psychiatric disorders were associated with the largest losses of HRQoL in all agegroups on 15D. On the EQ-5D, psychiatric and musculoskeletal disorders were associated with the largest impact on HRQoL up to 75 years of age, after which neurological disorders were more severe (Table 3).

Investigating the interactions between the severity of HRQoL impact for groups of conditions and age, only musculoskeletal and hearing problems displayed a statistically significant age-interaction on both measures. When individual conditions were investigated, only loss of hearing had statistically significant age interaction on both measures; loss of hearing had less impact at 65-74 years than at other ages.

Table 3. Prevalence of conditions. Marginal effects of conditions on health utility (SE), measured with 15D, by age-groups, adjusted for socioeconomic factors and other conditions. The results of the likelihood ratio test for age-condition interaction.

Condition	All (30- years)	30 - 44 years	45 - 54 years	55 - 64 years	65 - 74 years	75- years	Age-condition inter-action p-value
Number of chronic conditions	2.1	1.1	1.7	2.5	3.2	4.0	
Pulmonary disorders	12.8 %	8.4 %	10.9 %	14.2 %	20.2 %	18.6 %	
15D loss (SE)	-0.029 (0.003)***	-0.014 (0.005)**	-0.027 (0.007)***	-0.027 (0.008)***	-0.041 (0.009)***	-0.038 (0.011)***	0.047
Cardiovascular disorders	33.0 %	14.8 %	29.5 %	44.3 %	52.1 %	53.7 %	
15D loss (SE)	-0.020 (0.002)***	-0.006 (0.004)	-0.011 (0.004)**	-0.018 (0.004)***	-0.022 (0.006)***	-0.015 (0.010)	0.153
Musculoskeletal disorders	30.6 %	14.9 %	26.6 %	41.2 %	46.6 %	50.3 %	
15D loss (SE)	-0.036 (0.002)***	-0.022 (0.004)***	-0.038 (0.004)***	-0.036 (0.005)***	-0.032 (0.007)***	-0.019 (0.009)*	0.013
Hearing problems	22.5 %	10.1 %	18.3 %	29.7 %	35.6 %	42.2 %	
15D loss (SE)	-0.018 (0.002)***	-0.010 (0.005)*	-0.012 (0.004)**	-0.014 (0.005)**	0.004 (0.006)	-0.020 (0.008)*	0.027
Vision problems	8.3 %	0.7 %	3.0 %	7.5 %	18.5 %	32.7 %	
15D loss (SE)	-0.044 (0.005)***	-0.017 (0.011)	-0.035 (0.013)**	-0.025 (0.008)**	-0.023 (0.008)**	-0.029 (0.010)**	0.873
Psychiatric disorders	11.5 %	14.0 %	14.1 %	11.6 %	6.2 %	3.7 %	
15D loss (SE)	-0.048 (0.003)***	-0.051 (0.004)***	-0.063 (0.006)**	-0.047 (0.009)***	-0.059 (0.014)***	-0.054 (0.017)**	0.414
Neurological disorders	10.6 %	8.4 %	8.7 %	12.0 %	12.0 %	17.2 %	
15D loss (SE)	-0.016 (0.003)***	-0.014 (0.005)**	-0.005 (0.005)	-0.021 (0.008)**	-0.015 (0.010)	-0.035 (0.011)**	0.108
Disabilities by accident	13.5 %	9.5 %	12.3 %	16.2 %	16.6 %	20.5 %	
15D loss (SE)	-0.024 (0.004)***	-0.024 (0.005)***	-0.008 (0.006)	-0.019 (0.006)**	-0.025 (0.009)**	-0.041 (0.011)***	0.005
Other disorders	27.4 %	14.8 %	22.1 %	32.2 %	40.0 %	55.1 %	
15D loss (SE)	-0.030 (0.002)***	-0.017 (0.004)***	-0.022 (0.004)***	-0.032 (0.005)***	-0.026 (0.005)***	-0.032 (0.009)***	0.141

* p<0.05, ** p<0.01, *** p<0.001

5.2 The public health impact of chronic conditions

The public health impact of the 29 included chronic conditions was estimated by calculating the QALY losses associated with morbidity, separately for individual conditions and groups of conditions at different ages.

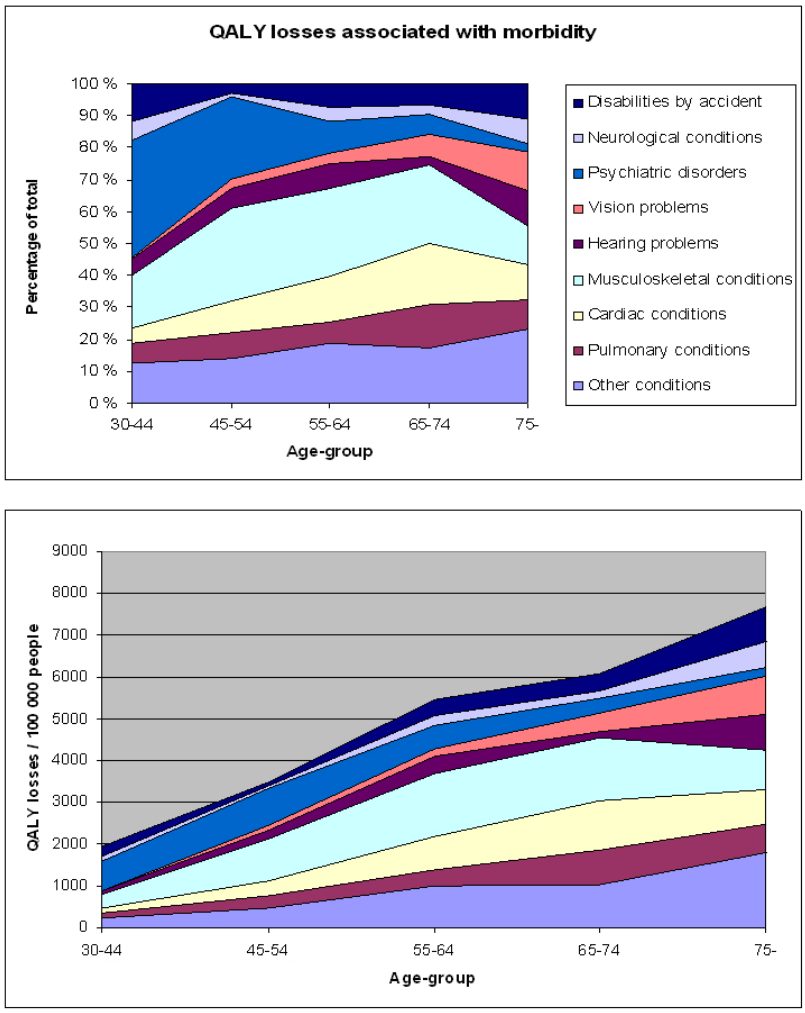
The QALY losses of individual conditions (Study I) are presented in Figure 1. Measured with 15D, the largest QALY losses were associated with depression, urinary incontinence and arthrosis of hip or knee. On EQ-5D, arthrosis of the hip and knee were associated with the largest loss of QALYs. Next, with practically equal impact came other arthrosis, back problems, depression and disabilities caused by accidents.

When the conditions were grouped (Study II, prevalence reported in table 3), musculoskeletal disorders were associated with 23% (15D) and 37% (EQ-5D) of the total annual QALY losses due to morbidity found in the study. Psychiatric disorders came second with 12% and 11% of the total, as measured with 15D and EQ-5D, respectively.

The impact of different groups of conditions on lost QALYs varied greatly by age. The absolute amount of lost QALYs per 100 000 persons on 15D and the relative proportions attributable to different conditions are presented in Figure 2. Psychiatric disorders were the largest cause of lost QALYs due to morbidity at ages under 45, representing 29% (EQ-5D) and 37% (15D) of the total for these ages. However, as the amount of QALYs lost associated with other disorders increased by age, psychiatric disorders were the only group of conditions where not only the relative but also the absolute amount of QALYs lost (per constant number of people) actually decreased in the oldest age-groups. Musculoskeletal disorders were associated with high loss of QALYs across all age groups, whereas the importance of vision problems increased dramatically with age.

In sum, although there were some statistically significant variations in the severity of conditions by age, the differences in prevalence were far greater and accounted for a majority of the differences in the public health impact of different conditions at different ages.

Figure 2. Relative and absolute QALY losses associated with morbidity, separately for age-groups and groups of conditions.



5.3 Ageing of the population and QALYs lost to chronic conditions

The Finnish population is ageing, so that according to official predictions the number of people aged over 64 will increase by around 70% between years 2005 and 2040, while the number of people aged over 30 will increase by 9% and the total population will grow only marginally.

The absolute yearly QALY losses associated with morbidity in Finland are presented in Figure 3 for 2005 population, and were predicted to years 2020 and 2040 using official predictions of Statistics Finland. If morbidity remains constant (i.e. the severity and prevalence of conditions by age remain similar) the absolute annual loss of QALYs due to morbidity will increase by 23% up to the year 2040 due to ageing of the population. The changes in relative importance of different conditions appear, however, modest.

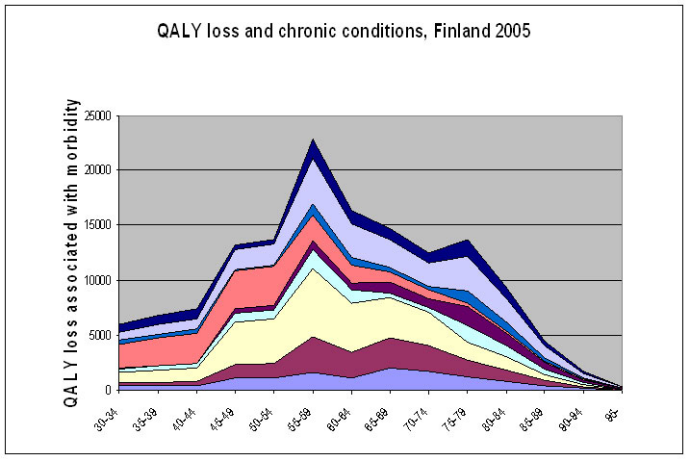
5.4 The HRQoL and QALY losses associated with depressive and anxiety disorders and alcohol dependence

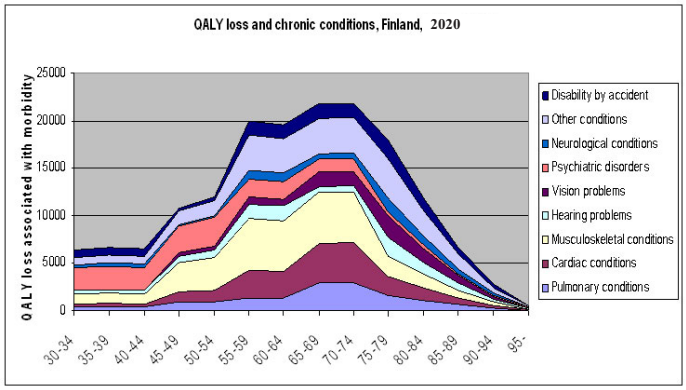
It was investigated how different depressive (major depressive disorder and dysthymia) and anxiety disorders (panic disorder, agoraphobia, social phobia and generalized anxiety disorder) and alcohol dependence associate with HRQoL at the individual and population levels. Furthermore, the effect of comorbidity between these psychiatric conditions and the dimensions of HRQoL that were affected was investigated. The prevalence of conditions, rates of comorbidity and unadjusted HRQoL scores are presented in Table 4.

The average unadjusted 15D (EQ-5D) score for the population was 0.91 (0.83), and 0.87 (0.72) for people with any psychiatric diagnosis. The lowest scores were reported by people with comorbid forms of dysthymia, GAD, agoraphobia and social phobia.

The magnitude of the HRQoL losses was further estimated with four different models. First, controlling for sociodemographic factors (age, gender, education, living arrangements and income), second, controlling for sociodemographics and somatic comorbidity and third, controlling for sociodemographics, somatic conditions and psychiatric comorbidity. Fourthly, pure forms of conditions were investigated separately, controlling for sociodemographics and somatic comorbidity. The results are presented in Figure 4 for 15D.

Figure 3. Absolute annual loss of QALYs associated with morbidity at different ages in Finland in 2005 and predictions for 2020 and 2040.





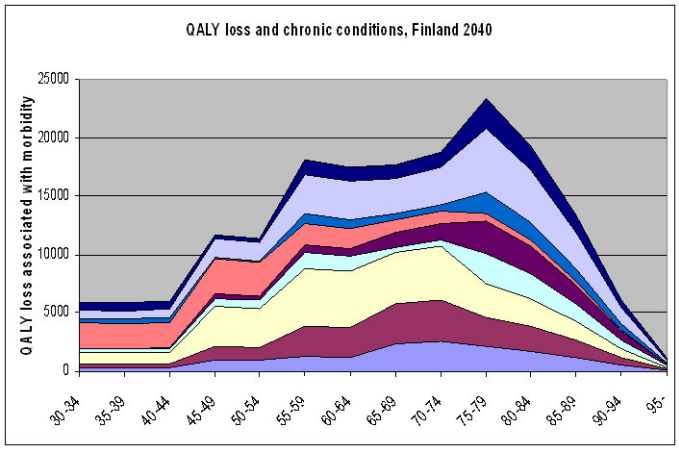
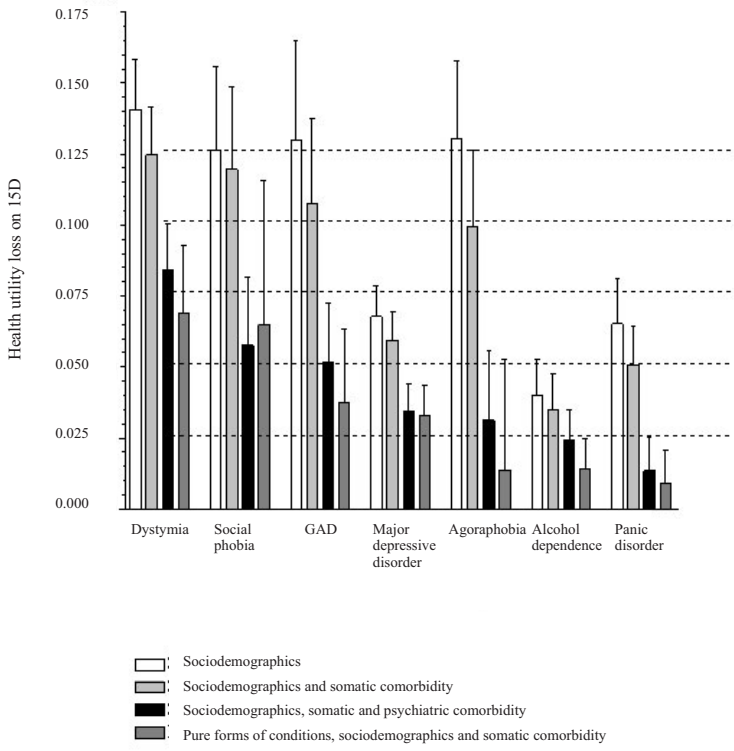


Table 4. Prevalence of psychiatric disorders, psychiatric comorbidity and unadjusted 15D and EQ-5D scores of respondents.

	Prevalence % (N)*	Proportion with psychiatric comorbidity	Mean 15D score (SE)	Mean EQ-5D score (SE)
Group of respondents				
Study population	- (6005)	12.2**	0.910 (0.001)	0.835 (0.003)
Disorder				
Any depressive disorder	6.5 (392)	39.2	0.840 (0.005)	0.729 (0.014)
Only depressive disorder	4.4 (272)	11.7	0.867 (0.006)	0.789 (0.013)
Any anxiety disorder	4.1 (242)	55.6	0.832 (0.007)	0.687 (0.018)
Only anxiety disorder	2.1 (127)	14.1	0.879 (0.008)	0.750 (0.021)
Alcohol dependence	3.9 (223)	23.3	0.893 (0.007)	0.829 (0.013)
Pure alcohol dependence	3.0 (173)	-	0.915 (0.006)	0.866 (0.012)
MDD	4.9 (298)	38.4	0.859 (0.006)	0.764 (0.014)
Pure MDD	3.1 (192)	-	0.889 (0.006)	0.833 (0.011)
Dysthymia	2.4 (147)	63.0	0.766 (0.009)	0.583 (0.024)
Pure dysthymia	0.9 (57)	-	0.810 (0.014)	0.687 (0.033)
Panic disorder	1.9 (114)	48.7	0.859 (0.009)	0.765 (0.022)
Pure panic disorder	1.1 (59)	-	0.908 (0.009)	0.821 (0.028)
Social phobia	1.0 (60)	77.1	0.801 (0.016)	0.659 (0.034)
Pure social phobia	0.2 (14)	-	0.891 (0.019)	0.729 (0.052)
Agoraphobia	1.0 (62)	84.3	0.781 (0.016)	0.622 (0.036)
Pure agoraphobia	0.2 (13)	-	0.818 (0.016)	0.636 (0.065)
GAD	1.3 (75)	68.3	0.783 (0.019)	0.589 (0.038)
Pure GAD	0.4 (24)	-	0.864 (0.018)	0.654 (0.046)

* Numbers are based on participants with complete M-CIDI information. Percentages are adjusted for the survey design.
** Proportion with any M-CIDI diagnosis.

Figure 4. HRQoL losses associated with psychiatric conditions, controlling for socioeconomic factors, somatic comorbidity, and psychiatric comorbidity and in pure forms of conditions, with 95% confidence intervals.

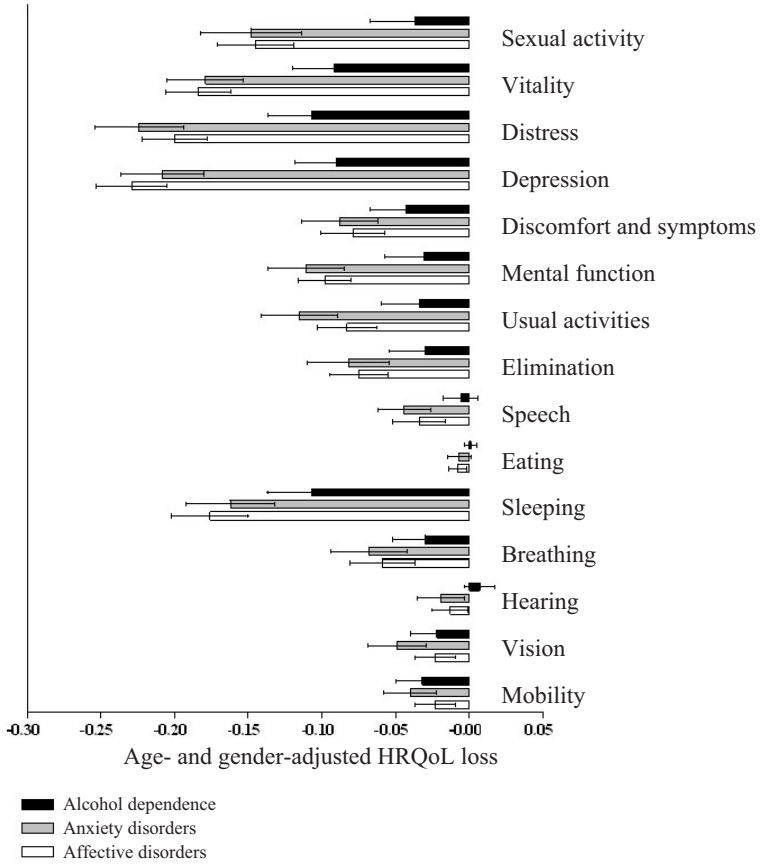


After controlling for sociodemographic variables and somatic conditions, the largest HRQoL losses were associated with dysthymia, agoraphobia, GAD and SP. Alcohol dependence had lowest impact, with panic disorder and MDD in between. Several disorders appeared more severe than the most severe somatic condition identified in Study I, Parkinson's disease, which was associated with a loss of -0.07 points on 15D.

Figure 4 also shows how adjusting for psychiatric comorbidity decreased the impact of individual disorders clearly. These decreases were relatively largest on anxiety disorders, especially agoraphobia, and smallest on alcohol dependence. After controlling for other psychiatric disorders, the largest losses of HRQoL were associated with dysthymia, SP and GAD. Considering pure forms of disorders, i.e. only those respondents receiving one M-CIDI diagnosis, the picture was similar: the largest HRQoL losses were found for dysthymia, SP and GAD

The 15D HRQoL profiles for alcohol dependence, anxiety- and depressive disorders are presented in Figure 5. The HRQoL profiles of alcohol dependence, anxiety- and depressive disorders were strikingly similar, only the magnitude of the effect of alcohol dependence is smaller on all dimensions. Equally, the dimensions of HRQoL most affected were the same for all disorders: depression, distress, vitality and sleeping. The decrease of HRQoL was widespread: a statistically significant decrease of HRQoL was found on most of the 15 dimensions covered by the 15D.

Figure 5. The 15D dimensions of HRQoL affected by alcohol dependence, depressive and anxiety disorders, controlling for age and gender.



5.5 Alcohol consumption, HRQoL and other measures of well-being

The association between HRQoL, subjective QoL, self-rated health (SRH), mental distress (GHQ-12) and alcohol consumption was investigated in Study IV. Alcohol consumption categories, aiming at equally sized deciles, are presented in Table 5. Women clearly consumed less alcohol and were more often abstainers than men.

Table 5. Alcohol consumption categories, for participants aged 30-64 years.

Men	N	Mean alcohol consumption g/week	Women	N	Mean alcohol consumption g/week
All men	2380	140	All Women	2603	41
0 g/wk 'Other abstainers'	270	0	0 g/wk 'Other abstainers'	735	0
0 g/wk 'Former drinkers'	147	0	0 g/wk 'Former drinkers'	90	0
1-7 g/wk	94	6	1-7 g/wk	237	5
8-24 g/wk	234	18	8-16 g/wk	281	13
25-49 g/wk	241	38	17-24 g/wk	221	21
50-73 g/wk	227	63	25-39 g/wk	273	33
74-105 g/wk	239	90	40-61 g/wk	248	50
106-146 g/wk	217	126	62-117 g/wk	263	83
147-228 g/wk	238	185	118-173 g/wk	130	142
229-348 g/wk	237	276	>173 g/wk	125	289
>348 g/wk	236	624			

The results of regression models investigating the association of alcohol consumption and the different outcomes are presented in figures 6 to 13, separately for both genders and each of the measures: 15D, subjective QoL, SRH and GHQ-12. Each graph presents two models, the first controlling for age, and the second controlling age, education, income and living arrangements.

For HRQoL, former drinkers scored worst on 15D on both raw scores and also when sociodemographic variables were controlled for. Only the most heavily drinking groups (women drinking an average of 289g (24 drinks) and men an average of 624g (52 drinks) per week) got statistically significantly lower 15D scores than abstainers who were not former drinkers. Moderate drinkers HRQoL scores were better than other abstainers, but these differences were clinically unimportant and also not statistically significant in the fully controlled models.

For other measures of well-being, women who were former drinkers scored worst on subjective QoL and SRH. Moderate drinkers had statistically significantly better SRH than other abstainers, but this was not observed on subjective QoL or GHQ-12. In contrast, the highest drinking groups had statistically significantly poorer subjective QoL and higher mental distress than other abstainers, but this was not found on SRH. For men, all three measures yielded similar results: former drinkers and the men who drank over 229g/week had statistically significantly worse scores than other abstainers. In the fully controlled models, other abstainers actually had the best scores, and there was no trend for a J-shaped association between well-being and drinking.

Figure 6. 15D Health-related quality of life differences (scale 0-1) associated with different alcohol consumption levels for women. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

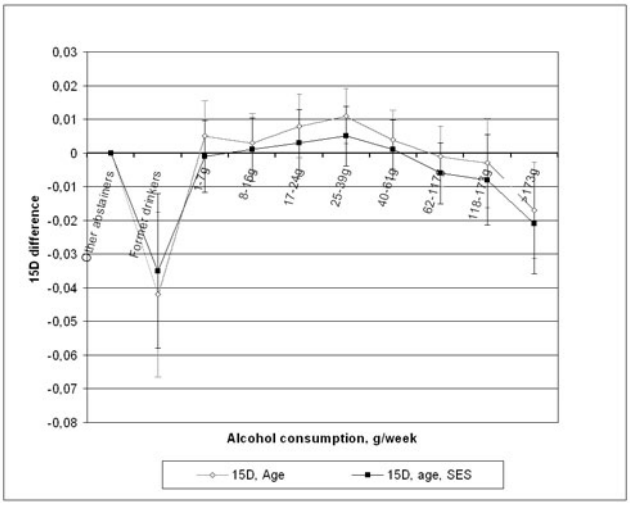


Figure 7. Subjective quality of life differences (scale 0-10) associated with different alcohol consumption levels for women. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

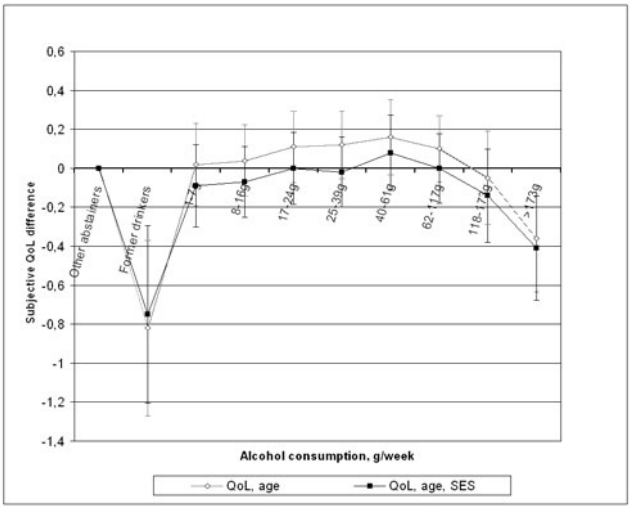


Figure 8. Self-rated health differences (scale 0-10) associated with different alcohol consumption levels for women. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

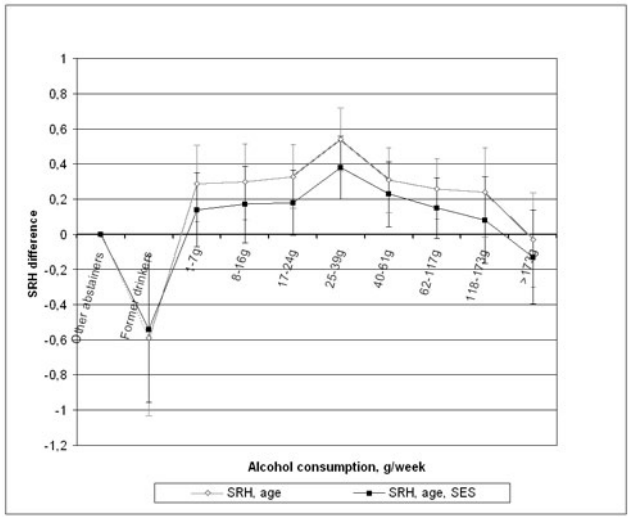


Figure 9. Mental distress differences (GHQ-12, scale 0-12 with higher scores indicating higher distress) associated with different alcohol consumption levels for women. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

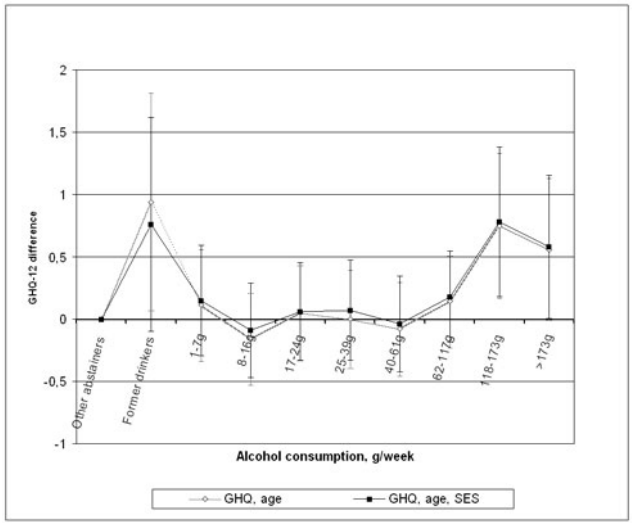


Figure 10. 15D Health-related quality of life differences (scale 0-1) associated with different alcohol consumption levels for men. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

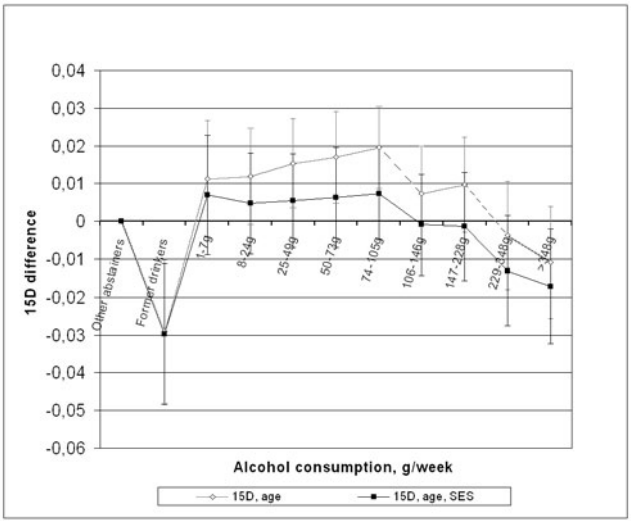


Figure 11. Subjective quality of life differences (scale 0-10) associated with different alcohol consumption levels for men. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

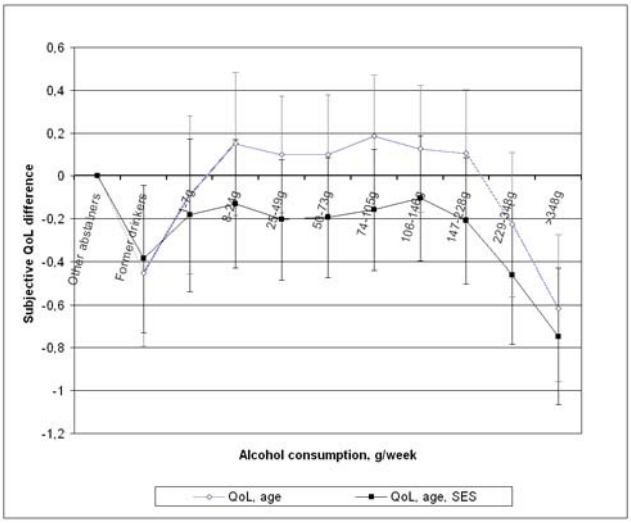


Figure 12. Self-rated health differences (scale 0-10) associated with different alcohol consumption levels for men. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.

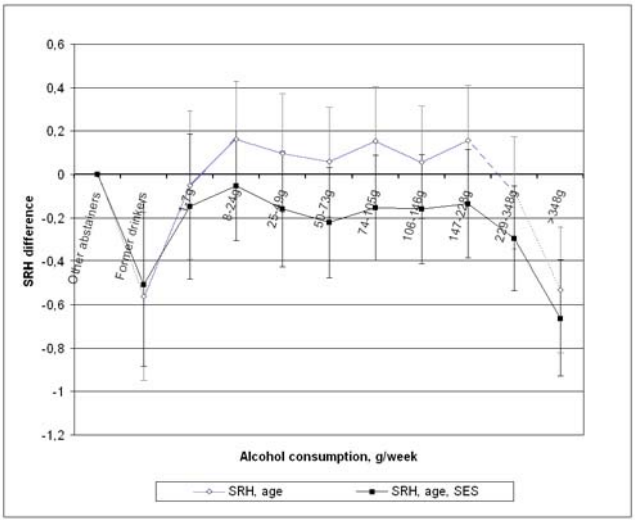
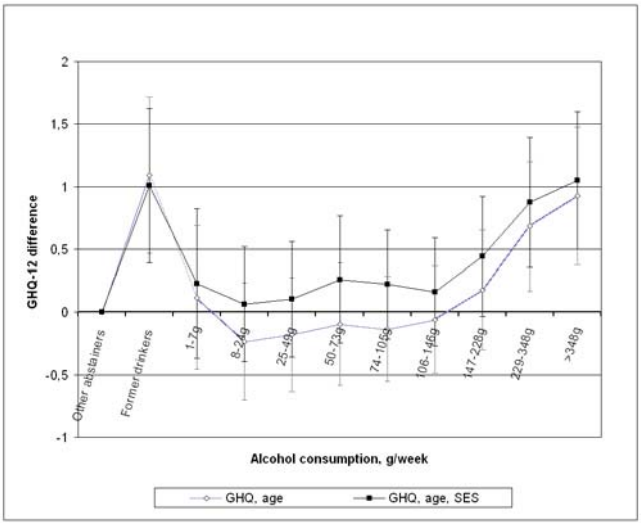


Figure 13. Mental distress differences (GHQ-12, scale 0-12 with higher scores indicating higher distress) associated with different alcohol consumption levels for men. Controlling for age, or age, education, income and living arrangements. 95% confidence intervals.



6. Discussion

The previous time that comparably valid and comprehensive health data was collected in Finland was the Mini-Finland Health Survey between 1978 and 1980. It did not include HRQoL measurement. Our study is based on the idea that knowledge of the HRQoL of the population and the loss of HRQoL associated with common chronic conditions is useful for rational health care and public health policy. This information may be used to identify interventions and public health programmes that could produce the largest public health improvements by showing how many QALYs could be saved by eliminating certain chronic conditions. Population-based reference values may also be used to gauge the extent to which populations in condition-specific cost-effectiveness studies or quality-improvement programmes are comparable to national averages (Sullivan, Lawrence et al. 2005).

Despite the recognised importance of measuring HRQoL in different diseases and in representative general population surveys, there are very few general population surveys using utility-based HRQoL measures and including several conditions. Despite the recognised public health burden of psychiatric disorders and the known challenges in diagnosing them in surveys, very few HRQoL surveys have included reliable diagnosis of psychiatric disorders. Despite the lack of a golden standard in HRQoL measurement and the wide variety of methods used to measure HRQoL, it has been rare to use more than one HRQoL measure simultaneously. This study aimed to overcome these weaknesses by measuring the utility-based HRQoL using two established instruments in a representative, general population sample of Finns using a thorough list of somatic conditions, reliable diagnostics of psychiatric disorders and alcohol consumption.

6.1 Principal findings

Investigating the HRQoL impact associated with major chronic conditions (Study 1) showed that at the individual level the most serious conditions on 15D were Parkinson's disease, anxiety disorders, depressive disorders and psychosis. EQ-5D emphasised the severity of musculoskeletal conditions, especially arthrosis. At the population level, the most severe conditions (largest losses of annual QALYs associated with morbidity on 15D) were depression, urinary incontinence and arthrosis of hip and knee.

Considering disorders in groups (Study II), the largest public health burden (loss of annual QALYs associated with morbidity on 15D) was found for musculoskeletal and psychiatric disorders, which were associated with 23% and 12% of the total disease burden identified in this study. Psychiatric disorders were associated with the largest health burden at ages 30 to 44, representing 37% of the total QALYs lost identified.

Investigating changes over age revealed that although the severity of some conditions varied with age, this variation was of little significance in comparison with the large variation in prevalence. The loss of HRQoL attributable to chronic conditions was found to increase fourfold when comparing people aged 30-44 to people aged over 75 years. The ageing of the Finnish population was estimated to lead to about 25% increase in the QALYs lost attributable to morbidity from chronic conditions up to year 2040, assuming unchanged morbidity patterns.

A detailed comparison of different anxiety, depressive and alcohol use disorders (Study III) showed that the commonly chronic conditions dysthymia, agoraphobia, GAD and SP were associated with the largest losses of HRQoL on individual level.

The HRQoL losses associated with dysthymia and GAD were larger than those associated with any of the somatic conditions investigated in Study I. This was partly explained by the finding that scores were statistically significantly reduced on most dimensions of HRQoL. Considering the public health impact of psychiatric conditions, the QALY loss due to morbidity associated with anxiety disorders was about a half of those associated with depressive disorders, and alcohol dependence was associated with about half of the burden of anxiety disorders.

Studying the association between alcohol consumption and HRQoL (Study IV) revealed that abstainers who were former drinkers got clearly worse scores in comparison to other abstainers, scoring worse than or equal to persons belonging to the decile that consumed most alcohol. This highlighted the importance of not investigating abstainers as one homogenous group, as this is likely to produce flawed estimates of the effects of abstaining on health. Considering moderate drinking, no statistically significant or clinically important associations between 15D and moderate alcohol consumption were observed after controlling for sociodemographic factors.

6.2 Comparison to previous studies

6.2.1 Comparison of severity of psychiatric and somatic conditions

This study identified Parkinson's disease, depressive disorder, psychosis and anxiety disorder as the four most severe disorders on 15D, i.e. showed that common psychiatric disorders have, on average, more severe effects on HRQoL than chronic somatic conditions. Study III showed that especially poor HRQoL was reported by people with dysthymia, GAD, SP and agoraphobia, which are typically chronic conditions (Yonkers, Bruce et al. 2003; Klein, Shankman et al. 2007). For example, the unadjusted HRQoL scores of patients suffering from dysthymia and GAD were below 0.8 on 15D and below 0.6 on EQ-5D - comparable to scores reported by people 20 years older and suffering from Parkinson's disease or heart failure.

Direct comparison to previous studies is however limited, as none of the representative general population surveys using utility-based HRQoL measures (presented in Table 1) included reliable diagnostics of several psychiatric disorders. Some surveys have relied on self-report (Fryback, Dasbach et al. 1993; Sullivan, Lawrence et al. 2005), used GHQ as measure of psychiatric distress (Burström, Johannesson et al. 2001) or depression screening questions (Johnson and Pickard 2000). Two studies used different sets of CIDI items to diagnose depression, but did not include any other psychiatric disorders (Wells and Sherbourne 1999; Manuel, Schultz et al. 2002).

However, the substantial impact of psychiatric disorders, particularly depression, in comparison to somatic conditions has been evident even when these varying measures were used. For example, a Swedish study that used GHQ-12 as an indicator for mental distress (with a low cut-off score of 1/2 and consequently high (21%) prevalence of distress) found that mental distress was associated with a lower adjusted EQ-5D score (-0.125) than any other of the seven included conditions (Burström, Johannesson et al. 2001). A US study using self-reported affective disorders (with a prevalence of 1%) found a smaller impact on EQ-5D (-0.07) (Sullivan, Lawrence et al. 2005), while another US study using QWB found -0.08 utilities for self-reported depression (prevalence of 4.6%) (Fryback, Dasbach et al. 1993). In both studies, depression was among the most severe of conditions, when at least age was adjusted for. Studies from Sweden and the USA, both using direct valuation techniques, found depression to be clearly the most severe condition, with twice the impact compared to the next severe of the circa 10 chronic conditions included. The utility losses associated with depression (measured with TTO) were almost identical in these studies: -0.09 in Sweden (Isacson, Bingefors et al. 2005) and -0.08 in the USA (Wells and Sherbourne 1999).

Considering the public health burden of diseases, the results of this study could be compared to studies using a related methodology, namely those measuring years lived with disability (YLD); this approach is used, for example, in the WHO burden of disease studies (Murray and Lopez 1996). In these studies, universal disability weights for each disorder are estimated by medical experts and combined with prevalence estimates. This contrasts with the method used in this study that measured the disability reported by the individuals directly. Also the included conditions always vary, so all comparisons must be treated as tentative. WHO has estimated that over 20 percent of all YLD globally can be attributed to psychiatric conditions (WHO 2001). In accordance with the results of this study, the WHO estimated psychiatric disorders to have the largest impact on YLD at ages under 60, although the proportion of disability attributed to psychiatric disorders by the WHO was even larger, around 50% at 30-44 years in Western Europe (WHO 2004), than in our study. The proportion of YLD explained by musculoskeletal disorders was much smaller in the WHO study or in a comparable Dutch study (Melse, Essink-Bot et al. 2000), and especially so at young ages and in comparison to our EQ-5D results. Also among Australians aged 35-54, psychiatric disorders accounted for over 30% and musculoskeletal disorders over 10% of YLD (Mathers, Vos et al. 1999). The Dutch study involved 48 conditions and listed the six largest causes of YLD as anxiety disorders, visual impairments, alcohol

dependence, depression, chronic lung diseases and hearing impairments (Melse, Essink-Bot et al. 2000). In general, the 15D results of this study were more in line with the WHO and other previous YLD results, than the EQ-5D results.

6.2.2 Comparing different psychiatric disorders

It is well established that affective and anxiety disorders cause significant distress, lowered HRQoL, and disability on several domains of life. The impact of alcohol use disorders generally appears smaller (Ormel, VonKorff et al. 1994; Bijl and Ravelli 2000; Alonso, Angermeyer et al. 2004; Sareen, Stein et al. 2005). The results of this study concur with this general picture: relatively comparable severity of anxiety and depressive disorders, and clearly smaller severity for alcohol use disorders. In a more detailed comparison, the typically chronic disorders dysthymia, agoraphobia, GAD and SP were found to be associated with larger losses of individual HRQoL than MDD, panic disorder or alcohol dependence.

Concerning previous studies, most mental health HRQoL surveys have used SF-36 (Ware and Sherbourne 1992) and related instruments. Only two of the studies reviewed in Table 1 included several of the psychiatric disorders diagnosed in the present study. A US survey (Sullivan, Lawrence et al. 2005) found that self-reported "affective disorders" were associated with larger health utility loss (loss of 0.07 on EQ-5D) than "anxiety, somatoform, dissociative or personality disorders" (-0.04). "Alcohol-related disorders" did not have a statistically significant association with the EQ-5D. A Swedish postal survey (Isacson, Bingefors et al. 2005) came to identical conclusions using a TTO exercise: 0.09 lost utilities for depression, and 0.045 lost for anxiety. The latter study controlled for the other conditions, whereas the former controlled for the number of conditions. A large US study of managed care patients (Wells and Sherbourne 1999) using both SG and TTO methods found that after adjustment for somatic conditions and socioeconomic variables, probable 12-month depression was associated with loss of 0.079 health utilities on TTO and 0.036 on SG. The results are well in line with our findings for depression (-0.09 for EQ-5D and -0.06 for 15D). Equally in line with the findings of this study was the US finding that dysthymia alone was clearly more severe (-0.08 on TTO) than MDD alone (-0.05). However, in contrast to US results, this study found anxiety disorders to be more severe than or equal to depression (-0.11 on EQ-5D, -0.05 on 15D). This difference may be due to differences in diagnostics: the present study used structured diagnostic interview, whereas the two other studies were based on self-report which is mirrored in widely varying prevalence of conditions. More generally, this highlights the importance of using structured diagnostic methods when estimating the burden of psychiatric disorders.

6.2.3 Alcohol consumption

Abstainers who were former drinkers were found to be quite different from other abstainers. Former drinkers got worse scores on all measures used, and the HRQoL scores of former drinkers were statistically significantly and clinically importantly below other abstainers. Positive associations between moderate alcohol use and SRH were observed for women, but this was not found for other measures, or for men, when sociodemographic variables were controlled for. Although there was a trend for improved HRQoL for moderate drinkers, this was neither statistically significant nor clinically important. Heavy drinkers showed a clear trend for worse health and well-being in comparison to moderate drinkers, although not all comparisons were statistically significant. Still, the negative impacts on HRQoL associated with heavy drinking could be considered relatively small, as it was below the 0.03 level of minimal clinical importance, and clearly lower than that found for common psychiatric conditions (as discussed above).

The author is not aware of previous surveys investigating alcohol consumption and utility-based HRQoL in the general population, and even clinical studies using utility-based HRQoL measures appear rare; a recent review on quality of life and alcoholism found 36 studies using 12 different QoL-related measures, but only one clinical study examined health utility (Donovan, Mattson et al. 2005). Clinical studies report far worse results for alcohol users than population studies (Foster, Powell et al. 1999; Foster, Peters et al. 2002) and can not be used to estimate average population level impact of alcohol use. A cohort study investigating 31-year old Finns included alcohol consumption and the 15D score; increasing alcohol consumption was associated with lower 15D score, but no J-shaped association was found (Häkkinen, Järvelin et al. 2006). Comparisons to surveys using non-utility HRQoL instruments (typically the SF-36) can be made, albeit with caution. Some studies using SF-36 have found former drinkers to score worse than other abstainers and moderate drinkers better than abstainers (Saito, Okamura et al. 2005; Stranges, Notaro et al. 2006) but there are also opposing results (van Dijk, Toet et al. 2004). The differences in results may be due to differing populations, response rates and classification of abstainers. Interestingly, however, none of these surveys found heavy drinkers to have lowered HRQoL as did this study.

Considering other measures than HRQoL, the improved health and well-being of moderate drinkers has been reported on several other instruments. A recent review on moderate drinking, mental health and quality of life (El-Guebaly 2007) identified five surveys investigating self-rated health and three investigating general mental health. Most of these observed beneficial effects associated with moderate drinking. Although most did not control for former drinkers (San Jose, van de Mheen et al. 1999; Guallar-Castillon, Rodriguez-Artalejo et al. 2001; Wang, Smith et al. 2006), some did and still found moderate drinkers to have better SRH than abstainers (Poikolainen, Vartiainen et al. 1996; Power, Rodgers et al. 1998; French and Zavala 2007). Interestingly, only the previous Finnish study (Poikolainen, Vartiainen et al. 1996) found former drinkers to be different

from other abstainers. Of the studies that have investigated life satisfaction (LS), a related concept to subjective QoL, or used GHQ (Hingson, Scotch et al. 1981; Roberts, Brunner et al. 1995; Koivumaa-Honkanen, Honkanen et al. 2000) most found moderate drinkers to have better well-being. However, this association mostly disappeared if sociodemographic factors were controlled for, and none of these studies separated former drinkers from other abstainers.

Although not statistically significant, this study still revealed a J-shaped trend suggesting better HRQoL for moderate drinkers in comparison to abstainers and heavy drinkers. However, the magnitude of improved HRQoL found for moderate alcohol users in this study could be considered negligible, as the highest point-estimate was 0.007 on 15D, clearly below the minimum limit for clinical importance, 0.03. The most consistent results supporting J-shaped benefits for moderate drinkers come from mortality studies (Gmel, Gutjahr et al. 2003; Di Castelnuovo, Costanzo et al. 2006; Rimm and Moats 2007) and those investigating a dichotomous measure or SRH (Poikolainen, Vartiainen et al. 1996; French and Zavala 2007). However, it is possible that although odds of poor SRH or premature death are in a J-shaped relation to alcohol consumption, the HRQoL gains of moderate alcohol consumption are clinically insignificant. Theoretically, this would not be surprising, given that the health benefits of moderate alcohol consumption appear related to cardiovascular diseases (CVD) (Rimm and Moats 2007). The health burden of CVD consists more of premature mortality and less of functional limitations and loss of HRQoL during lifetime (Manuel, Schultz et al. 2002). For example, people may be aware of having health problems like poor lipid profile, but this would not be expected to greatly influence the experienced HRQoL as long as there are no functional limitations. Thus, it is possible that the positive health effects of alcohol that appear via CVD may not be fully captured by HRQoL measurement. This suggests that mortality may be a sufficient metric for capturing most of the possible health impact of moderate alcohol use.

6.2.4 Age and the HRQoL impact of conditions

Both age and chronic conditions decrease HRQoL (Fryback, Dasbach et al. 1993; Alonso, Ferrer et al. 2004). The physical components of HRQoL are more strongly related to age and somatic conditions than the mental health components; some studies have even found mental components of HRQoL to improve with age (Singer, Hopman et al. 1999; Michelson, Bolund et al. 2000; Sprangers, de Regt et al. 2000). Positive associations between disease duration and mental health have also been observed (Singer, Hopman et al. 1999). Such findings have been interpreted to suggest that a psychological adjustment process enables people to maintain positive mental health despite physical disabilities due to somatic conditions and old age. As was also apparent also in this study, chronic somatic conditions typically affect older people, whereas common mental disorders appear at much younger age. This highlights the importance of adjusting for age when comparing the HRQoL losses of psychiatric disorders to most somatic disorders. For example, a Canadian study including 20 chronic conditions noted that depression was the only condition where age-adjusted HUI scores were lower than raw scores (Manuel, Schultz et al. 2002).

Previous studies have shown conflicting results regarding whether the individual severity of conditions on HRQoL varies by age (Fryback, Dasbach et al. 1993; Schultz and Kopec 2003). This study helps explain these differing results, because although some statistically significant differences in the severity of conditions at different ages were found, these were very small in comparison to the differences in prevalence. An overwhelming majority of differences in lost QALYs associated with morbidity at different ages was due to varying prevalence of conditions. Thus, little support was found for significant, individual adaptive processes that would cause the same conditions to have different impact on HRQoL at different ages. However, it is of course possible that the decline in prevalence of psychiatric disorders by age is due to these hypothesized psychological or social processes that also increase mental well-being and psychological components of HRQoL with age, relative to physical components.

6.3 Strengths and weaknesses

6.3.1 The survey

The most important strength of this study is that it reliably estimated the burden of the major chronic conditions as they occur in the population. This is an advantage over the YLD/DALY method, which estimates the disability weights and prevalence of conditions separately. In the HRQoL used in this study method, changes in prevalence due to variations in diagnostic threshold should at least partly be compensated by changes in measured severity, which can be important especially for psychiatric disorders. A representative, population based sample is necessary in order to estimate the true public health burden of disorders. Most HRQoL studies are based on clinical or otherwise selected samples, which make the results difficult to generalize. This study had a large sample including people living in institutions, oversampling of old people and high response rate yielding results that are representative of the Finnish population.

A thorough list of somatic conditions was included and, to the author’s knowledge, Health 2000 was the first survey to include reliably diagnosed psychiatric conditions and two different utility-based HRQoL measures. Psychiatric disorders can not be reliably diagnosed with questionnaires used in most previous surveys, which has led to either varying prevalence estimates or exclusion of psychiatric disorders in previous studies. Reliable diagnostics of psychiatric conditions is necessary in order to inform health policy and medical decision making: decisions can not be made from how many people report "anxiety" or "feeling depressed", but should be based on clearly defined syndromes that can ideally be treated with evidence-based methods. Using reliable diagnosis of alcohol use disorders was also necessary for identifying those abstainers with previous alcohol problems.

However, all chronic conditions could obviously not be included, and including only conditions that, based on participants' self-report, had been diagnosed by a physician may have led to underdiagnosis. Especially worth noticing is that Alzheimer's disease was not included, although it has previously been found to greatly impact on HRQoL (Schultz and Kopec 2003); Alzheimer's can not be reliably diagnosed or its impact on HRQoL reliably estimated using self-report. Also many important psychiatric disorders were not included due to practical reasons. This study protocol was long and rather demanding for the participants, so people with the most severe disorders were likely to drop out. Although the sample was relatively large, some conditions were rather rare in some age groups, leading to decreased statistical power. Considering this, the fact that most chronic conditions were statistically significantly associated with lowered HRQoL in most age groups suggests good construct validity of the HRQoL measures. A special case is psychosis, which can not be reliably diagnosed even with the CIDI interview method (Regier, Kaelber et al. 1998), so this study included psychoses if they were self-reported, or the physician conducting the health examination considered the participant to have a probable psychotic disorder. This method later showed to have good specificity but poor sensitivity (Perälä, Suvisaari et al. 2007), meaning that the public health impact of psychosis (Study I) and the group of mental disorders (Study II) are known to be underestimations. However, not all somatic conditions could be included either, but the study concentrates on the most common, chronic conditions.

A general limitation of the study is that the survey data were cross-sectional, so no firm conclusions about causality can be drawn; further longitudinal studies are warranted.

6.3.2 HRQoL measurement

There are two specific issues where the challenges of psychiatric epidemiology and HRQoL measurement meet: first, mental disorders may distort the way people report their HRQoL, and second, the descriptive diagnostic categorizations used in psychiatry may lead to measurement redundancy. Cognitive, affective or psychotic symptoms may distort the way the person perceives his/her HRQoL. The likelihood of this is may vary from one disorder to another, and according to disorder severity at the individual level (Katschnig, Freeman et al. 2006). If the HRQoL instruments and the diagnostic classification have similar domains this can lead to measurement redundancy. For example, both 15D and EQ-5D have dimensions with considerable overlap with diagnostic criteria of anxiety and depressive disorders. So, because feelings of anxiety and depression are a part of HRQoL as defined by these measures, it is not surprising that anxiety and depressive disorders influence HRQoL. However, this does not make the impact less real, nor does it discredit the main focus of this study: comparing the magnitude of the impact of different conditions on utility-based HRQoL. Furthermore, using the main alternative to HRQoL and QALYs - DALYs, i.e. disability-adjusted life years with expert-derived preference weights for diagnoses would also have been very problematic. This is especially true in psychiatry where, as this study also shows, diagnostic groups appear to hide the fundamental individual-level variation in the severity of the disorders.

A strength of the Health 2000 survey is that it included two different HRQoL instruments, the EQ-5D and the 15D. This permits a more valid estimation of health utility loss associated with different disorders because, as previous studies and this study also showed, different HRQoL measures can produce somewhat different results despite being utility-based. In particular the EQ-5D seems to differ from most other instruments in that it has a higher ceiling rate, longer scale and less continuous score distributions than other measures (Tengs and Wallace 2000; Franks, Hanmer et al. 2006). Thus, EQ-5D is problematic in (at least) general population studies, despite being one of the most evaluated and used HRQoL measures (Garratt, Schmidt et al. 2002; Räsänen, Roine et al. 2006). The 15D is more sensitive in detecting deviations from full health (Hawthorne, Richardson et al. 2001; Stavem, Bjornaes et al. 2001). Furthermore, the changes in the EQ-5D index were almost twice as large as those in the 15D index, again in line with previous findings (Hawthorne, Richardson et al. 2001). However, this study also found significant and systematic differences in the rank order of disease severity between the two measures. The EQ-5D appeared to emphasize the relative impact of musculoskeletal disorders and migraine, whereas the 15D emphasized the relative impact of lung diseases, psychiatric disorders, urinary incontinence and heart failure. This is problematic, as previous studies have suggested that the differences between health utility measures are primarily differences in magnitude of effects (which can be taken into account statistically) but not in the rank order of disorders (which is more difficult to control) (Franks, Hanmer et al. 2006). However, formal comparisons of the two HRQoL measures were not performed, as they were not included in the same wave of the survey and there was a delay of approximately one month between the measures.

Important theoretical problems in the use of preference-based HRQoL measures are the cross-national applicability of the results and use of same preferences for health utility estimation for all groups of people. If the valuations used to form the HRQoL scores differ significantly between countries, they accurately reflect only the preferences of the country where they were elicited. This could theoretically be behind the differences found between the 15D and the EQ-5D. However, the Finnish VAS-based EQ-5D valuations have been compared to those in USA (Johnson, Ohinmaa et al. 2000), UK and other European countries (Sintonen, Weijnen et al. 2003), and only minor differences between the countries were found. In addition, further analysis of the data of Study I using the Finnish VAS-based valuation algorithm for the EQ-5D produced no significant change in the differences between the 15D and the EQ-5D results. The applicability of a single set of population preferences to all people is, despite being the standard way of using HRQoL measures, a problematic assumption especially regarding the severity of conditions at different ages. Furthermore, even if the value people themselves would place

on health at different ages were constant, from the societal perspective people appear to value health benefits accruing to young higher than equal benefits for older people (Dolan, Shaw et al. 2005). This means that, although the health losses would grow with the ageing population by a quarter up to 2040 as estimated in Study II, it is unclear whether the patients themselves, or the society, will actually feel that the disease burden we need to be concerned about actually increases that much.

The statistical analysis of HRQoL measures is complex because they do not generally satisfy the distributional assumptions required by traditional OLS or Tobit regression models. The finding of this study that use of different statistical methods had a much smaller effect on the 15D than on the EQ-5D results was expected (Clarke, Gray et al. 2002), as the 15D has a lower censoring rate and more evenly distributed scores. It is reassuring that the choice of regression methods between OLS, Tobit or CLAD appears to have little significance for the 15D. However, this is not the case for the EQ-5D, so the Tobit estimates presented for the EQ-5D should be interpreted with this limitation in mind. Still, this study opted for Tobit analyses, as CLAD regression estimates the effects of explanatory variables on the median of HRQoL, whereas Tobit estimates the effects on the mean. The use of the median is problematic in the context of QALYs at the group level, because traditionally the average number of QALYs reflects the gains and losses of each individual. The differences in results between the 15D and the EQ-5D hardly arise from statistical factors, as they are observable in the raw scores and also persisted when the CLAD estimator was used. In sum, our study shows that if the length of the questionnaire is not a problem, 15D is preferable to EQ-5D in general population surveys.

Although this study aimed at estimating the individual, additive contribution of each conditions or group of condition to HRQoL, it is likely that in reality the effects are not always additive, i.e. comorbid forms of conditions might affect HRQoL differently from pure forms (Baumeister, Balke et al. 2005). This was investigated in Study III by analysing pure forms of conditions in addition to controlling for other conditions with regression techniques. The assumption for mostly additive effects between different DSM-IV disorders was supported by the similarity of these two estimates, but this was not tested for somatic conditions for practical reasons.

It is important to emphasise that the annual QALY loss estimates consider only morbidity and do not include mortality. The fraction of total QALYs lost due to morbidity is small for conditions with high mortality such as cancer and heart diseases. Morbidity accounts for most of the burden of musculoskeletal disorders, whereas mental, neurological and pulmonary disorders and accidents appear to fall in between (Manuel, Schultz et al. 2002). In other words, if mortality was included, this would increase the relative burden of most disorders except musculoskeletal. The relative importance of mortality also increases with age. For example, the Swedish burden of disease study (Peterson, Backlund et al. 1998) estimated that morbidity accounts for 68% of total disease burden at ages 15-44, 39% at 45-64, 30% at 65-84 and 37% at ages over 85 years. The predicted QALY losses in Finland for the year 2040 have the obvious limitation of assuming that the morbidity situation remains constant.

6.4 Implications for further research

This study has described the HRQoL of Finns with different chronic conditions. This is useful for health policy in many ways, but there are also important limitations suggesting further research. First, cross-sectional studies can not ascertain causality, so longitudinal research is warranted in order to more accurately decipher the impacts of diseases and disorders. Second, from a health policy perspective, the marginal effects of interventions and treatments in the real health care setting would be the ideal information needed for rational public health policy. In other words: the current study shows where the largest HRQoL losses - and largest theoretical gains - are. However, it does not show how, if at all, these gains can be realized. The results are important in guiding future research and development: an ideal way forward would be a follow-up study to the Health 2000 survey, including further HRQoL measurement, mortality and data on treatments received. The results are also directly important for health and social policy. There are plenty of studies showing what could be done to benefit people identified as having low HRQoL. For example, many people with depressive or anxiety disorders do not receive adequate treatment, or receive it too late (Alonso, Angermeyer et al. 2004; Melartin, Rytsälä et al. 2005; Wang, Berglund et al. 2005). Further, it may also be considered justified purely on ethical grounds to concentrate efforts of help on those who are worst off (Rawls 1972).

The present series of studies has shown a clear need for further studies estimating the impact different conditions have on HRQoL, including reliably diagnosed psychiatric disorders, using general population samples. The added complexity and costs following inclusion of reliable psychiatric interviews in surveys should not be used to justify excluding psychiatric conditions, as they are proved to cause a significant proportion of public health loss, especially at younger ages.

However, measuring only HRQoL of patients has obvious limitations, if the aim is to improve the global QoL of the whole population. First, a comprehensive QoL assessment needs to also address subjective life satisfaction and objective life circumstances. Second, it would be important to consider also the indirect effects of disorders on other peoples QoL, for example relatives and caregivers. Both of these issues are especially important for psychiatric disorders.

For psychiatric disorders, especially lacking are studies conducted on population-level anxiety disorders. This study suggests that the total loss of QALY caused by anxiety disorders is large and approaches that of depressive disorders. This finding requires replication, as the clinical and health policy implications can be significant.

Equally in need of replication is the finding that moderate alcohol consumption is associated with insignificantly improved HRQoL. The notion that moderate alcohol consumption is beneficial has penetrated the public widely, and alcohol consumption is

common, so the potential health policy implications of this finding may be large. It is possible that mortality studies capture most of the beneficial effects of alcohol. Due to complex causal pathways linking alcohol consumption, abstinence and HRQoL, other study designs than cross-sectional surveys are needed. Future studies should very carefully avoid the classification of former drinkers as abstainers.

As our studies have shown, HRQoL measurement also still needs theoretical improvements. If QALYs have validity, it is unacceptable that two measures claiming to measure the same thing yield such different results as shown in this study. However, in light of previous studies, this may be more a problem of the EQ-5D than the whole HRQoL field.

6.5 QALYs, rationing and health policy

In addition to the methodological problems of utility-based HRQoL measures, it is also still open how QALYs would be best used for resource allocation. Despite the temptation to opt for pure utilitarian maximising of QALYs, this can not be considered an adequate method for priority setting as such for several reasons (Holm, Sabin et al. 1998; Dolan, Shaw et al. 2005). First, HRQoL forms only a part of the whole of quality of life of individuals, and health care systems have many other legitimate purposes than maximising HRQoL, such as care, social cohesion, equality, safety and patient satisfaction that can not be captured by QALYs. In other words, directly applying of QALYs to rationing reduces the value of human life to HRQoL; hardly a humanistic approach (Arnesen and Nord 1999). Second, even if public health is obviously always related to real individuals' health, the same sum of public health (like the mean change in the HRQoL of the population concentrated in this study) can be produced by many different individual distributions of health. To exemplify some problems: a) the same aggregate HRQoL gain can be produced by increasing one patients HRQoL by 0.3 or thirty patients' by 0.01. b) is it of an equal societal or ethical value to increase someone's HRQoL from 0.2 to 0.4 or from 0.8 to 1.0? or c) what if the HRQoL of 100 people can be increased from 0.9 to 1.00, if someone's HRQoL is reduced from 0.3 to 0? Another important issue relates to age: are QALY gains equally valuable, if they fall on the young or the old? Even if we ignore the first concern and aim at maximising public health - however defined - we still need considerations of justice. Also empirical research suggests that people are generally willing to sacrifice quality of life maximisation in order to provide benefit to those with the worst health prospects, and prioritize young people over old people in accordance with the "fair innings" theory (Dolan, Shaw et al. 2005) . Third, from both ethical and economical points of view, it is important to know what the incremental and opportunity costs are, and who will bear them. Fourth, the lack of gold standard in HRQoL research and the differences in results provided by different measures (as shown in Study I) must be taken into account.

In sum, although exact-looking results that claim to show the impact of different conditions and treatments with three decimal places might be politically convenient, they may paradoxically in effect obstruct democratic health policy. A convincing argument can be made that the problems of rationing cannot be solved by rational, simple rules, but instead require a fair and politically transparent process of decisionmaking (Holm, Sabin et al. 1998; Culyer 2001; Daniels 2001; Ham and Coulter 2001).

The implication is that if rationing decisions are inherently political, the legitimacy of the decisions depends on the legitimacy of decision makers. Researchers are rarely legitimate policymakers, so if quality of life research wishes to legitimately influence health policy it is important to be transparent about the assumptions and limitations of the research - despite the temptation and opportunities for disguising value-decisions as scientific "evidence-based health policy" (Black 2001; Saarni and Gylling 2004). QALYs emphasise the preferences of people affected with different conditions. If democratic health policy should be based on preferences of health politicians - and not preferences the population or the patients - technocratic models based on QALY calculations may hinder this (Fayers and Machin 2007).

Practically and politically applicable, universally acceptable methods for setting health priorities are still much needed. Meanwhile, procedural model for rationing developed by Daniels and Sabin (Daniels and Sabin 1997; Daniels 2001), "accountability for reasonableness", based on Rawls (Rawls 1972) is a promising starting point. QALYs, as an expression of patient preferences, can have a legitimate place in priority setting. Considering the state of the art of QALY measurement, and the ethical issues discussed, presenting HRQoL profiles and mortality data separately in addition to combining them into QALYs is probably warranted in most cases.

7. Conclusions

This study aimed to fill the lack of general population studies with reliable psychiatric diagnostics and preference-based HRQoL measurement. This study has made clear that musculoskeletal and psychiatric disorders have a major impact on HRQoL of Finns. For psychiatric disorders, this is caused by the many dimensions of HRQoL these disorders influence, the relative importance of mental health dimensions to total HRQoL and the young age at which these disorders present. Although there is a lack of comparable, international studies, those that exist confirm these findings especially relating to psychiatric disorders. Anxiety disorders may need special attention, as their burden seems larger than previously thought. Considering moderate alcohol use, this study supports the current policy of not actively recommending anyone to start drinking, as the benefits commonly attributed to moderate alcohol consumption may be minor and mostly attributable to misclassification of former drinkers.

Quality of life research is important in bringing to the fore the true burden of different disorders in a way that respects the individual values of people. This paves the way for rational public health policymaking that focuses on targets where the biggest problems - and biggest potential gains - lie. Gains not just in health, but in better quality of life for all people. This is what health care and health research is for.

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2nd February 2008

Samuli Saarni

9. Appendices

1. Major preference-based HRQoL instruments

Major HRQoL instruments based on multi-attribute utility theory

Instrument	Dimensions	Scale
15D (Sintonen 1994; Sintonen 1995)	15	0.11 to 1.00
Assesment of Quality of Life (AQoL) (Hawthorne, Richardson et al. 1999; Hawthorne, Richardson et al. 2000)	4	-0.04 to 1.00
EuroQol EQ-5D (1990)	5	-0.59 to 1.00
Health Utilities Index, mark II (HUI II) (Feeny, Furlong et al. 1995; Torrance, Feeny et al. 1996)	7	-0.03 to 1.00
Health Utilites Index, mark III (HUI III) (Feeny, Furlong et al. 1995; Feeny, Furlong et al. 2002)	8	-0.36 to 1.00
Rosser-Kind Index (Rosser and Kind 1978)	2	-1.49 to 1.00
Quality of Well-being Index (QWB) (Kaplan and Anderson 1988)	4	0.00 to 1.00
Medical Outcomes Study Short Form - 6D (SF-6D) (Brazier, Usherwood et al. 1998)	6	0.46 to 1.00

2. The 15D questionnaire.

Please read through all the alternative responses to each question before placing a cross (x) against the alternative which best describes your present health status. Continue through all 15 questions in this manner, giving only one answer to each.

QUESTION 1. MOBILITY

1 ( ) I am able to walk normally (without difficulty) indoors, outdoors and on stairs.
2 ( ) I am able to walk without difficulty indoors, but outdoors and/or on stairs I have slight difficulties.
3 ( ) I am able to walk without help indoors (with or without an appliance), but outdoors and/or on stairs only with considerable difficulty or with help from others.
4 ( ) I am able to walk indoors only with help from others.
5 ( ) I am completely bed-ridden and unable to move about.

QUESTION 2. VISION

1 ( ) I see normally, i.e. I can read newspapers and TV text without difficulty (with or without glasses).
2 ( ) I can read papers and/or TV text with slight difficulty (with or without glasses).
3 ( ) I can read papers and/or TV text with considerable difficulty (with or without glasses).
4 ( ) I cannot read papers or TV text either with glasses or without, but I can see enough to walk about without guidance.
5 ( ) I cannot see enough to walk about without a guide, i.e. I am almost or completely blind.

QUESTION 3. HEARING

1 ( ) I can hear normally, i.e. normal speech (with or without a hearing aid).
2 ( ) I hear normal speech with a little difficulty.
3 ( ) I hear normal speech with considerable difficulty; in conversation I need voices to be louder than normal.
4 ( ) I hear even loud voices poorly; I am almost deaf.
5 ( ) I am completely deaf.

QUESTION 4. BREATHING

1 ( ) I am able to breathe normally, i.e. with no shortness of breath or other breathing difficulty.
2 ( ) I have shortness of breath during heavy work or sports, or when walking briskly on flat ground or slightly uphill.
3 ( ) I have shortness of breath when walking on flat ground at the same speed as others my age.
4 ( ) I get shortness of breath even after light activity, e.g. washing or dressing myself.
5 ( ) I have breathing difficulties almost all the time, even when resting.

QUESTION 5. SLEEPING

1 ( ) I am able to sleep normally, i.e. I have no problems with sleeping.
2 ( ) I have slight problems with sleeping, e.g. difficulty in falling asleep, or sometimes waking at night.
3 ( ) I have moderate problems with sleeping, e.g. disturbed sleep, or feeling I have not slept enough.
4 ( ) I have great problems with sleeping, e.g. having to use sleeping pills often or routinely, or usually waking at night and/or too early in the morning.
5 ( ) I suffer severe sleeplessness, e.g. sleep is almost impossible even with full use of sleeping pills, or staying awake most of the night.

QUESTION 6. EATING

1 ( ) I am able to eat normally, i.e. with no help from others.
2 ( ) I am able to eat by myself with minor difficulty (e.g. slowly, clumsily, shakily, or with special appliances).
3 ( ) I need some help from another person in eating.
4 ( ) I am unable to eat by myself at all, so I must be fed by another person.
5 ( ) I am unable to eat at all, so I am fed either by tube or intravenously.

QUESTION 7. SPEECH

1 ( ) I am able to speak normally, i.e. clearly, audibly and fluently.
2 ( ) I have slight speech difficulties, e.g. occasional fumbling for words, mumbling, or changes of pitch.
3 ( ) I can make myself understood, but my speech is e.g. disjointed, faltering, stuttering or stammering.
4 ( ) Most people have great difficulty understanding my speech.
5 ( ) I can only make myself understood by gestures.

QUESTION 8. ELIMINATION

1 ( ) My bladder and bowel work normally and without problems.
2 ( ) I have slight problems with my bladder and/or bowel function, e.g. difficulties with urination, or loose or hard bowels.
3 ( ) I have marked problems with my bladder and/or bowel function, e.g. occasional 'accidents', or severe constipation or diarrhea.
4 ( ) I have serious problems with my bladder and/or bowel function, e.g. routine 'accidents', or need of catheterization or enemas.
5 ( ) I have no control over my bladder and/or bowel function.

QUESTION 9. USUAL ACTIVITIES

1 ( ) I am able to perform my usual activities (e.g. employment, studying, housework, free-time activities) without difficulty.
2 ( ) I am able to perform my usual activities slightly less effectively or with minor difficulty.
3 ( ) I am able to perform my usual activities much less effectively, with considerable difficulty, or not completely.
4 ( ) I can only manage a small proportion of my previously usual activities.
5 ( ) I am unable to manage any of my previously usual activities.

QUESTION 10. MENTAL FUNCTION

1 ( ) I am able to think clearly and logically, and my memory functions well
2 ( ) I have slight difficulties in thinking clearly and logically, or my memory sometimes fails me.
3 ( ) I have marked difficulties in thinking clearly and logically, or my memory is somewhat impaired.
4 ( ) I have great difficulties in thinking clearly and logically, or my memory is seriously impaired.
5 ( ) I am permanently confused and disoriented in place and time.

QUESTION 11. DISCOMFORT AND SYMPTOMS

1 ( ) I have no physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
2 ( ) I have mild physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
3 ( ) I have marked physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
4 ( ) I have severe physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.
5 ( ) I have unbearable physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

QUESTION 12. DEPRESSION

1 ( ) I do not feel at all sad, melancholic or depressed.
2 ( ) I feel slightly sad, melancholic or depressed.
3 ( ) I feel moderately sad, melancholic or depressed.
4 ( ) I feel very sad, melancholic or depressed.
5 ( ) I feel extremely sad, melancholic or depressed.

QUESTION 13. DISTRESS

1 ( ) I do not feel at all anxious, stressed or nervous.
2 ( ) I feel slightly anxious, stressed or nervous.
3 ( ) I feel moderately anxious, stressed or nervous.
4 ( ) I feel very anxious, stressed or nervous.
5 ( ) I feel extremely anxious, stressed or nervous.

QUESTION 14. VITALITY

1 ( ) I feel healthy and energetic.
2 ( ) I feel slightly weary, tired or feeble.
3 ( ) I feel moderately weary, tired or feeble.
4 ( ) I feel very weary, tired or feeble, almost exhausted.
5 ( ) I feel extremely weary, tired or feeble, totally exhausted.

QUESTION 15. SEXUAL ACTIVITY

1 ( ) My state of health has no adverse effect on my sexual activity.
2 ( ) My state of health has a slight effect on my sexual activity.
3 ( ) My state of health has a considerable effect on my sexual activity.
4 ( ) My state of health makes sexual activity almost impossible.
5 ( ) My state of health makes sexual activity impossible.

3. The EQ-5D questionnaire

By placing a checkmark in one box in each group below, please indicate which statements best describe your own health state today.

QUESTION 1. MOBILITY
1 ( ) I have no problems in walking about
2 ( ) I have some problems in walking about
3 ( ) I am confined to bed

QUESTION 2. SELF-CARE
1 ( ) I have no problems with self-care
2 ( ) I have some problems washing or dressing myself
3 ( ) I am unable to wash or dress myself

QUESTION 3. USUAL ACTIVITIES (e.g., work, study, housework, family, or leisure activities)
1 ( ) I have no problems with performing my usual activities
2 ( ) I have some problems with performing my usual activities
3 ( ) I am unable to perform my usual activities

QUESTION 4. PAIN / DISCOMFORT
1 ( ) I have no pain or discomfort
2 ( ) I have moderate pain or discomfort
3 ( ) I have extreme pain or discomfort

QUESTION 5. ANXIETY / DEPRESSION
1 ( ) I am not anxious or depressed
2 ( ) I am moderately anxious or depressed
3 ( ) I am extremely anxious or depressed

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