Contribution of deaths related to alcohol use to socioeconomic variation in mortality: register based follow up study

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Abstract

Objective: To estimate the contribution of excessive alcohol use to socioeconomic variation in mortality among men and women in Finland.
Design: Register based follow up study.
Subjects: The population covered by the 1985 and 1990 censuses, aged ≥20 in the follow up period 1987-93.
Main outcome measures: Total mortality and alcohol related mortality from all causes, from diseases, and from accidents and violence according to socioeconomic position. The excess mortality among other classes compared with upper non-manual employees and differences in life expectancy between the classes were used to measure mortality differentials.
Results: Alcohol related mortality constituted 11% of all mortality among men aged ≥20 and 2% among women and was higher among manual workers than among other classes. It accounted for 14% of the excess all cause mortality among manual workers over upper non-manual employees among men and 4% among women and for 24% and 9% of the differences in life expectancy, respectively. Half of the excess mortality from accidents and violence among male manual workers and 38% among female manual workers was accounted for by alcohol related deaths, whereas in diseases the role of alcohol was modest. The contribution of alcohol related deaths to relative mortality differentials weakened with age.
Conclusions: Class differentials in alcohol related mortality are an important factor in the socioeconomic mortality differentials in Finland, especially among men, among younger age groups, and in mortality from accidents and violence.

Introduction

In all countries for which data exist, the lower socioeconomic classes have higher mortality than higher classes.[1 2] The possible causes of this gradient have been widely discussed,[3-5] but few quantitive estimates of the contribution of specific factors have been reported.[6 7]

Alcohol consumption is an important determinant of premature death, particularly among men.[8-10] Its role has usually been considered only in passing in accounts of causes of socioeconomic differentials in mortality, partly because explanatory studies based on epidemiological data have focused mainly on mortality from coronary heart disease, for which alcohol is not a major risk factor.

Our aim was to give a quantitive estimate of the contribution of excessive alcohol use to socioeconomic variation in mortality among Finnish men and women by category of cause of death. Comprehensive data from the death register that have been linked with census data offer a unique opportunity to study this problem. The data do not include information on consumption, but inferences about the role of alcohol are made on the basis of individual level, as given in death certificates.

Data and methods

The data used in this study were extracted from two large data files compiled by Statistics Finland, which include census records of all people covered by the 1985 and 1990 censuses linked with all death records for the years 1987-90 and 1991-3, respectively, by means of personal identification codes.[11] The analysis comprises men and women aged 20 and above in 1987-93. Social class could not be adequately measured for younger Finns in our data.

Deaths caused by excessive alcohol use were defined as those for which there was a reference to alcohol in the death certificate. They are here called alcohol related deaths and are described in detail in the appendix. There were 20 835 such deaths in the data (see table 1). Deaths for which the underlying cause was explicitly attributed to alcohol use constituted 40% of these deaths. In the 60% remaining, at least one of the contributory causes was either alcoholic intoxication or a disease explicitly attributed to alcohol use.

Socioeconomic position was measured by social class obtained from census records. It is based on own occupation for economically active people. Economically inactive family members—for example, housewives—are classified according to the head of the household. Data on earlier socioeconomic position were used for pensioners, students, unemployed people, and men in military service. More details about the classification are given elsewhere.[12]

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Table 1 Person year distribution and number and proportion of alcohol related deaths by social class, sex, and category of cause of death in population aged ⩾20, 1987-93

Sex and social class	Proportion (%) of person years	Alcohol related deaths* (proportion of all deaths)		
		All	Diseases†	Accidents and violence‡
Men				
Upper non-manual	14	1106 (9.6)	549 (5.5)	557 (37.8)
Lower non-manual	18	2175 (10.7)	1010 (5.7)	1165 (45.7)
Manual workers	50	11615 (13.7)	4900 (6.8)	6715 (52.3)
Farmers	11	1239 (3.3)	566 (1.6)	673 (27.3)
Other	8	1891 (12.4)	990 (7.5)	901 (45.6)
All	100§	18026 (10.7)	8015 (5.4)	10011 (47.0)
Women				
Upper non-manual	11	185 (2.1)	105 (1.3)	80 (13.7)
Lower non-manual	38	907 (2.9)	418 (1.4)	489 (22.3)
Manual workers	35	1332 (1.9)	662 (1.0)	670 (18.8)
Farmers	10	112 (0.3)	46 (0.1)	66 (5.3)
Other	6	273 (1.4)	147 (0.8)	126 (14.6)
All	100§	2809 (1.6)	1378 (0.8)	1431 (17.0)

*Definition of alcohol related deaths can be found in appendix.
†Underlying cause of death is disease (ICD-9 code <800).
‡Underlying cause of death is accidental or violent (ICD-9 code ⩾800).
§Men=12 380 000; women=13 615 000.

Two ways of measuring socioeconomic inequalities in mortality were applied. The first was based on mortality standardised for age and was calculated by using direct standardisation with the combined Finnish male and female populations in 1987-93 as the standard. The excess mortality among other classes compared with upper non-manual employees was defined as RR – 1, where RR is the ratio of the rates concerned. Confidence intervals for these ratios were calculated by using a formula given by Rothman.[13] The contribution of alcohol related mortality to inequality was obtained by comparing the excess mortality in all deaths and that in deaths not related to alcohol.

The second measure of inequality was the difference in life expectancy at age 20 between upper non-manual employees and other classes. Life tables for the classes were calculated in the conventional manner with five year age groups.[14] The reduction in life expectancy due to alcohol related mortality was calculated by using cause elimination life tables.[15] The contribution of alcohol to differences in life expectancy was then obtained by comparing the differences between upper non-manual employees and the other social classes in life expectancy and in the reduction in life expectancy due to alcohol.

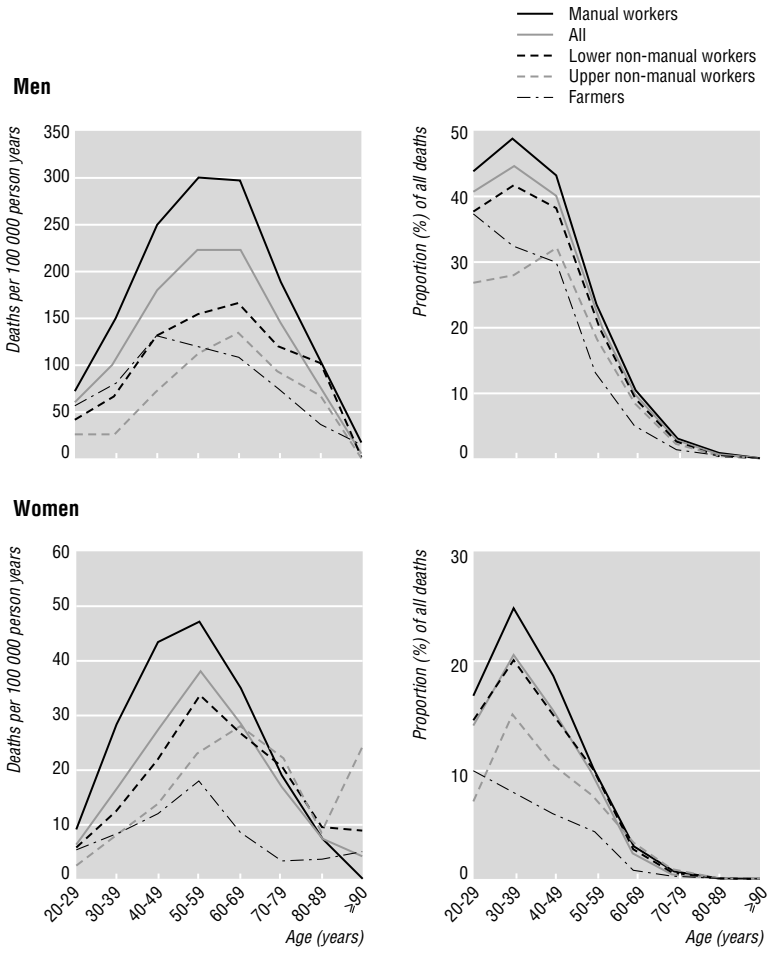

Fig 1 Alcohol related mortality (per 100 000 person years) and proportion of alcohol related deaths of all deaths by age and social class for men and women, 1987-93

Results

In the population aged 20 and above, 11% of all deaths in men and 2% of all deaths in women were alcohol related (table 1). The proportion was much larger in deaths from accidents and violence than in deaths from diseases: 47% of the former were alcohol related among men and 17% among women. Among men, the proportion of alcohol related deaths was the largest in manual workers even though their overall mortality was the highest as well. The relative impact of alcohol on mortality was the highest at ages 20-50, whereas absolute mortality related to alcohol use peaked at a later age, closer to 60 years (fig 1).

Among men, alcohol related mortality was almost three times higher among manual workers than among upper non-manual employees, and among women it was more than twice as high (table 2). Lower non-manual employees fell between these two classes, while farmers had a relatively low level of alcohol related mortality, especially among women. Generally, the differentials in alcohol related mortality were substantially larger than the differentials in overall mortality.

When alcohol related deaths were excluded, excess mortality among male manual workers diminished by 14%, whereas among women the decrease was fairly small at 4% (table 2). Alcohol related deaths thus accounted for 14% and 4% of excess mortality among male and female manual workers, respectively, compared with upper non-manual employees. The corresponding attributable proportions were somewhat lower among lower non-manual employees and in the group "others," whereas among farmers they were negligible or even reversed.

Table 3 shows the differences between upper non-manual employees and other classes in life expectancy at age 20 and in the estimated reduction in life expectancy due to alcohol. Among male manual workers 1.5 years (24%) of the total 6.2 year difference in life expectancy and among women 0.3 years (9%) of the 3.0 year difference were attributable to alcohol related deaths.

Alcohol related mortality from accidents and violence was as much as 3.5 times higher among male manual workers than among upper non-manual

employees and 2.7 times higher among women, while the corresponding ratios for diseases were 2.3 and 1.7 (table 4). The exclusion of alcohol related deaths from accidental and violent deaths diminished the excess mortality among manual workers by 49% in men and 38% in women. The corresponding decreases in manual workers' excess mortality from diseases were only a fraction of these figures because of the small proportion of alcohol related deaths among deaths from disease. Among both women and men, two thirds of the excess accidental and violent deaths of lower non-manual employees was attributable to alcohol related mortality.

The impact of alcohol related deaths on socioeconomic differentials from all cause mortality was higher in the younger age groups because of the larger proportions of accidental and violent deaths and of alcohol related deaths (table 5). There was a similar age pattern for deaths from disease. In accidental and violent deaths the effect of alcohol was substantial in all age groups.

Table 2 Age standardised rate ratios (95% confidence intervals) for all deaths, alcohol related deaths, and non-alcohol related deaths, by sex and social class in population aged ⩾20, 1987-93

Sex and class	All deaths	Alcohol related deaths	Non-alcohol related deaths	Proportion (%) of excess accounted for by alcohol*
Men				
Upper non-manual†	1.00 (1283‡)	1.00 (69‡)	1.00 (1215‡)	
Lower non-manual	1.21 (1.18 to 1.24)	1.55 (1.43 to 1.67)	1.19 (1.16 to 1.22)	9.0
Manual workers	1.54 (1.51 to 1.58)	2.85 (2.67 to 3.05)	1.47 (1.44 to 1.50)	13.6
Farmers	1.31 (1.28 to 1.34)	1.36 (1.25 to 1.49)	1.30 (1.27 to 1.34)	1.0
Other	1.45 (1.41 to 1.49)	2.46 (2.27 to 2.66)	1.39 (1.35 to 1.43)	12.8
All	1.38 (1.35 to 1.41)	2.13 (2.00 to 2.28)	1.33 (1.31 to 1.36)	11.3
Women				
Upper non-manual†	1.00 (777‡)	1.00 (14‡)	1.00 (763‡)	
Lower non-manual	1.13 (1.10 to 1.16)	1.33 (1.13 to 1.56)	1.13 (1.10 to 1.15)	2.8
Manual workers	1.34 (1.31 to 1.37)	2.14 (1.83 to 2.51)	1.33 (1.30 to 1.36)	4.2
Farmers	1.28 (1.25 to 1.31)	0.65 (0.50 to 0.85)	1.29 (1.26 to 1.33)	–4.0
Other	1.42 (1.38 to 1.45)	2.23 (1.84 to 2.70)	1.40 (1.37 to 1.44)	3.5
All	1.26 (1.23 to 1.28)	1.51 (1.29 to 1.76)	1.25 (1.22 to 1.28)	1.8

*Proportional difference between group's excess mortality in all deaths and that in non-alcohol related deaths: ((RR(all)-1)-(RR(non-alcohol related)-1))/((RR(all)-1)×100.
†Reference group.
‡Age standardised mortality (×100 000). Rates for other groups are obtained by multiplying this rate by the appropriate rate ratio.

Table 3 Effect of alcohol related deaths on difference in life expectancy at age 20 between other classes and upper non-manual employees, 1987-93

	Life expectancy at age 20		Difference in expectancy compared with upper non-manual workers (years)		Difference in years (%) attributable to alcohol*	
Social class	Men	Women	Men	Women	Men	Women
Upper non-manual	56.6	61.9	—	—	—	—
Lower non-manual	54.2	60.9	2.4	1.1	0.5 (20)	0.1 (8)
Manual workers	50.4	58.9	6.2	3.0	1.5 (24)	0.3 (9)
Farmers	52.8	59.5	3.8	2.4	0.4 (9)	–0.1 (–3)
Other	51.2	58.2	5.3	3.8	1.1 (21)	0.3 (7)
All	52.1	59.8	4.4	2.2	1.0 (21)	0.1 (6)

*Loss in life expectancy at age 20 due to alcohol is 1.0 years among upper non-manual men and 0.2 years among upper non-manual women. Numbers shown are differences from those in other groups.

Discussion

In the study period alcohol related deaths constituted over 10% of all deaths among men aged 20 and above and 2% among women. The proportions were considerably larger in accidental and violent deaths than in deaths from disease. Alcohol related mortality was substantially higher among manual workers than among upper non-manual employees. Our results show that alcohol consumption is an important cause of socioeconomic differentials in mortality in Finland, particularly among men and among the young and middle aged population. A large part of the differentials in accidental and violent deaths could be attributed to alcohol related deaths, whereas the influence of alcohol use on the differentials in mortality from diseases was modest. The impact of excessive alcohol use on the differences in life expectancy was even larger than its relative impact on the differences in mortality. This is because life expectancy as a measure of mortality gives greater weight to death at a younger age, and the proportion of alcohol related deaths is larger among younger than older adult age groups.

Generalisability of results

The findings concerning the Finnish population in 1987-93 cannot be generalised to other countries. The contribution of alcohol use to socioeconomic differentials in mortality is likely to be larger or smaller than reported here, depending on factors such as the nature of the differences in alcohol use between socioeconomic groups and the general level of mortality from alcohol related causes.

The only report known to us that estimated the contribution of alcohol to socioeconomic mortality differences concerned Sweden in 1981-6.[16] It reported a somewhat smaller effect than here, but the measure used for alcohol related deaths in that study would have covered only about 30% of alcohol related deaths covered by our measure.

The contribution of alcohol use is likely to be relatively small in countries such as the United Kingdom, where the overall mortality from both liver cirrhosis and from accidents and violence is relatively low[17] and class differences in mortality from liver cirrhosis seem to be small and irregular.[18] On the other hand, the contribution of alcohol is likely to be even larger than in Finland in countries such as France, where the alcohol related mortality is high and differences between occupational classes are large.[17 19]

Reliability of results

The reliability and the coverage of the information on alcohol related deaths in the Finnish death register were discussed in an earlier report.[10] It seemed that the gross underestimation of alcohol related causes of death in death certificates which was common in many other countries was not as severe a problem in Finland. Among the most important reasons was that the death certificate is not a public document in Finland, which practically eliminates social stigma related to alcohol related diagnoses—for example, the proportion of deaths from liver cirrhosis reported to be alcohol related was as high as 90% among men in Finland. It would be lower if strong social stigmatisation occurred. Also, the rate of necropsies is high in Finland, especially in accidental and violent deaths; medicolegal necropsies were carried out in more than 97% of all accidental and violent deaths among people aged

Table 4 Age standardised rate ratios (95% confidence intervals) for all deaths, alcohol related deaths, and non-alcohol related deaths whose underlying cause was disease or accident and violence, by sex and social class in population aged ⩾20, 1987-93

Sex, cause of death, class	All deaths	Alcohol related deaths	Non-alcohol related deaths	Proportion (%) of excess accounted for by alcohol*
Men				
Deaths from disease:				
Upper non-manual†	1.00 (1179‡)	1.00 (37‡)	1.00 (1141‡)	—
Lower non-manual	1.21 (1.17 to 1.24)	1.44 (1.29 to 1.61)	1.20 (1.17 to 1.23)	3.7
Manual workers	1.49 (1.46 to 1.52)	2.33 (2.12 to 2.57)	1.46 (1.43 to 1.50)	5.7
Farmers	1.28 (1.25 to 1.32)	1.01 (0.89 to 1.15)	1.29 (1.26 to 1.33)	–3.1
Other	1.41 (1.37 to 1.45)	2.36 (2.11 to 2.64)	1.38 (1.34 to 1.42)	7.6
All	1.35 (1.32 to 1.37)	1.80 (1.63 to 1.97)	1.33 (1.30 to 1.36)	4.3
Accidental and violent deaths:				
Upper non-manual†	1.00 (105‡)	1.00 (31‡)	1.00 (74‡)	—
Lower non-manual	1.26 (1.17 to 1.35)	1.67 (1.50 to 1.86)	1.08 (0.98 to 1.19)	68.2
Manual workers	2.14 (2.01 to 2.28)	3.47 (3.17 to 3.80)	1.58 (1.46 to 1.71)	49.3
Farmers	1.56 (1.44 to 1.67)	1.78 (1.58 to 2.01)	1.46 (1.33 to 1.60)	17.2
Other	1.89 (1.75 to 2.03)	2.58 (2.31 to 2.89)	1.59 (1.44 to 1.76)	33.4
All	1.73 (1.63 to 1.84)	2.53 (2.31 to 2.77)	1.39 (1.29 to 1.50)	46.5
Women				
Deaths from disease:				
Upper non-manual†	1.00 (732‡)	1.00 (8‡)	1.00 (724‡)	—
Lower non-manual	1.13 (1.10 to 1.16)	1.12 (0.90 to 1.39)	1.13 (1.10 to 1.16)	–0.1
Manual workers	1.33 (1.30 to 1.37)	1.73 (1.40 to 2.14)	1.33 (1.30 to 1.36)	1.3
Farmers	1.29 (1.26 to 1.33)	0.35 (0.23 to 0.53)	1.30 (1.27 to 1.34)	–3.6
Other	1.41 (1.37 to 1.45)	1.93 (1.49 to 2.50)	1.40 (1.36 to 1.44)	1.4
All	1.26 (1.23 to 1.29)	1.24 (1.02 to 1.52)	1.26 (1.23 to 1.29)	–0.1
Accidental and violent deaths:				
Upper non-manual†	1.00 (45‡)	1.00 (6‡)	1.00 (39‡)	—
Lower non-manual	1.11 (1.01 to 1.22)	1.63 (1.28 to 2.08)	1.04 (0.94 to 1.15)	67.6
Manual workers	1.48 (1.35 to 1.62)	2.70 (2.13 to 3.43)	1.30 (1.18 to 1.43)	38.0
Farmers	1.10 (0.98 to 1.23)	1.07 (0.75 to 1.52)	1.10 (0.98 to 1.25)	–4.5
Other	1.55 (1.39 to 1.74)	2.64 (1.98 to 3.51)	1.39 (1.23 to 1.57)	29.0
All	1.23 (1.13 to 1.34)	1.87 (1.49 to 2.36)	1.14 (1.03 to 1.25)	41.3

*Proportional difference between group's excess mortality in all deaths and that in non-alcohol related deaths: ((RR(all)-1)-(RR(non-alcohol related)-1))/((RR(all)-1)×100.
†Reference group.
‡Age standardised mortality (×100 000). Rates for other groups are obtained by multiplying this rate by appropriate rate ratio.

under 75 in 1987-93.[20] Some underestimation does occur, particularly in alcohol related deaths from such diseases as cancer of the upper aerodigestive tract (oropharynx, larynx, and oesophagus) and stroke. The earlier report suggested that the underestimation of alcohol related deaths from these diseases is about 10% of all alcohol related mortality or almost 30% of mortality from alcohol related disease.[10] Thus, the contribution of alcohol to socioeconomic differentials in mortality from disease may be somewhat underestimated here. On the other hand, some deaths not related to alcohol use may have been misclassified as alcohol related—for example, because it is not always possible to assess correctly the causal effect of a raised blood alcohol concentration on the death. The effect of these misclassifications on our results depends strongly on whether they have an association with social status. No evidence about this is available from Finland.

Table 5 Proportion of manual workers' excess mortality accounted for by alcohol* according to cause of death, sex, and age, 1987-93

Cause of death, age (years)	Men	Women
All causes		
20-34	49.0	24.0
35-64	19.4	12.0
65-74	2.1	–1.7
⩾75	1.8	–0.1
Deaths from disease		
20-34	44.2	–2.8
35-64	9.2	5.8
65-74	0.7	–1.3
⩾75	0.9	–0.0
Accidental and violent deaths		
20-34	46.0	50.5
35-64	42.7	29.6
65-74	22.3	–9.0
⩾75	38.2	0.5

*Proportional difference between group's excess mortality in all deaths and that in non-alcohol related deaths: ((RR(all)-1)-(RR(non-alcohol related)-1))/((RR(all)-1)×100.

Moderate alcohol consumption has been observed to prevent deaths from coronary heart disease.[21] A large survey from the United States showed that "moderate" or "frequent light" drinkers were more common in the upper social classes than in the lower ones, while abstinence was more common and heavy drinking slightly more common in the lower classes.[22] The evidence from Finland points in the same direction.[23] These results suggest that alcohol consumption may increase socioeconomic variation in mortality not only through more deaths caused by excess alcohol consumption in lower social classes, but also through a greater protective effect of alcohol against coronary disease in the higher classes. The confirmation of this hypothesis, and the estimation of the importance of it in a population, would require a survey on alcohol consumption large enough to estimate the consump-

Key messages

- Alcohol related deaths constituted 11% of all deaths in Finland among men aged 20 and above and 2% among women; the corresponding proportions were much larger for accidental and violent deaths and smaller for deaths from diseases
- Relative socioeconomic differentials were much larger in alcohol related mortality than in overall mortality, the largest rates being among manual workers
- Alcohol related mortality accounted for 14% of the mortality differentials between manual workers and upper non-manual employees among men, 4% among women, and 24% and 9% of the differentials in life expectancy, respectively
- The role of alcohol in the socioeconomic differentials was modest in deaths from diseases but substantial in accidental and violent deaths—for example, one half of the difference between upper non-manual employees and manual workers in accidental and violent mortality could be attributed to alcohol related deaths
- The impact of alcohol on relative socioeconomic mortality differentials increased with decreasing age

tion distribution in the population by sex, age, and socioeconomic position.

Alcohol use and socioeconomic variation in mortality

The framework of the Black report has been widely used in studies aiming to explain socioeconomic variation in mortality.[3] It divides the explanations into four types: artefact, social selection, cultural or behavioural, and materialist. In this classification, alcohol consumption and other health related behaviours belong to behavioural-cultural explanations. Alcohol consumption and the differentials in it, however, also have their causes, and some of these are "materialist." Problems in, for example, work or personal finances, the lack of opportunities to pursue leisure time activities, and inadequate parental resources to offer a stimulating environment for children may all be more common in lower socioeconomic groups and may increase the inclination towards heavy drinking. The part of the variation in mortality accounted for by alcohol consumption does not exclude the materialist explanation; excessive alcohol use can be partly seen as a pathway along which mortality and differentials in mortality are affected by material living conditions.

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Conflict of interest: None.

Table A1 Definition of alcohol related deaths and numbers of alcohol related deaths by diagnosis covered by study

Cause of death category	FCD code for underlying cause of death	No of deaths
Underlying cause of death is explicitly attributed to alcohol		8 268
Underlying cause of death is disease:		4 842
Alcoholic psychoses	291	218
Alcohol dependence syndrome	303	462
Alcoholic epilepsy	345 and 303	52
Alcoholic cardiomyopathy	4255	696
Alcoholic diseases of liver	5710, 5711, 5712, 5713	2 892
Alcoholic diseases of pancreas	5770D-F*, 5771C-D*	500
Alcoholic beriberi disease, alcoholic polyneuropathy, alcoholic gastritis	2650A*, 3575, 5353	22
Underlying cause of death is injury or poisoning:		3 426
Accidental poisoning by alcohol	E851†	2 478
Accidental poisoning by medicinal agents and alcohol	E849†	743
Alcohol poisoning undetermined whether accidentally or purposely inflicted	E970† and poisoning agent is alcohol	205
Underlying cause of death not explicitly attributed to alcohol, but at least one of contributory causes is either alcoholic intoxication (FCD-code 3050) or one of the diseases explicitly attributed to alcohol		12 567
Underlying cause is disease:		4 551
Diseases of circulatory system	(390-459)‡	3 028
Other diseases		1 523
Underlying cause is injury or poisoning:		8 016
Motor vehicle accident	(E801†, E802†)‡	699
Drowning or water traffic accident	(E81†, E910)‡	1 033
Accidental fall	(E88)‡	936
Suicide	(E95)‡	2 921
Other injury or poisoning		2 427
All deaths related to alcohol		20 835

*Five digit FCD code.
†Different code from ICD.
‡These categories were chosen to illustrate contents of supercategory.

Appendix

The Finnish Classification of Diseases 1987 (FCD; see table A1) has been used in coding the causes of death.[24] It is based on ICD-9 (international classification of diseases, ninth revision), but in part the Finnish classification is more detailed because five digit codes are used, and some categories have codes different from ICD.

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Effect of cleansing the birth canal with antiseptic solution on maternal and newborn morbidity and mortality in Malawi: clinical trial

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Abstract

Objective: To determine if cleansing the birth canal with an antiseptic at delivery reduces infections in mothers and babies postnatally.
Design: Clinical trial; two months of no intervention were followed by three months of intervention and a final month of no intervention.
Setting: Queen Elizabeth Central Hospital (tertiary care urban hospital), Blantyre, Malawi.
Subjects: A total of 6965 women giving birth in a six month period and their 7160 babies.
Intervention: Manual wipe of the maternal birth canal with a 0.25% chlorhexidine solution at every vaginal examination before delivery. Babies born during the intervention were also wiped with chlorhexidine.
Main outcome measures: Effects of the intervention on neonatal and maternal morbidity and mortality.
Results: 3635 women giving birth to 3743 babies were enrolled in the intervention phase and 3330 women giving birth to 3417 babies were enrolled in the non-intervention phase. There were no adverse reactions related to the intervention among the mothers or their children. Among infants born in the intervention phase, overall neonatal admissions were reduced (634/3743 (16.9%) *v* 661/3417 (19.3%), $P < 0.01$), as were admissions for neonatal sepsis (7.8 *v* 17.9 per 1000 live births, $P < 0.0002$), overall neonatal mortality (28.6 *v* 36.9 per 1000 live births, $P < 0.06$), and mortality due to infectious causes (2.4 *v* 7.3 per 1000 live births, $P < 0.005$). Among mothers receiving the intervention, admissions related to delivery were reduced (29.4 *v* 40.2 per 1000 deliveries, $P < 0.02$), as were admissions due to postpartum infections (1.7 *v* 5.1 per 1000 deliveries, $P = 0.02$) and duration of hospitalisation (Wilcoxon $P = 0.008$).
Conclusions: Cleansing the birth canal with chlorhexidine reduced early neonatal and maternal postpartum infectious problems. The safety, simplicity, and low cost of the procedure suggest that it should be considered as standard care to lower infant and maternal morbidity and mortality.

Introduction

Neonatal and maternal postpartum morbidity and mortality due to bacterial infections are substantial in developing countries. In areas with a high prevalence of HIV infection, such as sub-Saharan Africa, the HIV/AIDS epidemic has further increased paediatric and maternal morbidity and mortality.[1 2] In countries poor in resources, where many women do not receive antenatal care early in pregnancy,[3] simple and low cost methods to control infectious complications of the newborn babies and their mothers are greatly needed.

We conducted a large trial of cleansing the birth canal with chlorhexidine at Queen Elizabeth Central Hospital in Blantyre, Malawi. The primary objectives of this trial were to determine the effects of this cleansing on perinatal transmissions of HIV and other infections. Chlorhexidine is a well tolerated broad spectrum antiseptic which has been shown to reduce neonatal morbidity due to group B streptococcus[4 5]; it is capable of neutralising HIV.[6] The cleansing procedure at delivery did not significantly reduce the transmission of HIV from mother to child, except when membranes had been ruptured for more than four hours.[7] We report the effect of cleansing the birth canal on neonatal and maternal morbidity and mortality.

Methods

Women giving birth at Queen Elizabeth Central Hospital from June through November 1994 were studied. The protocol and consent forms were approved by institutional review boards in Malawi and the United States. Consent for washing the birth canal was sought when the woman was admitted to hospital during the intervention months. For all women, consent to be tested for HIV and enrolled in the study was obtained after delivery and before discharge from the hospital, when the woman was able to make decisions in private. The details of the study design and procedures have been described previously.[7] Individual randomisation into intervention and non-intervention was not possible in a busy labour room (about 15 000

deliveries a year), so the intervention and control groups were enrolled in the trial in time periods. During the first two months of the trial (June and July) there was no intervention. In the subsequent three months, August through October, the intervention was introduced. In November, the chlorhexidine solution was removed from the labour room and another control group was enrolled.

Women delivering in the non-intervention months received conventional delivery procedures as routinely practised in this hospital. This consisted of cleaning the external genitalia when conducting vaginal examinations, using sterile gloves with a solution of Savlon (cetrimide 1% and chlorhexidine gluconate 0.1%). There was no attempt to clean the interior mucosal surfaces of the birth canal. Also, after delivery, the babies were not washed with any solution. The Savlon solution was not available in the labour room during the months of the intervention.

The intervention consisted of manual cleansing of the birth canal with a 0.25% chlorhexidine gluconate solution in sterile water. Chlorhexidine was chosen on the basis of safety and its reported effects on group B streptococcus and HIV.[4 6] A nurse-midwife wrapped a cotton swab soaked in chlorhexidine solution on the examining fingers and wiped in a clockwise manner the entire birth canal and the external genitalia.[7] Vaginal examinations were done at admission and every four hours thereafter. Many women had only one (29.1%) or two (38.4%) washes because deliveries often occurred soon after admission.[3] Contraindications to vaginal examination included preterm labour, second stage labour, and placenta praevia. Babies born during the intervention phase were wiped with pads soaked in 0.25% chlorhexidine immediately after delivery. Midwives, nurses, and doctors who wiped the birth canal or the baby wore sterile gloves.

Babies developing neonatal problems before discharge were admitted to the special care baby unit, and readmissions (after discharge) were admitted to the paediatric nursery. Neonatal admissions included infants sent to the special care unit or paediatric nursery. The diagnosis of neonatal sepsis was made by paediatricians on the basis of clinical criteria of temperature $>38.0^{\circ}C$, poor feeding, and apnoea or irregular respiration. The clinical records for all babies who died in the hospital were reviewed by a paediatrician to verify causes of death.

The diagnosis of maternal postpartum infection was made by an obstetrician if the woman had frank puerperal sepsis or fever (temperature $>38^{\circ}C$) and had any of the following: offensive vaginal discharge, infected lochia, infected episiotomy or caesarean section wound, retained products of conception, or secondary postpartum haemorrhage. All women enrolled in the study were tested for HIV by examining cord blood samples for HIV antibodies (Genetic Systems HIV Enzyme Immuno-Assay, Seattle, USA).

Statistical analysis included comparison of rates and calculation of relative risks and 95% confidence intervals. An intent to treat analysis was performed, for which women and children were assigned to intervention or non-intervention phase according to time of delivery. The intervention phase therefore included 379 women (10% of women enrolled in the intervention group) who did not receive the intervention owing to unavoidable clinical contraindications such as premature labour and placenta praevia. Duration of hospitalisation was based on dates of admission to and discharge from the hospital. Analysis of hospital stay was restricted to women who gave birth vaginally to singletons with vertex presentation. As there was a preponderance of normal deliveries, the distribution of data on hospital stay was skewed; we therefore rank ordered the observations and used a non-parametric statistical test (Wilcoxon).

Results

The distribution of study participants and the characteristics of women and children enrolled in the trial are shown in tables 1 and 2. A total of 6965 women were enrolled; they had a total of 7160 babies. There were no complaints or complications related to the intervention in either the mother or the child. The staff had no difficulty in administering the intervention, which added little time to the routine vaginal examination.

Infants

The effects of the intervention on infant morbidity and mortality are summarised in table 3. During the intervention and non-intervention phases, 1295 infants were admitted to the hospital with neonatal problems. Among 3743 infants born during the intervention period, 634 (16.9%) were admitted, while among 3417 infants born during the non-intervention periods, 661 (19.3%) were admitted (relative risk = 0.88, 95% confidence interval 0.79 to 0.97).

Neonatal sepsis was diagnosed in 4.6% (29/634) of the admissions during the intervention period compared with 9.2% (61/661) in the non-intervention period (0.50, 0.32 to 0.76). Among 1134 babies admitted to the special care baby unit within 48 hours of delivery, neonatal sepsis was diagnosed in 2.8% (16/571) of the admissions in the intervention phase and 6.4% (36/563) in the non-intervention phase (0.60, 0.40 to 0.91). For babies admitted to the special care baby unit or paediatric nursery after 48 hours of delivery, the rate of sepsis was also lower, but the difference was not significant: 19% (13/70) among intervention babies and 28% (25/91) among non-intervention babies ($P = 0.24$).

Since fewer infants were admitted to the hospital during intervention months, we compared the rates of admissions for sepsis by month, using live births as the

Table 1 Women giving birth (n=7959) in six month period included in study of cleansing the birth canal, Queen Elizabeth Central Hospital, Blantyre, Malawi. Values are numbers (percentages)

	Total	No intervention	Intervention
Women enrolled in study	6965 (87)	3330 (48)	3635 (52)
Women excluded:	994 (13)	554 (56)	440 (44)
Complicated labour or delivery*	633 (64)	310 (49)	323 (51)
Birth before admission		140 (45)	140 (43)
Macerated stillbirth		97 (31)	99 (31)
Fresh stillbirth		41 (13)	62 (19)
Others*		32 (10)	22 (7)
Refused HIV testing	130 (13)	109 (84)	21 (16)
Baby died before enrolment	161 (16)	77 (48)	84 (52)
Reason not known	70 (7)	58 (83)	12 (17)
Babies enrolled in the study	7160	3417 (48)	3743 (52)

*Abortion, death of mother, exclusions based on clinician's decision.

Table 2 Characteristics of women and children. Values are numbers (percentages) unless specified otherwise

	Intervention	No intervention	P value for difference
Mothers	(n=3635)	(n=3330)	
Mean age (years)	24.5	24.6	0.48
Mean number of pregnancies	3.2	3.2	0.58
Mean years of schooling	5.4	5.5	0.21
Mean weight postnatally (kg)*	55.4	55.3	0.49
HIV positive	1105 (30.4)	1006 (30.2)	0.87
Clinical AIDS†	6 (0.2)	13 (0.4)	0.12
At delivery had:			
Perineal tear	549 (15.1)	554 (16.6)	0.09
Episiotomy	540 (14.9)	514 (15.4)	0.52
Rupture of membranes‡	1097 (30.2)	988 (29.7)	0.52
Delivery:			
Spontaneous vaginal	3050 (83.9)	2768 (83.1)	
Elective caesarean section	79 (2.2)	72 (2.2)	
Non-elective caesarean section	354 (9.7)	301 (9.0)	
Breech; vacuum extraction	150 (4.1)	177 (5.3)	
Vertex presentation of first baby	3517 (96.8)	3232 (97.1)	0.51
Babies	(n=3743)	(n=3417)	
Male	1891 (50.5)	1661 (48.6)	0.11
Multiple birth	219 (5.9)	178 (5.2)	0.26
Mean Apgar score at 1 minute	8.3	8.2	0.86
Mean Apgar score at 5 minutes	9.7	9.7	0.58
Mean weight (g)	2889.0	2882.0	0.54
Mean gestational age (weeks)	38.0	38.0	0.86

*Postnatal weight was determined on the second day after delivery. Data not available for 44 intervention and 54 non-intervention women.
†Two major and one minor signs.
‡More than 4 hours from rupture of membranes to delivery. Data missing for 275 intervention women and 229 non-intervention women (percentages based on 3360 intervention and 3101 non-intervention women on whom data were available).

Table 3 Effects of cleansing the birth canal on morbidity and mortality. Rates are per 1000 live births among infants and per 1000 deliveries among mothers

	Intervention		No intervention		
	No	Rate	No	Rate	Relative risk (95% CI)*
Infants	(n=3743)		(n=3417)		
Admissions:					
Overall	634	169.4	661	193.4	0.88 (0.79 to 0.97)
Due to sepsis	29	7.8	61	17.9	0.43 (0.28 to 0.67)
Mortality:					
Overall	107	28.6	126	36.9	0.78 (0.60 to 1.00)
Due to sepsis	9	2.4	25	7.3	0.33 (0.15 to 0.70)
Mothers	(n=3635)		(n=3330)		
Admissions:					
Overall	107	29.4	134	40.2	0.73 (0.57 to 0.94)
Due to sepsis	6	1.7	17	5.1	0.37 (0.13 to 0.82)
Mortality:					
Overall	4	1.1	5	1.5	0.73 (0.20 to 2.73)
Due to sepsis	0	—	0	—	—

Table 4 Mortality by cause among babies born at Queen Elizabeth Central Hospital during intervention and non-intervention phases

Cause of death	Intervention (n=3743)	Non-intervention (n=3417)	Relative risk (95% CI)
Alive	3636	3291	1.00
Infectious*	9	25	0.50 (0.29 to 0.88)
Congenital	2	5	0.54 (0.17 to 1.76)
Respiratory†	44	53	0.86 (0.69 to 1.08)
Preterm, low birth weight	12	11	0.99 (0.67 to 1.47)
Asphyxia	38	31	1.05 (0.85 to 1.30)
Other	2	1	1.27 (0.57 to 2.83)

*Including neonatal sepsis or septicaemia and meningitis.
†Including all causes of respiratory distress syndrome (hyaline membrane disease, meconium aspiration, and pneumonia).

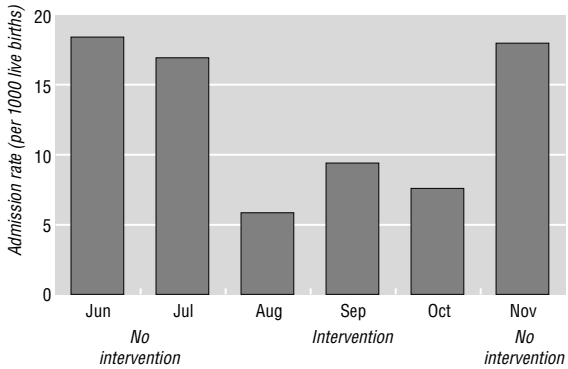

Fig 1 Admission for neonatal sepsis by month of birth, 1994

denominator. Figure 1 shows that the rates of admissions due to sepsis dropped immediately after the intervention was introduced and stayed substantially lower during the intervention compared with the non-intervention months (7.8 *v* 17.9 per 1000 live births; 0.43, 0.28 to 0.67).

Early neonatal mortality was lower during the intervention than the non-intervention periods (28.6 *v* 36.9 per 1000 live births; 0.78, 0.60 to 1.00). Mortality was 25% lower in August, when the intervention was introduced, than in July, when no intervention was in place (31.6 *v* 42.1 per 1000 live births; 0.75, 0.49 to 1.13). Likewise, mortality was 40% lower in October, when the intervention was still in progress, than in November, when the intervention was not being used (22.8 *v* 32.0 per 1000 live births; 0.71, 0.44 to 1.16). Table 4 shows the causes of death. Mortality from infectious causes was significantly lower during the intervention than the non-intervention phase (2.4 *v* 7.3 per 1000 live births; 0.50, 0.29 to 0.88). There were no significant differences in the other main causes of infant death.

Mothers

Of 3635 women who gave birth during the intervention period, 107 (29.1 per 1000 deliveries) were admitted to the hospital with postpartum problems, compared with 134 of 3330 women (40.2 per 1000 deliveries) who delivered during the non-intervention months (0.73, 0.57 to 0.94; table 3). Postpartum infection was diagnosed in 6 (5.6%) of the 107 women who delivered in the intervention period, compared with 17 (12.7%) of the 134 women who delivered in the non-intervention period. With the number of deliveries as the denominator, the postpartum infection rates were 1.7 and 5.1 per 1000 deliveries, respectively (0.37, 0.13 to 0.82). Postpartum infections were reduced in women infected with HIV and those not infected.

The median duration of hospitalisation was two days (range 0-64 days for women given intervention and 0-55 days for women not given intervention). Among 2947 intervention and 2686 non-intervention women who had uncomplicated vaginal deliveries of singletons, the mean duration of stay was 48.7 hours during the intervention period and 50.2 hours during the non-intervention period (Wilcoxon P = 0.008). The duration of stay for children was identical to that of their mothers.

Discussion

During the intervention we found significantly fewer neonatal admissions, fewer cases of neonatal and maternal postpartum sepsis, lower early neonatal mortality rates, and shorter duration of hospital stay. These results indicate that cleansing the birth canal at delivery has important public health benefits. We speculate that colonisation of the birth canal with potential pathogens is reduced, resulting in fewer infectious complications. We were not able to document infections by laboratory means because of limited facilities, but a follow up study to isolate and test the sensitivity of common organisms is being planned. The presence of pathogens, particularly group B streptococcus, in the birth canal is a known predisposing factor for neonatal sepsis.[4 5 8-11] In the pilot study of this trial during pregnancy, cervical and vaginal swabs for bacterial culture taken before and after a single birth canal cleansing with chlorhexidine showed that group B streptococcus and *Staphylococcus aureus* occurred less frequently.[12]

The reduction in neonatal sepsis during the intervention occurred mainly in babies admitted to the special care baby unit during the 48 hours after delivery. The beneficial effect may have been due to prevention of acute infections originating in the birth canal, such as early group B streptococcus infections. Reductions in the number of admissions for neonatal sepsis after 48 hours could be due to pathogens leading to late manifestations of sepsis.

There was an abrupt 25% reduction in early neonatal mortality with introduction of the intervention, and mortality increased when the intervention was stopped. Furthermore, only mortality due to infectious causes was significantly reduced. The reduction in overall mortality (8.3 per 1000 live births) beyond that explained by lower rates of infectious causes (4.9 per 1000 live births) may be due to underdiagnosis of sepsis, especially among deaths attributed to respiratory causes. Hospital data from the previous year showed no seasonal trend in neonatal mortality, but these data have limitations in comparability of the definition of early neonatal death and criteria for inclusions and exclusions. Rates of sepsis did not vary among babies born outside Queen Elizabeth Central Hospital but referred because of problems, suggesting lack of seasonal trends.

Alternative explanations for our results are unlikely. The study design allowed comparison of outcomes in intervention and non-intervention periods, as well as observations about changes in outcome related to the introduction or termination of the intervention. Comparison of data on women and children enrolled in the intervention and non-intervention phases (table 2) showed similar baseline characteristics, and because of our alternating scheme of enrolment, bias due to selection of participants is unlikely. More non-intervention than intervention women refused to give consent for HIV testing after delivery (table 1), but these women represented less than 2% (130/7959) of hospital deliveries. Perhaps the non-intervention women did not consent to HIV testing because they were approached about the study only after delivery, when they were eager to leave the hospital. It was not possible for women delivering in the non-intervention phase to receive the wash since neither the 0.25% chlorhexidine solution nor the sterile swabs were available in the labour room. The diagnoses of neonatal and maternal postpartum sepsis were made by hospital clinicians independent of the study. Hospital practices of admissions, readmissions, and discharges were the same during the intervention and non-intervention phases. Bias due to lack of blindness in the assessment of outcome is possible, but clinicians evaluating sepsis were not formally part of this study and information on characteristics of individual participants (such as enrolment in the study, whether the woman or baby has been washed, the number of washes, and the HIV status of the woman) was not available to clinicians. Cause of death of the child (before discharge from hospital) was abstracted from clinical records and verified by a paediatrician on criteria not based on the phase of the study. The modest reduction in hospital stay (3%) probably reflects inadequate measurement of duration.

The cleansing procedure was easily administered and took almost no extra time, and the cost of the chlorhexidine solution and cotton was less than US$0.10 per patient. None of the patients had complaints or complications related to the intervention. In a large Swedish study, however, a hypotensive episode occurred in one person (0.02%) exposed to chlorhexidine by lavage[4] and with many years of prior occupational exposure to chlorhexidine. Repeated deliveries using this intervention modality might thus result in sensitisation to chlorhexidine on rare occasions.

The beneficial effects, safety, simplicity, and low cost of the intervention encourage its adoption to reduce maternal and neonatal morbidity and mortality.

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Conflict of interest: None.

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Commentary: Sources of bias must be controlled

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Taha and colleagues address an important clinical issue, postpartum and neonatal infection. They conclude that infection is reduced by a more thorough cleansing procedure before vaginal examination during labour, combined with wiping the baby after delivery. The authors claim that alternative explanations of their results are unlikely—but, as they used a study design which could not ensure that the comparison was fair, the reported effects may be due to bias.

The most reliable way of comparing different forms of care is in a properly conducted randomised trial.[1] Non-randomised studies tend to report larger estimates of treatment effects than those using random allocation [2]; even among randomised trials, those in which there is poor concealment of allocation are associated with bias. [3] This study was not randomised and so there is no way of knowing, or proving, that there were no systematic differences (biases) between the two groups. The observed differences in outcome may be due to differences between the women in each group or the care they received, rather than a differential effect of the cleansing procedure on risk of infection. Simple, practical ways of randomising large numbers of people are available[4]; rather than being dismissed as impractical, these need to be developed for use within a wider variety of settings, particularly in developing countries.

Consent was given during labour for the new vaginal cleansing with chlorhexidine, but not the traditional perineal wash with Savlon. As Savlon was removed during the experimental period, it is unclear what happened if a woman refused. Consent for enrolment into the study was sought after delivery. The decision about eligibility and the woman's willingness to consent may therefore have been influenced by events related to the intervention. For example, women whose babies died "before enrolment" were excluded and there is no information about time or cause of death. If these women are included in the analysis of neonatal mortality the relative risk is smaller and no longer statistically significant (0.87; 95% confidence interval 0.71 to 1.05). The potential for bias would be less if all women delivering during the study period had been included in the analysis, and if only those not needing a vaginal examination (if delivered before admission, for example) or with a stillbirth before the first examination had been excluded.

Another potential source of bias is in how outcome is decided. The diagnoses of neonatal and maternal sepsis and cause of death were made by hospital clinicians who were "independent" of the study. In an open study such as this, however, clinicians could very easily have found out, or guessed, which cleansing procedure was used each month.

In view of these limitations, it is difficult to assess the true value of vaginal cleansing and wiping the baby in comparison to perineal cleansing. Also, data from a single study are rarely conclusive and should be put in the context of all available evidence.[5] A brief search of the Cochrane Controlled Trials Register[6] yielded citations of six possibly randomised studies evaluating vaginal cleansing with chlorhexidine.[7-12] The most reliable guide for clinical practice and future research would be a systematic review of all relevant studies with adequate control of bias.

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A person who profoundly affected my life

The eye doctor

Even before I became a teenager, I had set my heart on a future career to join the Royal Navy or to become a medical doctor. At the age of 12 in 1939 I was found to require spectacles. During the consultation the specialist, a Dr R W Greatorex, asked me if I had any plans for the future, and as a result of my reply he told me that, because of my eyes, I would not be accepted by the navy. He also informed me that his son was completing his medical training at St Thomas's Hospital in London. Following my preclinical training at Cambridge University, where there was then no local teaching hospital, I successfully applied to St Thomas's to complete my training. My choice of hospital had been decided by the conversation in 1939.

On the wall in the hospital chapel there is a memorial plaque commemorating the death of Lieutenant Thomas William Greatorex who died in May 1941, aged 26, from wounds received on active service in the Middle East. He had qualified in 1940.

I never met him.

Dr Eric Hainsworth, *retired general medical practitioner now living in Cornwall.*

Bone density and risk of hip fracture in men and women: cross sectional analysis

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Abstract

Objective: To determine the relative contribution of decline in bone density to the increase in risk of hip fracture with age in men and women.
Design: Incidence data of hip fracture from the general population were combined with the bone density distribution in a sample from the same population and with a risk estimate of low bone density known from literature.
Setting: The Netherlands.
Subjects: All people with a hospital admission for a hip fracture in 1993, and bone density measured in a sample of 5814 men and women aged 55 years and over in a district of Rotterdam.
Main outcome measure: One year cumulative risk of hip fracture by age, sex, and bone density measured at the femoral neck.
Results: A quarter of all hip fractures occurred in men. Men reached the same incidence as women at five years older. Controlled for age, the risk of hip fracture by bone density was similar in men and women. The risk of hip fracture increased 13-fold from age 60 to 80; decrease in bone density associated with age contributed 1.9 (95% confidence interval 1.5 to 2.4) in women and 1.6 (1.3 to 1.8) in men.
Conclusions: The risk of hip fracture by age and bone density is similar in men and women. The decrease in bone density associated with age makes a limited contribution to the exponential increase of the risk of hip fracture with age.

Introduction

The number of people with fracture of the hip is increasing rapidly and by the year 2050 may exceed 6 million a year worldwide, up from 1.6 million in 1990.[1] The aging of the population is the most important reason for this increase. In addition, the age specific incidence of hip fractures has also increased in several countries, including the Netherlands.[1,2] Hip fractures are a major cause of mortality and disability in elderly people and an important burden for the health services in many countries.[3]

As most hip fractures occur in women, most attention has focused on bone loss in women, predominantly around the menopause. Less is known about the relation of hip fractures with bone loss later in life, and the high incidence of hip fracture in older men is largely neglected.[4]

Detailed quantitive knowledge about the effect of age and bone density on the absolute risk of hip fracture is necessary to evaluate the potential benefit of interventions aimed exclusively at bone density. The association of low bone mass with an increased risk of hip fracture is well documented.[5] The strong increase of risk with age and the bone loss associated with age are also evident,[6] but the effect of both determinants together is poorly understood. This information could be obtained directly from follow up studies, but the numbers and time required make those studies difficult to accomplish. Combination of data can, however, lead to indirect estimates of the absolute risk comparable with the approach used previously to estimate the lifetime risk of hip fracture.[7]

In the present study we combined cross sectional data on bone mineral density from a population based sample of elderly men and women living independently with incidence data on hip fracture from a national registry in the Netherlands. In combination with data from the literature, this allowed us to estimate the effect of age and bone density on the risk of hip fracture in men and women.

Methods

Distribution of bone mineral density

The Rotterdam study, started in 1991, is a prospective follow up study of the occurrence and determinants of disease and disability in elderly people. The design of this study has been described.[8] The study focuses on four primary topics of research: neurogeriatric diseases, cardiovascular diseases, locomotor diseases, and ophthalmological diseases. All 10 275 men and women aged 55 and over living in a district of Rotterdam were invited to participate. The study was approved by the appropriate medical ethics committee, and participants provided written informed consent. From those eligible, 7983 participated, bringing the overall response rate of this study to 78%.

The baseline survey included an initial home interview followed by two visits to the research centre for a series of clinical examinations and laboratory assessments. Those baseline assessments included dual energy *x* ray absorptiometry scans of the femoral neck.

Methods of measuring bone mineral density and data on bone density in a subsample of 1762 subjects have been reported.[9] The present study used the data on femoral neck bone density from the total study population. This site was chosen because of the growing consensus that prediction of fractures is best done with site specific measurements.[3] People in nursing homes (11%) did not visit the research centre and thus were not eligible for bone density measurements.

We present the results for men and women separately, using the age on the day of the bone density measurement. The bone density distribution by age and sex is presented in 5 year age classes; additionally it was analysed continuously by linear regression. This regression model was extended with quadratic and cubic terms to detect a possible non-linear association between age and bone density. As obesity is well known to affect bone density,[9,10] and as in this study body mass index seemed to be related to age, it was added to the regression model as a potential confounder. The results are presented with 95% confidence intervals.

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Table 1 Mean (SD) height, weight, body mass index, and bone mineral density of elderly people, Rotterdam

	Men					Women				
Age	No	Height	Weight	Body mass index	Bone mineral density	No	Height	Weight	Body mass index	Bone mineral density
55-59	449	177.2 (6.8)	80.9 (10.7)	25.7 (2.9)	0.917 (0.133)	613	164.0 (6.2)	70.0 (11.0)	26.1 (3.9)	0.862 (0.129)
60-64	572	176.0 (6.5)	80.5 (11.3)	26.0 (3.2)	0.888 (0.121)	730	163.1 (6.1)	70.6 (11.2)	26.5 (3.9)	0.832 (0.126)
65-69	547	175.1 (6.4)	78.7 (10.4)	25.7 (2.9)	0.866 (0.131)	650	162.6 (6.1)	71.3 (10.9)	27.0 (3.9)	0.815 (0.134)
70-74	418	174.1 (6.3)	78.4 (10.5)	25.9 (3.0)	0.865 (0.138)	606	161.0 (6.2)	69.9 (10.9)	27.0 (4.0)	0.791 (0.129)
75-79	301	172.0 (6.3)	75.8 (9.8)	25.6 (2.9)	0.855 (0.145)	433	158.8 (6.2)	67.9 (11.2)	26.9 (4.2)	0.763 (0.126)
80-84	126	171.2 (6.8)	74.0 (9.7)	25.3 (3.2)	0.829 (0.139)	240	157.9 (5.9)	68.0 (10.8)	27.2 (4.1)	0.752 (0.127)
⩾85	33	170.1 (7.2)	71.9 (8.3)	24.9 (2.8)	0.804 (0.149)	96	157.3 (6.3)	67.1 (9.9)	27.1 (3.7)	0.729 (0.137)
Total	2446	174.9 (6.8)	78.8 (10.8)	25.7 (3.0)	0.876 (0.135)	3368	161.7 (6.5)	69.9 (11.1)	26.7 (4.0)	0.809 (0.134)

Distribution of hip fractures

The SIG (Foundation for Health Care Information) is a national registry that collects various data related to health care.[11] All admissions to hospital in the Netherlands are included in this registration as is most of the information from nursing homes. In the Netherlands virtually all patients with a hip fracture are treated clinically. Therefore, hospital data give accurate information about the incidence of hip fractures.

Data for hip fractures in 1993 (*International Classification of Diseases*, ninth revision (ICD-9) code 820xx) were collected from the detailed SIG hospital registration data. They were combined with Dutch demographic data for 1993 from the Dutch Central Bureau for Statistics.[12] The data were aggregated in one year age classes and a best fitting function estimated with the SPSS curve fitting facility.[13]

Probability of hip fracture

The relative risk for hip fractures, expressed as relative risk per SD decrease in bone density measured at the femoral neck, was estimated by Cummings et al to be 2.6 (95% confidence interval 1.9 to 3.6) in women.[14] Combining this relative risk with data on incidence and bone density made it possible to estimate the probabilities of hip fracture by age, sex, and bone density. The mathematical details are given in the appendix. We used the same relative risk estimate for men. We also estimated the isolated effects of aging and decline in bone density related to age and calculated confidence intervals for these separate effects by using the 95% confidence intervals of the relative risk per SD decrease in bone density.

Results

Distribution of bone mineral density

Table 1 shows the overall characteristics of the study population. From the 7086 people eligible, bone density data were obtained for 5814 (82%). This response rate remained above 70% up to the age of 85 years; in people aged over 85 the response dropped to 54%. Men were slightly younger than women (mean 67.6 (SD 7.6) years *v* 68.5 (8.3) years). The age at menopause was the same in all age groups (48.9 (5.2) years).

The bone density values, stratified by age and sex, were normally distributed, and the SD was almost constant over the age categories. Bone denisty declined linearly, and introducing quadratic and cubic terms did not improve the model. The apparent decrease in bone density at the femoral neck was 0.0046 (95% confidence interval 0.0040 to 0.0051) g/cm^2/year for women and 0.0031 (0.0024 to 0.0038) g/cm^2/year for men. Correction for body mass index changed those values only slightly (0.0050 g/cm^2/year for women and 0.0028 g/cm^2/year for men).

Distribution of hip fractures

In the Netherlands in 1993 there were 15 107 registered hospital admissions for hip fractures in a population of 15 million, a quarter of which occurred in men. The one year incidence of hip fracture (per 100 000) increased from around 40 at age 55-59 to about 3150 over age 95 in men and from around 40 to about 4450 in women. In each age group, the incidence of hip fracture in men was equivalent to that in women approximately five years younger. Figure 1 shows the one year cumulative incidence of hip fractures by age and sex with the fitted curves; details of these functions are given in appendix B.

Probability of hip fracture

From the preceding results we estimated the probability of hip fracture by age, sex, and bone density (appendix B). Figure 2 represents the association of the incidence of hip fracture with bone density at the femoral neck for different ages in men and women. Comparing an 80 year old woman with average bone density with a 60 year old woman, we found a relative risk for hip fracture of 13.6. When we separated the effects, age contributed 7.1 (5.7 to 8.8) to this relative risk, and age related decline in bone density contributed 1.9 (1.5 to 2.4). For men the relative risk was 12.7; the contribution of age was 8.2 (7.1 to 9.5) and of age related decline in bone density was 1.6 (1.3 to 1.8).

The magnitude of the relative risk per SD change in bone density affected the slope of the risk function (fig 3), which shows the curves for the central estimate

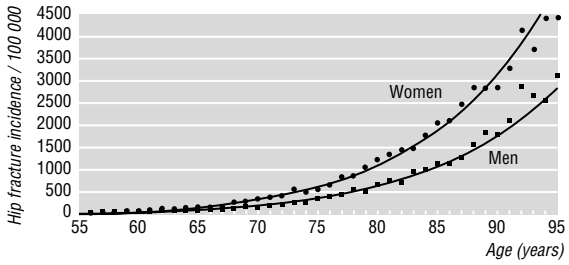

Fig 1 One year cumulative incidence of hip fracture per 100 000 population, Netherlands, 1993

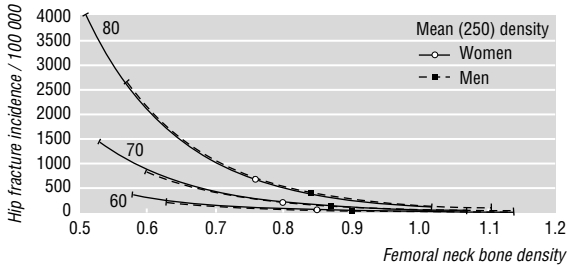

Fig 2 One year cumulative incidence of hip fracture by femoral neck bone density at ages 60, 70, and 80 in women and men

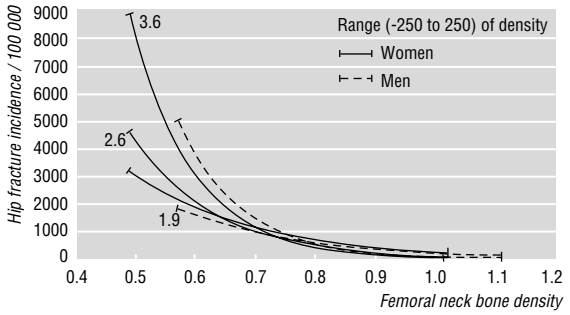

Fig 3 One year cumulative incidence of hip fracture in men and women aged 80 with a relative risk (per SD decrease of femoral neck bone density) of 2.6 and 95% confidence limits 1.9 and 3.6. For central estimate (2.6) solid and dotted lines overlap

(2.6) together with the curves at the lower and upper limits of the 95% confidence interval (1.9 to 3.6). As the incidence of hip fracture specific for age remains constant the risk of low bone density becomes higher, and the risk of high bone density becomes smaller when we assume a higher relative risk. The opposite happens at the lower confidence limit.

Discussion

After the age of 60 the incidence of hip fracture is consistently lower in men than in women of the same age. Men have about the same risk of hip fracture five years later than women. Though the age related decline in bone density is larger in women, the risk of hip fracture when age and bone density are considered together is remarkably similar in men and women. The five year difference in the age specific incidence of hip fracture between men and women can, in this study, be explained by the different bone density distributions at those ages.

Though the risk for hip fracture increased 13-fold from age 60 to age 80 in both men and women, the age related decline in bone density explained merely a doubling of this risk. The rest of the increased risk is explained by other determinants of risk that have been accounted for by using age as a surrogate and that are approximately equal in men and women. Previous research identified several skeletal and extraskeletal determinants.[15] Though bone density is not the main component of the increased risk of hip fracture in old age, risk would be substantially reduced if the age associated decline in bone density between the ages 60 and 80 could be excluded: a 36% reduction in men and 48% in women. Recent clinical trials indicate that part of this risk reduction might be achievable.[16 17]

Assumptions

The stronger effect of age on risk of fracture in general and of hip fracture in particular has been observed in women,[18] but previous studies were based on relatively small numbers of fractures. Our design allowed us to use the information from more than 15 000 hip fractures in the analysis. The data presented here, however, were derived from several sources, which involves some assumptions that need to be examined. We assumed that the distribution of femoral neck bone density in the Netherlands corresponds to the distribution in this study. Even though our sample was population based, it could have been influenced by selection bias: healthy people could have been overrepresented. The high response rates indicate that this effect was probably small.

More importantly, the sample included only people who were living independently. The more frail patients in nursing homes, presumably with lower average bone density, were excluded, resulting in an underestimation of the age associated decline of bone density. Fewer than 9% of elderly people aged under 80 were in nursing homes, but this proportion rose greatly at higher ages. This means that the validity of the data seems assured up to the age of 80, but that the effect of the age associated decline in bone density will probably be somewhat higher than estimated in the older age categories. The age associated decline in bone density that we found was of the same magnitude as in other cross sectional, population based studies, although the absolute levels are slightly higher.[19-21]

Finally, cohort effects cannot be excluded as the bone density data used in this study are cross sectional. If present, these cohort effects would affect the estimated rate of bone loss but not the risk function.

Other risk indicators

In the analysis, age was used as a surrogate marker for several risk indicators, including propensity to fall, types of fall, muscle strength, and bone quality. We used the distribution of bone density and the age related decline in bone density without correction for height, weight, or for the age at menopause as we were interested in the combined effect of these determinants. Moreover, the confounding effect of body mass index was small, and in women the age at menopause was unrelated to age at fracture.

Choice of relative risks

We assumed the relative risk of 2.6 per SD to be the same at all ages, and we also assumed this relative risk applies to the Netherlands. This relative risk estimate influences the slope of the association between incidence of hip fracture and bone density but it does not alter the level of those curves, as is clear from figure 3. It could, however, influence the contribution of the age related decline in bone density to the risk of hip fracture. But, even at the upper confidence limit, this merely doubles the risk over 20 years of aging. It was previously shown in women that bone mineral density predicted fractures equally well at different ages up to the age of 80.[22] Additionally, in a recent meta-analysis the relative risk estimate remained at 2.6 while the confidence interval narrowed slightly (2.0 to 3.5).[5] This same study also indicated that the estimates of relative

Key messages

- The risk of hip fracture increases exponentially with age in both men and women
- Men have about the same risk of hip fracture five years later than women
- The risk of hip fracture by age and bone density is similar in men and women
- The difference in age specific incidence is explained completely by the different bone density in men and women
- The contribution of decline in bone density to the exponential increase in risk of hip fracture with age is relatively small

risk for different measurement and fracture sites seem to be comparable in different parts of the world.

As no relative risk based on large samples was available for men we assumed the same relative risk in men and women, as others have suggested[23 24] and as was confirmed in a recent follow up study of bone density measurements in 752 men in Australia.[25] That study estimated the relative risk for hip fractures per SD lower bone density at the femoral neck at 2.9 (1.7 to 5.0). This seems compatible with our a priori assumption of no difference. When we applied this point estimate of 2.9 the results changed only slightly; the contribution of aging (age 60 to age 80) became 7.8 (6.1 to 10) and that of bone density decline 1.6 (1.3 to 2.1), supporting our conclusions.

Conclusions

The risk of hip fracture, when expressed as a function of bone density and age, is remarkably similar in men and women, and the difference in age specific incidence of hip fracture can be explained completely by the different distribution of bone density in men and women. Our results also show that the contribution of age associated decrease in bone density to the exponential increase of the risk of hip fracture with age is limited.

We are grateful to the participants of the Rotterdam study. We also thank the DXA technicians, L Buist and MB IJsselstijn, and all the other field workers in the research centre in Ommoord, Rotterdam.

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Conflict of interest: None.

Appendix A

To obtain the incidence of hip fracture specific for age, sex, and bone mineral density (BMD) we combined the BMD distribution in this population based sample, the observed incidence of hip fracture specific for age and sex in the Netherlands, and the relative risk for hip fractures per SD decrease in the femoral neck bone density as described by Cummings et al.[14] When we assume a constant relative risk per SD decrease of BMD, the age, sex and BMD specific incidence for hip fractures is given by:

$$p_{age,sex,BMD} = p_{age,sex} \cdot a^{-z} \quad (1)$$

where $p_{age,sex}$ denotes the incidence for people with mean BMD for that age and sex, where a is the relative risk per SD decrease in BMD, and where z is the BMD difference from the age and sex specific mean BMD expressed in SDs. The distribution of hip fractures by BMD in people of the same age and sex will then be given by the product of the risk of hip fracture specific for BMD given above and the BMD distribution in this same population, which we know is normal. The distribution of cases is therefore given by:

$$f_{age,sex}(z) = \frac{1}{\sqrt{2\pi}} \cdot e^{-0.5z^2} \cdot p_{age,sex} \cdot a^{-z}$$

The total incidence of hip fracture can be calculated by the integration of this distribution over the whole range of z. The incidence of hip fracture specific for age and sex is thus given by:

$$i_{age,sex} = \int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi}} \cdot e^{-0.5z^2} \cdot p_{age,sex} \cdot a^{-z} \cdot dz =$$

$$p_{age,sex} \cdot \int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi}} \cdot e^{-0.5z^2} \cdot a^{-z} \cdot dz$$

As the age and sex specific hip fracture incidence is known from population data, we can calculate $p_{age,sex}$.

$$p_{age,sex} = \frac{i_{age,sex}}{\int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi}} \cdot e^{-0.5z^2} \cdot a^{-z} \cdot dz} \quad (2)$$

From (1) and (2) it follows that:

$$p_{age,sex,BMD} = \frac{i_{age,sex}}{\int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi}} \cdot e^{-0.5z^2} \cdot a^{-z} \cdot dz} \cdot a^{-z} \quad (3)$$

In practice this means that, to obtain the incidence of hip fracture for people with mean BMD, the observed incidence specific for age and sex needs to be divided by a correction factor C, given by:

$$C = \int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi}} \cdot e^{-0.5z^2} \cdot a^{-z} \cdot dz$$

C equals 1 when a equals 1. In all other cases C is larger than 1. When $a = 2.6$, as is the central estimate in this article, the correction factor C equals 1.578541. (At the lower confidence limit (1.9) the correction factor is 1.228739 and at the upper limit (3.6) it is 2.271399.)

Appendix B

The one year cumulative incidence of hip fracture (per 100 000) in this article is estimated from population data. The best fitting curves are power functions given by:

$$i_{age,men} = 9.3 \cdot 10^{-15} \cdot age^{8.8431}$$

and

$$i_{age,women} = 5.9 \cdot 10^{-15} \cdot age^{9.0731}$$

The relation of femoral neck BMD with age is best described by a linear function:

$$BMD_{age,men} = 1.08586 - 0.0031 \cdot age$$

and

$$BMD_{age,women} = 1.121284 - 0.00456 \cdot age$$

With the conditions of normality and homoscedasticity fulfilled, and by assuming a relative risk of 2.6 per SD decrease of BMD at the femoral neck, the one year incidence of hip fracture (per 100 000) is thus given by (3):

$$p_{age,men,BMD} = \left(\frac{9.3 \cdot 10^{-15} \cdot age^{8.8431}}{1.578541} \right) \cdot 2.6^{\frac{1.08586 - 0.0031 * age - BMD}{0.135}}$$

and

$$p_{age,women,BMD} = \left(\frac{5.9 \cdot 10^{-15} \cdot age^{9.0731}}{1.578541} \right) \cdot 2.6^{\frac{1.121284 - 0.00456 * age - BMD}{0.134}}$$

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When I use a word …

Oe no!

As chairman of examiners in last year's preclinical examinations I was responsible for drafting the examiners' report. I circulated the first draft to my coexaminers. One of them asked me to change "fetus" to "foetus."

Fetus derives from the Latin word *feto*, I breed, but the spelling "foetus" has been around since at least the beginning of the seventh century. St Isidore, Archbishop of Seville, in a section entitled "De homine et partibus eius" in his *Originum sive etymologiarum libri* (*Books of Origins or Etymologies*), commonly known as the *Etymologiae* (published in about 620 AD), incorrectly wrote that it was derived from *foveo*, I keep warm: "Foetus autem nominatus, quod adhuc in utero foveatur" (XI, 1, 144).

The earliest English language citation in the *Oxford English Dictionary* (from 1398) uses the spelling "fetus," and it is not until 1594 that "foetus" is first recorded: "the Foetus of the Latines, and Embryon of the Greekes" (T B la Primaud). All this confused Samuel Johnson. In his dictionary he defined fetus as "Any animal in embryo" and foetus as "The child in the womb after it is perfectly formed; but before, it is called embryo."

Spelling does not, however, always accord with etymology, and it is wrong to be prescriptive. I prefer "fetus," but was prepared to capitulate if "foetus" was more commonly used. I therefore searched my computerised database of world bioscience literature since 1966. The results are shown in the table as percentage occurrences of the spelling "fetus" in the titles and abstracts of nearly 25 000 publications containing the word fetus or foetus.

Currently world wide "fetus" is used in 92% of publications, but there are regional variations. Not surprisingly, the figure is close to 100% in United States publications. In contrast, in English language titles and abstracts of non-English language publications the overall current figure is considerably lower (81%) and has been falling since 1966. In Britain, however, and in English language publications elsewhere it is currently as high as 90%, having in both cases increased significantly since 1966–82.

The striking increase in the use of "fetus" in Britain since 1966 is masked by the summary data. From about 1974 the frequency increased linearly to its current level, which it reached in 1985. But before that it was 67% in 1972–4, 42% in 1969–71, and only 17% in 1966-8. On the other hand, perhaps this rapid rise since the late 1960s is not so surprising—in October 1969 the *BMJ* first started to use "fetus" as its preferred spelling.

Jeff Aronson, *clinical pharmacologist, Oxford*

We welcome filler articles of up to 600 words such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake,* or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk.

Table 1 Percentage occurrences of "fetus" (rather than "foetus") in titles and abstracts of publications

Year	All publications (n=24 452)	United States (n=9511)	Britain (n=3842)	Other countries	
				In English (n=5407)	Not in English (n=5692)
1966-82	87	98	69	80	90
1983-9	92	98	90	87	87
1990-6	92	98	91	90	81