ORIGINAL ARTICLE

Non-malignant disease mortality in meat workers: a model for studying the role of zoonotic transmissible agents in non-malignant chronic diseases in humans

E S Johnson, Y Zhou, M Sall, M El Faramawi, N Shah, A Christopher, N Lewis

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See end of article for authors' affiliations

Correspondence to: Dr E S Johnson, Department of Epidemiology, School of Public Health, University of North Texas Health Science Center, 3500 Camp Bowie Boulevard, Fort Worth, TX 76107, USA; ejohnson@hsc.unt.edu

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Background: Current research efforts have mainly concentrated on evaluating the role of substances present in animal food in the aetiology of chronic diseases in humans, with relatively little attention given to evaluating the role of transmissible agents that are also present. Meat workers are exposed to a variety of transmissible agents present in food animals and their products. This study investigates mortality from non-malignant diseases in workers with these exposures.

Methods: A cohort mortality study was conducted between 1949 and 1989, of 8520 meat workers in a union in Baltimore, Maryland, who worked in manufacturing plants where animals were killed or processed, and who had high exposures to transmissible agents. Mortality in meat workers was compared with that in a control group of 6081 workers in the same union, and also with the US general population. Risk was estimated by proportional mortality and standardised mortality ratios (SMRs) and relative SMR.

Results: A clear excess of mortality from septicaemia, subarachnoid haemorrhage, chronic nephritis, acute and subacute endocarditis, functional diseases of the heart, and decreased risk of mortality from pre-cerebral, cerebral artery stenosis were observed in meat workers when compared to the control group or to the US general population.

Conclusions: The authors hypothesise that zoonotic transmissible agents present in food animals and their products may be responsible for the occurrence of some cases of circulatory, neurological and other diseases in meat workers, and possibly in the general population exposed to these agents.

Studies of disease risks in meat industry workers are important for two reasons: (1) to identify hazardous occupational exposures peculiar to the industry with the ultimate goal of mitigating their harmful effects; and (2) to identify the causes of diseases occurring in the general population that could originate from exposures to agents present in food animals and their products. This latter use has not been given much consideration apart from well known exceptions such as zoonotic tuberculosis, leptospirosis, brucellosis, botulism, anthrax, salmonella and *E coli*, etc. We propose that this warrants more serious examination than has so far been done, considering the extraordinarily large number of other transmissible agents in these animals whose role in human infection is unknown.

Considerable attention has been paid to substances present in animal food before and after cooking as risk factors for human diseases such as heart disease, diabetes,¹ and various cancers including cancer of the kidney, colon, breast, lung, etc.^{2–5} Before cooking, these exposures have included heme,^{6–7} fat or cholesterol,^{8–9} dioxins,¹⁰ whereas after cooking they include polycyclic aromatic hydrocarbons,¹¹ heterocyclic amines,¹² N'-nitroso compounds,¹³ and dioxins.¹⁰ However, the presence of these substances in animal food alone does not seem to explain the association with these diseases completely or adequately, and the associations have not been consistent.^{4–14} For example, in the study by Alavanja *et al.*,⁵ the observed association between consumption of red meat and lung cancer risk persisted even after controlling for total fat, saturated fat, cholesterol, and tobacco smoking. Therefore, alternative hypotheses are needed to explain these associations between consumption of animal products and different diseases in humans.

Cattle, pigs, sheep and poultry are the main sources of food for the vast majority of mankind, and they are naturally infected with a plethora of transmissible agents that include prions, viruses, bacteria, protozoa, fungi, etc, that are known to cause disease in these animals, including cancer and neurological diseases.^{15–16} In extensive reviews, we proposed that these agents could possibly be the origin of some cases of diseases that occur not only in meat workers but also in the general population, and that studies of disease risks in meat workers who have the highest exposures to these agents may help throw light on this issue.^{17–18} The rationale is that because occupational exposures are additional and much higher, any associated risks from these agents will be much easier to detect in workers than in subjects in the general population. Historically, there is precedence for this from experience with brucellosis, gastrointestinal tuberculosis, anthrax, etc, notwithstanding the traditional use of occupational populations to identify cancer risk from exposures such as asbestos, benzene, aniline dyes, polycyclic aromatic hydrocarbons, etc.

Within the meat industry, exposures to transmissible agents are expected to be highest for workers employed in manufacturing establishments where animals are slaughtered and processed. We therefore present the results for mortality from non-malignant diseases in subjects who during the entire length of their union membership worked either in abattoirs where cattle, pigs and sheep were slaughtered only, or were slaughtered and processed ($n = 4748$), or in meat processing

Abbreviations: CJD, Creutzfeldt-Jakob disease; ICD, International Classification of Diseases; PMR, proportional mortality ratio; SMR, standardised mortality ratio

plants where no slaughtering was performed but carcasses from animals slaughtered elsewhere were brought in for processing only ($n = 3772$), and in a control group of workers from the same union that were employed in a variety of non-meat establishments such as soft drinks manufacturing, oyster shucking, soup canning, etc, and who had never worked in the meat industry during their union membership ($n = 6081$). Initial and updated detailed results for cancer mortality in these workers have been presented before,^{19–21} as well as the results of limited investigation for non-malignant diseases in the initial follow-up period of 1949–80.^{22–23} These subjects were part of a larger cohort of 28 900 workers who were members of a local meat cutters' union in Baltimore, Maryland, and which also included workers in supermarkets and chicken slaughtering plants. The entire cohort has been previously described in detail.^{19–20} However in this report, which is restricted to mortality from non-malignant diseases in cattle/pig/sheep abattoirs and meat processing plant workers, follow-up is extended to the end of 1989, and we have investigated 134 distinct specific causes of death, as compared with fewer than 30 in the previous follow-up. The protocol for this study was approved by the National Institute of Environmental Health Sciences, NIH, USA, where the study was conducted.

METHODS

The study population was defined as all persons for whom dues were paid to the union at any time between July 1949 and December 1979, and the follow-up period is from 1 July 1949 to 31 December 1989. Methods of follow-up included (1) union records; (2) Social Security Administration Mortality Files; (3) Maryland Department of Motor Vehicle; (4) Maryland State Department of Vital Records; (5) National Death Index (NDI); (6) US Postal Service; (7) Pension Benefit Information Company (PBIC); and (8) personal contact by letter or telephone call. During the follow-up period a total of 1380 deaths were recorded among the abattoir workers, 1012 deaths in meat processing plant workers and 1202 deaths in the control group of non-meat workers. Because of the extensive methods of follow-up that were employed, and the fact that extensive searches for deceased individuals through the NDI, PBIC and the Maryland State Department of Vital Records were conducted, in the analysis subjects not identified as dead were assumed to be alive at the end of the study. The overwhelming majority of them were in fact known to be alive between 1985 and 1989 because they had driver's license renewals during that period.

Standardised mortality ratios (SMR) and proportional mortality ratios (PMR) were calculated using the OCMAP Plus software from the University of Pittsburgh.²⁴ The PMR analyses were included because information on all demographic variables including race was complete and available for all deceased subjects with death certificates on which the analysis was based ($n = 3594$). On the other hand, because information on race was not available in the union records, the race was unknown for subjects who were not deceased or were deceased but had no death certificates ($n = 11\ 007$). Thus in the SMR analyses all subjects without a death certificate were randomly assigned a race based on the racial distribution of the known deaths.

For the PMR analysis deaths from each cause were stratified by department, sex and race, and each stratum was subdivided according to age at entry into the cohort (5-year intervals) and calendar year (5-year intervals). For each cell, the proportion of all deaths due to a given cause in the US population was multiplied by the total number of deaths in the corresponding cell of the study population to get the expected number of deaths. The observed number of deaths and the expected

number of deaths in each cell were summed up across all strata to get the total observed and expected deaths. The ratio of observed to expected deaths is the PMR. The variance was calculated assuming a binomial distribution for the observations.²⁵

For the SMR analysis the study population was stratified by department, race and sex, and each stratum was subdivided according to age at entry into the cohort (5-year intervals) and calendar year (5-year intervals). Person-years were accumulated from 1 January 1949 for those who were already members of the union before that date. For those who became members later, person-years began on the date of membership. Person-years were enumerated up to the date of death, or date of termination of the study on 31 December 1989, whichever was earlier. Expected deaths were derived by multiplying the person-years in each cell by the corresponding gender-, calendar year-, age-specific mortality rate for the US general population. Observed and expected deaths for each cell were summed over all ages and calendar years, and over all strata, and the SMR estimated as the total observed number of deaths divided by the total expected. The 95% confidence intervals (CI) for the SMR were calculated according to a simple exact method that links both the Poisson and χ^2 distributions.²⁶

We also calculated for specific causes of death a relative SMR, defined as the ratio of the SMR obtained for the specific cause in the exposed group (abattoirs or meat processing plants) to that in the unexposed group of non-meat workers in the union, with confidence interval determined by a method for large samples.^{27–28} Results for relative SMRs will account for any variation between local mortality rates and US rates, and also to some extent for the healthy worker effect. Under certain conditions (which include homogeneity of SMRs across strata, and similarity of age distributions of the groups being compared) the relative SMR is equivalent to the odds ratio, and provides an estimate of the risk for a given cause of death in one group relative to that in another.²⁸

In nearly all cases no racial differences were observed in the results. Thus we present results for all males combined and for all females combined, and will point out racial differences where present.

RESULTS

In table 1, comparison of the age distributions of workers in abattoirs, meat processing plants, and the control group (non-meat) indicates no significant difference in their age structures. Table 2 gives the distributions of study subjects, person-years at risk, and deaths, by gender and race. The results in the tables 3 and 4 are for causes of death for which a statistically significant risk (SMR or PMR) was observed in at least one subgroup when the observed number of deaths was greater than one. It is seen that the SMR results for abattoirs and meat processing plants

Table 1 The distribution of year of birth in the Baltimore cohort

Interval	Abattoirs		Meat processing		Non-meat	
	n	%	n	%	n	%
1870–1900	143	3.01	93	2.47	131	2.16
1900–10	321	6.76	206	5.47	276	4.54
1910–20	1008	21.24	566	15.02	811	13.34
1920–30	1482	31.23	1148	30.47	1298	21.36
1930–40	980	20.65	1109	29.43	1611	26.51
1940–50	548	11.55	497	13.19	1135	18.67
1950–60	263	5.54	149	3.95	811	13.34
1960–70	1	0.02	0	0	5	0.08

*The overall test χ^2 statistic comparing the three groups indicated that there was no difference in their age distributions ($p = 0.37$).

Table 2 Number of subjects at risk, person-years at risk and number of deaths, by plant, race and sex, 1949–89)

	Males			Females		
	At risk, n	Person-years	Deaths, n	At risk, n	Person-years	Deaths, n
Abattoirs						
White	3083	90388.8	953	830	28244.7	189
Non-white	797	22463.1	234	38	1251.2	4
Total	3880	112851.9	1187	868	29495.9	193
Meat processing plants						
White	1678	48765.1	509	898	28459.0	183
Non-white	991	26261.7	291	206	5296.7	29
Total	2669	75026.8	800	1104	33755.7	212
Non-meat plants						
White	1995	46950.3	391	1107	32506.6	229
Non-white	1796	42000.5	343	1183	34981.3	239
Total	3791	88950.8	734	2290	67487.9	468

Cause of death was missing for a total of 83 deaths (16 in abattoirs, 26 in meatpacking plants, 41 in non-meat plants).

agree very closely with those of the corresponding PMRs as expected from theory,²⁹ as the all-causes SMRs in these groups were in general close to unity.

Increased risks of death from ICD 030–041 (other bacterial diseases) were observed in men and women in abattoirs and meat processing plants, and the relative SMRs were also modestly elevated. There were a total of 44 deaths in this category, and 41 (95%) were from ICD 038 (septicaemia).

A significant excess occurrence of deaths from subarachnoid haemorrhage (ICD 430) was observed only for males in meat processing plants, and the corresponding relative SMR was similarly elevated. No excess occurrence was seen in abattoirs or in the control group.

Deficits in deaths from occlusion/stenosis of the pre-cerebral and cerebral arteries (ICD 433, 434) were observed for males and females in abattoirs and meat processing plants, but not in the control group. In meat processing plants, the deficit was statistically significant in males.

High risks of death from acute and subacute endocarditis (ICD 421) were observed only in women in meat processing plants. Deaths from hypertensive disease (ICD 401–405) was not significantly elevated in meat workers, and in fact tended to be depressed although not statistically significant (results not shown).

Significant excesses of deaths from functional diseases of the heart (ICD 426, 427; conduction disorders, cardiac dysrhythmias) were observed in abattoirs and meat processing plants, but the increased risks seem confined to women in these departments when relative SMRs are considered.

Statistically significantly elevated risks for ischaemic heart disease (ICD 410–414) were observed in males in abattoirs and meat processing plants, but the relative SMRs were not elevated, and similar elevations were not statistically significant in females.

Excess of deaths from chronic nephritis (ICD 582) was observed in white males in abattoirs and white females in meat

Table 3 Cause-specific mortality in abattoirs (PMR, SMR, relative SMR)

Cause of death	Males				Females			
	Obs deaths, n	PMR (95% CI)	SMR (95% CI)	RSMR (95% CI)	Obs deaths, n	PMR (95% CI)	SMR (95% CI)	RSMR (95% CI)
Other bacterial diseases (ICD 030–041)	12	2.3 (1.3 to 4.0)	2.3 (1.2 to 4.0)	1.5 (0.6 to 4.1)	2	1.9 (0.5 to 7.4)	1.9 (0.2 to 6.9)	1.5 (0.3 to 7.5)
Ischaemic heart disease (ICD 410–414)	415	1.2 (1.1 to 1.3)	1.2 (1.1 to 1.4)	1.0 (0.8 to 1.2)	45	1.1 (0.8 to 1.4)	1.0 (0.8 to 1.4)	0.8 (0.6 to 1.2)
Acute & subacute endocarditis (ICD 421)	0				0			
Functional diseases of the heart (ICD 426, 427)	22	1.3 (0.9 to 2.0)	1.4 (0.9 to 2.1)	0.8 (0.4 to 1.5)	9	3.4 (1.8 to 6.2)	3.4 (1.6 to 6.5)	2.8 (1.2 to 6.8)
Subarachnoid haemorrhage (ICD 430)	2	0.4 (0.1 to 1.5)	0.4 (0.0 to 1.4)	0.4 (0.1 to 2.2)	2	1.1 (0.3 to 4.4)	1.1 (0.1 to 3.9)	1.8 (0.3 to 11.0)
Occlusion/stenosis pre-cerebral & cerebral arteries (ICD 433–434)	7	0.5 (0.3 to 1.1)	0.5 (0.2 to 1.0)	0.5 (0.2 to 1.4)	3	1.1 (0.4 to 3.5)	1.1 (0.2 to 3.2)	1.4 (0.4 to 5.3)
Cirrhosis, chronic liver disease, liver abscess, other (ICD 571–573)	39	1.1 (0.8 to 1.5)	1.1 (0.8 to 1.5)	1.0 (0.6 to 1.6)	1	0.2 (0.0 to 1.1)	0.2 (0.0 to 1.1)	0.3 (0.0 to 2.2)
Chronic nephritis (ICD 582)	7	2.6 (1.3 to 5.3)	2.2 (0.9 to 4.6)	1.1 (0.3 to 3.5)	0			
Other diseases of kidney & ureter (ICD 593)	6	3.5 (1.7 to 7.5)	3.3 (1.2 to 7.2)	1.7 (0.4 to 6.6)	1	3.9 (0.6 to 24.2)	3.6 (0.1 to 19.9)	0.8 (0.1 to 6.8)
Parkinson's disease (ICD 332)	4	2.5 (1.0 to 6.5)	2.7 (0.7 to 6.9)		0			
All Causes	1187		1.0 (1.0 to 1.1)	1.0 (0.9 to 1.1)	193		1.0 (0.9 to 1.2)	1.1 (0.9 to 1.3)

PMR, proportional mortality ratio; SMR, standardised mortality ratio; RSMR, relative SMR; ICD, 9th revision International Classification of Diseases.

Comparison group for PMR and SMR is the US general population.

Comparison group for relative SMR is the control group of union workers in non-meat companies.

Table 4 Cause-specific mortality in meatpacking plants (PMR, SMR, relative SMR)

Cause of death	Males				Females			
	Obs deaths, n	PMR (95% CI)	SMR (95% CI)	RSMR (95% CI)	Obs deaths, n	PMR (95% CI)	SMR (95% CI)	RSMR (95% CI)
Other bacterial diseases (ICD 030–041)	7	1.9 (0.9 to 3.9)	1.9 (0.8 to 3.9)	1.3 (0.4 to 3.8)	2	1.7 (0.4 to 6.8)	1.7 (0.2 to 6.3)	1.3 (0.3 to 6.7)
Ischaemic heart disease (ICD 410–414)	230	1.1 (1.0 to 1.2)	1.2 (1.1 to 1.4)	1.0 (0.8 to 1.2)	47	1.2 (0.9 to 1.5)	1.2 (0.8 to 1.5)	1.0 (0.7 to 1.4)
Acute & subacute endocarditis (ICD 421)	0				2	20.1 (7.6 to 53.4)	21.1 (2.6 to 76.3)	5.7 (0.5 to 62.9)
Functional diseases of the heart (ICD 426, 427)	22	2.1 (1.4 to 3.1)	2.1 (1.3 to 3.1)	1.2 (0.7 to 2.3)	11	3.9 (2.2 to 6.7)	3.9 (1.9 to 7.0)	3.3 (1.4 to 7.5)
Subarachnoid haemorrhage (ICD 430)	10	2.5 (1.4 to 4.6)	2.7 (1.3 to 5.0)	2.7 (0.8 to 8.6)	2	0.8 (0.2 to 3.2)	0.9 (0.1 to 3.4)	1.5 (0.3 to 9.0)
Occlusion/stenosis pre-cerebral & cerebral arteries (ICD 433–434)	2	0.2 (0.1 to 0.8)	0.2 (0.0 to 0.9)	0.2 (0.0 to 1.1)	1	0.4 (0.1 to 2.7)	0.4 (0.0 to 2.1)	0.5 (0.1 to 4.1)
Cirrhosis, chronic liver disease, liver abscess, other (ICD 571–573)	36	1.3 (0.9 to 1.8)	1.5 (1.0 to 2.0)	1.4 (0.8 to 2.2)	5	0.8 (0.3 to 1.8)	0.9 (0.3 to 2.1)	1.3 (0.4 to 3.8)
Chronic nephritis (ICD 582)	1	0.4 (0.1 to 2.9)	0.4 (0.0 to 2.4)	0.2 (0.0 to 1.7)	3	5.6 (2.1 to 15.2)	5.4 (1.1 to 15.9)	2.2 (0.5 to 8.6)
Other diseases of kidney & ureter (ICD 593)	2	1.5 (0.4 to 5.8)	1.5 (0.2 to 5.5)	0.8 (0.1 to 4.5)	1	2.7 (0.4 to 17.9)	2.9 (0.1 to 16.3)	0.7 (0.1 to 5.5)
Parkinson's disease (ICD 332)	1	1.3 (0.2 to 9.4)	1.3 (0.0 to 7.5)		0			
All Causes	800		1.1 (1.0 to 1.2)	1.1 (1.0 to 1.2)	212		1.1 (1.0 to 1.3)	1.2 (1.0 to 1.4)

PMR, proportional mortality ratio; SMR, standardised mortality ratio; RSMR, relative SMR; ICD, 9th revision International Classification of Diseases.

Comparison group for PMR and SMR is the US general population.

Comparison group for relative SMR is the control group of union workers in non-meat companies.

processing plants but not in any other groups or in the control group. The SMRs for other diseases of the kidney and ureter (ICD 593) were markedly elevated in abattoirs and meat processing plants, but the relative SMRs were not significantly elevated.

The SMR for cirrhosis/chronic liver disease/liver abscess/other (ICD 571–573) were significantly slightly elevated for white males in meat processing plants, but this was not seen in any other exposed group or in the controls.

Finally, an excess of deaths from Parkinson's disease (ICD 332) was evident in abattoirs and to a lesser extent in meat processing plants. However, all the deaths were confined to men, and no deaths were recorded in males in the control group.

We carried out analysis by latency for causes for which at least 10 deaths were observed (results not shown). These causes were other bacterial diseases (abattoir men only), ischaemic heart disease (men and women in abattoirs and meat processing plants), functional diseases of the heart (abattoir men and men and women in meat processing plants), cirrhosis (abattoir and meat processing plant men only), and subarachnoid haemorrhage (meat processing plant men only). Increased risks seemed to persist throughout the period of observation for all of these causes, except for other bacterial diseases in male abattoir workers for which no case occurred during the first 15 years of follow-up, and increased risk persisted thereafter. Interestingly, in male meat processing plant workers, similarly no case was observed during the first 20 years of follow-up, with elevated risk thereafter based on seven deaths.

DISCUSSION

There have been other cohort studies of mortality in meat workers, but emphasis has been on the report of excess cancer mortality.^{30–36} Information on mortality from non-malignant diseases has been sparse or non-informative because of the practice of combining several distinct causes of death into very broad categories. Thus, excess risks have been reported for diseases of the circulatory and digestive systems, endocrine,

nutritional and metabolic diseases, and benign neoplasms and cirrhosis of the liver.^{22 23 30 33 34 36} We had previously reported on cancer and non-cancer mortality in this cohort,^{21–23} but the present mortality update is the first time ever that cause-specific non-cancer mortality in this or any occupational group has been investigated in such detail. Previous studies have been hampered because available statistical software for analysing cause-specific mortality in occupational studies have all grouped individual causes into very broad groups, resulting in lack of information on specific causes. In this study we examined 134 specific causes of non-cancer deaths. To our knowledge no published cohort mortality study has investigated this many before.

The main findings in this study are the excess occurrences of septicaemia, endocarditis, cardiac dysrhythmias, subarachnoid haemorrhage, nephritis and other kidney diseases in this group of wholesale manufacturing meat workers. These conditions are well known to be clinically related and can all be caused by infection, and could fit into the cardio-mycotic-embolic syndrome which is well described in medical textbooks.^{37–39} The high aerosol and skin exposures to transmissible agents that are known to occur in this group of workers because of their propensity for cuts, lacerations, dermatitis and other injuries^{40–42} put them at high risk of these agents getting into the body and possibly causing an underlying bacteraemia/septicaemia. Once these agents get access to the circulatory system, they may spread to target organs—primarily the heart, brain and kidney. While this is one of other possible explanations for the occurrence of these excesses of deaths in the cohort, it should be emphasised that the excesses could well have arisen by chance because of the small numbers involved. Hence great caution should be exercised in the interpretation of the findings. At this time these results should be regarded as exploratory as it is the first time that they have been reported on, and their validity will depend on confirmation in other studies.

A statistically significant excess of deaths from liver disease was confined to males in meat processing plants, and could be a chance finding or related to alcohol intake or could also be

induced by occupationally acquired infection. Similarly, an excess of deaths from Parkinson's disease seem confined to men in abattoirs and meat processing plants, as none was observed in women in these plants or in the corresponding male controls. The cause of Parkinson's disease is unknown, but it is plausible that infection can cause damage to the cells of the substantia nigra in the brain, giving rise to the disease.

A case of bovine spongiform encephalopathy ("mad cow disease") has been diagnosed in a cow in the US.⁴³ New variant Creutzfeldt-Jakob disease (CJD) in humans is believed to be caused by the prion agent that causes "mad cow disease" in cattle. CJD has been previously linked with occupational and non-occupational exposure to animals, including butchers and other workers in the meat industry.⁴⁴⁻⁴⁶ Similarly, multiple sclerosis has been linked with exposure to sheep affected by swayback disease of the central nervous system⁴⁷ although, to date, no deaths from CJD or multiple sclerosis have been observed in this cohort. However, this and other cohort studies of meat workers may play an important role for monitoring diseases in humans hypothesised to be linked to exposure to zoonotic agents that are found in food animals, as further follow-up of these cohorts is extended.

The studied described above had certain deficiencies. The cause-specific SMRs may not be comparable across the three groups if the individual SMRs vary across age strata and the age distributions of the groups markedly differ. However, all three populations came from the same union and as is seen in table 1, the age distributions were quite similar. Also, in the SMR analyses, information on race was missing for subjects without a death certificate. However, the close agreement between the cause-specific SMR and PMR results predicted by theory when the all-causes SMRs are close to unity evident in these results indicates that any bias resulting from these two potential problems was probably minimal.²⁸⁻²⁹ Typical of retrospective cohort studies, the ability to control for important occupational and non-occupational confounding factors was limited, as was detailed information on exposure, and this could have affected interpretation of the results. For example, the slight excess of cirrhosis of the liver in males could be alcohol-related.

Secondly, it is possible that underlying risks may have been missed because of insufficient statistical power to detect risk from rarer outcomes. For several causes, elevated SMRs/PMRs that were not statistically significant but were based on one or two deaths were observed (results not shown), and these may well be indicative of potential risk. For example, the SMR for meningitis in all race/sex groups in meatpacking plants was 4.6 based on three deaths, while none was observed in the control group, and higher risks based on single deaths were observed in three of the four race/subgroups in abattoirs (not shown). Similarly, analysis by latency was primarily limited by lack of statistical power, although there is an indication that the increased occurrence of other bacterial diseases (septicaemia) is of late onset. At the end of this follow-up only 20% of the members of this cohort have died, thus further follow-up might well reveal more definite associations.

Thirdly, the classification into abattoirs and meat processing plants used in this study may not be sufficiently detailed enough for accurately depicting the expected exposure gradient of higher exposure to transmissible agents in abattoir workers than in those in meat processing plants, and could well explain why for example the risks of death from acute rheumatic fever and subarachnoid haemorrhage were higher in meat processing plants than in abattoirs. For example, abattoirs and meat processing plants were not separated according to whether they handled pigs, cattle or sheep. It is well known that although high rates of infection with some microbial agents like *bacillus anthracis*, *brucella* spp, *leptospira* spp, *staphylococcus aureus*,

streptococcus group A-E, G & L, *salmonella* spp and *E coli* are commonly encountered in workers in cattle, pig and sheep abattoirs and meat processing plants; high rates of others are found only in particular plants.⁴² For example, high rates of infection with *streptococcus suis* type II and *yersinia* spp are found only in plants that handle pigs; bovine pustular stomatitis and rabies viral infections are associated with workers who handle cattle; infection with the virus that causes orf is seen primarily in workers exposed to sheep.⁴² Many of the plants in this study handled a combination of these animals, although some handled one type predominantly. Related to this is the inability of the study to take into the account specific tasks performed which may be related to different exposures; for example, wrapping was predominantly a female activity throughout the industry.²⁰⁻⁴⁸ Although we focused mainly on transmissible agents, it is possible that some of the excess occurrence of deaths observed may well be related to other exposures such as fumes from the wrapping machine,⁴⁹ or even exposures such as nitrites and nitrosamines during curing,⁵⁰ or preservatives such as butylated hydroxytoluene or butylated hydroxyanisole which are known to enhance tumour formation in animals,⁵¹⁻⁵² or smoke during the smoking of meat,⁵³ which some of these workers could have been exposed to. It should be pointed out though that activities such as curing and smoking of meat are usually carried out by only a handful of individuals.

Fourthly, in this update of mortality in the cohort, employment history was not updated because of subsequent loss of data on dues payment in the union database that occurred after the first follow-up while the union was converting from a hard copy based record system to a computerised one. Thus we could not examine risk by duration of employment.

Finally, causes of death reported on in tables 3 and 4 represent the 10 causes out of 134 examined for which a statistically significant increase was observed in any race/sex group within any of the three departments investigated. Therefore, because of multiple comparisons, it is possible that some of the increased risks observed could have been chance occurrences, in spite of the fact that they all could be clinically related to each other from an underlying infective aetiology. Because of these limitations, the interpretation of the findings must be tempered with caution.

In spite of these deficiencies, the study is of importance and has obvious advantages. This is one of the largest studies of meat workers exposed to cattle, pigs and sheep to date, and the only study of this occupational group in the US. No study to date has examined so many specific causes of death in any occupational mortality study. The cohort was uniquely completely defined. Because of the exceptional recordkeeping system of this union, everyone who had ever been employed in these plants—for even just a few days—had a record, making selection bias an unlikely factor that would explain the findings. Similarly, the presence of the control group of non-meat workers from the same union permitted the control for the healthy worker effect and also for any geographic variation in rates between the local general population and the US general population. Finally, the results were consistent in so far as an underlying infective process could potentially give rise to all of them, and the increased risks for these causes were observed irrespective of whether the US general population or unexposed workers of the same union was used as the comparison group. In fact in some cases no deaths were observed in the non-meat group. This pattern strengthens the case for these observations to be real, particularly as lost persons were assumed to be alive in the analyses. Further follow-up of this cohort and other similar cohorts worldwide, and the conduct of case-control studies nested within these cohorts that will permit detailed characterisation of exposures

Main messages

- Workers who handle food animals or their products have high exposure to transmissible agents present in the animals or their products. The findings of this study indicate that these workers are at increased risks of dying from diseases of the heart and circulatory system, and neurological and kidney diseases, which may be caused by these agents.
- It is possible also that the occurrence of these diseases in the general population may be partly due to these agents.

Policy implication

This study confirms previous suggestions that these workers may be at risk of some of these diseases. There is therefore sufficient evidence for more detailed studies to be embarked on, and for consideration to be given to start adopting steps to minimise exposure to these agents in the workplace to protect workers' health.

and controlling for occupational and non-occupational confounding factors should be encouraged, because such studies will be important in shedding light on some of the interesting findings in this study. For the moment the findings in this study should be regarded as preliminary and as hypothesis generating, drawing attention to the possibility that zoonotic infections might play a role in the occurrence of these diseases even in the general population.

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Authors' affiliations

E S Johnson, Y Zhou, N Shah, A Christopher, Department of Epidemiology, University of North Texas Health Science Center, Fort Worth, TX, USA

E S Johnson, Y Zhou, M Sall, M El Faramawi, N Shah, A Christopher, N Lewis, Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA

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