

Adjusting for dependent comorbidity in the calculation of healthy life expectancy

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Abstract

Background

Healthy life expectancy – sometimes called health-adjusted life expectancy (HALE) – is a form of health expectancy indicator that extends measures of life expectancy to account for the distribution of health states in the population. The World Health Organization has estimated healthy life expectancy for 192 WHO Member States using information from health interview surveys and from the Global Burden of Disease Study. The latter estimates prevalent loss of health by cause, age and sex for populations. Summation of prevalence YLD across all causes would result in overestimation of the total average severity-weighted health state prevalence because of comorbidity between conditions. Earlier HALE calculations made adjustments for independent comorbidity in adding PYLD across causes. This paper presents a method for adjusting for dependent comorbidity using available empirical data.

Methods

Data from five large national health surveys were analysed by age and sex to estimate “dependent comorbidity” factors for pairs of conditions. These factors were defined as the ratio of the prevalence of people with both conditions to the product of the two total prevalences for each of the conditions. The resulting dependent comorbidity factors were used for all Member States to adjust for dependent comorbidity in summation of prevalence YLD across all causes and in the calculation of HALE. A sensitivity analysis carried out for order effects in the proposed calculation method.

Results

There was surprising consistency in the dependent comorbidity factors across the five surveys. The improved estimation of dependent comorbidity resulted in reductions in total PYLD per capita ranging from a few per cent in younger adult ages to around 8% in the oldest age group (80 years and over) in developed countries and up to 15% in the oldest age group in the least developed countries. The effect of the dependent comorbidity adjustment on estimated healthy life expectancies is small for some regions (high income countries, Eastern Europe, Western Pacific) and ranges from an increase of 0.5 to 1.5 years for countries in Latin America, South East Asia and Sub-Saharan Africa.

Conclusion

The available evidence suggests that dependent comorbidity is important, and that adjustment for it makes a significant difference to resulting HALE estimates for some

regions of the world. Given the data limitations, we recommend a normative adjustment based on the available evidence, and applied consistently across all countries.

Introduction

In the *World Health Report 2000*, the World Health Organization (WHO) reported for the first time on the average levels of population health for its 191 member countries using a summary measure that combines information on mortality and morbidity [1,2]. Because substantial resources are devoted to reducing the incidence of conditions that cause ill-health but not death and to reducing their impact on people's lives, it is important to capture both fatal and non-fatal health outcomes in any such measure of population health. Healthy life expectancy or health-adjusted life expectancy (HALE) is a form of health expectancy indicator which summarizes total life expectancy in terms of equivalent years of full health by taking into account the distribution of health states in the population [3].

Healthy life expectancy has previously been calculated for Canada and Australia using population survey data on disability [4-6]. The United States has adopted a public health policy goal to increase health-adjusted life expectancy (referred to as expected years of healthy life or YHL) and has used healthy life expectancy to measure progress towards this goal [7,8]. In calculating HALE for 191 WHO Member States for the World Health Report 2000, WHO carried out an analysis of 62 representative population health surveys which revealed substantial problems with comparability of self-report health status and disability data [2]. As a result disability, prevalence estimates from the Global Burden of Disease 2000 study (GBD 2000) [9] were used to adjust for biases in self-report data; the independent information on levels of population health provided by the health surveys was thus quite limited.

WHO undertook a Multi-Country Survey Study on Health and Responsiveness (MCSS) in 2000 and 2001 in collaboration with Member States using a standardized health status survey instrument together with new statistical methods for to adjust for biases in self-reported health. These new data, together with comprehensive analyses of epidemiological data for all regions of the world from the GBD 2000, and were used to calculate healthy life expectancy for WHO Member States for 2001 in a way that improves comparability across countries. Use of the Global Burden of Disease estimates of health state prevalences across Member States requires that these be added up across disease and injury causes. However, many people have more than one disease or injury, particularly at older ages. This comorbidity must be taken into account in adding up disease specific estimates if we are not to overestimate the average loss of health in the population. Additionally, the severity of health states associated with pairs of conditions, as measured by disability weights in the GBD 2000, may not simply be the sum of the two disability weights for the conditions. Its likely in many cases to be less than the sum, but in some cases there may be exacerbating effects on health states of having both diseases.

HALE calculation methods

Estimation of HALE for WHO Member States using Sullivan's method [10] requires three inputs: life tables and prevalences of various states of health together with appropriate severity weights. The development of WHO life tables and of health state

severity weights is described elsewhere [11,12], we focus here on the estimation of health state prevalences.

In order to measure comparable health state prevalences in populations, WHO undertook a Multi-Country Survey Study (MCSS) in 2000-2001 in collaboration with Member States using a standardized health status survey instrument together with new statistical methods to adjust for biases in self-reported health [13-16]. Because these surveys were carried out in only 61 Member States, a three-stage strategy was used to obtain comparable health state prevalences for all 192 Member States (Figure 1). Firstly, data from the GBD 2000 were used to estimate severity-adjusted prevalences by age and sex for all 192 countries for the year 2002 [17]. Secondly, data from the MCSS were used to make independent estimates of severity-adjusted prevalences by age and sex for 58 countries (three were excluded due to survey quality issues). Final prevalences for all countries were calculated based on the GBD 2000-based prevalences and the survey prevalences [17].

The GBD 2000 revisions have drawn on a wide range of data sources to develop internally consistent estimates of incidence, prevalence, duration and years lived with disability (YLD), for 135 major causes, for 17 sub-regions of the world [9]. As well as the standard incidence-based YLD, prevalence-based YLD rates were calculated, and adjusted for co-morbidity, giving direct estimates of the severity-weighted prevalence of health states attributable to each cause. Prevalence YLD measure the equivalent number of years of healthy life lost for prevalent cases of disease and injury and their sequelae, and are calculated as:

$$PYLD = prev \times DW$$

where *prev* is the number of prevalent cases of the condition in the population and *DW* is the disability weight for the condition (in the range 0-1).

When HALE estimates were first published in the World Health Report 2000, adjustments were made for independent comorbidity as described below. The methods used by WHO to calculate healthy life expectancy were peer-reviewed during 2001 and 2002 by the Scientific Peer Review Group (SPRG) constituted by the Director General, in response to a request by the WHO Executive Board. The SPRG's final report to the Director-General [18] made a number of technical recommendations which WHO has addressed in subsequent HALE calculations. In particular, methods were developed to take into account residents in health institutions and dependent comorbidity. This paper describes the approach for dealing with dependent comorbidity. Dependent comorbidity refers to the situation where the probability of having a pair of diseases is greater than the product of the probabilities for each disease, reflecting common causal pathways (for example common risk factors causing both diabetes and heart disease) and also that one disease may increase the risk of another.

Previous approaches for dealing with comorbidity

Barendregt and Bonneux have carried out a sensitivity analysis of health adjusted life expectancy to comorbidity between five diseases (ischaemic heart disease, congestive heart failure, cerebrovascular disease, lung cancer and chronic obstructive pulmonary disease). They assumed independent comorbidity: the probability of having two

diseases is the product of the probability or prevalence of each [19]. Through a sensitivity analysis, they concluded that the overall effect of comorbidity on estimated healthy life expectancy is small, and that simple assumptions on comorbidity disability weights will be acceptable, because the impact on HALE estimates will be minor.

For the first HALE calculations reported in the World Health Report 2000, all comorbidity between disease and injury causes was also assumed to be independent comorbidity [2]. Independent comorbidity is the situation where the probability of having two (comorbid) conditions is assumed to equal the product of the probabilities for having each of the diseases (Figure 2). In other words, if p_1 is the prevalence of disease 1 and p_2 the prevalence of disease 2, then the prevalence of disease 1 with disease 2 is given by:

$$p_{1+2} = p_1 + p_2 - p_1 \times p_2 = 1 - (1 - p_1) \times (1 - p_2)$$

The simplest approach to estimating the disability weight for the combined conditions 1 and 2 is to assume that the health state valuations (1-disability weight) are multiplicative, so that the combined weight is more severe than the weight for either condition on its own, and remains bounded by 0 and 1 [20]. If the disability weight for the combined conditions 1 and 2 is given by:

$$DW_{1+2} = 1 - (1 - DW_1) \times (1 - DW_2)$$

then the above two calculations can be combined into a single calculation for the combined prevalence YLD as follows:

$$PYLD_j = DW_j \times p_j$$

$$PYLD_{1+2} = 1 - (1 - PYLD_1) \times (1 - PYLD_2)$$

This formula can be generalized to deal with more than two causes as follows:

$$PYLD_{total} = 1 - \prod_i (1 - PYLD_i)$$

where \prod denotes the product operator. Additionally, for the second and third rounds of HALE estimates published in the World Health Reports 2001 and 2002 [21,22] dependent comorbidity was explicitly taken into account for Vitamin A deficiency and iron-deficiency anaemia (50% and 25% respectively assumed to be comorbid with protein-energy malnutrition), for diabetes with cardiovascular disease, and for chronic obstructive pulmonary disease with cardiovascular disease (comorbidity estimated from smoking prevalence data as common cause) [17].

Adjusting for dependent comorbidity

The approach outlined above for adjusting the sum of PYLD for independent comorbidity can be generalized to allow for dependent comorbidity. Let us define the comorbidity factor for two conditions as follows (see Figure 3):

$$f = \frac{Pr ev(condition1 + condition2)}{p_1 \times p_2}$$

Thus an f factor of 2 would indicate that the prevalence of conditions 1 and 2 together is twice as common as would be expected if the occurrence of the two conditions was independent. An f factor of 1 would indicate that the comorbidity is independent. Using this f factor, and the same assumption as above about the disability weight for the combined conditions, we can calculate the PYLD for conditions 1 and 2 as follows:

$$\begin{aligned} PYLD_{1+2} &= PYLD_1 + PYLD_2 - f_{12} \times PYLD_1 \times PYLD_2 \\ &= PYLD_1 + (1 - f_{12} \times PYLD_1) \times PYLD_2 \end{aligned}$$

When there are more than 2 causes, calculation of the total PYLD for all causes using the above approach would involve all pairwise f factors plus potential terms for higher order comorbidity between 3 or more conditions. This complexity can be avoided by taking a sequential approach to the calculation of the total PYLD, where at each step the PYLD for condition j+1 is added to the total PYLD for conditions 1 to j, and the required f factor is that for condition j with the total prevalence for conditions 1 to j:

$$PYLD_{1\dots j+1} = PYLD_{1\dots j} + (1 - f_{1\dots j, j+1} \times PYLD_{1\dots j}) \times PYLD_{j+1}$$

Methods

Data from five large national health surveys[23-27] in Australia, United States of America, Denmark and Belgium were analysed by age and sex to estimate “dependent comorbidity” f factors for pairs of conditions (see Table 1). These conditions were self-reported by survey respondents. To enable results for f factors to be compared and pooled across surveys, it was necessary to group self-reported conditions into broad disease and injury categories to avoid problems arising from differences in finer disease labels used. It was also decided that too many disease categories would be inappropriate given sample sizes and the low prevalences of many specific conditions. The final set of categories used were cardiovascular conditions and diabetes, chronic respiratory conditions, musculoskeletal conditions, nervous system conditions, mental disorders, and other conditions (including infectious diseases and injuries and their sequelae).

The Australian National Health Survey 1995 [28] was conducted on a multistage, cluster sample of households in all states and territories of Australia. Information was obtained by personal interviews of 53,751 persons. The survey contains detailed information on health status, including recent and long-term medical conditions experienced by respondents; recent health-related actions of respondents; information on life style factors such as smoking, alcohol consumption and exercise; and a range of socio-economic and demographic characteristics.

The Australian National Survey of Mental Health and Wellbeing 1997 [23,24] provide information from personal interviews of 10,600 persons on the prevalence of selected major mental disorders, the level of disability associated with these disorders, and the health services used and help needed as a consequence of a mental health problem for Australians aged 18 years or more. The response rate was 78%. Some

information was also collected on chronic physical conditions and disability. Data was gathered on health service use as a consequence of a mental health problem and on respondents' perceived need for health services. Also socio-demographic characteristics (such as labour force status, marital status and highest educational qualification) are included.

The US National Health Interview Survey 2000 [25] has information of health status, limitations and activities, health behaviour, AIDS, health care access and utilization, and socio-demographics. The interviewed sample for the adult component, which required self-response to all questions, was 32,374 persons 18 years and older. The response rate was 82.6%

The Danish Health and Morbidity Survey 1994 [27,29] contains information from 4,668 persons obtained from a representative national sample plus 2,119 persons from two Danish counties collected in the same year, resulting in a total sample of 6,787 adult persons over 16 years of age. The overall response rate to the interviews was 79%. Data were collected through a 45 minute interview together with a self-administered questionnaire to be mailed back within two weeks. The survey also contains a broad range of information about health status, diseases and symptoms and background information, such as age, sex, residence, education, profession and ethnicity.

The Belgian Health Interview Survey 1997 [26] consists of three parts: 1) a household survey with information on position in the household and demographic information such as age, sex, nationality, 2) a self-administrated questionnaire with information on perceived health, complaints and symptoms, life style behaviour, mental health, cardiovascular prevention, wellbeing, social life etc., and 3) a face-to-face interview about chronic diseases, limitations and handicaps, medicine consumption and use of health services, vaccinations, nutrition, physical activities, maternal and infant health, and a socio-economic profile. The survey is of 7,967 persons 15 years and older in Belgium's three regions the Flemish Region, the Walloon Region and the Brussels Region. The overall response rate was 60.5%.

The resulting f factors from analysis of these surveys were compared and averaged to give a final set of dependent comorbidity factors which were used for adjusting the summation of PYLD across causes by age and sex for each country in the calculation of HALE for 2002 reported in the World Health Reports 2003 and 2004 [30,31]. For these estimates, PYLD were adjusted for dependent comorbidity using the cumulative method outlined above and the following sequence of cause groups: cardiovascular disease and diabetes, chronic respiratory diseases, musculoskeletal diseases, sight or hearing loss, Group 1 conditions (communicable, maternal, perinatal and nutritional conditions), injuries, other diseases, neurological diseases, mental disorders.

A sensitivity analysis was carried out of the impact of the magnitude of the f factor on the adjustment to total PYLD. The f factors were assumed to be the same across all sequential condition groups and varied from 1 (independent comorbidity) through to 5. Another sensitivity analysis was carried out for the sensitivity of the HALE estimates to the sequencing of the disease and injury groups for the dependent comorbidity adjustments. Results are reported below.

Results

Table 2 shows the f factors calculated from the 5 survey datasets. Differences in the comprehensiveness in self-reported conditions collected in the various surveys meant that f factors for some categories could not be calculated for some of the surveys. However they have been included in the table for comparison. There was surprising consistency in the f factors across the five surveys, both in terms of the magnitudes and the age patterns. The f factors were typically around 1.5 to 2 at older ages, around 3 to 5 at middle ages and higher at younger ages (where prevalences are typically low). An f factor of 5 at middle ages signifies that the prevalence of the comorbid pair of conditions is five times higher than would be expected by chance alone based on the observed prevalences for each of the conditions considered separately,

A final set of f factors were calculated by averaging the f factors across surveys and applying these f factors to a slightly more detailed set of sequential cause categories. The dependent comorbidity factors shown in Table 3 were used for all Member States to adjust for dependent comorbidity in summation of prevalence YLD across all causes, as there was insufficient evidence to justify use of different f factors in different regions of the world.

Figure 4 shows the results for males aged 80 years and over for a typical developing country. Simple addition of PYLD across causes without any adjustment for comorbidity results in a total PYLD of 0.85 (an average health state equivalent to severe Alzheimer's disease or quadriplegia). Adjustment for independent comorbidity ($f=1$) reduces this to around 0.59, still a health state more severe than blindness. As the f factor increases up to 5, the average health state valuation reduces to around 0.33, not as severe but still a state of considerable health problems.

The overall effect of the introduction of the dependent comorbidity adjustment is a reduction across all countries in the total PYLD rate by age and sex from the GBD 2000 country estimates, and hence an increase in healthy life expectancy. The amount of change varies somewhat across regions. The improved estimation of dependent comorbidity resulted in reductions in total PYLD per capita ranging from a few per cent in younger adult ages to around 8% in the oldest age group (80 years and over) in developed countries and up to 15% in the oldest age group in the least developed countries.

Figure 5 illustrates the impact of the dependent comorbidity adjustment on regional healthy life expectancy at birth in 2002. The bars labelled 2002 were calculated using the 2002 country life tables, the health state valuations from the MCSS surveys and the Global Burden of Disease estimated PYLD for 2002 with dependent comorbidity adjustments. The bars labelled 2001 show the same healthy life expectancies calculated with the Global Burden of Disease inputs replaced by estimated PYLD for 2001 with independent comorbidity adjustments. The differences are slight for low mortality countries, Eastern Europe, China and the Western Pacific. In contrast, the dependent comorbidity adjustments increase healthy life expectancy by around 0.5 to 1.5 years for Latin America, South East Asia and Sub-Saharan Africa.

The analysis of the surveys was repeated to calculate f factors for sequentially cumulative cause groups using three different orderings of the cause groups, in order

to test the sensitivity of the results to the assumed order. The three orders are shown in Table 4.

The age standardized PYLD rate per capita (a number between 0 and 1 corresponding to the average health state valuation) is shown in Table 5 for the three orderings for a developing country (Ghana) and a developed country (Sweden). Dependent comorbidity adjustment of any kind makes a big difference to the total PYLD rate, there are also some smaller differences between the results for the three orderings. The corresponding differences in HALE at birth are shown in the 2 right hand columns of Table 5. Adjustment for dependent comorbidity increases HALE by around 1 year for both males and females in Ghana and for females in Sweden, and by around 0.5 years for males in Sweden. The ordering of the condition groups in carrying out the adjustment makes some difference also, with a range of around 0.3 years for males in Sweden and females in Ghana, and around 0.6 years for males in Ghana and females in Sweden.

Discussion and conclusions

A number of studies have examined the impact of comorbidity on overall levels of disability or functioning, usually for a selected small group of conditions. Although some of these also provide information on the probability of comorbidity for condition pairs, this has been a less obvious focus of research relating to comorbidity.

One large study of the impact of comorbidity of common impairments in older people on Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) found that only a few combinations including vision and hearing loss acted to further exacerbate the effects of other impairments on disability [32]. A number of studies in Mexican-Americans, Americans, Canadians and Koreans have found that depression and comorbid medical conditions interact to increase the probability of depression and to reduce the health-related quality of life [33-39]. Certain physical conditions have also been found to be associated with a significantly increased likelihood of panic attacks [40,41].

A recent Dutch study of 1,673 non-institutionalized chronic disease patients found synergistic effects of combinations of diabetes, cardiovascular disease and chronic respiratory disease with a higher risk of physical disability than could be expected from their separate effects [42]. However, while these types of studies tell us that the disability associated with a comorbid state may be greater than the disability associated with either condition, they have not addressed the issue of whether the disability weights would be additive or sub-additive, as has been assumed in the methods outlined above.

The improved estimation of dependent comorbidity resulted in reductions in total PYLD per capita ranging from a few per cent in younger adult ages to around 8% in the oldest age group (80 years and over) in developed countries and up to 15% in the oldest age group in the least developed countries. This has resulted in an upward adjustment in the HALE estimates for WHO Member States reflecting the consistent evidence from health surveys that dependent comorbidity is common for most conditions.

To date, this evidence is based on health surveys from developed countries, and it will be important to extend this analysis to health surveys in developing countries. However, in extending the analysis, it will be difficult to take into account the known differences in reporting behaviour for illnesses and impairments between people in developing and developed countries [43,44]. Many surveys have shown that people in developing countries report much lower prevalences of illnesses and impairments. In part this is due to lower access to health services resulting in less awareness of illnesses, and in part to difference implicit standards for labelling and reporting health problems. Such differences will make it difficult to interpret whether differences in f factors between self-report data in developing and developed countries are real or are a result of differences in reporting behaviours.

We have chosen to apply the f factors, derived in our analysis of five large surveys in four countries, to all countries as a normative evidence-based adjustment for dependent comorbidity as it seems unlikely that unbiased evidence on differences in dependent comorbidity across countries and regions is feasible in the near future.

The sensitivity to order of adjustment, noted above in the sensitivity analysis, is also a result of using self-report data from surveys for the estimation of f factors. If a consistent set of disease prevalences were used for the estimation of f factors and for the calculation of PYLD then the sequential cumulative adjustment method must be independent of order (this can be shown mathematically). Because we are using f factors derived from self-report survey data, and applying them to GBD estimates of prevalences derived from synthesis of epidemiological data from population studies using carefully defined case definitions for diseases and their sequelae, the results may depend on the order of adjustment. This is because the GBD prevalences are not necessarily consistent with the survey self-report prevalences.

The only way to properly solve this problem is to carry out a very large population survey in which prevalences are ascertained using appropriate diagnostic tests and GBD case definitions. This would be so expensive as to almost certainly never be likely to be carried out. It would certainly be possible to obtain more rigorous data on dependent comorbidity for some selected condition pairs, but this would not help us solve the full comorbidity adjustment problem.

The order that we have chosen for the adjustment of HALE gives an increase in HALE at the lower end of the range. In other words, it is a more conservative adjustment than given by the other orderings. If it is possible to obtain analyses of f factors for condition pairs based on more objective case definitions consistent with those used in the GBD 2000, then it might be possible to take these into account in adjusting for dependent comorbidity in HALE. The analyses reported here could be used to make an initial determination of the most important condition pairs for dependent comorbidity adjustment (this would take into account prevalence, severity and best estimate of f factors). Such a short list of important pairs could then be used to search for empirical evidence to improve the adjustments for these pairs.

Another area requiring further investigation is the estimation of disability weights for comorbid pairs of conditions. The usual techniques for eliciting health state valuations either present valuers with a pure health state description (using the Euroqol or HUI or similar multi-domain health state description tool) or with a disease label.

Sometimes the disease label is supplemented with a health state description [45] or the respondent is asked to write the health state description for the disease label they are valuing (MCSS). Extending these approaches to comorbid pairs of conditions seems to present a lot of difficulty. The respondents are either guessing what the impact of the pair of conditions is on the health state profile, or there is a need for that to be provided from empirical studies. In the absence of such studies, the multiplicative assumption used here seems a reasonable step.

Barendregt and Bonneux concluded in their earlier paper that, ignoring comorbidity is an attractive option because of the difficulty of bring empirical data to bear and the complex adjustments required, and that simple assumptions will probably serve because the impact on HALE estimates is minor [19]. We have shown that the available evidence suggests that dependent comorbidity is important, and that adjustment for it makes a significant difference to resulting HALE estimates. Given the data limitations, a normative adjustment based on the available evidence, but applied consistently across all countries, seems to be the most justifiable approach. This is the approach that has been taken for the calculation of HALE for WHO Member States in recent World Health Reports [30,31].

Competing interests

None declared.

Authors' contributions

CM conceived the approach to adjustment for dependent comorbidity, KMI and SB carried out analyses of the five health surveys, CM and KMI undertook sensitivity analyses, calculations of healthy life expectancies and initial drafting of the paper. All three authors contributed to the writing of the paper.

Acknowledgements

We wish to acknowledge useful discussions with Christopher JL Murray, Joshua Salomon and Niels Tomijima. Niels Tomijima also carried out calculations of PYLD rates for countries using the dependent comorbidity adjustments described in this paper.

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Figures

Figure 1 Estimation of severity-adjusted health state prevalences for calculation of HALE

Figure 2 - Independent comorbidity

Figure 3 - Dependent comorbidity

Figure 4 - Sensitivity of average health state valuation to dependent comorbidity factor f

Variation of average health state valuation for age group 80 and over with assumed value of dependent comorbidity factor f (same factor assumed for all disease pairs): example for males in a developing country.

Figure 5 - A comparison of regional healthy life expectancy at birth in 2002 calculated with and without dependent comorbidity adjustment

Healthy life expectancy (HALE) and Lost Health Expectancy (LHE) at birth in 2002, calculated using as inputs the Global Burden of Disease estimated PYLD for 2002 with dependent comorbidity adjustments (bars labelled 2002) and the Global Burden of Disease estimated PYLD for 2001 with independent comorbidity adjustments (bars labelled 2001).

Tables

Table 1 - Five population health surveys used in analysis

Year of survey, sample size, and abbreviation used in other tables.

Abbreviation	Survey	Year	Sample size
AUSNHS	Australian National Health Survey	1995	53,700
AUS NMHS	Australian National Survey of Mental Health and Wellbeing	1997	10,600
US NHIS	US National Health Interview Survey	2000	32,375
Denmark	Danish Health and Morbidity Survey	1994	6,786
Belgium	Belgian Health Interview Survey	1997	7,967

Table 2 - Comorbidity factors from five population surveys
Comorbidity factors for cumulative cause groups by age and sex

Survey	Combinations	Males					Females				
		<30	30-44	45-59	60-74	75+	<30	30-44	45-59	60-74	75+
AUSNHS	Cardiovascular + respiratory	114.77	43.84	7.93	4.05	7.36	48.36	16.14	9.72	6.03	6.80
	Previous + musculoskeletal	5.91	8.73	5.12	2.84	4.27	5.77	5.68	4.89	3.84	4.31
	Previous + other	3.87	2.58	1.72	1.40	1.72	3.87	2.64	1.78	1.38	1.65
	Previous + nervous	4.88	3.47	2.25	1.64	2.13	4.72	3.28	1.94	1.47	1.92
	Previous + mental	2.93	2.01	1.43	1.20	1.45	2.87	1.98	1.47	1.25	1.43
AUS NMHS	Cardiovascular + respiratory	--	--	9.66	3.76	4.05	41.99	35.78	14.62	6.12	4.53
	Previous + musculoskeletal	37.19	33.12	8.47	3.47	3.52	27.62	21.66	11.54	5.13	4.21
	Previous + other	23.44	15.85	4.03	2.07	2.21	19.34	10.31	3.56	1.91	1.89
	Previous + mental	4.76	4.83	2.29	1.44	1.73	4.25	3.93	2.09	1.37	1.46
US NHIS	Cardiovascular + respiratory	9.97	4.10	1.80	2.59	1.77	8.14	4.12	2.20	1.42	2.37
	Previous + musculoskeletal	7.07	3.55	1.64	2.38	1.56	4.78	3.07	1.89	1.31	2.24
	Previous + other	2.00	2.00	1.56	1.22	1.22	1.92	1.92	1.57	1.27	1.27
	Previous + mental	1.84	1.84	1.46	1.15	1.15	1.65	1.65	1.39	1.17	1.17
Denmark	Cardiovascular + respiratory	32.71	32.71	14.05	6.04	6.04	41.56	41.56	15.63	5.87	5.87
	Previous + musculoskeletal	13.49	13.49	5.76	2.46	2.46	14.38	14.38	7.43	3.84	3.84
	Previous + other	4.15	4.15	2.61	1.64	1.64	4.35	4.35	2.66	1.63	1.63
	Previous + nervous	4.08	4.08	2.63	1.69	1.69	4.46	4.46	2.73	1.67	1.67
	Previous + mental	3.12	3.12	2.09	1.40	1.40	3.20	3.20	2.05	1.32	1.32
Belgium	Cardiovascular + respiratory	33.02	33.02	11.66	4.12	4.12	43.21	43.21	15.74	5.73	5.73
	Previous + musculoskeletal	11.06	11.06	5.28	2.52	2.52	11.12	11.12	6.31	3.58	3.58
	Previous + mental	5.90	5.90	3.27	1.81	1.81	5.72	5.72	3.48	2.12	2.12

Table 3 - Final dependent comorbidity factors

Dependent comorbidity factors used in the calculation of all-cause PYLD per capita

Condition pair	Males								Females							
	0-4	5-14	15-29	30-44	45-59	60-69	70-79	80+	0-4	5-14	15-29	30-44	45-59	60-69	70-79	80+
CVD + diabetes	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
+ respiratory*	26.2	26.2	26.2	15.1	5.9	3.7	3.7	3.6	25.0	25.0	25.0	16.1	7.4	3.7	4.0	4.2
+ Musculoskeletal	10.9	10.9	10.9	9.0	3.9	2.7	2.6	2.5	9.1	9.1	9.1	7.6	4.6	2.8	3.0	3.3
+ Sight or hearing loss	5.2	5.2	5.2	4.3	2.3	1.6	1.6	1.7	5.0	5.0	5.0	3.9	2.3	1.5	1.6	1.6
+ Group1***	5.2	5.2	5.2	4.3	2.3	1.6	1.6	1.7	5.0	5.0	5.0	3.9	2.3	1.5	1.6	1.6
+ Injuries	4.9	4.9	4.9	4.2	2.6	1.7	1.8	1.9	4.8	4.8	4.8	4.0	2.4	1.6	1.7	1.9
+ Other diseases	5.2	5.2	5.2	4.3	2.3	1.6	1.6	1.7	5.0	5.0	5.0	3.9	2.3	1.5	1.6	1.6
+ Neurological	4.5	4.5	4.5	3.8	2.3	1.6	1.5	1.5	4.5	4.5	4.5	3.8	2.3	1.6	1.5	1.5
+ Mental disorders	4.1	4.1	4.1	3.9	2.2	1.4	1.5	1.6	3.9	3.9	3.9	3.5	2.2	1.5	1.5	1.5

*The first condition of each pair is the cumulative prevalence of having one or more of the conditions in preceding rows.

*** Communicable diseases, maternal and perinatal conditions and nutritional deficiencies.

Table 4 - Three orderings of cumulative condition groups for sensitivity analysis

Three orderings of cumulative condition groups for analysis of dependent comorbidity factors and sensitivity of dependent comorbidity adjustments to condition ordering.

Order 1	Order 2	Order 3
Cardiovascular + respiratory	Musculoskeletal + nervous system	Mental + respiratory
Previous + musculoskeletal	Previous + Cardiovascular	Previous + musculoskeletal
Previous + injuries	Previous + respiratory	Previous + Cardiovascular
Prev + nervous system	Previous + Group 1	Prev + nervous system
Previous + Group 1	Previous + other	Previous + Group 1
Previous + other	Previous + mental	Previous + other
Previous + mental	Previous + injuries	Previous + injuries

Table 5 - Sensitivity analysis of ordering of cumulative condition groups

Three orderings of cumulative condition groups for analysis of dependent comorbidity factors and sensitivity of dependent comorbidity adjustments to condition ordering.

	Age-standardized prevalence		HALE at birth	
	Male	Female	Male	Female
Ghana				
Independent comorbidity	0.151	0.096	46.8	48.9
Order 1	0.134	0.089	47.8	49.9
Order 2	0.128	0.088	48.1	50.0
Order 3	0.128	0.085	48.5	50.3
Sweden				
Independent comorbidity	0.066	0.044	70.5	72.6
Order 1	0.062	0.042	70.9	73.3
Order 2	0.060	0.041	71.0	73.6
Order 3	0.056	0.039	71.2	73.9

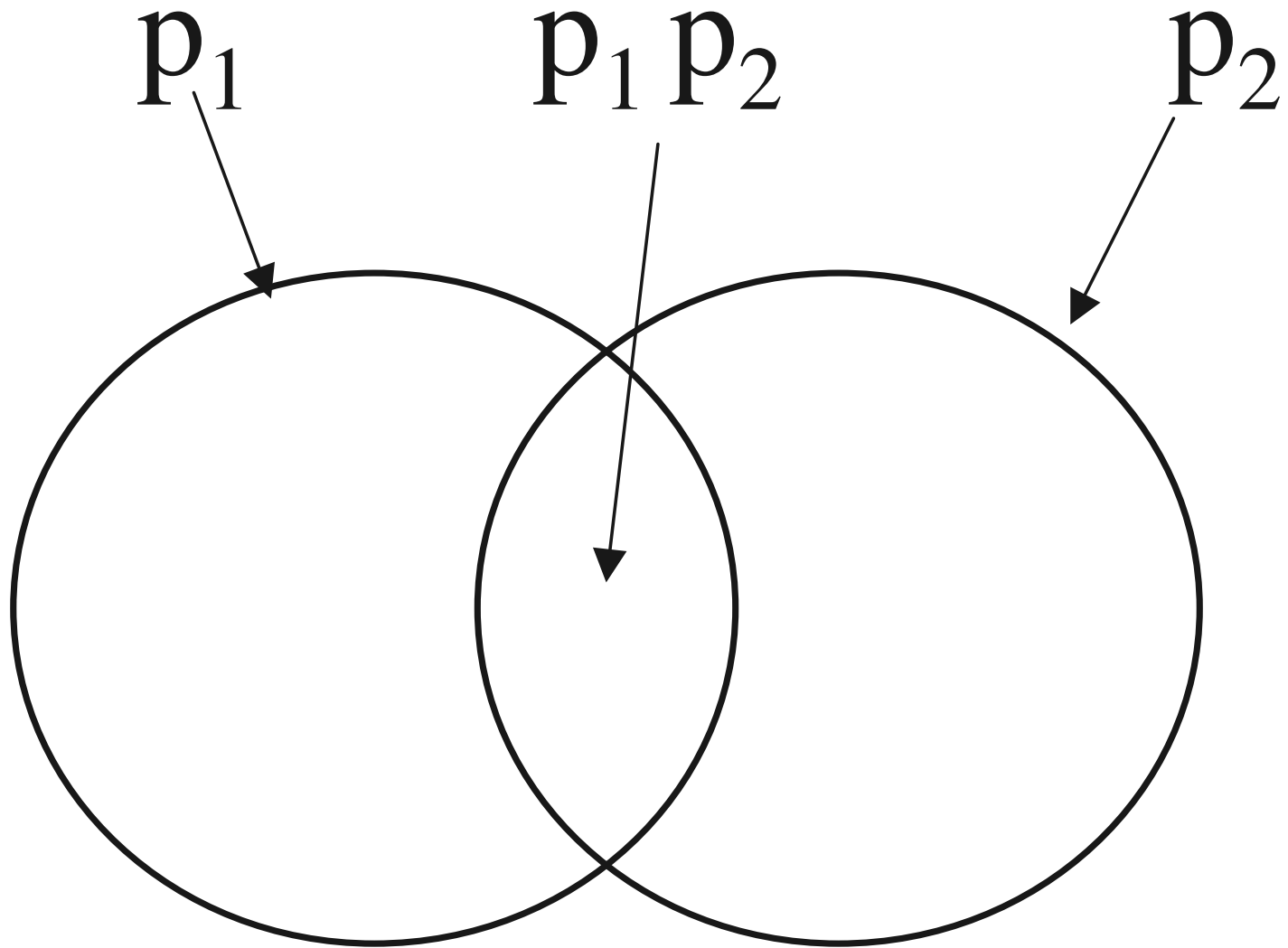


Figure 1

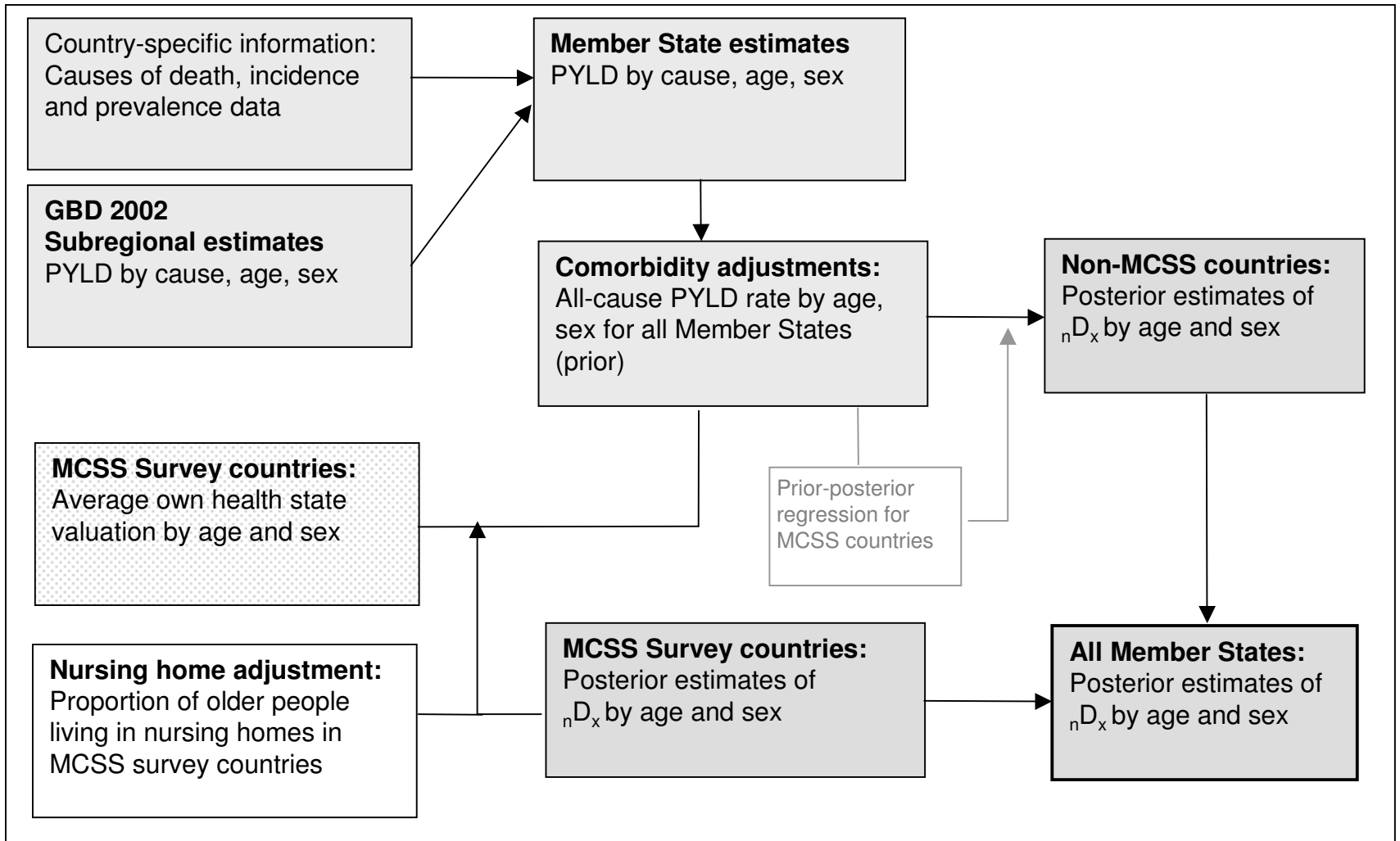


Figure 2

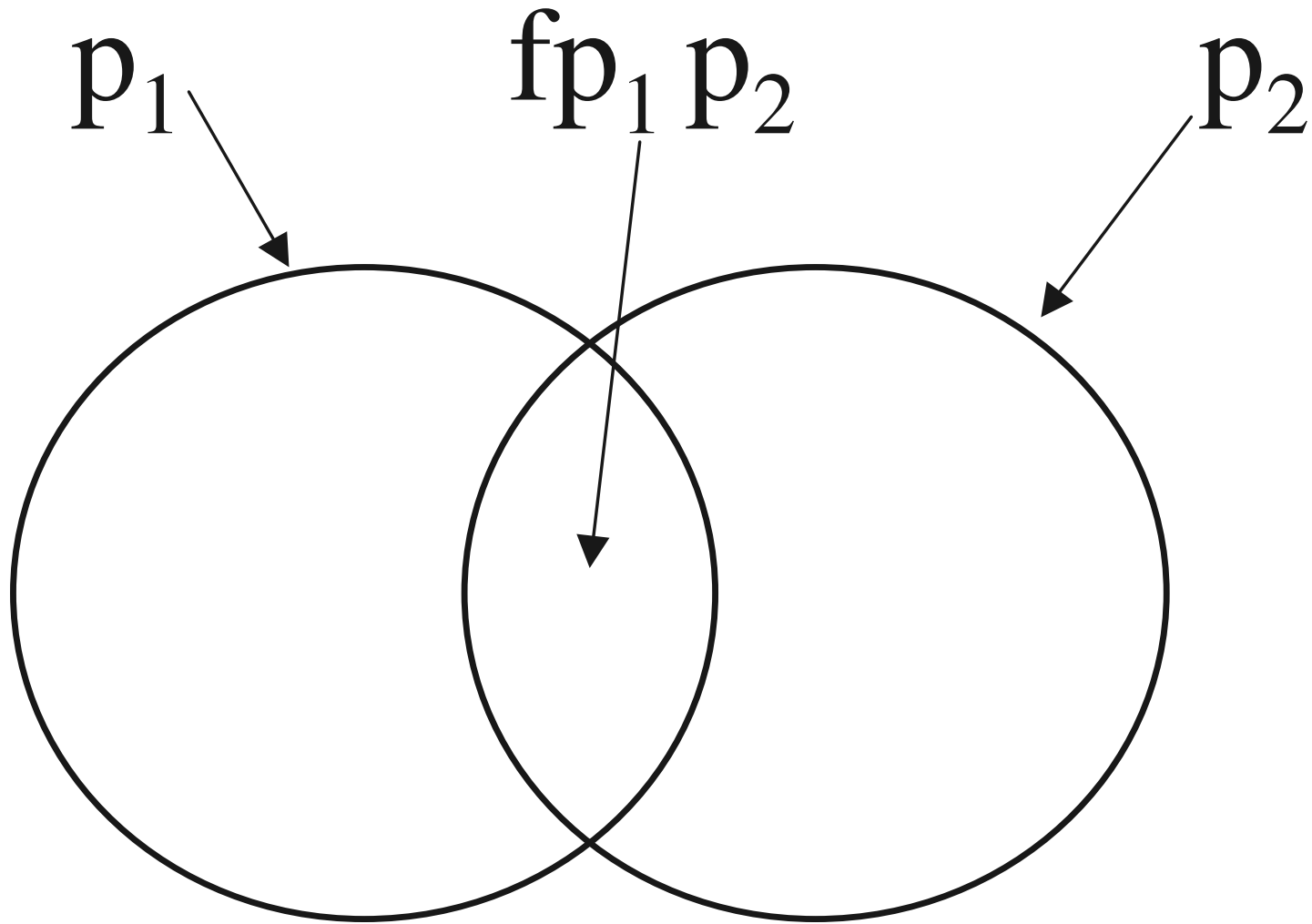


Figure 3

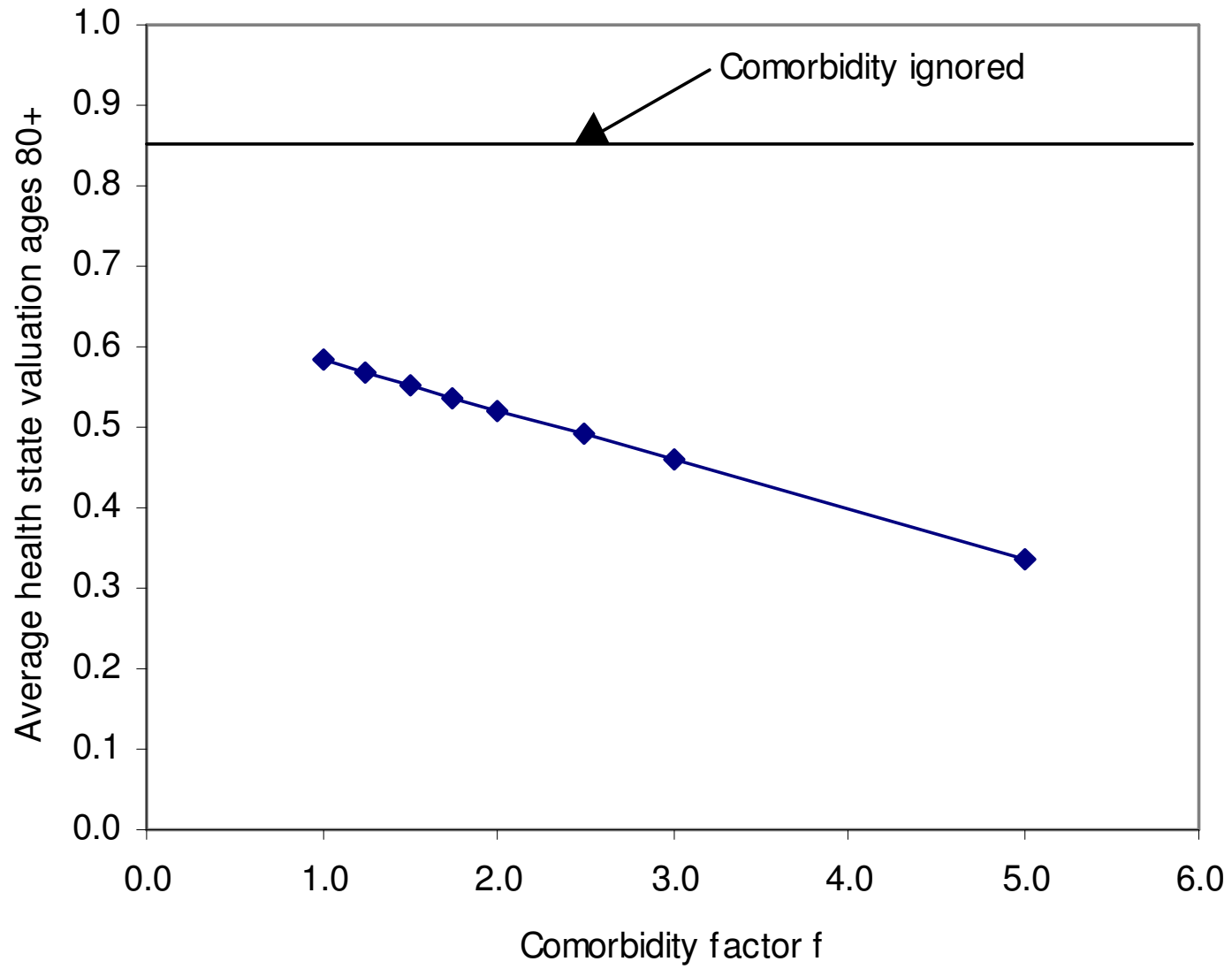


Figure 4

Males

Females

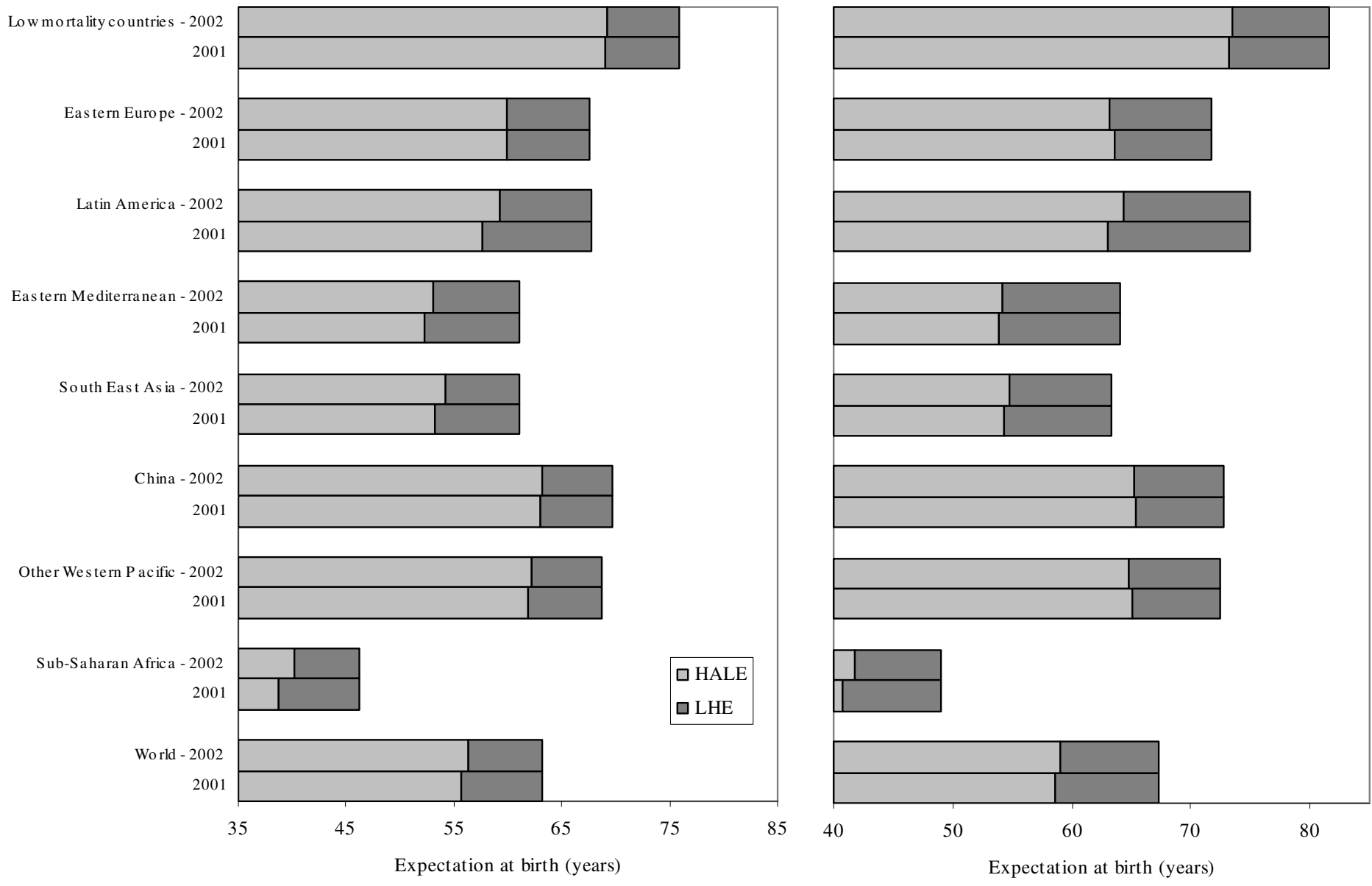


Figure 5