ORIGINAL ARTICLE

Occupational risk of salmonellosis and campylobacteriosis: a nationwide population-based registry study

Janneke W Duijster,[1] Eelco Franz,[1] Jacques J C Neefjes,[2] Lapo Mughini-Gras[1,3]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/oemed-2019-105868).

[1]Center for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands
[2]Oncode Institute and Department of Cell and Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands
[3]Institute for Risk Assessment Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands

Correspondence to
Dr Lapo Mughini-Gras, Center for Infectious Disease Control, RIVM, Bilthoven 3720 BA, The Netherlands; lapo.mughini.gras@rivm.nl

Received 8 April 2019
Revised 24 June 2019
Accepted 7 July 2019

Check for updates

To cite: Duijster JW, Franz E, Neefjes JJC, *et al*. *Occup Environ Med* 2019;**76**:617–624.

ABSTRACT

Objectives Occupational exposure to animals and foods thereof is a poorly characterised risk factor for salmonellosis and campylobacteriosis, the main causes of bacterial gastroenteritis in the Western world. We performed a population-based registry study in the Netherlands to assess whether differences exist in the incidence of reported salmonellosis and campylobacteriosis cases among occupational groups, and whether they can be explained by differences in the magnitude of exposure to these pathogens, as defined by serology.

Methods Person-level occupational data for all Dutch residents were linked to lab-confirmed salmonellosis and campylobacteriosis data, and to serological data from a previous national serosurvey. SIRs for salmonellosis and campylobacteriosis among occupational sectors and specific high-risk occupations were calculated based on the total employed population. Moreover, *Salmonella* and *Campylobacter* seroincidence rates were compared among sectors and high-risk occupations.

Results Occupational exposure to live animals or manure and working in the sale of animal-derived food products were associated with significantly increased risks of salmonellosis (SIR 1.55–1.82) and campylobacteriosis (SIR 1.36–1.65). Moreover, incidences were significantly higher in specific industrial sectors, as well as healthcare and social work sectors. Mean seroincidence rates ranged from 1.28 to 2.30 infections/person-year for *Campylobacter*, and from 0.36 to 0.99 for *Salmonella*, with only slightly higher rates for people in high-risk occupations.

Conclusions Significant differences in reported salmonellosis and campylobacteriosis incidence exist among occupational sectors, with the highest incidence in those persons occupationally exposed to live animals. These differences are only partially reflected in the serology.

Key messages

What is already known about this subject?

- Occupational contact with animals or animal-derived (food) products is a poorly characterised risk factor for *Salmonella* and *Campylobacter* infections, the leading causes of bacterial gastroenteritis worldwide.

What are the new findings?

- Significant differences exist in the incidence of reported salmonellosis and campylobacteriosis cases among occupational groups.
- These differences are only partially explained by differences in infection pressure by these pathogens, as defined by serology.

How might this impact on policy or clinical practice in the foreseeable future?

- As *Salmonella* and *Campylobacter* infections cause a serious health burden, identifying occupations at risk of acquiring these infections may provide important target for control activities.
- Targeting education and prevention strategies, for instance, may help understand the transmission routes in these occupational groups as to reduce disease burden and provide a better picture of the epidemiology of these occupationally acquired infections.

BACKGROUND

Salmonella and *Campylobacter* are the main causes of bacterial gastroenteritis in the Western world, including the European Union.[1] In the Netherlands, the annual number of salmonellosis cases is estimated at ~27 000, whereas for campylobacteriosis, this number is twofold to threefold higher.[2] In terms of disability-adjusted life years (DALY), both pathogens are estimated to cause altogether over 4000 DALYs in the Netherlands every year, with the associated cost amounting to ~€75 million/year. Such burden is mainly attributable to possible sequelae beyond gastroenteritis (ie, Guillain-Barré syndrome, reactive arthritis, irritable bowel syndrome and inflammatory bowel disease).[3 4] Surveillance of salmonellosis and campylobacteriosis in the Netherlands is based on voluntary reporting of a network of diagnostic laboratories capturing mainly cases with more severe symptoms. Besides the main and extensively researched route of transmission via food, *Salmonella* and *Campylobacter* infections may be acquired through contact with animals or manure.[5 6] The risk of *Salmonella* or *Campylobacter* transmission via contact with animals or manure has been shown to be significant in specific cohorts, including people occupationally exposed to live animals or animal-derived products (eg, farmers and abattoir workers).[7 8] Studies assessing salmonellosis and campylobacteriosis incidence across different types of occupations on a national level are scarce.[9] Therefore, the aim of this study was to assess whether differences exist in the incidence of reported salmonellosis and campylobacteriosis cases among occupational groups, and whether they can be explained by differences in the magnitude of exposure to these pathogens, as defined by serology.

METHODS

Data and study population

We linked two national registries and a national serosurvey in the Netherlands (~17 million inhabitants). One registry included deidentified person-level data on occupation as derived from Statistics Netherlands (CBS), which records the occupation of all Dutch residents at any moment in time based on tax returns. Occupations are coded based on the European Nomenclature of Economic Activities (NACE) (second revision) classification of productive economic activities, which is part of the integrated International Standard Industrial Classification of All Economic Activities (ISIC) system.[10] NACE codes consist of five digits, allowing for four hierarchical levels (ie, sections, divisions, groups, classes).[10] At the time of analysis, the data set included data for 12 566 846 individuals of legal working age with recorded type of occupation (5-digit level) and the dates of start and end of employment, between January 1999 and December 2016.

The second data set contained data on reported human salmonellosis and campylobacteriosis cases in the Netherlands, derived from the national laboratory surveillance network coordinated by the Dutch National Institute for Public Health and the Environment. Estimated population coverage is 64% and 52% for salmonellosis and campylobacteriosis, respectively.[11] At the time of analysis, the data set included 27 425 records of culture-confirmed non-typhoid *Salmonella* infection and 31 855 records of culture-confirmed *Campylobacter* infections (both among outpatients and hospitalised patients), with relevant metadata (ie, gender, birth date, residence location). The salmonellosis data set contained data between January 1999 and December 2016, whereas campylobacteriosis data between January 2004 and December 2016.

The third data set contained serological data for *Salmonella* and *Campylobacter* from participants of a population-based cross-sectional serosurvey in the Netherlands in 2006–2007. This serosurvey has already been presented in detail before.[12] Briefly, participants provided a blood sample and completed an epidemiological questionnaire. In total, serum samples from 7904 individuals were available, 1304 of which were tested for anti-*Salmonella* and anti-*Campylobacter* IgA, IgM and IgG concentrations (optical density values) using a mixed ELISA based on lipopolysaccharides of *S.* Enteritidis and *S.* Typhimurium[13 14] and an acid glycine extract of *C. jejuni* strain SSDZ-01[15] as capture antigens. This data set has been used in several previous studies on immunodynamic modelling of *Salmonella*[16 17] and *Campylobacter* infections.[18–20]

Data linkage and exposure/outcome definition

All three data sets were transferred to CBS, which acted as trusted third party for data anonymisation by adding a unique Record Identification Number (RIN), based on persons' gender, birth date and residence location. On generation of the RINs, all the personal identifiers were removed, and the RINs were then used for linkage to the study data.[21] We limited the analyses to people aged 16–69 years, as compulsory education applies until 16 years and almost all people retire by the age of 70 years. The data set was cleared from duplicate isolations of the same *S. enterica* subsp *enterica* serovar or *Campylobacter* sp within 3 months after the initial infection. Participants of the serosurvey with start of employment after the sampling date were excluded. We excluded also participants who ended employment >1 year before the sampling date, to account for waning immunity, leaving 733 participants with *Salmonella* and/or *Campylobacter* serology data for analysis.

The structure of the NACE framework allows for analysis at different classification levels. We performed the first analysis at the division level where all occupations are mutually classified into 86 divisions, hereafter also referred to as 'sectors'. Due to revision of the NACE classification in 2008, some occupations could not be classified into a single sector in the period before the revision; hence, these were excluded from the analysis. The serology analysis was performed at section level due to sample size constraints. In total, 21 sections exist, each containing one or multiple sectors (mutually classified). To test for differences between *Salmonella* serovars, these were classified as *S.* Typhimurium and its monophasic variant (35.3%), *S.* Enteritidis (35.8%), and other serovars (28.9%). Based on the type of sample the *Salmonella* isolate originated from (ie, faeces, blood, urine, and so on), *Salmonella* infections were classified as enteric (faeces, 91.1%), septicaemic (blood, 3.7%) or others (mostly urinary tract and wound infections, 5.2%). For *Campylobacter*, the analysis was limited to the most frequently reported species in the Netherlands: *C. jejuni* (92.9%) and *C. coli* (7.1%); further information on the *Campylobacter* isolates was not available.

Statistical analysis

Time at risk (age ≥16) started at the date of employment and ended at the date of first reported *Salmonella* or *Campylobacter* infection, end date of that employment (when this corresponded to the start of an unemployment period) or the end of the study period (1 January 2017), whichever occurred first. As long as no *Salmonella* or *Campylobacter* infection occurred, individuals were allowed to re-enter the study cohort at any point in time in case of intermittent employment periods and shifts between occupations, and they could be included in multiple sectors (either subsequently or simultaneously). Accounting for an average reporting delay of 3 weeks,[11] the reporting date of *Salmonella* or *Campylobacter* infection minus 3 weeks was used for analysis. An event was therefore defined as a reported salmonellosis or campylobacteriosis case with estimated date of infection during an employment period. Separate analyses were performed for *Salmonella* and *Campylobacter*, allowing for occurrence of both infections in one individual.

Incidence rates (IR) per 100 000 person-years at risk of salmonellosis and campylobacteriosis in the employed population were calculated by *Salmonella* serovar and type of infection, *Campylobacter* sp, gender, age (5-year bands) and calendar year. SIRs for salmonellosis and campylobacteriosis were calculated for each occupational sector by dividing the observed number of reported *Salmonella* and *Campylobacter* infections by the expected number of infections based on the IRs in the employed population (matched by gender, age and calendar year); 95% CIs were estimated based on Poisson distribution of person-time data. For sectors with significantly increased or decreased SIRs and ≥10 cases, analyses were stratified by *Salmonella* serovar, *Campylobacter* sp, gender and age group (16–19, 20–29, 30–39, 40–49, ≥50 years). Next, based on the 5-digit NACE codes, we classified 42 occupations with potential risk of occupational exposure to *Salmonella* and/or *Campylobacter* into three specific groups (online supplementary table S1). Those risk groups entailed occupations with possible contact with live animals or manure (eg, farmers and abattoir workers), occupations in food production/preparation (eg, bakers, cooks/chefs) and occupations in sale of animal-derived products (eg, butchers). Overall and stratified SIRs of salmonellosis and campylobacteriosis were calculated for each of these high-risk groups using the rates in the employed population as reference. Cumulative incidence plots with years of employment as timescale were made to graphically display the risk of infection in the risk groups versus the employed population.

Seroincidence rates for *Salmonella* and *Campylobacter* infections, defined as the average number of infections per person-year, were determined based on the optical density values of serum IgA, IgG and IgM as described in detail elsewhere.[20] Briefly, we used the European Centre for Disease Prevention and Control's (ECDC) seroincidence calculator tool (https://ecdc.europa.eu/en/publications-data/seroincidence-calculator-tool), which uses the combination of IgG, IgM and IgA values at a given point in time to estimate the time since seroconversion, thereby providing an estimate of the annual 'force of infection' for each individual using a Bayesian back-calculation model. This model is based on the kinetics of IgG, IgM and IgA observed during previous longitudinal studies of adult patients with stool culture-confirmed *Salmonella* or *Campylobacter* infections, which provided reference values for peak levels and decay rates of Ig concentrations and their relationship over time. Following the analytical approach of Monge *et al*,[18] we tested for differences in log-transformed seroincidence rates between sections using a multivariate linear regression model including also gender and years of employment as covariates. We then compared seroincidences in high-risk occupations with those of other occupations. All statistical analyses were performed using STATA V.14.2. P values <0.05 were considered statistically significant.

RESULTS

Cohort description

The cohort consisted of 12 566 831 individuals aged 16–69 years employed between 1999 and 2016 (online supplementary figure S1). People entering the cohort after the start of the study (1 January 1999) had a median age of 17 years (IQR: 16–29). Overall, 8220 individuals with a reported *Salmonella* infection during employment were observed, corresponding to an IR of 6.51 infections per 100 000 person-years at risk (95% CI 6.36 to 6.65). Online supplementary table S2 shows the IRs of salmonellosis by serovar, type of infection, gender and age group. Highest IRs were observed for age groups 16–19 years (IR: 12.72, 95% CI 11.94 to 13.50) and 20–29 years (IR: 10.85, 95% CI 10.45 to 11.24). Infection occurred after a median of 5 years of registered employment (IQR: 2–9).

For *Campylobacter,* the study period was limited to 2004–2016, with a total of 11 615 429 people in the cohort, of which 14 352 with a reported *Campylobacter* infection. The overall IR was 15.54 infections per 100 000 person-years at risk (95% CI 15.29 to 15.79). As for salmonellosis, the IRs for campylobacteriosis were higher in the younger age groups (online supplementary table S2). The median time of registered employment at infection was 5 years (IQR: 2–8).

Increased occupational risks

Among the 86 sectors, a median of 31 *Salmonella* infections (IQR: 11–87) and 53 *Campylobacter* infections (IQR: 19–149) were reported. Online supplementary table S3 shows the SIRs of salmonellosis and campylobacteriosis per sector. Among sectors with ≥10 reported cases, 12 sectors showed a significantly increased SIR for salmonellosis, campylobacteriosis or both (table 1, online supplementary tables S4–S15). The highest SIRs were observed for the sector 'veterinary activities', with a twofold increased risk for salmonellosis (SIR 2.03, 95% CI 1.22 to 3.37) and campylobacteriosis (SIR 1.96, 95% CI 1.33 to 2.87). Most reported cases within this sector were female (salmonellosis: 80.0%; campylobacteriosis: 84.6%) and aged 20–29 years (online supplementary table S4). Increased SIRs, mainly for campylobacteriosis, were found in five industrial sectors, including the manufacturing of chemicals, paper and machinery, and the extraction and supply of petroleum, gas and electricity. Among these sectors, SIRs were only significant for males (salmonellosis: 1.40–1.42; campylobacteriosis: 1.44–2.59) and people aged ≥30 years. Within the 'other manufacturing' sector, reported cases were mostly attributable to the occupation 'social employment' (*Salmonella* n=165; *Campylobacter* n=301), whereas the other occupations within this sector had <15 reported cases each. Social employment includes customised and supervised occupations for people with physical or mental disabilities. Most cases were reported among people being ≥40 years (salmonellosis: 69.4%; campylobacteriosis: 77.7%). Marginally increased risks were also observed among healthcare and social workers (mean SIR 1.13 salmonellosis; mean SIR 1.17 campylobacteriosis), with most cases being females (77.6%–92.5% salmonellosis; 76.7%–90.2% campylobacteriosis). SIRs for salmonellosis were highest in the youngest age group (16–19 years), whereas this was not the case for campylobacteriosis (online supplementary tables S11–S13). In the healthcare sector, most cases were reported among people working within hospitals (salmonellosis: n=413; campylobacteriosis: n=833). Within 'residential care activities', which includes occupations in nursing homes, psychiatric hospitals, home care for elderly and disabled people, reported infections were evenly distributed across occupations, with SIRs higher for males (online supplementary table S12). Furthermore, an increased risk for campylobacteriosis was found for the 'accommodation' sector (eg, hotels and campsites), with highest risks in the younger age groups (online supplementary table S14).

Decreased occupational risks

Twelve sectors (with ≥10 cases) showed a significantly lower SIR for salmonellosis and/or campylobacteriosis (online supplementary table S3, S16–27). SIRs were 0.77–0.85 for salmonellosis and 0.62–0.92 for campylobacteriosis (table 1). Some of these sectors are 'white collar' sectors, which includes jobs at professional, administrative or managerial level, generally associated with a higher socioeconomic status (SES). No consistent differences were observed among age groups or gender in the white collar sectors. Within the educational sector, risk was significantly reduced only for females (SIR 0.83, 95% CI 0.74 to 0.94 salmonellosis; SIR 0.85, 95% CI 0.78 to 0.93 campylobacteriosis).

High-risk occupations

Online supplementary table S28 shows the characteristics of the three high-risk groups. The group occupationally exposed to live animals or manure ('live animals') consisted of 240 993 and 172 978 people for the salmonellosis and campylobacteriosis analysis, respectively, with the majority being male (63.5%). Within this group, 93 *Salmonella* and 147 *Campylobacter* infections were reported. The second group included 2 037 210 people with occupational exposure through food production/

Table 1 Sectors with significantly increased or decreased SIRs for overall salmonellosis and/or campylobacteriosis

	Salmonellosis			Campylobacteriosis		
Sector	Obs	Exp	SIR (95% CI)	Obs	Exp	SIR (95% CI)
Higher SIRs						
Veterinary activities	15	7.4	2.03 (1.22 to 3.37)**	26	13.3	1.96 (1.33 to 2.87)**
Manufacture of chemicals	59	42.6	1.38 (1.07 to 1.79)*	112	81.0	1.38 (1.15 to 1.66)**
Manufacture of paper (products)	15	19.5	1.03 (0.64 to 1.66)	51	34.1	1.50 (1.14 to 1.97)**
Extraction of crude petroleum and natural gas	6	3.4	1.75 (0.79 to 3.89)	16	6.3	2.54 (1.56 to 4.15)***
Electricity, gas, steam and air conditioning supply	17	23.2	0.73 (0.46 to 1.18)	67	43.9	1.53 (1.20 to 1.94)**
Manufacture of machinery and equipment	59	45.5	1.30 (1.01 to 1.67)*	114	124.7	0.91 (0.76 to 1.10)
Other manufacturing	183	115.8	1.58 (1.37 to 1.83)***	323	230.7	1.40 (1.26 to 1.56)***
Human health activities	550	492	1.12 (1.03 to 1.21)*	1123	918.6	1.22 (1.15 to 1.30)***
Residential care activities	559	478.3	1.17 (1.08 to 1.27)***	981	835.4	1.17 (1.10 to 1.25)***
Social work activities without accommodation	362	331.6	1.09 (0.98 to 1.21)	686	620.5	1.11 (1.03 to 1.19)**
Accommodation	102	95.5	1.06 (0.87 to 1.28)	213	155.0	1.37 (1.20 to 1.57)***
Activities of households as employers of domestic personnel	26	23.2	1.12 (0.76 to 1.65)	82	57.8	1.42 (1.14 to 1.76)**
Lower SIRs						
Architectural and engineering activities; technical testing and analysis†	79	102.8	0.77 (0.62 to 0.96)*	162	191.3	0.85 (0.73 to 0.99)*
Computer programming and consultancy†	80	91.9	0.87 (0.70 to 1.08)	149	240.5	0.62 (0.53 to 0.73)***
Financial service activities†	125	145.8	0.86 (0.72 to 1.02)	200	256.3	0.78 (0.68 to 0.90)***
Activities auxiliary to financial services and insurance activities†	59	58.8	1.01 (0.78 to 1.30)	72	100.1	0.72 (0.57 to 0.91)**
Activities of head offices; management consultancy activities†	134	141.5	0.95 (0.80 to 1.12)	191	279.0	0.68 (0.59 to 0.79)***
Activities of membership organisations†	74	81.1	0.91 (0.73 to 1.15)	113	140.0	0.81 (0.67 to 0.97)*
Education	428	502.3	0.85 (0.78 to 0.94)**	857	934.6	0.92 (0.86 to 0.98)*
Crop and animal production and hunting	105	119.2	0.88 (0.73 to 1.07)	141	181.2	0.78 (0.66 to 0.92)**
Construction of buildings	64	64.1	1.00 (0.78 to 1.27)	141	169.7	0.83 (0.70 to 0.98)*
Wholesale trade	403	431.5	0.93 (0.85 to 1.03)	716	845.7	0.85 (0.79 to 0.91)***
Land transport	157	185.1	0.85 (0.73 to 0.99)*	365	345	1.06 (0.95 to 1.17)
Services to buildings and landscape activities	184	176.2	1.04 (0.90 to 1.21)	247	287.5	0.86 (0.76 to 0.97)*

*p<0.05; **p<0.01; ***p<0.001.
†White collar sector.
CI, Confidence Interval; Exp, expected numbers; Obs, observed numbers; SIR, Standardized Incidence Rate.

preparation ('food production') for the salmonellosis analysis and 1 666 621 people for the campylobacteriosis analysis, with 423 and 762 salmonellosis and campylobacteriosis cases, respectively. The third group included 244 051 people involved in the sale of animal-derived food products ('food sale') for the salmonellosis analysis and 178 427 for the campylobacteriosis analysis, in which 78 salmonellosis and 109 campylobacteriosis cases were reported. Analysis of the three risk groups showed a significantly increased risk for both salmonellosis and campylobacteriosis in the live animals group and in the food sale group (table 2, figure 1). For salmonellosis, the SIR was 1.82 (95% CI 1.49 to 2.23) for the live animals group and 1.55 (95% CI 1.24 to 1.93) for the food sale group. In both groups, risk was most pronounced for *S.* Typhimurium, whereas the risk for serovars other than Enteritidis and Typhimurium was not significantly elevated. SIRs were generally higher in the younger age groups (table 2).

Serology

Data from 732 serosurvey participants remained for analysis (294 males; 438 females). Mean age at sampling was 37 years (SD: 12). Duration of registered employment (since ≥1999) at sampling increased with age, from a median of 1.1 year (IQR: 0.5–2.2) for those aged 16–19 years to 7.8 years (IQR: 7.4–8.2) for people ≥50 years.

Mean seroincidence adjusted for gender and years of employment was 0.74 infections/person-year (95% CI 0.73 to 0.75, n=721) for *Salmonella* and 1.81 infections/person-year (95% CI 1.80 to 1.83, n=725) for *Campylobacter* (table 3). Seroincidence in females versus males was slightly lower for *Salmonella* (exp(b): 0.915 (95% CI 0.770 to 1.086, p=0.308)) and slightly higher for *Campylobacter* (exp(b): 1.086 (95% CI 0.996 to 1.185, p=0.062)), though both non-significant. Age at sampling and years of employment showed a significant positive association with *Salmonella* and *Campylobacter* seroincidences; however, due to high collinearity between these two variables, we only considered years of employment (exp(b): 1.074 (95% CI 1.036 to 1.113) per year of employment for *Salmonella*; exp(b): 1.038 (95% CI 1.019 to 1.057 for *Campylobacter*)). Serology data were available for 19 occupational sections (table 4). Mean seroincidence of *Salmonella* per section ranged from 0.36 to 0.99 infections/person-year. No significant differences were observed in the seroincidence for *Salmonella* between sections (ie, comparisons of each section vs all others). Among sections with ≥10 participants, seroincidences were highest in the sections 'transportation and storage', 'financial and insurance activities' and 'real estate activities'. For *Campylobacter*, the mean seroincidence ranged from 1.28 to 2.30 infections/person-year, with a significantly higher seroincidence rate in the 'other service activities' section (2.30; 95% CI 2.18 to 2.43) compared with other sections. Table 4 shows the seroincidence for *Salmonella* and *Campylobacter* in people exposed to the high-risk occupations: for both pathogens, seroincidence was slightly increased in these high-risk occupations (exp(b): 1.08, 95% CI 0.75 to 1.56, p=0.677, for *Salmonella*; exp(b): 1.03, 95% CI 0.86 to 1.24, p=0.732, for *Campylobacter*), although non-significant.

Table 2 SIRs for salmonellosis and campylobacteriosis by risk group

	Live animals			Food production			Food sale		
Salmonellosis									
Gender	Obs	Exp	SIR (95% CI)	Obs	Exp	SIR (95% CI)	Obs	Exp	SIR (95% CI)
Overall	93	51.5	1.82 (1.49 to 2.23)***	423	445.1	0.95 (0.86 to 1.05)	78	50.5	1.55 (1.24 to 1.93)***
Male	60	32.0	1.88 (1.46 to 2.42)***	195	202.5	0.96 (0.84 to 1.11)	32	19.6	1.63 (1.15 to 2.30)**
Female	33	19.1	1.73 (1.23 to 2.43)**	228	242.5	0.94 (0.83 to 1.07)	46	30.8	1.49 (1.12 to 1.99)**
Salmonella serovar									
Typhimurium	38	13.6	2.79 (2.03 to 3.84)***	130	137.4	0.95 (0.80 to 1.12)	32	14.4	2.23 (1.58 to 3.15)***
Enteritidis	34	20.0	1.70 (1.21 to 2.38)**	177	167.9	1.05 (0.91 to 1.22)	31	20.1	1.54 (1.08 to 2.19)*
Other	21	17.4	1.20 (0.78 to 1.85)	116	139.7	0.83 (0.69 to 1.00)*	15	16.0	0.94 (0.57 to 1.56)
Type of infection									
Enteric	89	47.7	1.87 (1.52 to 2.30)***	399	418.5	0.95 (0.86 to 1.05)	74	47.4	1.56 (1.24 to 1.96)***
Septicaemic	0	1.5	–	9	10.3	0.87 (0.45 to 1.68)	2	1.2	1.71 (0.43 to 6.83)
Other†	4	1.9	2.06 (0.77 to 5.48)	15	16.3	0.92 (0.56 to 1.53)	2	1.9	1.05 (0.26 to 4.21)
Age (years)									
16–19	22	7.18	3.07 (2.02 to 4.66)***	155	147.7	1.05 (0.90–1.23)	30	14.3	2.09 (1.46 to 2.99)***
20–29	33	18.3	1.80 (1.28 to 2.53)**	164	185.0	0.89 (0.76–1.03)	26	17.9	1.45 (0.99 to 2.13)
30–39	18	9.1	1.99 (1.25 to 3.15)**	46	41.8	1.10 (0.82 to 1.47)	8	6.5	1.23 (0.61 to 2.45)
40–49	12	8.1	1.49 (0.85 to 2.62)	31	35.2	0.88 (0.62 to 1.25)	10	5.9	1.69 (0.91 to 3.15)
≥50	8	8.4	0.95 (0.47 to 1.90)	27	35.3	0.77 (0.53 to 1.12)	4	5.8	0.69 (0.26 to 1.84)
P trend	<0.001			0.123			0.026		
Campylobacteriosis									
Gender	Obs	Exp	SIR (95% CI)	Obs	Exp	SIR (95% CI)	Obs	Exp	SIR (95% CI)
Overall	147	88.9	1.65 (1.41 to 1.94)***	762	744.3	1.02 (0.95 to 1.10)	109	80.1	1.36 (1.13 to 1.64)**
Male	94	57.2	1.64 (1.34 to 2.01)***	366	345.9	1.06 (0.96 to 1.17)	36	33.7	1.07 (0.77 to 1.48)
Female	53	31.7	1.67 (1.28 to 2.19)***	396	398.4	0.99 (0.90 to 1.10)	73	46.4	1.57 (1.25 to 1.98)***
Campylobacter sp									
Jejuni	140	82.9	1.69 (1.43 to 2.00)***	718	696.0	1.03 (0.96 to 1.11)	99	74.8	1.32 (1.09 to 1.61)**
Coli	7	6.0	1.17 (0.56 to 2.45)	44	48.3	0.91 (0.68 to 1.22)	10	5.3	1.89 (1.02 to 3.51)*
Age (years)									
16–19	29	9.5	3.05 (2.12 to 4.39)***	216	213.2	1.01 (0.8 to 1.16)	28	18.4	1.52 (1.05 to 2.20)*
20–29	43	26.5	1.62 (1.20 to 2.19)**	333	296.7	1.12 (1.01 to 1.25)*	38	25.2	1.51 (1.10 to 20.7)*
30–39	15	13.8	1.08 (0.65 to 1.80)	65	73.6	0.88 (0.69 to 1.13)	17	10.6	1.60 (1.00 to 2.58)
40–49	26	17.0	1.52 (1.04 to 2.24)*	70	75.8	0.92 (0.73 to 1.17)	18	12.4	1.45 (0.92 to 2.30)
≥50	34	22.0	1.55 (1.11 to 2.17)*	78	85.0	0.92 (0.74 to 1.15)	8	13.4	0.60 (0.30 to 1.19)
P trend	<0.001			0.909			0.070		

*p<0.05; **p<0.01; ***p<0.001.
†*Salmonella* isolated from urine or wounds.
CI, Confidence Interval; Exp, expected numbers; Obs, observed numbers; SIR, Standardized Incidence Rate.

DISCUSSION

We assessed the distribution of reported salmonellosis and campylobacteriosis cases, as well as the magnitude of exposure to these pathogens, among different occupational groups in the Dutch-employed population. We identified significantly increased SIRs for both salmonellosis and campylobacteriosis in several occupations. These observations can be explained by a combination of multiple coexisting factors entailing exposure levels to the pathogens, susceptibility to infection and medical awareness/knowledge associated with the occupations in question.

The risk of reported salmonellosis and campylobacteriosis was almost twofold higher in people in the 'live animals' group, presumably caused by increased exposure to both pathogens. Similar, although stronger, associations were found in a registry study in the USA where the relative risk of salmonellosis and campylobacteriosis among people working in occupations including farming was respectively 10-fold and threefold higher compared with other occupations,[9] whereas in another study, 17% of the campylobacteriosis cases reported occupational exposure to animals.[7] Among people with occupational exposure to animal-derived food products, we observed a significantly increased risk of infection in the 'food sale' group and in the 'accommodation' sector. However, we did not observe it in the overall risk group involved in food production/preparation. Acquired immunity against *Salmonella* and *Campylobacter* might be an explanation for the latter observation. Furthermore, SIRs (for salmonellosis and/or campylobacteriosis) were significantly higher in five industrial sectors, mainly those associated with the use of chemicals. Long-term exposure to chemical substances is associated with altered composition of gut microbiota, resulting in dysregulation of the gut mucosal immune function, which in turn might lead to adverse health effects and possibly increased susceptibility to enteric infections.[22] Generally, frailty and low SES are risk factors for increased morbidity and mortality of disease.[23] This could explain the increased SIRs among people working in the 'other manufacturing' sector,

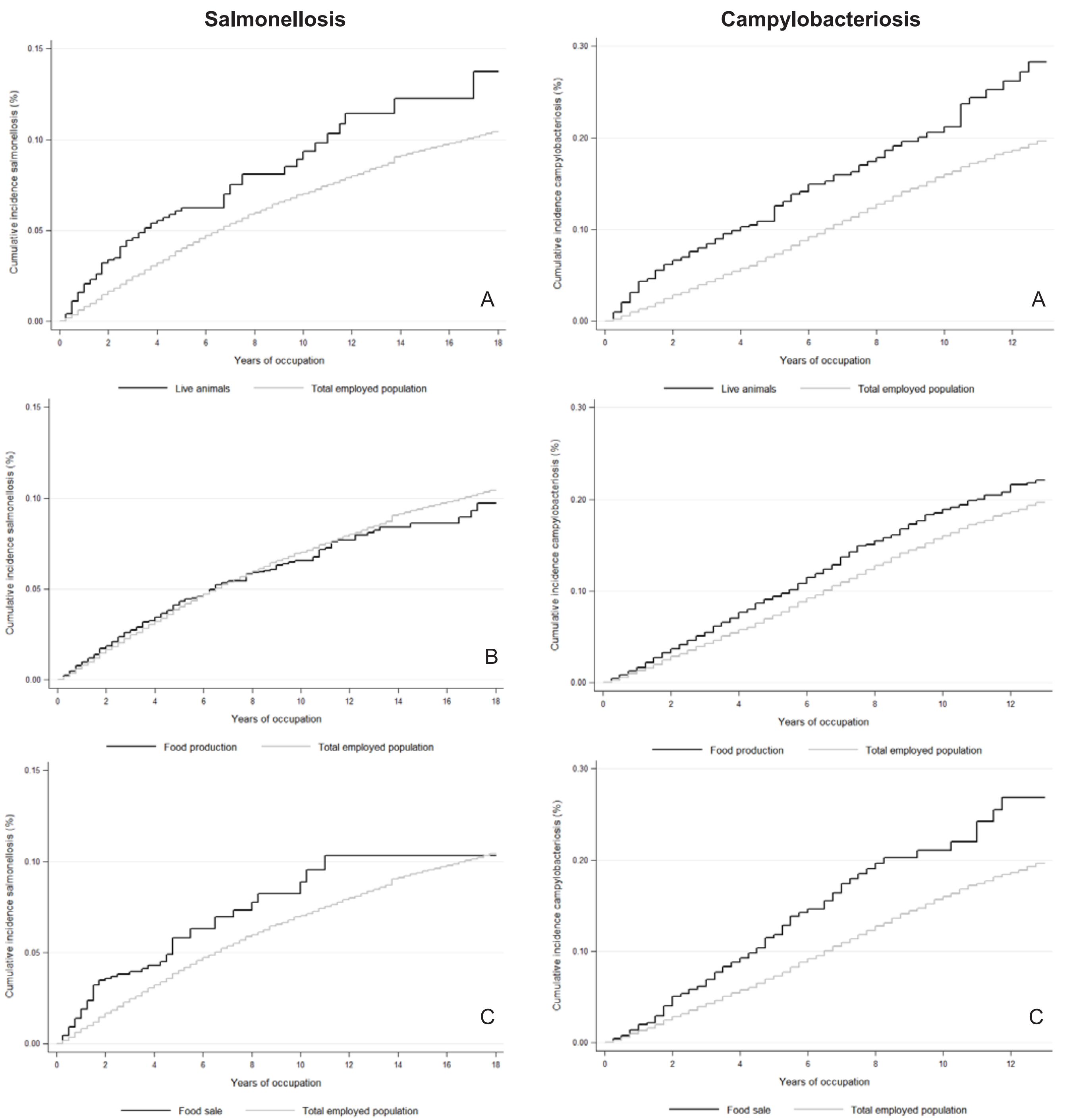

Figure 1 Cumulative incidence (CI) plots of salmonellosis and campylobacteriosis by risk group. (A) Live animals. (B) Food production. (C) Food sale.

whereas the decreased SIRs among people working in 'white collar' sectors could be explained by a higher educational level, SES and general health. Moreover, marginally higher SIRs were observed among people working in healthcare and social work. An underlying factor might be increased infection pressure in such facilities, as nosocomial outbreaks and outbreaks in long-term care facilities are documented for *Salmonella*.[24 25] On the other hand, the increased SIRs might also be partially attributable to increased healthcare-seeking behaviour caused by medical awareness/knowledge among people working in these sectors. Shift work, being common in healthcare and industrial sectors, has been proposed to increase the risk of infection as an indirect result of sleep rhythm and health behaviour on the immune function.[26 27] In addition to the infection risk from occupational exposure, the observed distribution of salmonellosis and campylobacteriosis cases in our study is, to some extent, influenced by surveillance/detection bias, potential healthy worker effect, as well as the confounding effect of lifestyle, which we could not fully control for.[28] Indeed, here we could not account for other potential risk factors related to, for example, eating habits, pet ownership, travel and ethnicity, which might have played a role as well. Moreover, the study period covered 17 years in which diagnostics of gastrointestinal infections and hygiene standards in, for example, abattoirs, might have changed. However,

Table 3 Mean and 95% CI of seroincidence rates (ie, number of infections/person-year) of *Salmonella* and *Campylobacter*, by age at sampling

Age at sampling (years)	*Salmonella*			*Campylobacter*		
	n	Mean*	95% CI	n	Mean*	95% CI
16–19	49	0.52	0.51 to 0.53	49	1.53	1.27 to 1.83
20–29	176	0.69	0.68 to 0.71	178	1.76	1.73 to 1.78
30–39	193	0.78	0.77 to 0.80	194	1.87	1.86 to 1.89
40–49	160	0.78	0.77 to 0.80	159	1.86	1.84 to 1.88
≥50	143	0.79	0.77 to 0.81	145	1.87	1.84 to 1.89
Total	721	0.74	0.73 to 0.75	725	1.81	1.80 to 1.83

*Adjusted for gender and years of employment at time of sampling.
CI, Confidence Interval.

we consistently used the same type of data (ie, culture-confirmed *Salmonella* and *Campylobacter* infections, as culture is still performed for antimicrobial resistance determination after positive PCR screening) and temporal trends in reported salmonellosis/campylobacteriosis were not assessed, that is, data were analysed retrospectively by including (cumulative) employment time of each individual in each sector, and not chronological time per se. Thus, while the strength of some associations might differ between periods, our study was meant to provide overall estimates for the average effects of occupation during the whole study period.

Salmonellosis and campylobacteriosis IRs are based on laboratory-confirmed cases reported to public health surveillance. These cases constitute only a small fraction of all cases occurring in the community and are usually patients with severe or prolonged symptoms. The extent of under-reporting is influenced by healthcare-seeking behaviours and patient-related sensitivity of the healthcare and surveillance systems (eg, patients with travel history or those with underlying chronic diseases are more likely to undergo increased medical scrutiny on presentation of symptoms). Serology allows us to assess infection risks independently of these factors, as it also includes asymptomatic infections, hence it sheds light on the epidemiology of *Salmonella* and *Campylobacter* from a different perspective.[18] We found the seroincidence to be only slightly associated with occupational groups with a higher incidence of reported salmonellosis and campylobacteriosis cases. Previous studies comparing seroincidence rates among countries have found no significant correlations with incidence of reported cases, with seroincidence rates being up to 130-fold higher than reported incidence.[17] Besides surveillance artefacts, possible explanations could be the intrinsic limitations of seroincidence data, such as differential antibody decay over time in different groups of the population. It is difficult to predict how this may have affected the seroincidence estimates of our high-risk groups. If the antibody response is stronger, seroincidence would be overestimated. However, if frequent infections induce a weaker immune response, especially lower IgM production, seroincidence would be underestimated, as pointed out before.[17]

A limitation of the NACE classification is that a person's NACE code is based on the economic activity of the company/organisation employing the linked person, rather than the actual job tasks. The proportion of people employed via an employment agency differs among sectors, with most people in the 'employment activities' sector working in industry (24% males; 14% females).[29] This might affect the observed risk of infection among occupational groups. Furthermore, serological data were limited by the sample size of serosurvey participants

Table 4 Mean and 95% CI of seroincidence rates (number of infections/person-year) of *Salmonella* and *Campylobacter*, by section

Section	*Salmonella*		*Campylobacter*	
	n	Mean (95% CI)†	n	Mean (95% CI)†
Agriculture, forestry and fishing	6	0.77 (0.57 to 1.04)	8	1.62 (1.46 to 1.79)
Manufacturing	76	0.70 (0.67 to 0.73)	76	1.78 (1.74 to 1.82)
Electricity, gas, steam and air conditioning supply	4	0.44 (0.31 to 0.63)	4	1.55 (1.21 to 1.98)
Water supply; sewerage, waste management and remediation activities	4	0.36 (0.25 to 0.53)	4	1.28 (1.06 to 1.56)
Construction	36	0.61 (0.57 to 0.68)	35	1.72 (1.66 to 1.78)
Wholesale and retail trade	133	0.63 (0.61 to 0.65)	134	1.81 (1.77 to 1.84)
Transportation and storage	26	0.99 (0.91 to 1.09)	26	1.76 (1.69 to 1.84)
Accommodation and food service activities	29	0.48 (0.44 to 0.51)	29	1.78 (1.71 to 1.85)
Information and communication	19	0.76 (0.69 to 0.84)	19	1.57 (1.51 to 1.64)
Financial and insurance activities	35	0.97 (0.91 to 1.04)	36	2.07 (1.98 to 2.15)
Real estate activities	10	0.95 (0.80 to 1.13)	10	1.64 (1.51 to 1.78)
Professional, scientific and technical activities	61	0.68 (0.64 to 0.71)	60	1.81 (1.77 to 1.86)
Administrative and support service activities	109	0.67 (0.65 to 0.68)	108	1.72 (1.69 to 1.75)
Public administration and defence; compulsory social security	47	0.77 (0.73 to 0.81)	48	1.89 (1.84 to 1.94)
Education	72	0.78 (0.75 to 0.82)	73	1.82 (1.78 to 1.87)
Human health and social work activities	167	0.70 (0.68 to 0.72)	169	1.78 (1.76 to 1.80)
Arts, entertainment and recreation	20	0.45 (0.43 to 0.49)	20	1.54 (1.48 to 1.59)
Other service activities	21	0.91 (0.84 to 0.99)	21	2.30 (2.18 to 2.43)**
Activities of households as employers	2	0.95 (0.72 to 1.26)	2	2.26 (1.96 to 2.62)
High-risk occupations‡	43	0.65 (0.60 to 0.70)	44	1.69 (1.64 to 1.75)
All occupations	721	0.74 (0.73 to 0.75)	725	1.81 (1.80 to 1.83)

**p<0.01
†Adjusted for gender and years of employment at time of sampling.
‡Risk groups 'live animals', 'food production' and 'food sale' combined.
CI, Confidence Interval.

in some sectors (probably due to participation bias), which hampered comparisons between groups. In conclusion, we found significantly increased occupational risks for salmonellosis and campylobacteriosis among people with occupational exposure to animals or animal-derived products, healthcare and social workers, as well as people working in specific industrial sectors. Seroincidence in these high-risk groups was only slightly increased, suggesting possible differential antibody response and decay over time (on increased exposure to *Salmonella* and *Campylobacter*) in different groups. Campylobacteriosis and salmonellosis should be considered when workers in occupations at increased risk for infection have symptoms compatible with these diseases. Although the exact transmission routes in these occupational groups are yet to be fully understood, targeting education and prevention strategies may help reduce disease and provide a better understanding of these occupationally acquired infections.

Contributors All authors conceived and designed the study. JWD performed the data analysis together with LMG. JWD drafted the paper. All authors have substantially contributed to critical interpretation of the results and drafting/revising of the paper.

Funding This study was supported by the Dutch Ministry for Public Health, Welfare and Sport via the 'ZonMw' (grant number 522004001).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The serosurvey (PIENTER-2) was approved by the Medical Ethics Testing Committee of the Foundation ofTherapeutic Evaluation of Medicines (METC-STEG) in Almere (ISRCTN 20164309). This study was performed on deidentified data and no person identifying information was generated.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

REFERENCES

1 European Food Safety Authority and European Centre for Disease Prevention and Control (EFSA and ECDC). The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2017. *EFSa Journal* 2018;16:e05500.
2 NationalInstitute for Public Health and the Environment (RIVM). Staatvan Zoönosen 2017 [State of Zoonotic Diseases 2017]. Bilthoven: RIVM, 2018.
3 Mangen MJ, Friesema IHM, Pijnacker R, *et al*. *Disease burden of food-related pathogens in the Netherlands, 2017*. 2018. Bilthoven: RIVM, 2018.
4 Mangen M-JJ, Bouwknegt M, Friesema IHM, *et al*. Cost-Of-Illness and disease burden of food-related pathogens in the Netherlands, 2011. *Int J Food Microbiol* 2015;196:84–93.
5 Mughini-Gras L, Enserink R, Friesema I, *et al*. Risk factors for human salmonellosis originating from pigs, cattle, broiler chickens and egg laying hens: a combined case-control and source attribution analysis. *PLoS One* 2014;9:e87933.
6 Mughini Gras L, Smid JH, Wagenaar JA, *et al*. Risk factors for campylobacteriosis of chicken, ruminant, and environmental origin: a combined case-control and source attribution analysis. *PLoS One* 2012;7:e42599.
7 Su C-P, Stover DT, Buss BF, *et al*. Occupational Animal Exposure Among Persons with Campylobacteriosis and Cryptosporidiosis - Nebraska, 2005-2015. *MMWR Morb Mortal Wkly Rep* 2017;66:955–8.
8 Ellström P, Hansson I, Söderström C, *et al*. A prospective follow-up study on transmission of Campylobacter from poultry to abattoir workers. *Foodborne Pathog Dis* 2014;11:684–8.
9 Su C-P, de Perio MA, Fagan K, *et al*. Occupational Distribution of Campylobacteriosis and Salmonellosis Cases - Maryland, Ohio, and Virginia, 2014. *MMWR Morb Mortal Wkly Rep* 2017;66:850–3.
10 Eurostat. NACE Rev. 2—Statistical classification of economic activities, 2008. Available: http://ec.europa.eu/eurostat/web/nace-rev2
11 van Pelt W, de Wit MAS, Wannet WJB, *et al*. Laboratory surveillance of bacterial gastroenteric pathogens in the Netherlands, 1991-2001. *Epidemiol Infect* 2003;130:431–41.
12 van der Klis FRM, Mollema L, Berbers GAM, *et al*. Second National serum bank for population-based seroprevalence studies in the Netherlands. *Neth J Med* 2009;67:301–8.
13 Mollema L, De Melker HE, Hahné SJM, *et al*. PIENTER 2-project: second research project on the protection against infectious diseases offered by the National immunization programme in the Netherlands 2010.
14 Strid MA, Dalby T, Mølbak K, *et al*. Kinetics of the human antibody response against Salmonella enterica serovars enteritidis and typhimurium determined by lipopolysaccharide enzyme-linked immunosorbent assay. *Clin Vaccine Immunol* 2007;14:741–7.
15 Ang CW, Krogfelt K, Herbrink P, *et al*. Validation of an ELISA for the diagnosis of recent Campylobacter infections in Guillain-Barré and reactive arthritis patients. *Clin Microbiol Infect* 2007;13:915–22.
16 Simonsen J, Teunis P, van Pelt W, *et al*. Usefulness of seroconversion rates for comparing infection pressures between countries. *Epidemiol Infect* 2011;139:636–43.
17 Falkenhorst G, Simonsen J, Ceper TH, *et al*. Serological cross-sectional studies on Salmonella incidence in eight European countries: no correlation with incidence of reported cases. *BMC Public Health* 2012;12:523.
18 Monge S, Teunis P, Friesema I, *et al*. Immune response-eliciting exposure to Campylobacter vastly exceeds the incidence of clinically overt campylobacteriosis but is associated with similar risk factors: a nationwide serosurvey in the Netherlands. *J Infect* 2018;77:171–7.
19 Ang CW, Teunis PFM, Herbrink P, *et al*. Seroepidemiological studies indicate frequent and repeated exposure to Campylobacter spp. during childhood. *Epidemiol Infect* 2011;139:1361–8.
20 Teunis PFM, van Eijkeren JCH, Ang CW, *et al*. Biomarker dynamics: estimating infection rates from serological data. *Stat Med* 2012;31:2240–8.
21 Mughini-Gras L, Schaapveld M, Kramers J, *et al*. Increased colon cancer risk after severe Salmonella infection. *PLoS One* 2018;13:e0189721.
22 Jin Y, Wu S, Zeng Z, *et al*. Effects of environmental pollutants on gut microbiota. *Environ Pollut* 2017;222:1–9.
23 Mughini-Gras L, Pijnacker R, Heusinkveld M, *et al*. Societal burden and correlates of acute gastroenteritis in families with preschool children. *Sci Rep* 2016;6:22144.
24 Lee MB, Greig JD. A review of nosocomial Salmonella outbreaks: infection control interventions found effective. *Public Health* 2013;127:199–206.
25 Greig JD, Lee MB. Enteric outbreaks in long-term care facilities and recommendations for prevention: a review. *Epidemiol Infect* 2009;137:145–55.
26 Mohren DCL, Jansen NWH, Kant IJ, *et al*. Prevalence of common infections among employees in different work schedules. *J Occup Environ Med* 2002;44:1003–11.
27 Almeida CMOde, Malheiro A. Sleep, immunity and shift workers: a review. *Sleep Sci* 2016;9:164–8.
28 Spierenburg EAJ, Smit LAM, Heederik D, *et al*. Healthy worker survivor analysis in an occupational cohort study of Dutch agricultural workers. *Int Arch Occup Environ Health* 2015;88:1165–73.
29 CBS. De uitzendbranche in Nederland sinds 2005. retrieved at 4 February 2019 from, 2017. Available: https://www.cbs.nl/nl-nl/achtergrond/2017/43/de-uitzendbranche-in-nederland-sinds-2005