Infectious Diseases Attributable to Household Crowding in New Zealand: A Systematic Review and Burden of Disease Estimate

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1. Executive Summary

Context

The incidence of serious infectious diseases (IDs), notably respiratory, skin and enteric infections, is increasing in New Zealand (NZ). Ethnic and socioeconomic inequalities are large and rising, with markedly higher rates of IDs for Māori and Pacific peoples relative to European/Other. It is important to identify factors that may be contributing to this burden of disease, particularly factors that can be modified.

Household crowding is a plausible risk factor for transmission of IDs. Exposure to household crowding is very unequal across ethnic groups in NZ. The 2006 Census showed that for children <15 years, exposure to extreme crowding (2+ bedroom deficit) was 9.9% for Māori and 20.9% for Pacific children compared with 1.8% for European/Other.

As recently as 2001, a Ministry of Social Policy review of the effects of household crowding on health concluded that the evidence was inconclusive and more research was needed. This study therefore aimed to review the literature and summarise the evidence linking household crowding to IDs to provide a base for estimating the impact of exposure to household crowding on rates of serious IDs in NZ.

Objective

We aimed to identify and summarise cross-sectional, case-control, cohort and intervention studies from the international published literature that investigated the relationship between different degrees of exposure to household crowding density and the outcome of close contact infectious disease (CCIDs). Studies examining participants of any age group from any country were eligible.

We then aimed to estimate the impact of exposure to household crowding on the burden of serious IDs in NZ.

Data Sources

A systematic literature search examined articles published before 8th July 2012 in Medline, Embase, Scopus, Web of Science, Index New Zealand, Cochrane Library and the journal Lancet Infectious Disease. Additional articles were identified by searching references and expert recommendation.

Study Selection

There were 9,852 articles identified. Based on a review of their abstracts, full texts of 838 studies were obtained for further assessment. Of these, 345 studies were eligible for the narrative synthesis. And of these, 116 provided odds ratios or risk ratios adjusted for age and socioeconomic status and were therefore eligible for meta-analysis. Combined estimates were calculated for ten different categories of CCIDs based on 82 studies.

Data Synthesis

Over half of the identified studies (55%, 189/345) demonstrated a statistically significant association between greater household crowding and increased risk of CCID, whereas only 1% (5/345) showed a beneficial effect from crowding. No randomised trials were identified and only one study investigated a crowding reduction intervention.

Where a combined estimate was possible, nine out of ten CCID categories demonstrated a statistically significant association between greater household crowding and increased disease risk, after taking into account the effect of age and socioeconomic status. People living in households with the greatest vs. least crowding density had increased odds of CCID ranging from 1.13 (gastroenteritis) to 3.78 times greater risk (tuberculosis). More than half of the meta-analyses (6/10) were focussed on studying how crowding impacts on children, and predominantly children less than six years old.

Main findings and data quality

This collection of meta-analyses reveals a consistent association between crowding and a range of CCIDs across a variety of settings and study designs. Meta-analyses reliant on observational studies are considered low quality evidence for causality and may be somewhat overstated by reporting bias and incomplete retrieval. However, narrative review results of a much larger group of studies support the meta-analysis results.

The most robust meta-analysis effect estimates provided evidence that household crowding was associated with increased risk of gastroenteritis (OR 1.13, CI 1.01-1.26), pneumonia / lower respiratory tract infection (LRTI) (OR 1.69, CI 1.34-2.13 and RR 1.36, CI 1.09-1.69), *Haemophilus influenzae (Hib)* disease (OR 1.74, CI 1.27-2.37) and respiratory syncytial virus (RSV) bronchiolitis, when cohort (4.44, CI: 2.45-8.04) and case-control data (OR 1.31, CI: 0.85-2.01) were considered separately. There were also statistically significant associations between household crowding and risk of hepatitis A (OR 1.53, CI 1.23-1.90), *H. pylori* infection (OR 1.82, CI 1.55-2.14), meningococcal disease (OR 2.13, CI 1.38-3.29), tuberculosis (OR 3.78, CI 1.78-8.13) and trachoma (OR 2.07, CI 1.06-4.06). The later meta-analyses were less robust due to greater unexplained heterogeneity (where study variability results in observed effects being more different from each other than would be expected from chance alone). Although there was a positive association between upper respiratory tract infection (URTI) and household crowding, this relationship did not reach statistical significance (OR 1.39, CI 0.69-2.79 and RR 1.63, CI 0.88-3.02). All estimates may be somewhat overstated due to publication bias (where positive results are more likely to be published than results of studies that are not statistically significant).

For five of these outcomes (gastroenteritis, pneumonia, bronchiolitis, *Hib* disease, and tuberculosis) there were additional studies that reported unique outcomes so could not be included in the combined analyses. About half (8/15) of these additional studies found significant positive associations between the disease in questions and household crowding. The specific diseases were: toxoplasma gondii infection, typhoid fever, wheeze associated with RSV, *Haemophilus influenzae* carriage, tuberculin positivity (2 studies), and tuberculosis meningitis.

This review identified a further 21 eligible studies covering 16 specific infectious diseases. The outcomes were too heterogeneous to allow for combined estimates. A majority (13/21) found significant positive associations between the disease in questions and household crowding. These diseases were: giardiasis, intestinal parasites (3 studies), influenza-like-illness (2 studies), measles, varicella-zoster infection, invasive GAS infection, pediculosis, Epstein–Barr virus infection, infectious illness warranting hospitalisation, and communicable disease symptoms.

The evidence base of high-quality research studies was relatively large for some important outcomes, such as gastroenteritis and pneumonia, and for some specific infectious diseases, such as *Helicobacter pylori* infection, tuberculosis, *Hib* disease, meningococcal disease and hepatitis A. For other important diseases the published evidence base was very small, notably for skin infections and rheumatic fever. For these conditions, there were insufficient high quality studies to produced combined estimates of the effect of exposure to household crowding.

Estimated burden of ID from exposure to household crowding

We used a burden of disease (BoD) analysis to estimate the contribution of exposure to household crowding to the incidence of serious IDs in NZ. This approach used the effect measures obtained from the meta-analyses, combined with the estimated prevalence of exposure to household crowding in NZ derived from the 2006 Census, to estimate the population attributable fraction (PAF) of IDs from household crowding. These PAFs were applied to hospitalisation incidence data for these IDs (average annual numbers for 2007-11) to estimate hospitalisations attributed to household crowding. This approach was repeated for nine categories of IDs (trachoma was excluded as there is no transmission in New Zealand and URTI was included with the uncertainty around this estimate reflected by the confidence intervals).

We estimated that 1,343 (CI 182-2843) hospitalisations per year in NZ are attributed to household crowding. This total is 10% of the 13,680 hospital admissions a year from these diseases (which represent about one fifth of the total 75,706 annual ID hospitalisations in NZ over the 2004-08 period[1]). However, it is important to recognise that this current analysis was restricted to just nine categories of IDs for which summary estimates of the contribution of household crowding could be made. Due to a lack of high quality published studies, no pooled estimates were possible for many important IDs, such as skin infections and rheumatic fever. In addition, most of these estimates apply to restricted age groups, further under-estimating the likely burden of IDs in the total population.

There are very large ethnic inequalities within this disease burden. For European/Others exposure to household crowding is estimated to cause 331 (CI 20-779) admissions a year, or 5% of IDs (in the nine disease groups examined). For Asian peoples exposure to household crowding is estimated to cause 108 (CI 23-206) admissions a year, or 13% of IDs. For Māori the contribution from household crowding is higher, with an estimated 790 (CI 106-1540) hospitalisations a year or 17% of ID admissions, and for Pacific peoples the estimated contribution is 692 (CI 136-1184) admissions a year or 25% of ID admissions in the disease groups examined.

The contribution of exposure to household crowding is particularly large for some diseases. Meningococcal disease predominantly occurs in children (0-16 years) and

the meta-analysis shows that risk is strongly associated with exposure to household crowding. For Pacific children (where 45% are exposed to household crowding), an estimated 34% of disease burden and in Māori children (where 28% are exposed to household crowding) an estimated 23% of disease burden can be attributed to this exposure. By comparison, the estimate is only 9% in European/Other children (where only 8% are exposed to household crowding).

Conclusions

The findings of this review support the conclusion that household crowding is a very important risk factor for transmission of most major categories of close-contact infectious diseases. Restricting our analysis to the highest quality studies (n=116), and those where there were multiple published works looking at similar outcomes, allowed us to produce combined estimates of the effect of household crowding on ten infectious diseases outcomes. In nine out of ten of these outcomes there was a statistically significant positive relationship between household crowding and the risk of disease (and in the remaining one the effect was positive but not statistically significant).

This systematic review also supports the conclusion that ethnic inequalities in household crowding in NZ are making a large contribution to inequalities in the risk of infectious disease. Children are not only disproportionately exposed to household crowding in NZ, but evidence suggests they may be disproportionately affected by the consequences of this exposure.

Crowding reduction interventions have potential to reduce the burden of CCIDs in NZ. The Housing New Zealand Corporation (HNZC) Healthy Housing Programme included crowding reduction and was associated with a marked decline in hospitalisation for children participating in the Programme. Policies to improve housing affordability are suggested in order to address household crowding in NZ. This includes increasing the number and proportion of social and affordable houses, improving accessibility to social and affordable housing for all ethnic groups, and ensuring housing subsidies and supplements are available for low income households with the most need, particularly large families with children.

Future crowding reduction programmes could be implemented in a way that supports high quality evaluation thus adding to the very small evidence base we currently have of intervention studies in this area. The gold standard of evidence for causality would be from a staggered intervention trial, where one group would be randomly allocated to a comprehensive crowding reduction programme and a second group would receive the intervention at a later time.

2. Introduction

New Zealand has experienced a marked increase in rates of serious infectious diseases (IDs), notably respiratory, enteric and skin infections.[1] These diseases show significant inequalities with rates that are more than twice as high for Māori and Pacific peoples relative to European/Others and almost three times higher for those living in the most deprived neighbourhoods compared with the least deprived.[1] Large inequalities have been reported for many specific IDs including tuberculosis,[2] acute rheumatic fever,[3] meningococcal disease,[4] childhood pneumonia[5] and skin infections.[6] In the 2009 H1N1 influenza pandemic, hospitalisation rates were 3.0 times higher for Māori and 6.7 times higher for Pacific peoples than for the European/Other ethnic grouping.[7] These inequalities are most marked for close-contact infectious diseases (CCIDs), those which are transmitted between people.[8]

Exposure to household crowding in NZ is highly patterned by age, ethnicity and socioeconomic status.[9,10] The distribution of exposure to household crowding is unequal with higher levels for children relative to adults, and for Māori and Pacific relative to European/Other.[10] Households in rental accommodation are more likely to be crowded (11%) than those in dwellings owned with a mortgage (4%) or mortgage-free (2%).[11] Many tenants are children, with 45% of HNZC tenants being less than 18 years of age, with a median age of 20 years (compared with the national median age of 36 in 2006).[12] Crowding varies by region in NZ with the highest level of household overcrowding in Manukau City (24% of people), followed by Opotiki and Porirua.

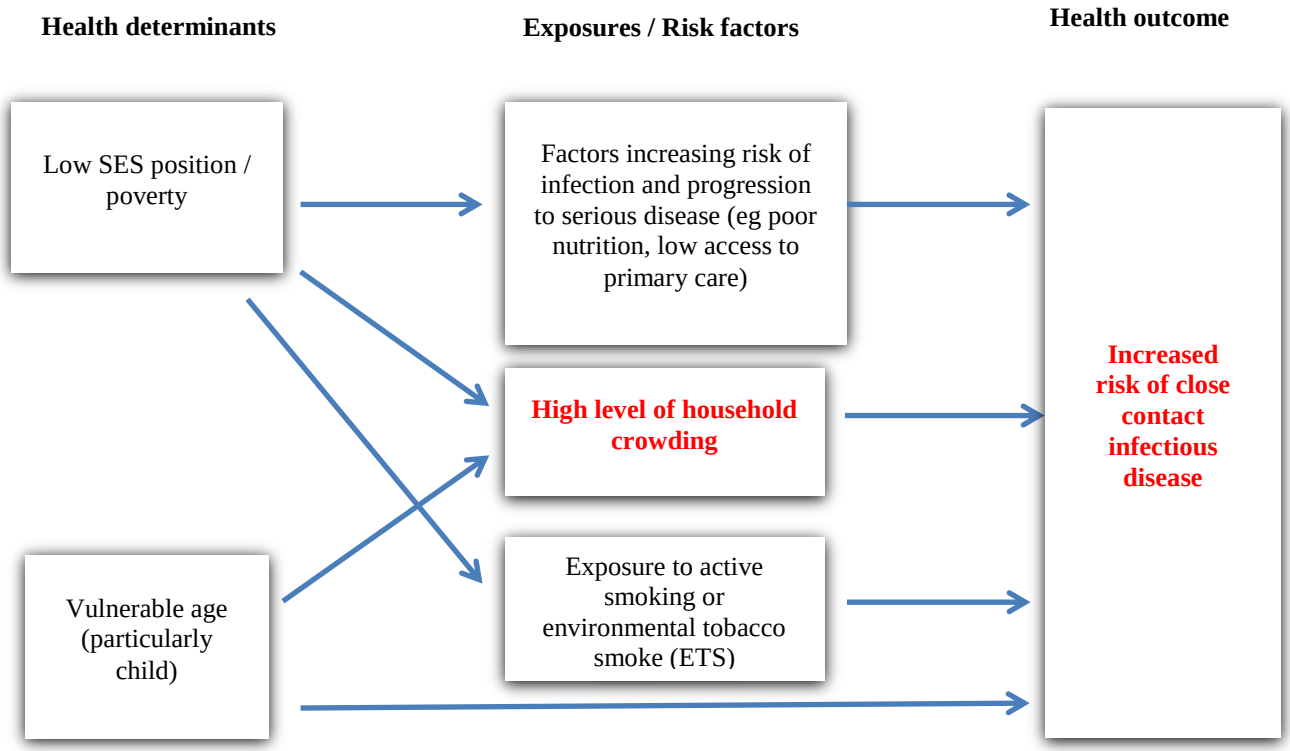
The broad causal pathway linking household crowding to an increased risk of CCIDs is shown in Figure 1. This figure also shows major health determinants (notably age and socioeconomic status) that influence the risk of CCIDs through their association with household crowding and other pathways.

In 2001, a Ministry of Social Policy review of the effects of household crowding on health concluded that the available evidence was inconclusive and more research was needed.[13] Since then, household crowding has become more widely acknowledged as an important health determinant. NZ research has identified exposure to household crowding as an important risk factor for IDs,[14] notably meningococcal disease,[15] tuberculosis,[16] rheumatic fever[17] and pneumonia.[18] The Ministry of Social Development included exposure to household crowding as an indicator of economic wellbeing in all of its annual Social Reports from 2001 to 2010.[19]

The strength of a systematic review and meta-analysis is that multiple study results can be combined in a consistent and robust manner. This process minimises the play of chance, of which small studies are particularly at risk, and reduces bias that may be introduced by investigators' inherent beliefs.

This systematic review aimed to identify and summarise the international published literature from cross-sectional, case-control, cohort and intervention studies that investigate the relationship between high vs. low household crowding density and a CCID outcome. Studies examining participants of any age group from any country were eligible. Meta-analysis was used to summarise the association between crowding and CCID, independent of age and socioeconomic status.

Figure 1: Proposed relationship between household crowding and infectious disease risk, including major confounders



3. Method

3.1. Broad approach

A systematic review of the international literature was conducted to investigate the association between household crowding density and CCIDs. A transparent search strategy and predefined set of eligibility criteria were applied to identify the most relevant studies. The results of the studies were combined both qualitatively (by narrative synthesis) and quantitatively (by meta-analysis) to give an overall picture of the available evidence. Our methods were steered by the PRISMA guidelines for reporting systematic reviews and meta-analyses.[20] The review protocol was registered on PROSPERO.

3.2. Search strategy

A systematic strategy was developed, piloted and implemented to search library databases. The search is up to date as of the 6th July 2012. Databases searched were Medline (1966 to 2012), Embase (1988 to 2012), Scopus, Web of Science, Index New Zealand and the Cochrane Library. The journal Lancet Infectious Disease (highest rated infectious disease journal) was examined more closely for relevant articles by applying simplified search terms.

A small number of articles were identified by expert recommendation. Additional articles for each CCID were identified by exploring the references of the most recent eligible articles. At least one review article was also identified from Google Scholar for each infectious disease and searched for references. If referenced articles met the eligibility criteria they were added to the full text screening.

The search strategy was developed to identify all articles measuring household crowding in combination with any one of a broad set of IDs. Key word searches were used for each of the databases with the addition of customised MeSH terms for Medline and Embase. The majority of studies were published in journals. Studies could be from any year of publication limited only by the limits of each database. The search was limited to human and English language categories.

A pilot search was carried out in Medline to identify studies that referenced household crowding and CCIDs, using the terms; "crowding" (MeSH), "overcrowding" (key word) and "household density" (key word). Infectious origins were detected using the following high-level mesh terms; "bacterial infections and mycoses", "virus diseases" and "parasitic diseases". The pilot highlighted the assortment of measurements that are used to assess household crowding (Table 1). This information informed the final search strategy.

We aimed to identify household crowding studies with search terms that encompassed the concepts of both people and space, including ratios of the number of people in a household per the number of rooms, people per metre^2, bedroom sharing and house area. Each of these aspects was identified using adjacent search term functions (within three words) available in all four key databases. Although it was rarely used, house area was also adopted as a density measure because it has the potential to differentiate between different levels of crowding density for families of a similar size.

The number of people in a household was initially considered to be an eligible crowding measure, however, it was later excluded because it had limited specificity as

a density measure and furthermore it identified an unmanageably large number of potential papers. Bed sharing was excluded because it is more of a behavioural exposure than housing related. Therefore, we chose to concentration this review on measures of household crowding that specifically focus on density including concepts of both people and space (See eligibility criteria).

Table 1: Crowding measures used in different studies (most are continuous or categorical measures rather than binary)

Measure	Frequency
People per house (including adults or children per house)	12
People per room	26
People per bedroom	10
People per bed or bed sharing	1
Square metres per person	3
House size below threshold (eg 1 room, <x square meters)	3
Total	**55**

The pilot search on crowding and infectious disease also identified which CCIDs, syndromes and microbes have a literature base that investigates an association with household crowding. The IDs identified in the pilot were aligned with specific search terms in the final search strategy (

Table 2). In this way, the sensitivity of the search was maximised for these IDs. Furthermore, the breadth of CCIDs identified by the search was maximised by including broad infectious disease terms such as "communicable disease", "viral infection", and "bacterial infection". An example of the search strategy is presented in Table 3 showing the combination of MeSH terms and keywords used in Medline. The search was adapted to search Embase, Scopus and Web of Science but used similar terms.

Table 2: Close contact infectious disease search terms used in the search strategy

ID category	Type of infectious disease	Search terms used
Enteric	Gastroenteritis, Rotavirus	diarrhoea or vomiting or gastritis or gastroenteritis or rotavirus
	Helicobacter pylori infection	helicobacter
	Hepatitis A	hepatitis
Respiratory	Pneumonia	pneumonia
	Respiratory tract infection	respiratory tract infection, bronchitis or Pneumococc*
	Bronchiolitis / Respiratory syncytial virus (RSV) infection	respiratory syncytial virus or bronchiolitis
	Otitis media	otitis
	Meningococcal disease	mening* or encephalitis or sepsis
	Haemophilus influenzae type b	haemophilus
	Influenza	influenza
	Tuberculosis	tubercul*
	Acute rheumatic fever, Group A Streptococcus (GAS)	rheumatic fever or Streptococc*
Skin and eyes	Skin infection / cellulitis	skin infect* or cellulitis
	Head lice	pediculosis capitis or head lice
	Staphylococcal infection / Methicillin resistance Staphylococcus aureus (MRSA)	staphylococc*
Blood-borne	Hepatitis B/C	hepatitis

Table 3: Medline search strategy

Exposure: crowding	Outcome: infectious disease	Limits
MeSH terms	MeSH terms	
Crowding/	exp Communicable Diseases/ or exp bacterial infection/ or exp virus infection/ or exp parasitosis/	Human
or bed sharing/		English
Keywords	or exp meningococcosis / or exp tuberculosis/ or exp rheumatic fever/ or exp Haemophilus Infection/ or exp pneumonia/ or exp otitis media/ or respiratory syncytial virus infection/ or exp bronchiolitis/ or exp respiratory tract infection/ or exp gastroenteritis/ or exp acute diarrhea/ or exp infectious diarrhea/ or Vomiting/ or helicobacter infection/ or exp skin infection/ or cellulitis/ or exp conjunctivitis/ or exp acute hepatitis/ or exp chronic active hepatitis/ or exp chronic hepatitis/ or exp infectious hepatitis/ or exp virus hepatitis/ or rotavirus infection/ or exp Influenza/	
crowd*		
or overcrowd*		
or per room		
or ((People or person or persons or child* or adult or adults or resident or residents or member*) adj3 (room* or bed* or area or m2 or square meter* or square metre* or ft2 or square feet*))	Keywords	
or ((bed* or room*) adj3 (sharing or share))	Mening* or encephalitis or sepsis or tubercul* or rheumatic fever or Haemophilus or pneumonia or otitis or respiratory syncytial virus or bronchiolitis or bronchitis or respiratory tract infection or gastroenteritis or diarrhea or Vomiting or gastritis or helicobacter or skin infect* or cellulitis or conjunctivitis or Hepatitis or Pediculosis capitis or head lice or rotavirus or Influenza or Staphylococc* or Streptococc* or Pneumococc*	
or ((hous* or home) adj3 (area or m2 or square meter* or square metre* or ft2 or square feet* or size or density))		

3.3. Selection criteria

Eligibility criteria were used to limit our selection of studies to those most relevant to our research question. If a study did not meet any one of the following criteria it was not eligible for narrative synthesis or meta-analysis.

Inclusion and exclusion criteria

We were interested in studies from any population. No exclusions were made based on age or country in order to ensure the broadest range of evidence was examined. Study populations with a high risk of disease were also eligible, such as infants born prematurely with higher risk of infection, or patients presenting with symptoms (such as dyspepsia) that might be a result of the infectious disease of interest (*H. pylori*).

The study was required to evaluate household crowding density as an exposure variable. Eligible crowding measures included: the number of household members per number of rooms; persons per area (such as m^2); number of persons sharing the same bedroom; and any measure of house area (e.g. number of rooms or m^2). Crowding measures excluded were the number of occupants per household, number of siblings in the household and bed sharing (however, studies with these measures of crowding were full text screened to determine whether additional crowding measures had also been used). Mass gathering, prison, military, workplace, day care and institutional care measures of crowding, were not eligible. Studies that had a CCID outcome but did not indicate household crowding in the title or abstract were only included where there was some indication that crowding may have been measured, such as reference to a multivariate analysis or housing factors.

A statistical comparison was required between greater and lesser levels of household crowding density. Any statistical measure was eligible for narrative synthesis such as an odds ratio (OR), rate ratio (RR), beta coefficient or difference between two means. Only ORs and RRs were combined in the meta-analysis.

Studies that reported any outcome measure of CCID were eligible. Outcome measures of infection included incidence, prevalence, severity (e.g. hospitalisation) and mortality. Objective identification of CCID was required such as laboratory detection of a particular pathogen (active infection or carriage) and / or a clearly defined clinical syndrome attributable to infectious disease. CCIDs are spread by person-to-person contact in the community and include respiratory, enteric (faecal-oral), skin and potentially blood borne infections such as those shown in

Table 2. Hospital acquired IDs were excluded because they are more likely to relate to hospital factors than housing factors. Asthma, allergy and vector-borne infections, such as malaria, were not considered CCIDs (though infectious disease is likely to contribute to exacerbations of chronic diseases such as asthma).

Any quantitative study design with an individual level of analysis was eligible, including cohort, case-control and cross-sectional studies. These criteria excluded ecological study designs and neighbourhood measures of crowding. Our focus here was on non-randomised observational studies. Systematic reviews, case studies and case series (<20 participants) were excluded.

Screening

The first step was to screen the titles and abstracts identified in the search. References from the database search were imported into a reference manager and duplicates were removed. The title (+/- abstract) of each study was assessed as to whether it might meet the eligibility criteria. Potentially eligible studies were then categorised by CCID. Some articles simultaneously investigated two or more CCIDs and were categorised by each of them. CCID categories were the same as those used in the search strategy with the subsequent addition of intestinal parasites; cytomegalovirus, Epstein Barr virus or herpesvirus; measles, mumps, rubella or varicella (chicken pox); scabies; conjunctivitis; trachoma; and studies which combined multiple IDs.

Every effort was made to obtain full text articles for the set of potentially eligible articles, irrespective of the journal in which they were published.

The second step involved screening the full texts of each study to assess whether they met the eligibility criteria. The outcome of screening was documented. For each study, eligibility criteria were assessed in the following order: study design; infectious disease outcome; household crowding density measure; and an appropriate comparison group.

Screening and the full text extraction was carried out by one reviewer (AM) who consulted another reviewer (MB) where required.

Narrative synthesis and meta-analysis

Studies that met all of the eligibility criteria were included in the narrative synthesis.

To be eligible for meta-analysis, studies were additionally required to provide an OR or RR (or data to calculate this) that was adjusted for confounding from age and socioeconomic status (see Figure 1). Although tobacco smoke exposure is also an important risk factor for respiratory infections, we considered it too restrictive to also require adjustment for this exposure. Adjustment for low socioeconomic status provides some adjustment for tobacco smoke exposure given the association between low socio-economic status and tobacco use.

Adjustment for confounding could be made by stratification, standardisation and/or regression. If a multivariate analysis was used to estimate the OR, both age and socioeconomic status had to be considered for the model, even if these variables were excluded from the final model because they had no predictive value or no confounding value. Socioeconomic status was defined as any measure of income, occupation, education, deprivation, residence or housing amenity factors (such as the presence of a toilet).

3.4. Data collection and analysis

Extraction of data

Key information from all eligible studies was extracted into a spread sheet. Data included: country; age of participants; exposure measure; outcome measure; study

design; number of subjects; crude measure of effect; direction of the effect; and statistical significance.

A spread sheet was developed and piloted for the full text extraction of studies eligible for meta-analysis. The following information was extracted for each study outcome:

1. Identifiers
    a. Disease of interest
    b. Author, year
2. Study design
    a. Study design (e.g. cross-sectional, case-control, cohort)
    b. Outcome measure (most crowded vs. least crowded category)
    c. Exposure measure in crowded vs. not crowded
    d. If case-control studies: how were the cases selected and matched?
    e. Socioeconomic status variable(s) adjusted for (or considered in brackets)
    f. How was age adjusted for?
    g. If respiratory: What smoking or indoor smoke variables were adjusted for? (or considered in brackets)
    h. Other crowding variables adjusted for
    i. Any other variables adjusted for
3. Study population:
    a. Country
    b. Years that study was carried out
    c. Incidence or prevalence of the infectious disease of interest
    d. Was the study population high risk or population representable?
    e. What was the age range of the population studied?
    f. How many study participants (if case control: broken down by cases and controls)
4. Unadjusted measure of effect
    a. OR: odds ratio / RR: rate ratio
    b. LCI: lower 95% confidence interval
    c. UCI: upper 95% confidence interval
    d. P-value if CI unavailable
5. Adjusted measure of effect (from an eligible model with the most number of variables)
    a. OR: odds ratio / RR: rate ratio
    b. LCI: lower 95% confidence interval
    c. UCI: upper 95% confidence interval
    d. P-value if CI unavailable

For each specific CCID, meta-analysis was carried out when two or more eligible studies measured the same outcome using the same measure of effect (OR or RR). If there was a choice between different eligible models in a study, the model that adjusted for the greatest number of variables was selected.

Avoiding duplication

Some articles contributed data to more than one CCID, for example, if a cohort study investigated both gastroenteritis and pneumonia as outcomes, both would be included in our results. If a study stratified results by sub-populations and no overall measure of

effect was available, each strata's results was considered as a separate study for the purposes of analysis. For example, some studies stratified results by two separate age groups and each group was analysed separately.

Within each CCID we aimed to limit the contribution of any one study to the overall result. If more than one article used the same study data, the most recent article was selected for extraction. Where a study investigated two outcomes for the same infectious disease, one outcome was selected for inclusion in the review. The choice of included outcome was based the most objective measure (for example a laboratory test is more objective than reported symptoms), the measure most comparable with other studies (for example prevalence was more common than disease severity), a combined measure or, failing that, the more common outcome.

If there was two or more eligible crowding exposures, then one was selected based on the following order of priority: ratio of persons to the number of rooms (prioritising childhood exposure over adult exposures); area per person; persons per bedroom (prioritising siblings closest in age over parents in same bedroom); house area or other. This order is based on the validity of each measure in quantifying household crowding density, potential relevance to CCID transmission and the frequency that each measure is used in the literature.

3.5. Synthesis of results

Narrative synthesis of eligible study outcomes was carried out to summarise the overall scope of the available literature. The proportion of studies that demonstrated statistically significant associations between household crowding and ID was reported, along with whether the effect was positive or negative.

A sub-group of studies with adjusted estimates from the narrative synthesis was then summarised by meta-analysis. Meta-analysis combines study data to calculate summarised effect estimates. Our methods are based on Cochrane Handbook guidance.[21]

Data were entered into Revman5 software and forest plots were created using random effects analysis to allow for heterogeneity between studies. The inverse variance function was selected to input study data. This required that odds ratios were converted into natural logarithms [ln(OR)] and standard errors were calculated from the 95% confidence intervals using the following formula[22]:

$$SE[\ln(OR)] = [\ \ln(\text{upper limit}) - \ln(\text{lower limit})\ ] / 3.92$$

If confidence intervals were not given, but a p-value was reported, the standard error was calculated from the p-value.[22] This assumes a Wald test is used to calculate the reported p-value and uses the following formula:

$$SE[\ln(OR)] = \ln(OR) / Z_{(\text{p-value})}$$

Heterogeneity occurs when the variability in study participants, interventions, outcomes, design and methods results in observed effects being more different from each other than would be expected from chance alone.[21] Heterogeneity between studies was assessed by visual inspection and the I^2 statistic.[21] I^2 describes the percentage of variability in effect estimates that is due to differences between studies rather than sampling error (chance).

For example I^{2} =

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

Where numbers were adequate, sub-group meta-analysis was considered to investigate heterogeneity. Pre-specified sub-groups were study design, high and low income country and high and low quality studies. Sub-groups later considered included low vs. high risk study populations, and child vs. adult exposure to crowding.

3.6. Risk of bias in individual studies

Non-randomised study outcomes are subject to greater bias than randomised studies. For this reason we limited the meta-analysis to studies which adjusted for two major identified confounders: age and socioeconomic status. The meta-analysis combined only the adjusted measures of effect. In this way we aimed to demonstrate the impact of household crowding independent of age and socioeconomic status.

3.7. Risk of bias across studies

Funnel plots produced by RevMan5 were used to describe potential publication bias if more than eight studies were combined in each meta-analysis. Risk of publication bias based on the symmetry of the funnel plots was evaluated as high, moderate or low.

The narrative synthesis provides another layer of analysis to view the wider collection of studies (irrespective of whether they adjust for confounding) and comment on the association between crowding and ID.

3.8. Burden of infectious disease from household crowding

The burden of disease (BoD) analysis combined the results of the systematic review, described in the previous parts of this report, with other data to estimate the burden of IDs that can be attributed to household crowding. These other data sources were two related reports prepared for the Ministry of Health which examined the incidence of CCIDs[8] and the distribution of household crowding in NZ,[10] as well as a published paper on the incidence of serious IDs in NZ.[1]

Environmental BoD methodology can be applied to estimate the expected proportion of a health outcome (in this case IDs) that can be attributable to a particular environmental exposure (in this case household crowding).[133] We have previously used this method to estimate the burden of tuberculosis that can be attributed to household crowding in Europe.[134]

The first step is to estimate the population attributable fraction (PAF) which is the proportion of disease burden attributable to exposure to household crowding, calculated using the following formula:

$$\text{Population attributable fraction (PAF)} = \frac{p\,(RR-1)}{p\,(RR-1)+1}$$

This estimate is based on the effect measure (OR or RR) obtained from the systematic review (Table 6) combined with the prevalence of exposure to household crowding (p). ORs were substituted for RRs where RRs were not available. ORs are a reasonable approximation and do not substantially (at the very most 5%) overestimate the RR because the summary estimates are small (all ORs < 4) and incidence of hospital admission is low (< 2% per annum).[135] These methods make the assumption that the association is causal.

The measure of disease incidence was acute and arranged overnight hospitalisations, as previously reported.[1] We consider that these events provide a reasonably consistent measure of the burden of serious IDs in NZ. The PAF was applied to the incidence of each ID in the age group of participants that contributed to the combined effect measures (eg, if the meta-analysis was for gastroenteritis in children aged <5 years, then we applied the PAF to hospitalisation rates for this condition in this age group). The incidence rates were based on average hospital admissions over the 2007-11 period.

For most ID categories, we simply used hospitalisations for the disease outcomes that best matched the PAF conditions. The one exception was for *H. pylori* infection, where we used hospitalisations for the known sequelae of infection (non-cardia gastric cancer, peptic ulcer, chronic gastritis and duodenitis). The justification is that *H. pylori* infection is considered the predominant cause of these diseases.[1]

The analysis by ethnic group used four ethnicity categories: European/Other, Māori, Pacific, and Asian. We used 'total response' ethnicity, meaning that those recording multiple ethnicities were included in all of the ethnic groups that they nominated so some individuals were effectively counted more than once. This approach was consistent across the numerator (hospitalisations), denominator (2006 Census population), and crowding exposure (again based on 2006 Census data[10]).

It is important to recognise that this current analysis has been restricted to just nine categories of IDs where estimates of the contribution of household crowding have been made (trachoma was excluded because transmission does not occur in NZ). In addition, most of these estimates apply to restricted age groups. Due to a lack of high quality published, no pooled estimates have been possible for many important IDs, such as skin infections and rheumatic fever. For 'Pneumonia/lower respiratory tract infection' we have chosen to use the estimate for the wider age range (0-5 years) derived from case-control and cross sectional studies, instead of the estimate from the narrower age range (0-3 years) derived from cohort studies. We have also retained results for 'Upper respiratory tract infections' even though results for the two meta-analyses (case-control and cross-sectional studies in children 0-18 years, and cohort studies in 0-2 year olds) were not significant. We retained this category as findings from both meta-analyses showed a consistently positive association and the uncertainty could be demonstrated in our hospital admissions estimates. Again, we selected the results for the wider age group (0-18 years) rather than the findings for the narrower age group (0-2 year olds). When calculating the total burden of IDs attributable to crowding exposure, we removed bronchiolitis (J21) and *Hib* (J14) from the pneumonia/LRTI category to avoid double counting.

4. Results

4.1. Study selection

Over 18,000 articles were identified from database searching including 3,178 from Medline, 4,453 from Embase, 5,045 from Scopus, 5,466 from Web of Science, 4 from the Cochrane library, 110 from Index New Zealand and 130 from Lancet Infectious Diseases. A further 111 articles were identified from reference searching and 9 were identified by expert recommendation.

The screening and selection process is illustrated by the flowchart in Figure 2. After removing duplicate articles 9,852 records remained and were screened by title and abstract. Common reasons for exclusion at this stage included the absence of infectious disease outcome, eligible household crowding measure or eligible study design.

A total of 838 studies were assessed by full text screening. Of these, 493 were excluded from further analysis because they did not meet the eligibility criteria (Table 4). The most common reason for exclusion at this stage was the absence of an eligible household crowding density measure (311/838 records) and an inadequate study design (112/838 records), which includes some exclusions for articles presenting duplicate study results. The screening process culminated in 345 studies eligible for narrative synthesis.

Figure 2: Identification and selection of eligible studies

Flowchart adapted from PRISMA.[20] (*Studies were counted more than once if results were given for more than one study population e.g. when results were stratified by country or results were given for more than one infectious disease.)

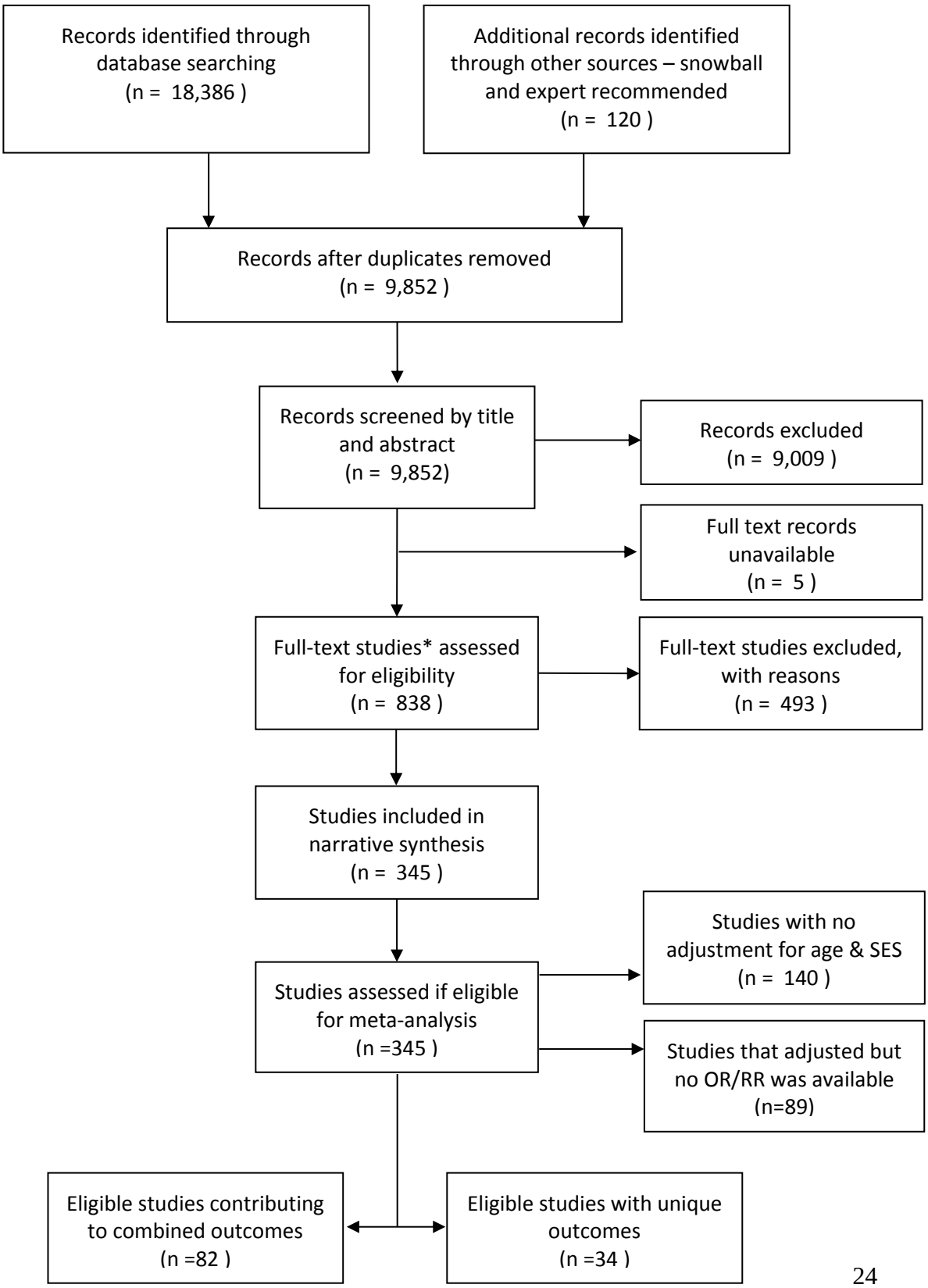


Table 4. Full text records assessed according to type of infectious disease showing the reasons for exclusion from narrative synthesis. Studies included in meta-analysis had to adjust for socioeconomic status and age.

Close-contact Infectious Disease	Number full text studies screened	Studies excluded with reasons				Studies Included	
		Study design	Infect. disease outcome	HH crowd. density expos.	Compa-rison group	Narrative synthesis	Meta-analysis
Enteric infection							
Gastroenteritis*	**81**	9	3	37	3	29	10
*Helicobacter pylori**	**99**	3	4	28	1	63	28
Hepatitis A*	**37**	4	0	17	1	15	7
Giardia and cryptosporidium	**9**	0	0	5	1	3	1
Intestinal parasites	**31**	2	1	18	0	10	3
Respiratory tract infection							
Pneumonia / lower respiratory tract infection*	**33**	3	0	5	0	25	7
Bronchiolitis / Respiratory syncytial virus*	**44**	5	14	13	0	12	5
Upper respiratory tract infection*	**90**	13	6	25	1	45	10
Meningococcal disease*	**27**	2	0	8	1	16	7
*Haemophilus influenzae type b**	**25**	4	0	3	1	17	7
Tuberculosis*	**73**	25	3	18	5	22	12
Otitis Media	**17**	1	0	6	0	10	3
Influenza	**22**	7	1	10	0	4	2
Measles, Mumps, Rubella, Chicken pox	**25**	5	1	14	0	5	2
Rheumatic fever, RHD, GAS	**36**	6	0	13	2	15	4
Skin & eye infection							
Conjunctivitis	**5**	0	0	3	0	2	0
Trachoma*	**7**	1	0	3	0	3	2
Staphylococcus aureus (MRSA)	**8**	2	0	5	0	1	0
Pediculosis (lice)	**20**	1	1	7	0	11	1
Scabies	**19**	3	1	8	1	6	0
Other skin infection	**29**	1	1	16	0	11	1
Blood born infection							
Hepatitis B	**23**	2	1	11	1	8	0
Hepatitis non-A, non-B	**8**	1	0	6	0	1	0
Other							
Cytomegalovirus	**9**	1	0	5	0	3	0
Epstein Barr virus, Herpes virus	**9**	0	0	6	0	3	2
Multiple infectious disease	**22**	6	5	7	0	4	2
Other infectious disease	**22**	4	4	13	0	1	0
Other outcomes/exposures	**8**	1	6	1	0	0	0
Total	**838**	**112**	**52**	**311**	**18**	**345**	**116**

*Disease included in meta-analysis

4.2. Narrative synthesis

After full assessment, 345 studies were selected for narrative synthesis. The largest group of outcomes was for respiratory infections (131), followed by enteric infections (120), skin and eye infection (34) and blood borne infections (9). The study populations tended to reflect the populations most affected by the diseases in question. For example, studies of bronchiolitis involved young children (<3 years of age) and studies of invasive bacterial infections focused on children (generally <18 years). A handful of studies focussed on persons particularly at risk of disease such as family contacts of a tuberculosis patient.

No randomised study designs were identified investigating the association between household crowding and CCID. All eligible studies were non-randomised studies i.e. observational in nature. One intervention study[24] is included in the analysis. This cohort study investigated the impact of a housing intervention on crowding and infectious disease in an indigenous Australian community.

Cross-sectional studies were the predominant investigation method used by studies identified here (185/345 studies) followed by cohort (84/345) and case-control studies (76/345). Diseases where infection may be less clinically apparent have tended to be investigated using cross-sectional studies such as is the case for *Helicobacter pylori* infection and hepatitis A, where prevalence of infection can be identified by specific serological testing. Serious acute diseases with conspicuous clinical presentations lend themselves well to case-control studies, notably meningococcal disease, *H. influenzae type b (Hib)* disease and tuberculosis.

More than half of the studies in the narrative synthesis (189/345, 55%) found a statistically significant positive association between greater household crowding and CCID risk. Less than half of the studies (151, 44%) found no statistical evidence of an association and 5 (1%) found a significant negative association (Table 5). The proportion of studies with evidence of an association was relatively similar across respiratory (51%), enteric (59%) and skin/eye infections (59%).

More than two-thirds of studies investigating hepatitis A, intestinal parasites, meningococcal disease, otitis media and pediculosis identified a statistically significant positive association. Conversely, only one-third of studies investigating gastroenteritis, upper and lower respiratory tract infections and tuberculosis identified a statistically significant positive association. This pattern may be related to the magnitude of the true association, chance findings, confounding bias and/or the greater chance of measurement bias in syndrome diagnoses (based on symptoms) compared to the greater accuracy afforded by laboratory diagnosis of a specific infectious agent.

Table 5. Narrative synthesis of study outcomes which investigate the role of household crowding as a risk factor for close contact infectious disease

	Statistical significance of study outcomes at the 95% level						Total studies
	+	(%)	ns	(%)	-	(%)	
Enteric infection							
Gastroenteritis*	11	38	18	62	0	0	29
*Helicobacter pylori**	39	62	24	38	0	0	63
Hepatitis A*	11	73	4	27	0	0	15
Giardia and cryptosporidium	2	67	1	33	0	0	3
Intestinal parasites	8	80	2	20	0	0	10
Respiratory tract infection							
Pneumonia / lower respiratory tract infection*	9	36	14	56	2	8	25
Bronchiolitis - Respiratory syncytial virus*	7	58	5	42	0	0	12
Upper respiratory tract infection*	17	38	26	58	2	4	45
Meningococcal disease*	12	75	4	25	0	0	16
*Haemophilus influenzae type b**	9	53	8	47	0	0	17
Tuberculosis*	8	36	14	64	0	0	22
Otitis Media	7	70	2	20	1	10	10
Influenza	3	75	1	25	0	0	4
Measles, Mumps, Rubella, Chicken pox	4	80	1	20	0	0	5
Rheumatic fever, RHD, GAS	9	60	6	40	0	0	15
Skin & eye infection							
Conjunctivitis	2	100	0	0	0	0	2
Trachoma*	2	67	1	33	0	0	3
Staphylococcus aureus (MRSA)	0	0	1	100	0	0	1
Pediculosis (lice)	8	73	3	27	0	0	11
Scabies	3	50	3	50	0	0	6
Other skin infection	5	45	6	55	0	0	11
Blood born infection							
Hepatitis B	5	63	3	38	0	0	**8**
Hepatitis non-A, non-B	1	100	0	0	0	0	1
Other							
Cytomegalovirus	2	67	1	33	0	0	3
Epstein Barr virus, Herpes virus	2	67	1	33	0	0	3
Multiple infectious disease	2	50	2	50	0	0	4
Other infectious disease - toxoplasma	1	100	0	0	0	0	1
Total	**189**	55	**151**	44	**5**	1	**345**

*included in the meta-analysis, + =statistically significant positive association between greater household crowding and increased infectious disease, ns =non-significant association, - = statistically significant negative association showing crowding as beneficial

4.3. Meta-analysis

Combined estimates were produced from 82 studies for ten different categories of CCIDs. A further 36 studies were eligible for meta-analysis, but had largely unique outcomes, so could not be combined. Some studies were not eligible for meta-analysis because no OR or RR was available (89 studies removed) or the study had not adjusted for age and socioeconomic position (136 studies removed).

For the combined estimates covering ten different CCIDs, nine showed statistically significant results i.e. persons experiencing the greatest vs. least levels of household crowding had increased risk of disease. The increased odds of infection ranged from 1.13 times the risk of gastroenteritis to 3.78 times the risk of tuberculosis (Table 6). Although upper respiratory tract infections had a positive association with household crowding, this association was not statistically significant (OR 1.39, CI 0.69-2.79 and RR 1.63, CI 0.88-3.02). A summary of the meta-analyses is presented in Table 6.

The ability to conduct meta-analysis reflects the greater number of studies carried out investigating the association of these particular CCIDs with household crowding exposure (Table 5). There are some notable omissions of CCIDs that narrowly missed out on meta-analysis. Pediculosis (lice) studies, for example, were limited by their quality and were less likely to control for confounding from age and socioeconomic status. Several studies investigating rheumatic fever, intestinal parasites and other skin infections did control for confounding and were eligible for meta-analysis; however study outcomes were unique and unable to be combined. These studies are also discussed and presented in the tables below.

Included studies were more likely to investigate the impact of household crowding density on children than adults. All meta-analyses included studies with children as participants. Six out of ten meta-analyses focussed primarily on children, the majority of whom were less than six years old.

The most robust meta-analysis effect estimates provided evidence that higher crowding was associated with increased risk of pneumonia / lower respiratory tract infection (OR 1.69, CI 1.34-2.13 and RR 1.36, CI 1.09-1.69), gastroenteritis (OR 1.13, CI 1.01-1.26), *Haemophilus influenza* disease (OR 1.74, CI 1.27-2.37) and respiratory syncytial virus (RSV) bronchiolitis - when cohort (4.44, CI 2.45-8.04) and case-control data (OR 1.31, CI 0.85-2.01) were considered separately. Other meta-analyses were less robust due to greater unexplained heterogeneity (variation in individual study results), with statistically significant associations between household crowding and hepatitis A (OR 1.53, CI 1.23-1.90), meningococcal disease (OR 2.13, CI 1.38-3.29), *H. pylori* infection (OR 1.82, CI 1.55-2.14), tuberculosis (OR 3.78, CI 1.78-8.13) and trachoma (OR 2.07, CI 1.06-4.06). The association was not statistically significant for household crowding and upper respiratory tract infection (OR 1.39, CI 0.69-2.79 and RR 1.63, CI 0.88-3.02).

Individual study results are presented in forest plots (Figure 3, Figure 4, Figure 6, Figure 7, Figure 8, Figure 9, Figure 10, Figure 11, Figure 12, Figure 13). Study characteristics are summarised in corresponding tables. To investigate publication biases between included studies, a funnel plot is presented for the *H. pylori* meta-analysis (Figure 5), because this is the only outcome with sufficient studies.

For five of these outcomes (gastroenteritis, pneumonia, bronchiolitis, *Hib* disease, and tuberculosis) there were additional studies that reported largely unique outcomes. These results are summarised below:

- A further five (6 outcomes) studies of gastroenteritis had largely unique outcomes so could not be included in the combined meta-analysis. Two of these studies found positive associations between disease risk and crowding (toxoplasma gondii, typhoid fever). Two found no significant association (bacillary dysentery, diarrhoeal deaths). And one found a weak protective effect (carriage of multiple drug resistant E coli).
- A further study of pneumonia/lower respiratory infection had a unique outcome and so could not be included in the combined meta-analysis. This study (mortality from respiratory infection) did not find a significant association between disease risk and crowding
- A further study of RSV had a unique outcome, reported wheeze, so could not be included in the combined meta-analysis. It found a significant association between disease risk and crowding.
- A further study of *Hib* had a unique outcome, *Hib* nasopharyngeal carriage, so could not be included in the combined meta-analysis. It found a significant association between carriage risk and crowding.
- A further five studies of tuberculosis had largely unique outcomes: symptoms of tuberculosis, self-reported tuberculosis, tuberculin skin test positive (two studies), and tuberculosis meningitis, so could not be included in the combined meta-analysis. Three studies (the two tuberculin studies and the one on tuberculosis meningitis) found a significant association between disease risk and crowding and two did not (symptoms of tuberculosis, self-reported tuberculosis).

This review identified a further 21 eligible studies covering 16 specific infectious diseases (there were three eligible studies of otitis media, two of influenza-like illness and three of rheumatic fever and its sequelae). The outcomes were too heterogeneous to allow for combined estimates but have been tabulated in blocks of related diseases.

- Amongst the enteric diseases, there was one cross sectional study of giardia and three other studies of specific intestinal parasites. All showed statistically significant associations between crowding and disease.
- Amongst the respiratory diseases, three eligible studies looked at different forms of otitis media (OM) with two finding no significant relationship between disease risk and measures of household crowding and one finding a protective effect for chronic otitis media. Two cohort studies of influenza-like illness both found a significant positive relationship between disease risk and measures of household crowding. A cohort study of measles and a cross sectional study of varicella-zoster virus antibodies each found a significant positive relationship between disease risk and measures of household crowding. None of the three eligible studies of rheumatic fever and its sequelae (rheumatic fever incidence, rheumatic heart disease (RHD) prevalence, and RHD mortality) found a significant positive relationship between household crowding and disease risk. However, one study of invasive GAS infection did find a significant positive relationship between household crowding and disease risk.
- Amongst studies of superficial infections a study of pediculosis (head lice) found a significant positive relationship between disease risk and measures of household crowding whereas there was no significant association for skin infections.

- There were a further four eligible studies that were difficult to put into a specific transmission category. One study of Epstein–Barr virus (EBV) found a significant positive relationship between disease risk and measures of household crowding. A single study of Human Herpesvirus 8 (HHV8) did not find a significant association. One case-control study of infectious illness warranting hospitalisation and one prevalence study of communicable disease symptoms found a significant positive relationship between disease risk and measures of household crowding.

Table 6: Summary of findings table for meta-analyses investigating association between household crowding density and close contact infectious diseases

Infectious disease outcome	studies eligible for meta-analysis (combined in summary effect)[a]	study design	age of participants	summary effect (95% C.I.)	I^2
Enteric					
Gastroenteritis	10(4)	cx	0-5yo	OR 1.13 (1.01,1.26)	33%
Helicobacter pylori	27(27)	cx/cohort†	0+yo	OR 1.82 (1.55,2.14)	87%
Hepatitis A	7(7)	cx/cohort†	0+yo	OR 1.53 (1.23,1.90)	72%
Giardia and intestinal parasites	4(0)	Meta-analysis not possible			
Respiratory tract					
Pneumonia / lower respiratory tract infection	2(4)	cx/ccs	0-5yo	OR 1.69 (1.34,2.13)	0%
	(6)	cohort	0-3yo	RR 1.36 (1.09,1.69)	26%
Bronchiolitis - respiratory syncytial virus	5(4)	ccs/cohort	0-3yo	OR 2.24 (1.14,4.38)	84%
Upper respiratory tract infection	4(3)	cx/ccs	0-18yo	OR 1.39 (0.69,2.79)	84%
	(3)	cohort	0-2yo	RR 1.63 (0.88,3.02)	65%
Meningococcal disease	7(7)	ccs	0-16yo*	OR 2.13 (1.38,3.29)	69%
Haemophilus influenzae type b	7(6)	ccs	0-6yo	OR 1.74 (1.27,2.37)	47%
Tuberculosis	12(7)	ccs/cx†	15+yo^	OR 3.78 (1.75,8.13)	90%
Otitis media	3(0)	Meta-analysis not possible			
Influenza	2(0)	Meta-analysis not possible			
Measles, mumps, rubella, chicken pox	2(0)	Meta-analysis not possible			
Rheumatic Fever	4(0)	Meta-analysis not possible			

Skin and eye					
Trachoma	2(2)	cx	0+yo	OR 2.07 (1.06,4.06)	94%
Pediculosis (lice)	1(0)	Meta-analysis not possible			
Other skin infection	1(0)	Meta-analysis not possible			
Other					
Epstein Barr Virus, Herpesvirus	2(0)	Meta-analysis not possible			
Multiple infectious disease	2(0)	Meta-analysis not possible			

[a]=number of studies eligible for meta-analysis with the number of studies contributing to the combined estimate in brackets, I^2 is the proportion of heterogeneity between studies, *=one study was 16+yo, ^=one study was <15yo, †= only one study with this design, n=number of study outcomes, cx=cross-sectional, ccs=case-control study, n=study outcomes

4.3.1. Study level limitations

In all meta-analyses the quality of evidence for causality is regarded as low by Cochrane collaboration standards because we were reliant on non-randomised observational studies.[21] The grade of evidence quality is reduced further for meta-analyses where there are poor quality study designs (e.g. with poor control for important confounders), unexplained heterogeneity (where study variability results in observed effects being more different from each other than would be expected from chance alone) and evidence of publication bias (where studies with negative effects may be less likely to be published resulting in a bias towards positive findings in systematic reviews).

Considerable heterogeneity was present for *H. pylori*, upper respiratory tract infection, tuberculosis, trachoma and bronchiolitis. Substantial (slightly less than considerable) heterogeneity was evident for hepatitis A and meningococcal disease. Three out of ten meta-analyses had low to moderate heterogeneity, which is not likely to have an important effect on the conclusions. The random effects analysis carried out allows for this variation between included studies.

Sub-group meta-analysis was not possible for most IDs, due to the small number of studies involved and the similarity of study designs within each ID. For *H. pylori* infection 26/27 studies were cross-sectional designs, limiting the ability to stratify based on study design. However, some sub-group analysis was possible within the *H. pylori* and bronchiolitis meta-analyses. In the bronchiolitis meta-analysis, sub-group analysis by study design helped explain the heterogeneity.

All estimates may be somewhat overstated due to publication bias. This was only able to be assessed by funnel plot for *H. pylori* infection, where many studies would be required to shift the summary estimate. Therefore the risk of this sort of bias was considered low to moderate for this outcome.

The inclusion of only English language papers may have introduced bias, however the evidence of this occurring in systematic reviews is conflicting.[21] Some studies have shown greater and lesser estimates from non-English vs. English published studies.

When Moher and colleagues examined inclusion and exclusion of trials reported in a language other than English, the exclusion of non-English-language trials did not significantly affect the results.[25]

A proportion of gastroenteritis, *H. pylori*, *Hib* disease, pneumonia / lower respiratory tract infection, upper respiratory tract infection and meningococcal disease studies tended to adjust for additional crowding variables in the ORs/RRs they reported. This adjustment may have slightly diluted the overall combined effect estimate in these meta-analyses.

There is also the possibility that residual confounding was unable to be measured and controlled for, such as from age and socioeconomic status or other factors. This may have overestimated the summary effect measures.

4.4. Enteric infection

Meta-analysis was carried out for three enteric infections; gastroenteritis, *H. pylori* infection and Hepatitis A. In addition, eligible studies of giardia and intestinal parasites were also described, but had unique outcomes so could not be combined.

4.4.1. Gastroenteritis meta-analysis

Data from three cross-sectional articles were considered here as four separate studies in the analysis (Table 7). Children less than five years old living in more crowded households experienced a small increase in the risk of gastroenteritis (diarrhoeal illness); OR 1.13 (CI 1.01-1.26) (Figure 3). Although the increased risk borders on statistical non-significance, there is greater reliability accredited by the preciseness of the estimate and the low to moderate heterogeneity between studies. All studies are representative samples and include participants of a similar age group. Confounding was well adjusted for. Gastroenteritis is a symptomatic diagnosis here and not classified by laboratory methods. This increases the chance of misclassification bias that may have lowered the OR closer towards no effect.

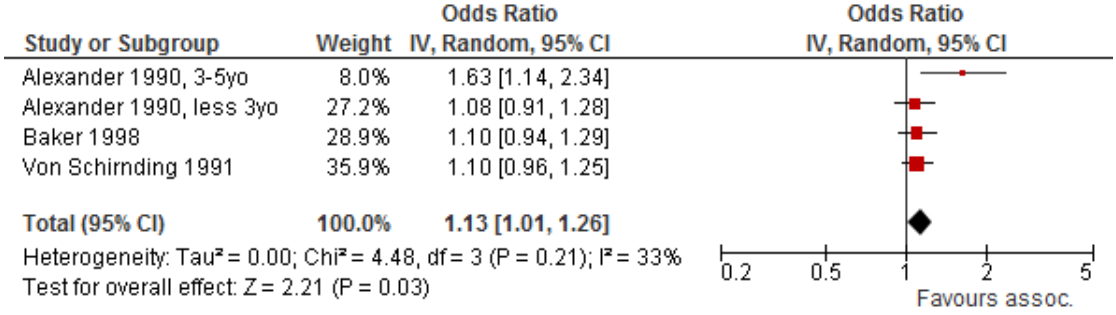
In addition, a further five articles studying gastroenteritis were eligible for inclusion in the meta-analysis, but had unique outcomes so could not be included in the combined meta-analysis. Two of these studies found positive associations between disease risk and crowding (*toxoplasma gondii*, typhoid fever). Two found no significant association (bacillary dysentery, diarrhoeal deaths) and one found a weak protective effect (carriage of multiple-drug-resistant-*E. coli*).

Table 7: Gastroenteritis meta-analysis study and population characteristics

Author, year	design	outcome	exposure	place	incid.	population	age	n	measure of effect
Combined outcomes:									
Alexander, 1990[26]	cx	acute gastrointestinal illness resulting in doctor visits, hospitalisations, restricted activity days, or bed disability days	high household crowding, upper 25 percent	US	2%	national survey	3-5yo	2094	OR 1.63 (0.89 - 1.83)
Alexander, 1990[26]	cx	acute gastrointestinal illness resulting in doctor visits, hospitalisations, restricted activity days, or bed disability days	high household crowding, upper 25 percent	US	2%	national survey	<3yo	2751	OR 1.08 (0.86 - 1.20)
Baker, 1998[27]	cx	mother identified if child had diarrhoea	more than one person per room vs. one or fewer	UK	26%	infants, all pregnant women in three health districts	6mo	8488	OR 1.10 (0.94 - 1.29)
Von Schirnding, 1991[28]	cx	diarrhoeal disease	more than two people per room	South Africa	9%	African American people living in urban areas representative sample	0-5yo	1227	OR 1.10 (1.00 - 1.30)
Unique outcomes:									
Emond[29], 1997	cohort	secondary bacillary dysentery in a household	more than one person per room	UK	40%	preterm infants 24-32wks gestation	0-12 mo	102	RR 1.57 (0.92 - 2.67)
Emond[29], 1997	cohort	secondary bacillary dysentery in a household	more than one person per room	UK	27%	term infants	0-12 mo	192	RR 0.85 (0.30 - 2.38)
Seidman[30], 2009	cx	carriage of multiple drug resistant *E. coli*	number of people per number of rooms	India	38%	children attending primary school	<10yo	119	OR 0.70 (0.52 - 0.94)
Jones[31], 2001	cx	*toxoplasma gondii* IgG seropositivity	one or more persons per room vs. less than 0.5	US	23%	adjusted to be representative of whole US population	20+yo	12566	OR 1.27 (1.02 - 1.59)
Hosoglu[32], 2006	ccs	typhoid fever: *S. typhi* on blood culture	more than 2.25 members per room (mean of all participants)	Turkey	NR	patients from area surrounding hospital	15+yo	64 cases + 128 controls	OR 3.31 (1.58 - 6.92)
Victora[33], 1988	ccs	diarrhoeal deaths	more than 5.0 people per room vs. 2.5 or less	Brazil	NR	recruited from hospitals and coroners	<12mo	170 cases +340 controls	OR 1.20 (0.50 - 2.50)

*cx=cross-sectional study, incid.=incidence, NR=not reported

Figure 3: Gastroenteritis meta-analysis forest plot



4.4.2. Helicobacter pylori infection meta-analysis

H. pylori infection accounted for the largest group of eligible studies investigating household crowding and CCID and 26/27 were cross-sectional designs (Table 8). The estimate of effect is therefore relatively precise (Figure 4). Independent of age and socioeconomic status, persons experiencing the greatest household crowding had 1.82 (1.55-2.14) times increased odds of *H. pylori* infection, compared to those experiencing least crowding. This combined estimate should be considered in light of heterogeneity and potential publication bias.

The outcome measure for *H. pylori* infection is laboratory defined and relatively unlikely to be subject to substantial measurement bias. Most studies use serology (or saliva) to measure antibodies which indicate previous infection. Other measures such as C-urea breath test and gastric biopsy determine current infection.

There is considerable heterogeneity (87%) in this meta-analysis. We sought to explore the reason for this by doing sub-group analysis that stratified results by outcome measure (current infection vs. previous infection - antibodies), age of exposure (child vs. adult), low or high income country, study population prevalence of *H. pylori* infection (<40% vs. 40+%) and gastrointestinal symptoms.

The only stratification that significantly altered the summary effect was stratifying by whether participants had gastrointestinal symptoms. If symptoms were present, there was less risk of *H. pylori* infection for individuals in crowded households (OR 1.28, CI 1.19- 1.39, I^2 0%, n=4) than there was for individuals in the strata without symptoms who were in greater vs. less crowded households (OR 1.99 CI 1.64, 2.42, I^2 88%, n=24). Heterogeneity remained in the later estimate.

The funnel plot (Figure 5) indicates low to moderate risk of publication bias. It would require several studies with quite different outcomes to substantially reduce the magnitude of the combined effect.

Table 8: *Helicobacter pylori* infection meta-analysis study and study population characteristics

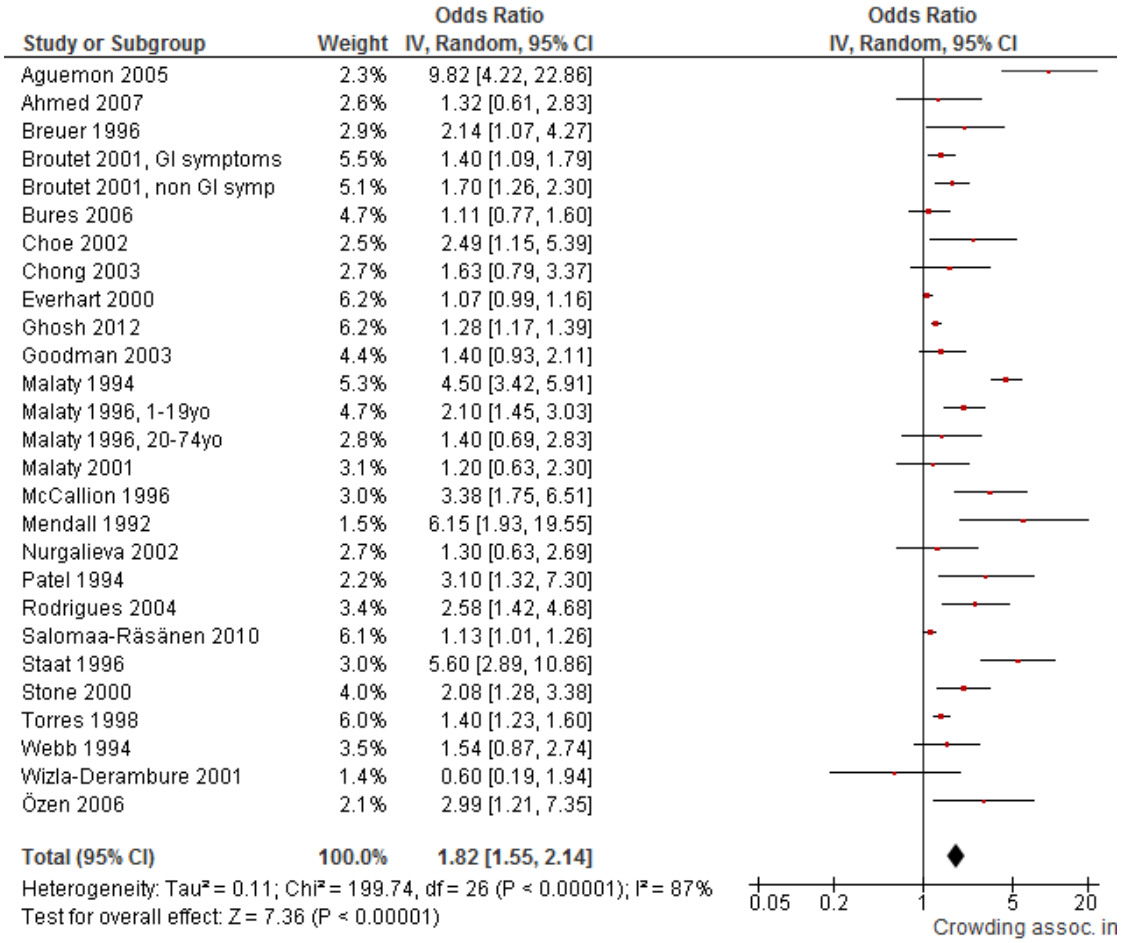
Author, year	study design	outcome	exposure	place	incid.	study population	age	n	measure of effect
Combined outcomes:									
Aguemon, 2005[34]	cx*	serology	more than three persons sharing a room to sleep vs. not sharing room	Benin	62%	healthy individuals in urban and rural households	2-74yo	446	OR 9.82 (4.30 - 23.31)
Ahmed, 2007[35]	cx	gastric biopsy x3 and PCR	members divided by rooms: high vs. low	Pakistan	80%	upper gastrointestinal symptoms who were not treated for H pylori	30-79yo	200	OR 1.32 (0.61 - 2.83)
Breuer, 1996[36]	cx	serology	persons per room in household at 8yo	Germany	39%	all blood donors	18-61yo	260	OR(linear) 2.14 (1.07 - 4.26)
Broutet, 2001[37]	cx	salivary IgG	more than one person per room growing up	France	46%	patients consulting gastroenterologist with upper digestive tract symptoms	18+yo	1582	OR 1.40 (1.10 - 1.80)
Broutet, 2001[37]	cx	salivary IgG	more than one person per room growing up	France	25%	patients consulting gastroenterologist with non-upper digestive tract symptoms	18+yo	1450	OR 1.70 (1.20 - 2.20)
Bures, 2006[38]	cx	C-urea breath test	shared room with siblings vs. own room	Czech Republic	42%	general practice catchments	5+yo	1350	OR 1.11 (0.77 - 1.60)
Choe, 2002[39]	cx	serology	two or more in house divided by number of rooms vs. less than two	Korea	43%	two schools - one athletics and one not	15-17yo	660	OR 2.49 (1.15 - 5.39)
Chong, 2003[40]	cx	serology	sharing bedroom (may be sharing a bed) vs. single	US	17%	children referred to hospital, GI referral and non-GI referral participants	1-18yo	992	OR 1.63 (0.79 - 3.37)
Everhart, 2000[41]	cx	serology	number of household residents divided by the total number of rooms (excluding bathrooms): 7 levels vs. least crowded	US	33%	adults in national nutrition survey	20+yo	7465	OR(linear) 1.07 (0.99 - 1.16)
Ghosh, 2012[42]	cx	salivary PCR	members divided by rooms: high vs. low	India	85%	all asymptomatic	20+yo	1500	OR 1.28 (1.17 - 1.39)
Goodman, 2003[43]	cx	serology	more than one household member per room vs. one or fewer household members per room	US	67%	all pregnant women	17-47yo	727	OR 1.40 (0.93 - 2.11)
Malaty, 1994[44]	cx	serology	three or more people divided number of rooms vs. less than one	US	54%	Black and Hispanic volunteers who had completed high school, through local advertisements	19-49yo	151	OR 4.50 (3.30 - 5.70)
Malaty, 1996[45]	cx	serology	more than three vs. less than one persons per room	Russia	44%	children	1-19yo	307	OR 2.10 (1.20 - 2.50)
Malaty, 1996[45]	cx	C-urea breath test	more than three vs. less than one persons per room	Russia	88%	adults	20-74yo	213	OR 1.40 (1.10 - 4.50)
Malaty, 2001[46]	cx	serology	one bedroom home vs. three or more bedroom home	US	24%	children from 13 licensed day care centres, primarily enrolling minority children from low-middle socioeconomic classes	2-16yo	356	OR 1.20 (0.60 - 2.20)

Table 8 continued…

Author, year	study design	outcome	exposure	place	incid.	study population	age	n	measure of effect
McCallion, 1996[47]	cx	serology	more than one person per room vs. less than 0.7 persons per room	UK	32%	children in hospital for routine non-gastrointestinal day surgery	3-15yo	367	OR 3.38 (1.75 - 6.50)
Mendall, 1992[48]	cx*	serology	1.30 or more persons per room in childhood vs. 0.70 or less persons per room in childhood	UK	32%	consecutive patients attending a health screening clinic in general practice	18-82yo	208	OR 6.15 (1.84 - 18.60)
Nurgalieva 2002[49]	cx	serology	more than three members divided by rooms vs. less than two members per rooms	Kazak-stan	80%	unrelated healthy individuals	10-60yo	289	OR 1.30 (0.70 - 3.00)
Özen, 2006[51]	cx	C-urea breath test	more than one persons per room	Turkey	57%	asymptomatic children	8-17yo (at follow up)	136	OR 2.99 (1.21 - 7.35)
Patel, 1994[52]	cohort	saliva ELISA	more than one person per room	UK	11%	random sample of 30 primary schools in Edinburgh	6-7yo	554	OR 3.10 (1.30 - 7.20)
Rodrigues, 2004[53]	cx	C-urea breath test	more than two persons per room vs. one person per room	Brazil	56%	children random selected from urban neighbourhood	6mo-14yo	353	OR 2.58 (1.40 - 4.60)
Salomaa-Rasanen, 2010[54]	cx	serology	for every increase of one person per room	Finland	12%	all individuals invited from population register	15-40yo	3316	OR(linear) 1.13 (1.01 - 1.26)
Staat, 1996[55]	cx	serology	two or more vs. less than 0.5 persons divided by numb rooms	US	25%	national health and nutrition survey	6-19yo	2581	OR 5.60 (2.90 - 10.90)
Stone, 2000[56]	cx	serology	persons per room in childhood	UK	15%	general population sample	21-55yo	1431	OR(linear) 2.08 (1.28 - 3.38)
Torres, 1998[57]	cx	serology	3.6 or more persons per room vs. 1.5 or fewer persons per room	Mexico	66%	national serological survey	1-39yo	11605	OR 1.40 (1.23 - 1.60)
Webb, 1994[58]	cx	serology	greater than one person per room vs. less than one person per room	UK	37%	male factory workers	18-65yo	471	OR 1.54 (0.87 - 2.75)
Wizla-Derambure, 2001[59]	cx	gastric biopsy	more than person per room, excluding kitchen and bathroom	France	7%	high risk: children requiring a endoscopy	2-17yo	436	OR 0.60 (0.20 - 2.10)

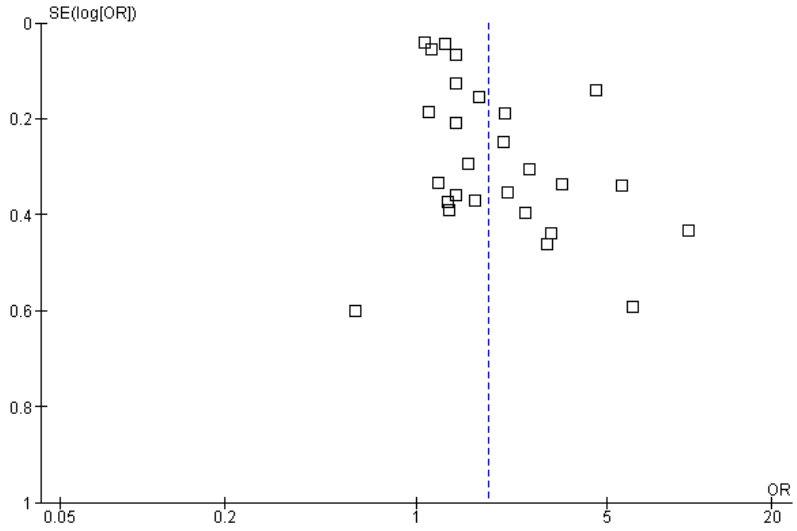
*cx=cross-sectional

Figure 4: *Helicobacter pylori* meta-analysis forest plot



*Note: The odds ratios in the forest plot may differ slightly from the odds ratios reported by the studies shown in Table 8, because the inverse variance function in RevMan automatically calculates the confidence intervals from the inputted natural log of the odds ratio and its standard error.

Figure 5: *Helicobacter pylori* funnel plot



4.4.3. Hepatitis A meta-analysis

Six studies were included in the meta-analysis investigating the association between household crowding and hepatitis A serology (Table 9). Five out of six used a cross-sectional study design. For persons experiencing the greatest vs. least household crowding, there was 1.53 times increased odds of Hepatitis A infection. This estimate may be exaggerated by publication bias. Measurement bias is relatively less unlikely.

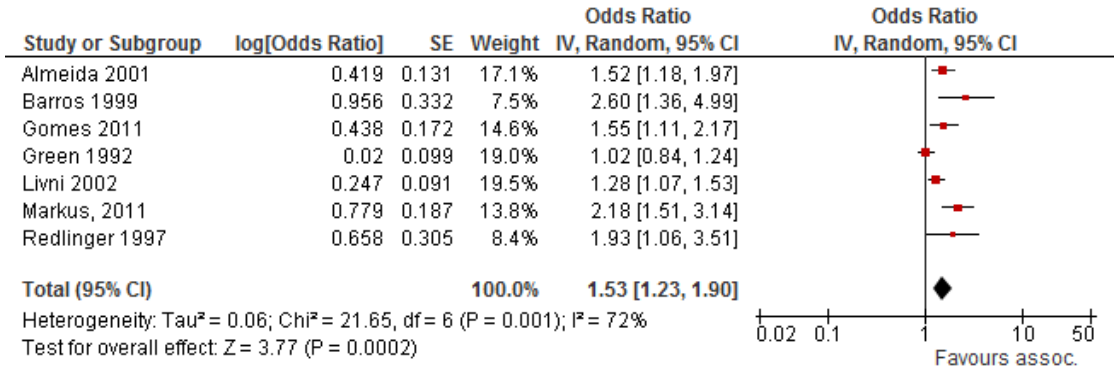
There was substantial heterogeneity (I^2 66%) amongst these six studies. This does not appear to be due to year of publication, study design or country income. There appears to be a slight trend to a greater magnitude of effect for studies including only children and study populations with a lower incidence of hepatitis A.

Table 9: Hepatitis A meta-analysis study and study population characteristics adjusted

Author, year	study design	outcome	exposure	place	Incid.	study population	age	n	measure of effect
Combined outcomes:									
Almeida, 2001[60]	cohort	anti-HAV antibodies	more than three persons per room vs. less than two	Brazil	58%	population survey of households, non-immunised	0+yo	3271	OR 1.52 (1.18 - 1.97)
Barros, 1999[61]	cx*	anti-HAV antibodies	more than two persons per room vs. less than one person	Portugal	28%	students attending public and private schools randomly selected	6-19yo	667	OR 2.60 (p=0.004)
Gomes, 2011[62]	cx*	anti-HAV antibodies	more than one person per bedroom vs. one only	Brazil	64%	school children	7-14yo	462	OR 1.55 (1.11 - 2.18)
Green, 1992[63]	cx*	anti-HAV antibodies	people per room at 10yo	Israel	57%	serving in permanent army	21-30yo	1153	OR (linear) 1.02 (0.84 - 1.24)
Livni, 2002[64]	cx*	anti-HAV antibodies	persons per room	Israel	48%	hospital workers	21-70yo	478	OR (linear) 1.28 (1.05 - 1.50)
Markus[65], cx 2011		HAV antibodies	living in a household with one or more inhabitant per room	Brazil	20%	outpatients from one hospital	1-14yo	901	OR 2.18 (1.51 - 3.14)
Redlinger,cx* 1997[66]		anti-HAV antibodies	one or more persons per rooms vs. fewer than one	US	17%	school students	3-7yo	523	OR 1.93 (1.06 - 3.50)

cx=cross-sectional

Figure 6: Hepatitis A meta-analysis forest plot



4.4.4. Giardia and intestinal parasites

Four studies with unique outcomes (including cross sectional studies of giardia and three infections) were eligible for meta-analysis in the giardia and intestinal parasite group (Table 10). All studies showed statistically significant associations between crowding and disease.

Table 10: Studies eligible for meta-analysis with unique outcomes in the giardia and intestinal parasite group.

Giardia and intestinal parasites									
Author, year	study design	outcome	exposure	place	occur.	population	age	n	measure of effect
Unique outcomes:									
Silva[67], 2009	cx	giardia lamblia	living in a two bedroom house or smaller vs. more than two bedrooms	Brazil	26%	representative household survey	6-71mo	405	OR 2.30 (1.40 - 3.80)
Carneiro[68], 2002	cx	ascaris lumbricoides - prevalence	"crowding"	Brazil	12%	census of eleven rural communities	<14yo	760	RR 6.84 (2.27 - 20.55)
Cazorla[69], 2006	cx	pinworm: E. vermicularis	three or more persons per room vs less than three	Venezuela	63%	six kindergartens and two primary schools in six rural communities	2-12yo	427	OR 1.88 (1.73 - 3.22)
Pullan[70], 2008	cx	Coinfection: N. americanus + S. Mansoni	one or more rooms per person	Brazil	41%	household survey	0+yo	1208	OR 2.35 (1.25 - 4.25)

4.5. Respiratory tract infections

Meta-analysis was carried out for six respiratory tract infections and syndromes: Pneumonia / lower respiratory tract infection; Bronchiolitis / respiratory syncytial virus; Upper respiratory tract infection; Meningococcal disease; *Hib* disease; and Tuberculosis. In addition, eligible studies of otitis media (middle ear infection); Influenza; Measles, mumps, rubella, varicella (chicken pox); and Rheumatic fever (RHD, GAS) were also described but had largely unique outcomes so could not be combined.

4.5.1. Pneumonia / lower respiratory infection meta-analysis

Two meta-analyses were carried out for studies investigating the association between pneumonia / lower respiratory tract infection and household crowding: one for cohort studies reporting RRs and the other for ORs reported by case-control and cross-sectional studies (Table 11). Studies examined children of similar age groups from a

mix of low and high income countries. There was low heterogeneity. The small number of studies prevents funnel plot analysis. Reliance on syndrome identification may have led to an increased chance of misclassification bias and underestimated these measures of effect.

Combined data from four case-control and observational studies showed that children less than five years old exposed to greater household crowding had 1.69 times the odds of pneumonia than children exposed to the least crowding (Figure 7). The recent NZ study[18] had similar results to the two Brazilian studies.

Combined cohort study data for children less than three years old suggests that the increased risk of lower respiratory tract infection from the greatest level of household crowding is 1.36 times (CI: 1.12-2.31) that of children experiencing the least crowding (Figure 7).

A further study of pneumonia/lower respiratory infection had a unique outcome and so could not be included in the combined meta-analysis. This study (mortality from respiratory infection) did not find a significant association between disease risk and crowding (Table 11).

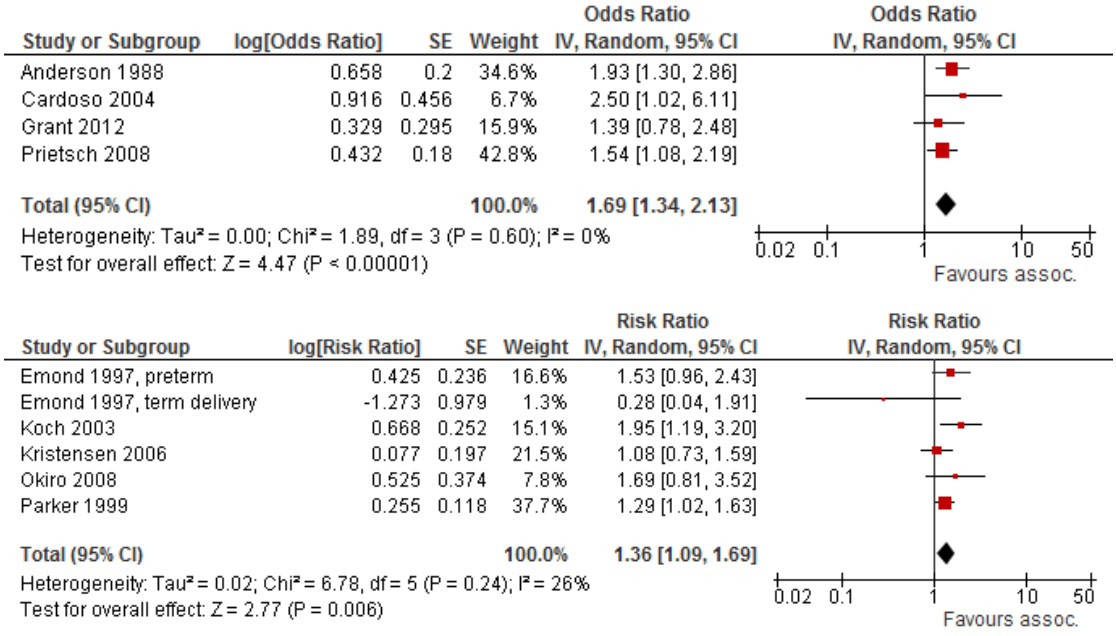
Table 11: Pneumonia / lower respiratory infection meta-analysis study and study population characteristics

Author, year	study design	outcome	exposure	place	occur.	population	age	n	measure of effect
Combined outcomes:									
Anderson, 1988[71]	ccs	acute LRTI	number persons sleeping in same room as child	US	NR	four hospitals with all patients admitted with bronchiolitis or pneumonia, asthma considered, patients with no underlying condition	0-24mo	102 cases + 199 controls	OR 1.93 (p=0.001)
Cardoso, 2004[72]	ccs	LRI, acute bronchitis, acute bronchiolitis, or pneumonia (not asthma)	four or more persons sharing the child's bedroom	Brazil	NR	five public hospitals	2-59mo	396 cases + 336 controls	OR 2.50 (1.02 - 6.09)
Prietsch, 2008[73]	cx	ALRI	four or more persons per bedroom vs. two or fewer	Brazil	24%	sample of children residing in urban area	0-59mo	775	OR 1.54 (1.08 - 2.19)
Grant, 2012[18]	ccs	community-acquired pneumonia (hospitalised and non-hospitalised)	more than one person per room vs. one person or less	New Zealand	NR	children presenting to a public hospital	<5yo	428 cases + 351 controls	OR 1.39 (0.78 - 2.48)
Emond, 1997[29]	cohort	LRTI	more than one person per room vs. one per room	UK	46%	preterm infants 24-32wks gestation	0-12mo	102	RR 1.53 (0.96 - 2.42)
Emond, 1997[29]	cohort	LRTI	more than one person per room vs. one per room	UK	26%	term infants	0-12mo	192	RR 0.28 (0.04 - 1.86)
Koch, 2003[74]	cohort	LRI	two children sleeping in the same room as child vs. none	Greenland	1.59 per 100 days		0-2yo	288	RR 1.95 (1.19 - 3.19)
Kristensen, 2006[75]	cohort	URTI and LRTI	two or more children in same bedroom vs. one	South Africa	1.56 per child year	pregnant women enrolled over 4 months from four antenatal clinics	<1yo	579 children, 118 650 days	RR 1.08 (0.73 - 1.58)
Okiro, 2008[76]	cohort	LRTI - all cause = cough or difficulty	3 siblings <6y sleeping in same room vs. none	Kenya	NR	coastal , birth cohort, lived close to hospital	<3 years	857 LRTI - all	RR 1.69 (0.81 - 3.51)

		breathing associated with one element of respiratory distress						cause cases in 439 cohort	
Parker, 1999[77]	cohort	severe RTI (pneumonia & bronchitis)	more than two persons in a one-roomed dwelling, three in two rooms, five in three rooms; eight persons or more in four rooms and more than two persons per room in houses of five rooms or more	UK	0.34 per child-year	Newcastle thousand families study	0-12mo	982	RR 1.29 (1.02 - 1.62)
Unique outcomes:									
Victora, 1989[78]	ccs	mortality from respiratory infection (broncho-pneumonia, bronchiolitis, pneumonia, acute otitis media, and other)	five or more vs. 1-2.5 people per bedroom	Brazil	NR	all infants from two cities	0-1yo	127 cases + 254 controls	OR 1.85 (0.86 - 3.99)

*ccs=case-control, #cx=cross-sectional, ^LRTI=lower respiratory tract infection, NR=not reported

Figure 7: Pneumonia / lower respiratory infection meta-analysis showing combined odds ratios and combined rate ratios forest



4.5.2. Bronchiolitis / respiratory syncytial virus meta-analysis

Five eligible studies were included in the meta-analysis investigating the association between household crowding and respiratory syncytial virus (RSV) infection, of which four had a similar outcome and could be combined (Table 12).

In children less than three years old with the greatest levels of household crowding, the overall risk of symptomatic respiratory syncytial virus (RSV) infection was 2.24 times greater than those with the least household crowding. This is an imprecise estimate based on a small number of studies with considerable heterogeneity (84%).

Studies were therefore stratified according to study design. This appeared to account for a proportion of the heterogeneity. In the combined estimate from two case-control studies there was now no evidence of an association between crowding and risk of hospitalisation with respiratory syncytial virus infection (OR 1.31, CI 0.85-2.01, I^2 63%). Data from a single cohort study were combined to suggest a 4.44 (CI: 2.45-8.04, I^2 0%) times increased risk of respiratory syncytial virus lower respiratory infection for infants sharing the same bedroom with two or more others.

Another systematic review of crowding and RSV has recently been published.[79] That review had broader eligibility criteria and was limited by heterogeneity so meta-analysis was not carried out. It reports on 20 studies of which 16 found a statistically significant association between a crowding variable (widely defined) and RSV in under five year olds. Using a more precise measure of household crowding density in the narrative synthesis of this review, we identified 15 relevant studies of which 7 report a significant association with crowding. Both our results and the published review suggest that crowding is associated with RSV.

In addition a further study of RSV was eligible for inclusion in the meta-analysis, but had a unique, less objective outcome, reported wheeze, and so could not be included in the combined meta-analysis (Table 12). It found a significant association between disease risk and crowding.

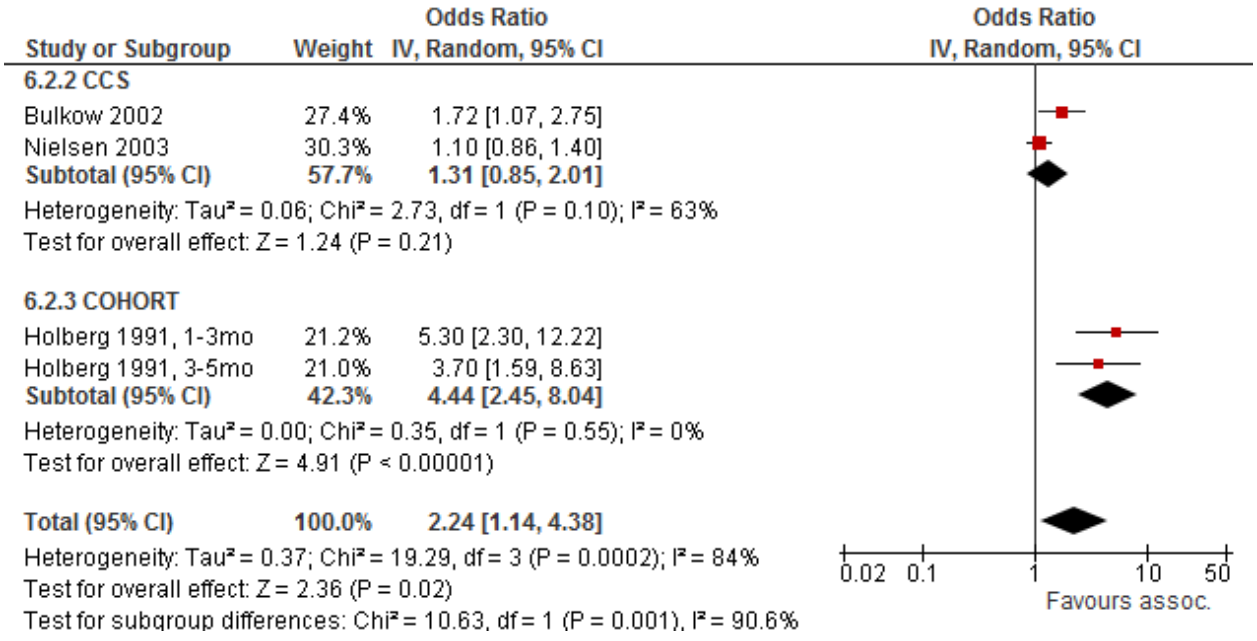
Table 12: Respiratory syncytial virus meta-analysis study and study population characteristics

Author, year	study design	outcome	exposure	controls	place	study population	age	n	measure of effect
Combined outcomes:									
Bulkow, 2002[80]	ccs*	NPA +ve on Ag detection or culture whilst hospitalised	two or more persons per room	matched on age and region of residence, with no RSV in preceding year	USA (Alaska)	remote location, 85% Eskimo, high rates of hospitalisat-ion with RSV	< 3yo	204 cases + 338 controls	OR 1.72 (p=0.024)
Nielsen, 2003[81]	ccs*	RSV hospitalisation, nasopharyngeal sample positive within two days of admission	less than 22 square meters per person	community controls matched on age, sex and municipality	Denmark	all children admitted with RSV infection from two counties	<2yo	1252 cases + 6260 controls	OR 1.10 (0.87 - 1.42)
Holberg, 1991[82]	cohort	LRI infants diagnosed by their paediatrician and then tested to be RSV positive on either culture or immunofluorescence	two or more others sharing the same bedroom vs. one or no	-	USA (Arizona)	healthy infants enrolled at birth	**1-<3mo**	579	OR 5.30 (2.30 - 12.20)

	(first episode only)	others						
Holberg, 1991[82] cohort	LRI infants diagnosed by their paediatrician and then tested to be RSV positive on either culture or immunofluorescence (first episode only)	two or more others sharing the same bedroom vs. one or no others	-	USA (Arizona)	healthy infants enrolled at birth	**3-<5mo**	600	OR 3.70 (1.60 - 8.70)
Unique outcomes:								
Baker[27], 1998 cx	prevalence maternal reported wheeze	more than one person per room vs. one or fewer persons per room	-	UK	infants, all pregnant women in three health districts	**6mo**	8450	OR 1.26 (1.06 - 1.49)

*ccs=case-control, cx=cross-sectional study

Figure 8: Respiratory syncytial virus bronchiolitis meta-analysis forest plot



4.5.3. Upper respiratory tract infection meta-analysis

Two meta-analyses were carried out for studies investigating the association between upper respiratory tract infection (URTI) and household crowding: one for cohort studies reporting RRs and the other for ORs reported by case-control and cross-sectional studies (Table 13). URTIs are defined as those which do not meet the criteria for lower respiratory infections and pneumonia and are typically less severe.

Combined data from two cross-sectional studies and one case-control study, showed that children experiencing greater household crowding had an estimated 1.39 times the odds of URTI (not significant) than children experiencing the least crowding (Figure 9). There is substantial heterogeneity in these studies. One study of older children in

China actually showed that living in houses with less than three rooms was protective against infection.

Combined data from three cohort studies from high income countries suggests that the best estimate of increased risk of URTI for children less than two years old experiencing the greatest level of household crowding is 1.63 times (not significant) that of children experiencing the least crowding (Figure 9). There is moderate heterogeneity.

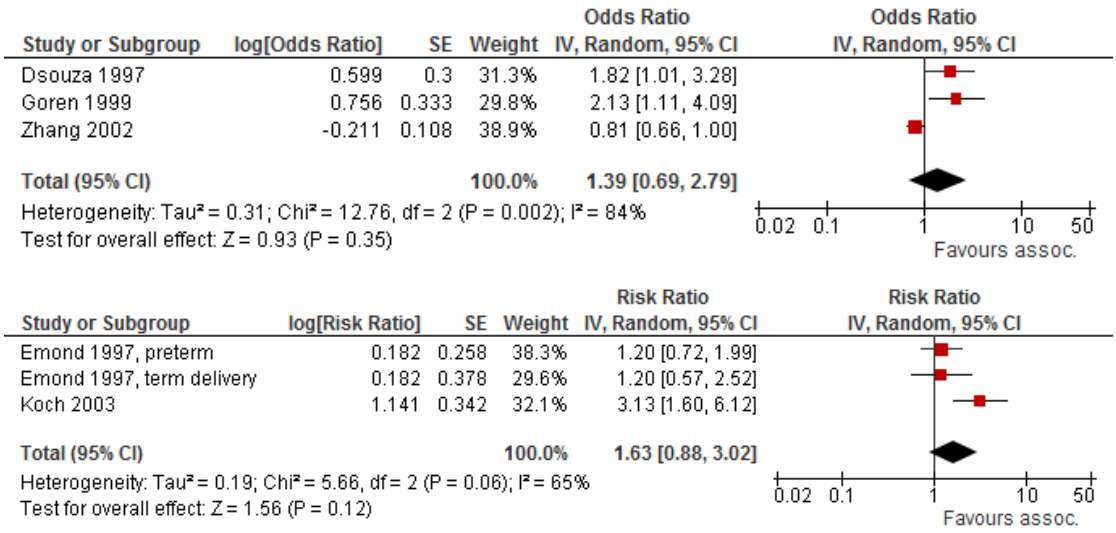
Reliance on syndrome identification of the outcome may lead to an increased chance of misclassification bias and underestimate these measures of effect.

Table 13: Upper respiratory tract infection study population characteristics

Author, year	study design	outcome	exposure	place	occur.	population	age	n	measure of effect
Combined outcomes:									
Dsouza, 1997[83]	cx	cough and runny nose, with or without fever reported by the mother	total house area / number of people living in the house is 1.48m2 or less vs. greater than 1.48m2	Pakistan	15%	children of families in a squatter settlement	unknown	698	OR 1.82 (1.01 - 3.28)
Zhang, 2002[84]	cx	reported ever hospitalised for respiratory symptoms	less than three rooms vs. three or more rooms	China	14%	elementary school students and their families chosen from an urban district and a suburban district in each of four cities	5-16yo	7392	OR 0.81 (p=0.05)
Goren, 1999[85]	cx	cough without cold	average persons per room	Israel	NR	children from participating schools in two communities	7-13yo	976	OR (linear) 2.13 (1.11 - 4.10)
Emond, 1997[29]	cohort	URTI recorded on parent held record	more than one person per room	UK	49%	preterm infants 24-32wks gestation	0-12mo	102	RR 1.20 (0.72 - 1.98)
Emond, 1997[29]	cohort	URTI recorded on parent held record	more than one person per room	UK	30%	term infants	0-12mo	192	RR 1.20 (0.57 - 2.51)
Koch, 2003[74]	cohort	URTI	two adults sleeping in the same room as child vs. none	Greenland	1.59 episodes per 100 child days at risk	open cohort of Inuit children in a single town	0-2yo	288	RR 3.13 (1.60 - 6.11)

*ccs=case-control, #cx=cross-sectional, ^RTI=respiratory tract infection, NR=not reported

Figure 9: Upper respiratory tract infections meta-analysis showing combined odds ratios and combined rate ratios forest plots



4.5.4. Meningococcal disease meta-analysis

Five case-control articles from high income countries contributed to seven study outcomes investigating the association between household crowding and meningococcal disease (Table 14). All studies, except for one, were limited to children.

Persons experiencing the greatest vs. least household crowding had 2.13 times increased odds of meningococcal disease. The estimate of effect was imprecise and there was substantial heterogeneity (I^2 69%). This may have been contributed to by the range of crowding measures investigated.

The NZ study[15] recorded a particularly large OR compared to studies in other high income settings. Ascertainment of meningococcal disease included laboratory and non-laboratory measures in the majority of studies. All studies adjusted for smoking, 4/7 adjusted for an additional crowding variables and 6/7 adjusted for other additional variables.

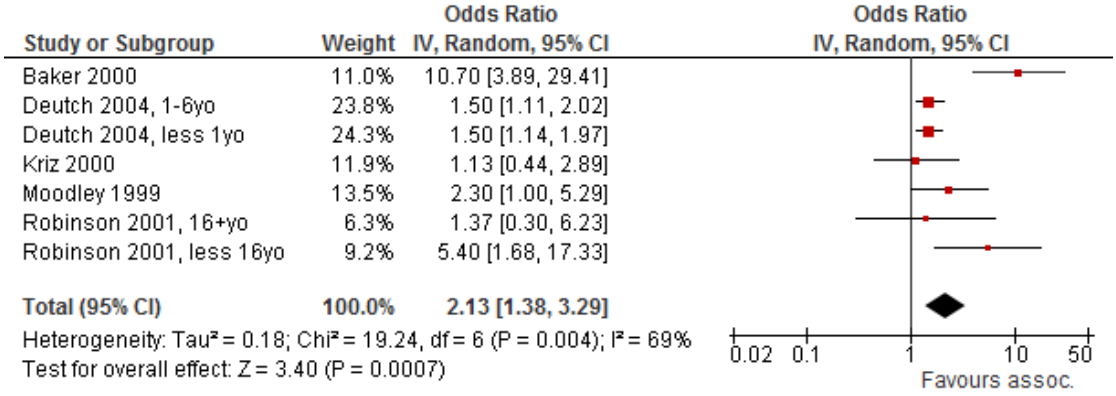
Table 14: Meningococcal disease meta-analysis study and study population characteristics

Author, year	study design	outcome	exposure	controls	place	study population	age	n	measure of effect
Combined outcomes									
Deutch, 2004[86]	ccs	hospitalisation for meningococcal disease - discharge code	<20m^2 per person vs. >50m^2	Civil registry community controls matched on age and gender	Denmark	nationwide population based	1-6y	1,222 cases + 24,549 controls (74%)	OR 1.50 (1.10 - 2.00)
Deutch, 2004[86]	ccs	hospitalisation for meningococcal disease - discharge code	<20m^2 per person vs. >50m^2	Civil registry community controls matched on age and gender	Denmark	nationwide population based	≤1yo	1,222 cases + 24,549 controls (36%)	OR 1.50 (1.10 - 1.90)

Kriz, 2000[87]	ccs	lab and non-lab confirmed invasive meningococcal disease	more than one person per room	from same school matched for age, sex and place of residence	Czech Republic	school children	<15 years	68 cases + 135 controls	OR 1.13 (0.44 - 2.88)
Moodley, 1999[88]	ccs	lab and non-lab confirmed meningococcal disease	>2.5 equivalent people per bedroom (where a child <10y = 0.5 persons)	hospitalised controls from trauma	South Africa	metropolitan area	<14 years	70 cases + 210 controls	OR 2.30 (1.00 - 5.30)
Robinson, 2001[89]	ccs	lab and non-lab confirmed meningococcal disease	normally shares a bedroom	matched on age, sex and socioeconomic status	Australia	state notifications	16+yo	40 cases + 80 controls	OR 1.37 (0.30 - 6.20)
Robinson, 2001[89]	ccs	lab and non-lab confirmed meningococcal disease	normally shares a bedroom	matched on age, sex and socioeconomic status	Australia	state notifications	<16 years	47 cases + 94 controls	OR 5.40 (1.70 - 17.50)
Baker, 2000[15]	ccs[1]	lab and non-lab confirmed meningococcal disease	number of adults (10+yo) per number of rooms	community controls matched on age and ethnicity	New Zealand	children presenting to public hospital	<8yo	202 cases + 313 controls	OR(linear) 10.70 (3.90 - 29.50)

[1]ccs=case-control

Figure 10: Meningococcal disease meta-analysis forest plot



4.5.5. Haemophilus influenzae disease meta-analysis

Six study results were included in the meta-analysis investigating the association between household crowding and *Hib* disease (Table 15). All studies were case-control designs in high income countries. For children <6 years old experiencing the greatest level of household crowding there was a 1.74 times increased odds of *Hib* disease, compared to children with the least household crowding (Figure 11). The association with crowding is further strengthened by only a moderate degree of heterogeneity (I^2 47%).

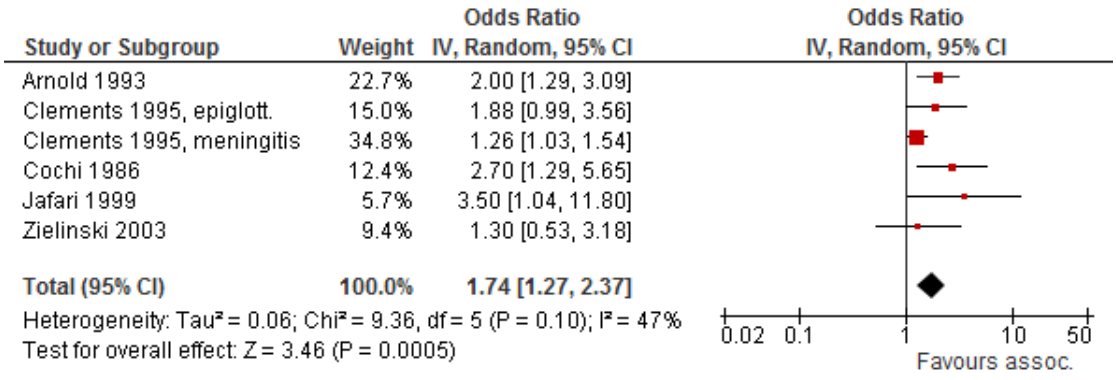
In addition a further study of *Hib* was eligible for inclusion in the meta-analysis, but had a unique outcome (*Hib* nasopharyngeal carriage) so could not be included in the combined meta-analysis (Figure 11). It found a significant association between carriage risk and crowding.

Table 15: *Haemophilus influenzae* type b study and study population characteristics

Author, year	study design	outcome	exposure	controls	place	study population	age	n	measure of effect
Combined outcomes:									
Arnold, 1993[90]	ccs*	invasive Hib	two or more vs. less than 1.5 persons to the number of bedrooms	matched on age	US	population based: children hospitalised	<6yo	295 cases + 590 controls	OR 2.00 (1.30 - 3.10)
Clements, 1995[91]	ccs*	invasive Hib epiglottitis	child shared a bedroom vs. did not share	day surgery hospital controls	Australia	children hospitalised	<5yo	83 cases + 367 controls	OR 1.88 (0.99 - 3.55)
Clements, 1995[91]	ccs*	invasive Hib - meningitis	each additional child per bedroom	day surgery hospital controls	Australia	children hospitalised	<5yo	76 cases + 367 controls	OR(linear) 1.26 (1.03 - 1.54)
Cochi, 1986[92]	ccs*	invasive Hib	child shared a bedroom vs. did not share	random sample of children matched on age	US	population based surveillance of hospitals and laboratories	2-59mo	102 cases + 530 controls	OR 2.70 (1.30 - 5.70)
Jafari, 1999[93]	ccs*	Hib disease	more than one person per room vs. one or fewer	controls matched by age and county of birth	US	population based, partially vaccinated	2-18mo	40 cases + 93 controls	OR 3.50 (1.03 - 11.70)
Zielinski, 2003[94]	ccs*	Hib meningitis	apartment size of 47m2 or less vs. >47m2	controls matched on age and immunisation centre	Poland	nested within a population based surveillance study	≤5yo	55 cases + 155 controls	OR 1.30 (0.50 - 3.00)
Unique outcomes:									
Sekhar[95], 2009	cx	*H. influenzae* nasopharyngeal carriage	more than two persons per room vs. two or fewer	NA	India	household sample	0-24yo	997	OR 9.20 (2.30 - 36.10)

ccs=case-control, cx=cross-sectional study

Figure 11: *Haemophilus influenzae* type b disease meta-analysis forest plot



4.5.6. Tuberculosis meta-analysis

Twelve studies of tuberculosis disease and infection were eligible for meta-analysis (Table 16).

Six case-control studies and one cross-sectional study contributed to the meta-analysis investigating the association in adults between household crowding and tuberculosis. Tuberculosis was defined in 6/7 studies as pulmonary tuberculosis. The combined effect estimate was the largest of all the CCID meta-analyses with 3.78 times increased odds of tuberculosis in the most crowded compared to the least crowded households.

There was considerable heterogeneity (I^2 90%) and an imprecise effect estimate with a 95% confidence interval of 1.75-8.13. Studies were carried out in a range of settings, mainly in low-moderate income countries. Two large studies account for 36% of the combined result and both have ORs close to no effect. This is in contrast to the other contributing studies which have higher effect estimates. There appears to be little reason why the association would be different between the two groups of studies, however the threshold used to define crowding exposure is less severe in the two larger studies showing less effect.

In addition a further five studies of tuberculosis were eligible for inclusion in the meta-analysis, but had largely unique outcomes (symptoms of tuberculosis, self-reported tuberculosis, tuberculin skin test positive [two studies], and tuberculosis meningitis) so could not be included in the combined meta-analysis. Three studies (the two tuberculin studies and the one on tuberculosis meningitis) found a significant association between disease risk and crowding and two did not (symptoms of tuberculosis, self-reported tuberculosis) (Table 16).

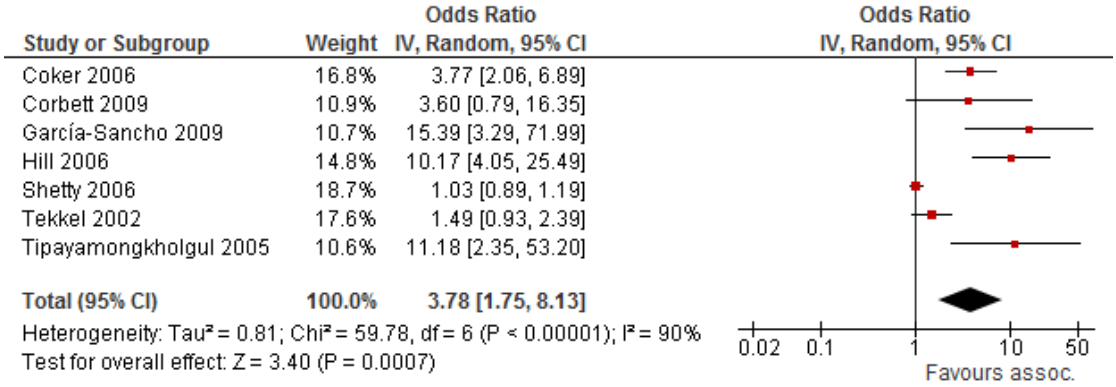
Table 16: Tuberculosis meta-analysis study and study population characteristics

Author, year	study design	outcome	exposure	controls	place	study population	age	n	measure of effect
Combined outcomes:									
Coker, 2006[96]	ccs[1]	pulmonary tuberculosis culture confirmed	least vs. most living space per person	age and sex matched controls	Russia	those recruited to WHO DOTS programme and randomly selected controls	adults	334 cases + 334 controls	OR 3.77 (2.06 - 6.88)
Corbett, 2009[97]	cx[c]	pulmonary tuberculosis culture confirmed	more than four persons per number of rooms in the dwelling vs. less than two	NA	Zimbabwe	forty-six study neighbourhoods	16+yo	10092	OR 3.60 (0.80 - 16.50)
Garcia-Sancho, 2009[98]	ccs[1]	pulmonary tuberculosis sputum culture positive	one room household vs. more than one room	sex matched controls	Mexico	females living in small communities	adults	42 cases + 84 controls	OR 15.40 (3.30 - 72.08)
Hill, 2006[99]	ccs[1]	pulmonary tuberculosis sputum culture positive	at least 4 persons and at least 2 persons per room in a household vs. less than 4 persons and less than 2 people sleeping per	age and sex matched clinic controls	Gambia	presenting to a health clinic	15+yo	100 cases + 200 controls	OR 10.17 (4.08 - 25.63)

			room on average						
Shetty, 2006[100]	ccs[1]	pulmonary tuberculosis - new cases in pulmonary outpatients	more than two persons per room vs. less than two	age and sex matched controls from among relatives visiting non tuberculosis patients in hospital	India	new cases of pulmonary tuberculosis seen at outpatients	15-83yo	189 cases + 189 controls	OR 1.03 (0.89 - 1.19)
Tekkel, 2002[101]	ccs[1]	pulmonary tuberculosis - verified by European definition	more than one person per room vs. one or fewer	population registry controls matched by sex, age and region	Estonia	admitted to hospital	15+yo	248 cases + 248 controls	OR 1.49 (0.93 - 2.39)
Tipayam-ongkholgul, 2005[102]	ccs[1]	tuberculosis - hospital diagnosed - 50% pulmonary, 36% lymph nodes	five or more persons per room vs. one person or less	age and sex matched hospital controls	Thailand	diagnosed and treated at one hospital	<15yo	130 cases + 130 controls	OR 11.18 (2.35 - 53.20)
Unique outcomes:									
Goldhaber-Fiebert, 2011[103]	cx	symptoms of tuberculosis (haemoptysis and persistent cough) (sensitivities between 65 and 70% and specificities between 55 and 75%)	people per room		World Health Survey	forty six mainly low and middle income countries	adults	124545	OR (linear) 1.04 (0.98 - 1.09)
Mishra, 1999[104]	cx	self-reported tuberculosis	number of persons per room		India	national health survey	20+yo	260162	OR 0.96 (0.85 - 1.09)
Tornee, 2005	cx	tuberculin skin test positive	persons per rooms		Thailand	household contacts of tuberculosis patients	<15yo	480	OR 5.19 (2.65 - 8.69)
Elliott, 1993[105]	cohort of contacts	tuberculin skin test positive	three or more persons per room vs. less than two		Zambia	tuberculosis contacts	0+yo	348	OR 3.13 (p=0.022)
Thilothamm al, 1996[106]	ccs	tuberculosis meningitis laboratory confirmed	more vs. less living space in square feet per person	hospital controls from the seizure clinic with febrile convulsions block matched for age and sex	India	hospital cases,	6mo-12yo	107 cases + 321 controls	OR 1.64 (1.02 - 2.64)

[1]ccs=case-control, [c]cx=cross-sectional

Figure 12: Tuberculosis meta-analysis forest plot



4.5.7. Otitis media

Three studies looking at different forms of otitis media (OM) (previous acute OM episodes, middle ear effusion prevalence, chronic OM) were eligible for meta-analysis (Table 17). Two found no significant relationship between disease risk and measures of household crowding and one found a protective effect for chronic otitis media.

Table 17: Studies eligible for meta-analysis with unique outcomes in the otitis media group

Author, year	study design	outcome	exposure	place	incid.	population	age	n	measure of effect
Unique outcomes:									
Homøe, 1999[107]	cx	previous acute OM episodes	persons per room	Green-land	33%	children born in Greenland	3,4,5,8yo	591	OR (linear) 1.24 (0.88 - 1.74)
Strachan, 1990[108]	cx	middle ear effusion prevalence	more than one person per room vs. less than one	UK	9%	three schools	6-7yo	879	OR 1.05 (0.70 - 1.57)
Kim, 1993[109]	ccs	chronic OM	four or more living rooms vs. one living room	Korea	3%	population sample of households	0+yo	201 cases + 8910 controls	RR 0.50 (0.32 - 0.80)

OM=otitis media, cx=cross-sectional, ccs=case-control,

4.5.8. Influenza

Two cohort studies of influenza-like illness were eligible for meta-analysis, however one gives an OR and the other a RR so they were not combined (Table 18). Both found a significant positive relationship between disease risk and measures of household crowding.

Table 18: Studies eligible for meta-analysis with unique outcomes in the influenza group

Author, year	design	outcome	exposure	place	occur.	population	age	n	measure of effect
Unique outcomes:									
Forshey[110], 2010	cohort contacts	influenza like illness	2-2.9 residents per room vs. less than one	Peru	39.8 episodes per 1000 person-years	population surveillance across 45 city blocks	0+yo	1534	OR 1.56 (1.17- 2.08)
Gordon[111], 2009	cohort	influenza like illness	five or more people per the number of rooms vs. less than three	Nicaragua	34.8 episodes per 100 person-years	patients of a public primary care facility	2-11yo	2615	RR 1.18 (1.04-1.34)

4.5.9. Measles, mumps, rubella, and varicella (chicken pox)

One cohort study of measles and a cross sectional study of varicella-zoster virus antibodies were eligible for meta-analysis (Table 19). Both found a significant positive relationship between disease risk and measures of household crowding.

Table 19: Studies eligible for meta-analysis with unique outcomes in the measles, mumps, rubella, varicella group

Author, year	study design	outcome	exposure	place	incid.	population	age	n	measure of effect
Unique outcomes:									
Dayan, 2004[112]	cx	Varicella-zoster virus antibodies	more than two per bedroom vs. two or fewer	Argentina	99%	women attending public health care setting in four cities and one rural area	15-49yo	2803	OR 2.70 (1.22 - 5.99)
Silfverdal, 2009[113]	cohort	clinical measles	quintiles of person per room at 5yo	UK	50%	all children born in one week of April 1970 living in Great Britain	0-10yo	10207	OR 1.36 (1.14 - 1.62)

cx=cross-sectional,

4.5.10. Rheumatic fever, heart disease and group A streptococcus

For the rheumatic fever group, four eligible studies were identified (Table 20). Only one showed a positive association with crowding and it investigated invasive group A streptococcus infection.

Other syntheses of the literature on crowding and rheumatic fever are available.[114,115] These reviews appear to have taken a broader approach by including more eligible crowding measures and including a greater range of study designs (such as ecological studies). Both these literature reviews are similar to this review, in that the studies identified were heterogeneous and no meta-analysis was undertaken.

Table 20: Studies eligible for meta-analysis with unique outcomes in the rheumatic fever, rheumatic heart disease, and invasive GAS group

Author, year	design	outcome	exposure	place	occur.	population	age	n	measure of effect
Unique outcomes:									
Oli[116], 1999	cx	rheumatic heart disease prevalence	number of persons per bedroom (two or more in univariate analysis)	Ethiopia	6.4 per 1000	school children in an urban area	10-15yo	9378	OR (linear) 1.00 (0.84 - 1.13)
Factor[117], 2005	ccs	invasive Group A strep: isolation of strep. pyogenes from normally sterile site	fewer rooms in the home	US	NR	non-institutionalised residents , population based	<18yo	38 cases + 78 controls	OR 1.49 (1.14 - 1.96)
Vlajinac[118], 1991	ccs	rheumatic fever incidence	more than two persons per room	Yugoslavia (Serbia Proper)	NR	all cases in region identified through reports to health administration	0-19yo (8.1% >20yo)	148 cases + 444 controls	RR 1.35 (0.61 - 3.00)
Coggon[119], 1993	cohort retros-pective	mortality from rheumatic heart disease	one or more persons per room vs. less than 0.50	UK	NR	Chesterfield township	0+ yo	8138	OR 1.00 (0.40 - 2.30)

RHD=rheumatic heart disease, GAS=Group A Streptococcus, NR=not reported

4.6. Skin and eye infection

Meta-analysis was carried out for trachoma. In addition, eligible studies of skin infections and pediculosis (head lice) were also described, but had largely unique outcomes so could not be combined.

4.6.1. Trachoma meta-analysis

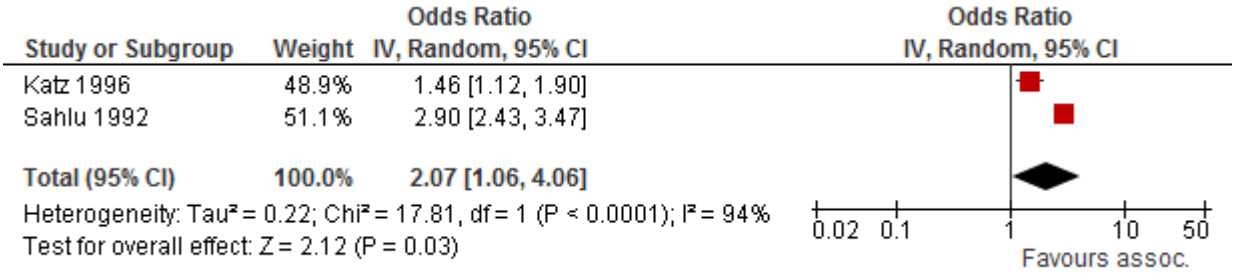
Two cross-sectional studies from low income countries were included in the meta-analysis investigating the association between household crowding and trachoma (Table 21). For individuals in the most crowded households there was a 2.07 times increased odds of trachoma. However, the estimate is imprecise and there is considerable unexplained heterogeneity (I^2 94%). In fact the confidence intervals of each study do not overlap. Heterogeneity is not accounted for by age, country income, incidence of infection, outcome measure or exposure measure.

Table 21: Trachoma study and study population characteristics

Author, year	study design	outcome	exposure	place	incid.	study population	age	n	measure of effect
Combined estimates:									
Katz, 1996[120]	Cx*	trachoma on examination	five or more people per room vs. less than five	Nepal	24%	population sample house-to-house census	24-76mo	836	OR 1.46 (1.03 - 1.75)
Sahlu, 1992[121]	cx	trachoma on examination	four or more per room vs. three or less	Ethiopia	27%	rural population representative	0+yo	1222	OR 2.90 (2.49 - 3.56)

*=cross-sectional

Figure 13: Trachoma meta-analysis forest plot



4.6.2. Other skin infection and pediculosis

One study of skin infection and one of pediculosis (head lice) were eligible for meta-analysis (Table 22). The pediculosis study found a significant positive relationship between disease risk and measures of household crowding whereas there was no significant association for skin infections.

Table 22: Studies eligible for meta-analysis with unique outcomes in the skin infection and pediculosis (lice) group

Author, year	study design	outcome	exposure	place	incid.	population	age	n	measure of effect
Unique outcomes:									
Bailie, 2012[24]	cohort / intervention	positive change in skin infection reported by carer between baseline and follow-up	reduction of two or more persons per bedroom over study period vs. baseline	Australia	NR	children before and after in a housing intervention cohort	<=7yo	302	OR 1.81 (0.82 - 4.02)
Mahmud, 2011[122]	cx	head lice	3.5 or more persons per room vs. less than 3.5	Australia	6%	women in national survey	12+yo	2321	OR 1.50 (1.10 - 2.10)

NR=not reported

4.7. Other infections

One study of Epstein–Barr virus (EBV) and one of Human Herpesvirus 8 (HHV8) were eligible for meta-analysis (Table 22). The EBV study found a significant positive relationship between disease risk and measures of household crowding whereas there was no significant association for HHV8.

Two other eligible studies looked at multiple infectious diseases (Table 24). One was a case-control study of infectious illness warranting hospitalisation and one was a prevalence study of communicable disease symptoms. Both found a significant positive relationship between disease risk and measures of household crowding.

Table 23: Studies eligible for meta-analysis with unique outcomes in the Epstein Barr Virus, Herpesvirus group

Author, year	study design	outcome	exposure	place	incid.	population	age	n	measure of effect
Unique outcomes:									
Anderson, 2008[123]	cx	HHV8 Abs	one or more person per room vs. less than one	US	1%	national survey weighted to be representative	6-17yo	4166	OR 1.10 (0.40 - 2.90)
Crowcroft, 1998[124]	cx	EBV	child shares a bedroom	UK	56%	population representative sample of school children	11yo	552	OR 1.78 (1.14 - 2.79)

Table 24: Studies eligible for meta-analysis with unique outcomes in multiple infectious diseases groups

Author, year	study design	outcome	exposure	controls	place	incid.	population	age	n	measure of effect
Unique outcomes:										
Berg, 1991[125]	ccs	infectious illness warranting hospitalisation (including *Hib*, N meningitidis)	sharing a bedroom	community controls matched on age and primary health clinic	US	NR	excluded if had underlying condition, no phone or unable to attend day care	3-59 mo	193 cases + 193 controls	OR 2.40 (1.35 - 4.27)
Booth, 1976[126]	cx	prevalence of communicable disease based on symptoms	1. Kitchen set in wall of another room. 2. Number of hours respondent is awake and at home when the number of people is equal to or greater than the number of rooms. 3. Number of hours respondent is awake and at home when the number of people in the room with the respondent is two or more.		Canada	0%	males - white urban intact families selected for crowded neighbour-hood and household conditions	adults	213	OR 2.69 (p<0.05)

NR=not reported

4.8. New Zealand studies

The following section summarises studies conducted in NZ to investigate the health effects of household crowding. These studies are briefly summarised here because of their particular relevance to NZ. This section of the results is therefore outside the scope of the systematic review. However, two of the studies described here were eligible for inclusion in the meta-analysis.[15,18]

- Meningococcal disease – A case-control study was conducted during the early stages of the serogroup B epidemic to identify risk factors for disease in children <8 years.[15] This was a large study that collected multiple measures of crowding along with data on potential confounders. It found that the risk of disease was strongly associated with crowding as measured by the number of adult and adolescent household members per room (OR 10.7, CI 3.9-29.5). This effect would mean that if a family living in an average sized house of six rooms increased the number of adolescents or adults by one there would be a 50% increase in risk of meningococcal disease for a child living in the same household. If they increased the number by two adolescents or adults there would be a doubling of risk, by four adolescents or adults a 5-fold increase in risk, and by six a 10.7-fold increase.[15]
- Rheumatic fever (RF) – An ecological study was conducted of all 1,249 new RF hospitalisations in NZ, 1996-2005.[17] This study used the percentage of crowded households (measured using the Canadian National Occupancy Standard) in a neighbourhood (census area unit) as the exposure measure. It used a multivariate model (zero inflated negative binomial) that included household income (Jensen Equivalised Annual Household Income) and proportion of children 5-14 years in the neighbourhood. It found a significant independent risk from the crowding exposure. The incidence rate ratio (IRR) for the risk of RF in relation to the percentage of household crowding was: Total pop=1.065 (CI 1.052-1.079), Children 5-14 years=1.040 (CI 1.029–1.050), Māori and Pacific children 5-14 years=1.022 (CI 1.010–1.034). The IRR of 1.065 in the full model means that for every 1% increase in the average crowding level of a Census Area Unit (CAU) there would be a 6.5% increase in the expected RF count in that CAU, assuming the other variables were held constant. This means that if we used the least crowded quintile of housing as a reference (median crowding level of 0.77%), we would expect the RF count in the most crowded quintile (median crowding level of 12.03%) to be approximately 88% higher if all the other variables were held constant (based on an approximately 11% increase in crowding level).[17]
- Rheumatic fever - An earlier study described 240 cases of RF in Auckland, NZ, over the 1981-84 period.[127] It found that RF cases tended to come from crowded households. However, it did not have a control population so it is hard to evaluate the findings.
- Tuberculosis – An ecological study was conducted of all 1898 notified TB cases in NZ over the 2000-04 period.[16] This study used percentage of crowded households (measured using the Canadian National Occupancy Standard) in the neighbourhood (Census Area Unit) as the exposure measure. It used a multivariate model (negative binomial) that included household income (Jensen Equivalised Annual Household Income), migration, age, and existing TB burden in the neighbourhood. It found statistically significant associations between TB incidence and household crowding in both the total population (IRR 1.05, CI 1.02-

1.08) and in NZ-born people <40 years (IRR 1.08, CI 1.04-1.12). TB incidence was also associated with migration and income. The IRR of 1.05 in the full model means that for every 1% increase in the average crowding level of a CAU there would be a 5% increase in the expected TB count in that CAU, assuming the other variables were held constant. This means that if the least crowded quintile of housing was used as a reference (median crowding level of 0.94%), the TB count in the most crowded quintile (median crowding level of 9.49%) would be expected to be approximately 41% higher if all the other variables were held constant (based on an approximately 8% increase in crowding level). For NZ-born people aged <40 years, with an IRR of 1.08, the effect would be even stronger with the expected TB count approximately 71% higher in the most crowded quintile.[16]

- Pneumonia – A recently published case-control study in Auckland[18] demonstrating the increased risk of pneumonia hospitalisation for children exposed to household crowding (OR 2.87, CI 1.33-6.41) and mould in the child's bedroom (OR 2.39, CI 1.25-4.72). The American Crowding Index was used as the measure of crowding where the house is considered crowded if there is more than one person per room.
- Crowding reduction as part of the HNZC Healthy Housing Programme (HHP) – The three objectives of the HHP were described by the former HNZC CEO Michael Lennon as being, 'to reduce state housing overcrowding, reduce the risk of meningococcal disease and other infectious disease, and conduct independent and external evaluation of the pilot scheme prior to any rollout implementation.' [128] The HHP had an initial pilot from January 2001 to June 2002 with the main programme starting in 2003. Initial evaluation of the programme was based on qualitative interviews of 30 selected households and all available HHP providers. The authors concluded that the health goals of the initial HHP had been strengthened by its 'evolution' into a more holistic approach to promoting household well-being.[129] Initial quantitative evaluation of the HHP found a significant reduction in acute hospitalisations for younger participants in the HHP (a 23% reduction for those aged 5-34 years).[130] However, the study could not separate the contribution of crowding reduction from the other components of the intervention.[131] A more extensive evaluation used a control population.[132] This evaluation found that for children (<20 years of age), participation in the HHP was associated with a statistically significant fall in the total number of acute and arranged hospitalisations of 27% (CI -43% to -6%) in the year following completion of the HHP interventions. The effect of the HHP appeared more marked for the most intensive intervention, crowding reduction, which was associated with the largest reduction of 61% (CI -79% to -26%) in acute and arranged admissions.[132] Although CCID dropped by 69% (CI -91% to +1%) in the crowding reduction sub-group, this decline was of marginal statistical significant.

4.9. Burden of infectious disease from household crowding

Results of the burden of disease analysis are shown in Table 25. These estimates have been made for nine categories of infectious disease using estimates from meta-analyses (Table 6). Trachoma was excluded as there is no transmission in New Zealand. URTIs were retained, with the uncertainty around this estimated effect reflected by the confidence intervals (which overlap one).

The greatest absolute numbers of hospital admissions attributable to household crowding correspond to the most common CCID admission categories. In the age groups studied, bronchiolitis (667, CI 89-1399), pneumonia/LRTI excluding bronchiolitis and *Hib* disease (296, CI 154-455) and URTIs (177, CI -158-668) accounted for the greatest number of hospital admissions attributable to household crowding.

For the diseases included in the meta-analyses, the total number of hospitalisations attributed to household crowding is estimated to be 1,343 (CI 182-2843) per year. This total is 9.8% of the 13,680 hospital admissions a year from these diseases (which represent about one fifth of the total 75,706 ID hospitalisations a year in NZ over the 2004-08 period[1]).

This analysis has also looked at the estimated contribution of exposure to household crowding for different ethnic groups. Despite their smaller populations, Māori (Table 27) and Pacific (Table 28) ethnic groups each had more hospital admissions per year attributable to household crowding than European/Others (Table 26). For European/Others exposure to household crowding is estimated to cause 331 (CI 20-799) admissions a year or 5% of the total 7,224 admissions a year for these groups of diseases. For Asian peoples exposure to household crowding is estimated to cause 108 (CI 23-206) admissions a year, or 13% of IDs. For Māori the contribution from exposure to household crowding is higher, with an estimated 790 (CI 106-1540) hospitalisations a year which is 16.8% of the 4,703 hospitalisations a year from these diseases. For Pacific peoples the estimated contribution from exposure to household crowding is similar to Māori with 692 (CI 136-1184) admissions a year. However, for Pacific peoples the relative contribution is the highest seen for any ethnic group, with an estimated 24.7% of 2,802 admissions per year attributable to this exposure for the IDs included in the analysis. The relatively larger contribution of household crowding to Māori and Pacific disease incidence is largely because exposure to household crowding is much higher for these populations. In addition, Māori and Pacific peoples have rates of hospitalisation for serious infectious diseases that are two to three times higher than those of the European/Other population. Consequently, these ethnic groups experience a greater absolute effect from any exposure that increases their risk of infectious disease.

The contribution of exposure to household crowding is particularly large for some diseases affecting Māori and Pacific peoples. Meningococcal disease predominantly occurs in children (0-16 years) and the meta-analysis shows that risk is strongly associated with exposure to household crowding. For Pacific children (where 45% are exposed to household crowding) an estimated 34% of disease burden and in Māori children (where 28% are exposed to household crowding) an estimated 23% of disease burden can be attributed to this exposure. By comparison, the estimate is only 9% in European/Other children (where only 8% are exposed to household crowding).

Table 25: Estimated burden of infectious disease in New Zealand attributable to household crowding, 2007-11, Total population

Infectious disease outcome	No. studies[a]	Age group	Meta-analysis summary effect (95% C.I.)	Prevalence household crowding in this age group (%)[b]	Number of hospital admissions per year[c]	Number of annual admissions attributable to household crowding (95% C.I.)[d]	Hospital admission rate (per 100,000 persons of this age per year)[c]	Hospital admission rate attributable to crowding (95% C.I.)[d]
Enteric								
Gastroenteritis	4	0-5yo	OR 1.13 (1.01,1.26)	17	2371	**51 (4-100)**	713	**15 (1-30)**
Hepatitis A	7	0+yo	OR 1.53 (1.23,1.90)	10	11	**0.6 (0.3-0.9)**	0.27	**0.01 (0.01-0.02)**
Helicobacter pylori	28	0+yo	OR 1.82 (1.55,2.14)	10	1511	**119 (82-159)**	38	**2.9 (2.0-3.9)**
Respiratory tract								
Bronchiolitis from respiratory syncytial virus	4	0-3yo	OR 2.24 (1.14,4.38)	17	3848	**667 (89-1,399)**	1749	**303 (40-636)**
Haemophilus influenzae	6	0-6yo	OR 1.74 (1.27,2.37)	17	10	**1.1 (0.4-1.8)**	2.5	**0.3 (0.1-0.5)**
Pneumonia / lower respiratory tract infection	4	0-5yo	OR 1.69 (1.34,2.13)	17	6692	**699 (364-1,073)**	2013	**210 (109-323)**
	6	0-3yo	RR 1.36 (1.09,1.69)	17	6315	**362 (95-659)**	2870	**165 (43-300)**
Upper respiratory tract infection	3	0-18yo	OR 1.39 (0.69,2.79)	17	2919	**177 (-158-668)**	264	**16 (-14-60)**
	3	0-2yo	RR 1.63 (0.88,3.02)	17	1752	**169 (-36-446)**	1062	**102 (-22-270)**
Meningococcal disease	7	0-16yo	OR 2.13 (1.38,3.29)	17	66	**10 (4-18)**	6.7	**1.1 (0.4-1.8)**
Tuberculosis	17	15+yo	OR 3.78 (1.75,8.13)	9	109	**21 (7-42)**	3.5	**0.7 (0.2-1.3)**

[a] Number of studies contributing to summary estimate

[b] The prevalence of household crowding (one or more bedrooms in deficit) is taken from the 2006 Census [136]

[c] Annual hospital admission numbers and rates are based on average overnight admissions from 2007-11 from the National Minimum Data Set, with the following ICD codes: Gastroenteritis (A00-A09, K529, K528, R11), Hepatitis A (B15), Sequelae of *H. pylori* infection (non-cardia gastric cancer [C161-C169], peptic ulcer [K25-K28], gastritis and duodenitis [K293-295]), Bronchiolitis (J21), Hib disease (J14, A413, A492), Pneumonia/LRTI (A481, A482, B59, J09-J18, J20- J22), Upper respiratory tract infection (J00-J06, J32, J340, J36, J37, J390, J392), Meningococcal disease (A39) and Tuberculosis (A15-A19, N740, N741, J65).

[d] The following formula is used to calculate the proportion of admissions attributable to crowding:

$$PAF = \frac{p(RR-1)}{p(RR-1)+1}$$

Table 26: Estimated burden of infectious disease in New Zealand attributable to household crowding, 2007-11, European/Other

Infectious disease outcome	No. studies[a]	Age group	Meta-analysis summary effect (95% C.I.)	Prevalence household crowding in this age group (%)[b]	Number of hospital admissions per year[c]	Number of annual admissions attributable to household crowding (95% C.I.)[d]	Hospital admission rate (per 100,000 persons of this age per year)[c]	Hospital admission rate attributable to crowding (95% C.I.)[d]
Enteric								
Gastroenteritis	4	0-5yo	OR 1.13 (1.01,1.26)	8	1528	**16 (1-32)**	639	**7 (1-13)**
Hepatitis A	7	0+yo	OR 1.53 (1.23,1.90)	5	7	**0.17 (0.01-0.28)**	0.22	**0.01 (0.00-0.01)**
Helicobacter pylori	28	0+yo	OR 1.82 (1.55,2.14)	5	999	**37 (25-50)**	33	**1.2 (0.8-1.7)**
Respiratory tract								
Bronchiolitis from respiratory syncytial virus	4	0-3yo	OR 2.24 (1.14,4.38)	8	1442	**132 (16-310)**	908	**83 (10-195)**
Haemophilus influenzae	6	0-6yo	OR 1.74 (1.27,2.37)	8	4	**0.25 (0.1-0.4)**	1.6	**0.1 (0.0-0.2)**
Pneumonia / lower respiratory tract infection	4	0-5yo	OR 1.69 (1.34,2.13)	8	2772	**147 (74-232)**	1158	**61 (31-97)**
	6	0-3yo	RR 1.36 (1.09,1.69)	8	2567	**73 (19-136)**	1617	**46 (12-86)**
Upper respiratory tract infection	3	0-18yo	OR 1.39 (0.69,2.79)	10	1865	**71 (-60-286)**	237	**9 (-8-36)**
	3	0-2yo	RR 1.63 (0.88,3.02)	8	1065	**52 (-10-150)**	895	**43 (-9-126)**
Meningococcal disease	7	0-16yo	OR 2.13 (1.38,3.29)	8	24	**2 (1-4)**	3.4	**0.3 (0.1-0.5)**
Tuberculosis	17	15+yo	OR 3.78 (1.75,8.13)	4	30	**3 (1-6)**	1.3	**0.1 (0.0-036)**

[a] Number of studies contributing to summary estimate

[b] The prevalence of household crowding (one or more bedrooms in deficit) is taken from the 2006 Census [136]

[c] Annual hospital admission numbers and rates are based on average overnight admissions from 2007-11 from the National Minimum Data Set, with the following ICD codes: Gastroenteritis (A00-A09, K529, K528, R11), Hepatitis A (B15), Sequelae of *H. pylori* infection (non-cardia gastric cancer [C161-C169], peptic ulcer [K25-K28], gastritis and duodenitis [K293-295]), Bronchiolitis (J21), Hib disease (J14, A413, A492), Pneumonia/LRTI (A481, A482, B59, J09-J18, J20- J22), Upper respiratory tract infection (J00-J06, J32, J340, J36, J37, J390, J392), Meningococcal disease (A39) and Tuberculosis (A15-A19, N740, N741, J65).

[d] The following formula is used to calculate the proportion of admissions attributable to crowding:

$$PAF = \frac{p(RR-1)}{p(RR-1)+1}$$

Table 27: Estimated burden of infectious disease in New Zealand attributable to household crowding, 2007-11, for Māori

Infectious disease outcome	No. studies[a]	Age group	Meta-analysis summary effect (95% C.I.)	Prevalence household crowding in this age group (%)[b]	Number of hospital admissions per year[c]	Number of annual admissions attributable to household crowding (95% C.I.)[d]	Hospital admission rate (per 100,000 persons of this age per year)[c]	Hospital admission rate attributable to crowding (95% C.I.)[d]
Enteric								
Gastroenteritis	4	0-5yo	OR 1.13 (1.01,1.26)	27	595	**20 (2-39)**	746	**25 (2-49)**
Hepatitis A	7	0+yo	OR 1.53 (1.23,1.90)	22	1	**0.11 (0.05-0.17)**	0.2	**0.02 (0.01-0.03)**
Helicobacter pylori	28	0+yo	OR 1.82 (1.55,2.14)	22	284	**44 (31-57)**	50	**8(5-10)**
Respiratory tract								
Bronchiolitis from respiratory syncytial virus	4	0-3yo	OR 2.24 (1.14,4.38)	27	1871	**468 (68-891)**	3522	**881 (128-1,677)**
Haemophilus influenzae	6	0-6yo	OR 1.74 (1.27,2.37)	27	3.8	**0.6 (0.3-1.0)**	4.1	**0.7 (0.3-1.1)**
Pneumonia / lower respiratory tract infection	4	0-5yo	OR 1.69 (1.34,2.13)	27	2861	**448 (240-667)**	3586	**561 (301-836)**
	6	0-3yo	RR 1.36 (1.09,1.69)	27	2749	**243 (65-430)**	5173	**457 (122-810)**
Upper respiratory tract infection	3	0-18yo	OR 1.39 (0.69,2.79)	27	905	**86 (-83-296)**	367	**35 (-34-120)**
	3	0-2yo	RR 1.63 (0.88,3.02)	27	587	**85 (-20-207)**	1473	**214 (-49-519)**
Meningococcal disease	7	0-16yo	OR 2.13 (1.38,3.29)	27	33	**8 (3-13)**	14.7	**3.4 (1.4-5.6)**
Tuberculosis	17	15+yo	OR 3.78 (1.75,8.13)	19	25	**9 (3-14)**	6.7	**2.4 (0.9-3.9)**

[a] Number of studies contributing to summary estimate

[b] The prevalence of household crowding (one or more bedrooms in deficit) is taken from the 2006 Census [136]

[c] Annual hospital admission numbers and rates are based on average overnight admissions from 2007-11 from the National Minimum Data Set, with the following ICD codes: Gastroenteritis (A00-A09, K529, K528, R11), Hepatitis A (B15), Sequelae of *H. pylori* infection (non-cardia gastric cancer [C161-C169], peptic ulcer [K25-K28], gastritis and duodenitis [K293-295]), Bronchiolitis (J21), Hib disease (J14, A413, A492), Pneumonia/LRTI (A481, A482, B59, J09-J18, J20- J22), Upper respiratory tract infection (J00-J06, J32, J340, J36, J37, J390, J392), Meningococcal disease (A39) and Tuberculosis (A15-A19, N740, N741, J65).

[d] The following formula is used to calculate the proportion of admissions attributable to crowding:

$$PAF = \frac{p(RR-1)}{p(RR-1)+1}$$

Table 28: Estimated burden of infectious disease in New Zealand attributable to household crowding, 2007-11, Pacific peoples

Infectious disease outcome	No. studies[a]	Age group	Meta-analysis summary effect (95% C.I.)	Prevalence household crowding in this age group (%)[b]	Number of hospital admissions per year[c]	Number of annual admissions attributable to household crowding (95% C.I.)[d]	Hospital admission rate (per 100,000 persons of this age per year)[c]	Hospital admission rate attributable to crowding (95% C.I.)[d]
Enteric								
Gastroenteritis	4	0-5yo	OR 1.13 (1.01,1.26)	44	360	**19 (2-37)**	866	**47 (4-89)**
Hepatitis A	7	0+yo	OR 1.53 (1.23,1.90)	41	1.4	**0.25 (0.12-0.38)**	0.53	**0.09 (0.05-0.14)**
Helicobacter pylori	28	0+yo	OR 1.82 (1.55,2.14)	41	169	**42 (31-53)**	63	**16 (12-20)**
Respiratory tract								
Bronchiolitis from respiratory syncytial virus	4	0-3yo	OR 2.24 (1.14,4.38)	44	1072	**379 (62-641)**	3846	**1358 (223-2,300)**
Haemophilus influenzae	6	0-6yo	OR 1.74 (1.27,2.37)	44	1.6	**0.4 (0.20.6)**	3,3	**0.8 (0.4-1.2)**
Pneumonia / lower respiratory tract infection	4	0-5yo	OR 1.69 (1.34,2.13)	44	1840	**429 (239-611)**	4427	**1,031 (576-1,470)**
	6	0-3yo	RR 1.36 (1.09,1.69)	44	1770	**242 (67-412)**	6349	**868 (242-1,479)**
Upper respiratory tract infection	3	0-18yo	OR 1.39 (0.69,2.79)	45	402	**60 (-64-178)**	328	**49 (-53-146)**
	3	0-2yo	RR 1.63 (0.88,3.02)	44	269	**58 (-15-126)**	1286	**279 (-72-605)**
Meningococcal disease	7	0-16yo	OR 2.13 (1.38,3.29)	45	17	**6 (2-8)**	15.1	**5.1 (2.2-7.6)**
Tuberculosis	17	15+yo	OR 3.78 (1.75,8.13)	39	14	**7 (3-10)**	8.3	**4.3 (1.9-6.1)**

[a] Number of studies contributing to summary estimate

[b] The prevalence of household crowding (one or more bedrooms in deficit) is taken from the 2006 Census [136]

[c] Annual hospital admission numbers and rates are based on average overnight admissions from 2007-11 from the National Minimum Data Set, with the following ICD codes: Gastroenteritis (A00-A09, K529, K528, R11), Hepatitis A (B15), Sequelae of *H. pylori* infection (non-cardia gastric cancer [C161-C169], peptic ulcer [K25-K28], gastritis and duodenitis [K293-295]), Bronchiolitis (J21), Hib disease (J14, A413, A492), Pneumonia/LRTI (A481, A482, B59, J09-J18, J20- J22), Upper respiratory tract infection (J00-J06, J32, J340, J36, J37, J390, J392), Meningococcal disease (A39) and Tuberculosis (A15-A19, N740, N741, J65).

[d] The following formula is used to calculate the proportion of admissions attributable to crowding:

$$PAF = \frac{p(RR-1)}{p(RR-1)+1}$$

Table 29: Estimated burden of infectious disease in New Zealand attributable to household crowding, 2007-11, Asian peoples

Infectious disease outcome	No. studies[a]	Age group	Meta-analysis summary effect (95% C.I.)	Prevalence household crowding in this age group (%)[b]	Number of hospital admissions per year[c]	Number of annual admissions attributable to household crowding (95% C.I.)[d]	Hospital admission rate (per 100,000 persons of this age per year)[c]	Hospital admission rate attributable to crowding (95% C.I.)[d]
Enteric								
Gastroenteritis	4	0-5yo	OR 1.13 (1.01,1.26)	24	208	**6 (0-12)**	718	**22 (2-42)**
Hepatitis A	7	0+yo	OR 1.53 (1.23,1.90)	41	2	**0.2 (0.1-0.4)**	0.7	**0.1 (0.0-0.1)**
Helicobacter pylori	28	0+yo	OR 1.82 (1.55,2.14)	41	96	**13 (9-17)**	27	**4 (3-5)**
Respiratory tract								
Bronchiolitis from respiratory syncytial virus	4	0-3yo	OR 2.24 (1.14,4.38)	24	134	**31 (4-60)**	703	**161 (23-314)**
Haemophilus influenzae	6	0-6yo	OR 1.74 (1.27,2.37)	24	0.4	**0.1 (0.0-0.1)**	1.2	**0.2 (0.1-1.3)**
Pneumonia / lower respiratory tract infection	4	0-5yo	OR 1.69 (1.34,2.13)	24	337	**48 (25 -72)**	1166	**165 (88- 248)**
	6	0-3yo	RR 1.36 (1.09,1.69)	24	294	**23 (6-42)**	1539	**122 (32-218)**
Upper respiratory tract infection	3	0-18yo	OR 1.39 (0.69,2.79)	22	166	**13 (-12-47)**	162	**13 (-12-46)**
	3	0-2yo	RR 1.63 (0.88,3.02)	24	111	**14 (-3-36)**	772	**101 (-23-251)**
Meningococcal disease	7	0-16yo	OR 2.13 (1.38,3.29)	22	1.2	**0.2 (0.1-0.4)**	1.3	**0.3 (0.1-0.4)**
Tuberculosis	17	15+yo	OR 3.78 (1.75,8.13)	19	45	**16 (6-26)**	16	**6 (2-9)**

[a] Number of studies contributing to summary estimate

[b] The prevalence of household crowding (one or more bedrooms in deficit) is taken from the 2006 Census [136]

[c] Annual hospital admission numbers and rates are based on average overnight admissions from 2007-11 from the National Minimum Data Set, with the following ICD codes: Gastroenteritis (A00-A09, K529, K528, R11), Hepatitis A (B15), Sequelae of *H. pylori* infection (non-cardia gastric cancer [C161-C169], peptic ulcer [K25-K28], gastritis and duodenitis [K293-295]), Bronchiolitis (J21), Hib disease (J14, A413, A492), Pneumonia/LRTI (A481, A482, B59, J09-J18, J20- J22), Upper respiratory tract infection (J00-J06, J32, J340, J36, J37, J390, J392), Meningococcal disease (A39) and Tuberculosis (A15-A19, N740, N741, J65).

[d] The following formula is used to calculate the proportion of admissions attributable to crowding:

$$PAF = \frac{p(RR-1)}{p(RR-1)+1}$$

5. Discussion

In this discussion we summarise and discuss the key findings from this review. We also assess the strengths and weaknesses of this analysis and consider the implications of our findings for policy and further research.

5.1. Key findings

A large body of evidence from non-randomised observational studies was identified demonstrating an association between household crowding density and CCIDs. No randomised trials were identified and only one study investigated the impact of a crowding reduction intervention.

More than half of the studies in the narrative synthesis (189/345, 55%) found a statistically significant positive association between greater household crowding and CCID risk. Fewer than half of the studies (151, 44%) found no statistical evidence of an association and a very small minority (5, 1%) found a significant negative association (Table 5). The proportion of studies with evidence of an association was relatively similar across respiratory (51%), enteric (59%) and skin/eye infections (59%).

Of the studies included in the narrative synthesis, 116 met additional criteria for inclusion in a meta-analysis, that is they included a quantitative measure of the effect of crowding exposure (an OR or RR) and they included adjustment for age and SES. Within this group of higher quality studies, meta-analysis of combined outcomes was possible for 82 studies across ten different CCIDs (Table 6). Nine out of ten of these combined analyses demonstrated a statistically significant association between greater household crowding and infectious disease risk. For the one exception, upper respiratory tract infections, there was a positive association with household crowding, but this association was not statistically significant (OR 1.39, CI 0.69-2.79 and RR 1.63, CI 0.88-3.02). These associations were independent of age and socioeconomic status. Increased odds of infection for persons experiencing the greatest vs. least household crowding ranged from 1.13 times increased odds for gastroenteritis to 3.78 times for tuberculosis.

The most robust combined measures were for gastroenteritis, pneumonia/lower respiratory tract infection, *Hib* disease and respiratory syncytial virus (RSV) bronchiolitis. Associations between household crowding and risk of hepatitis A, *H. pylori* infection, meningococcal disease, tuberculosis and trachoma were less robust due to greater unexplained heterogeneity (variation in individual study results).

Over half of the meta-analyses (6/10) focussed on the impact of household crowding on children, with the vast majority of participants less than six years old. CCIDs with the most consistent results are some of the most frequent and increasing reasons for hospital admission, particularly among children.[1]

For five of these outcomes (gastroenteritis, pneumonia, bronchiolitis, *Hib* disease, and tuberculosis) there were additional studies that reported largely unique outcomes so could not be included in the combined analyses. About half (8/15) of these additional studies found significant positive associations between the disease in question and household crowding. These diseases were: toxoplasma gondii, typhoid fever, wheeze

associated with RSV, *Hib* carriage, tuberculin positivity (2 studies), and tuberculosis meningitis. Most of the remainder (5/14) found no significant positive associations between the disease in questions and household crowding: bacillary dysentery, diarrhoeal deaths, mortality from respiratory infection, symptoms of tuberculosis, and self-reported tuberculosis. One study found a weak protective effect (carriage of multiple drug resistant *E. coli*) associated with household crowding.

This review identified a further 21 eligible studies covering 16 additional specific infectious diseases. The outcomes were too heterogeneous to allow for combined estimates. A majority (13/21) found significant positive associations between the disease in questions and household crowding. These diseases were: giardia, intestinal parasites (3 studies), influenza-like illness (2 studies), measles, varicella-zoster infection, invasive GAS infection, pediculosis, Epstein–Barr virus infection, infectious illness warranting hospitalisation, and communicable disease symptoms. Most of the remainder (7/21) found no significant positive associations between the disease in questions and household crowding: otitis media (2 studies), rheumatic fever incidence, rheumatic heart disease (RHD) prevalence, RHD mortality, skin infections and Human Herpesvirus 8 infection. One study found a protective effect for chronic otitis media associated with household crowding.

The evidence base of high-quality research studies was relatively large for some important syndromes, such as gastroenteritis and pneumonia, and for some specific infectious diseases, such as *H. pylori* infection, tuberculosis, *Hib* disease, meningococcal disease and hepatitis A. For other important syndromes and diseases the research base was very limited, notably for skin infections and rheumatic fever. For these later diseases, there were insufficient high quality studies to produce combined estimates of the effect of exposure to household crowding so no conclusions can be drawn about the impact of this risk factor.

We used a burden of disease analysis to estimate the contribution of exposure to household crowding to the incidence of serious IDs in NZ. This approach used the effect measures obtained from the meta-analyses combined with the estimated prevalence of exposure to household crowding in NZ to estimate the population attributable fraction (PAF) of IDs from household crowding. This estimate was then applied to hospitalisation incidence data for nine categories of IDs to estimate hospitalisations attributed to household crowding. The total was estimated to be 1,343 (CI 182-2843) per year. This total is 9.8% of the 13,680 hospital admissions a year from these diseases (which represent about one fifth of the total 75,706 annual ID hospitalisations in NZ over the 2004-08 period[1]).

There are very large ethnic inequalities with this disease burden. For European/Others exposure to household crowding is estimated to cause 331 (CI 20-799) admissions a year, or 4.6% of IDs (in the nine groups examined). For Asian peoples exposure to household crowding is estimated to cause 108 (CI 23-206) admissions a year, or 12.7% of IDs. For Māori the contribution from exposure to household crowding is higher, with an estimated 790 (CI 106-1540) hospitalisations a year or 16.8% of ID admissions, and for Pacific peoples the estimated contribution is 692 (CI 136-1184) admissions a year, or 24.7% of ID admissions.

The contribution of exposure to household crowding is particularly large for some diseases. For example, meningococcal disease predominantly occurs in children (0-16 years) and the meta-analysis shows that risk is strongly associated with exposure to household crowding. For Pacific children (where 45% are exposed to household

crowding) an estimated 34% of disease burden and in Māori children (where 28% are exposed to household crowding) an estimated 23% of disease burden can be attributed to this exposure. By comparison, the estimate is only 9% for European/Other children (where only 8% are exposed to household crowding).

5.2. Strengths and limitations

The strength of this systematic review is the ability to simultaneously explore the impact of household crowding density across a breadth of CCID outcomes. We were able to pivot our search strategy on household crowding density and investigate the expanse of potential infectious disease outcomes. In this way, it was immediately obvious which outcomes have been most investigated (such as *H. pylori*, meningococcal disease) and which outcomes lack a large body of quality research investigating the impact of household crowding (such as influenza, rheumatic fever, and skin infections).

Inclusion of ten different infectious outcomes (diseases and syndromes) in the meta-analysis enables us to investigate the consistency of results across different CCIDs, study designs, settings and differences in quality. In this way we can see which populations, or indeed age groups, have been most investigated and for which there is the most evidence of an association with crowding. The consistency of meta-analysis results across a variety of study designs and a wide variety of settings supports the importance of household crowding in the aetiology of CCID.

5.2.1. Biological plausibility

The contribution of household crowding to increased rates of CCIDs has a high degree of biological plausibility. The potential for an infectious disease to spread from person to person in a population is summarised by the reproduction number. The reproduction number (R_0) is driven by the risk of transmission per contact (β), the number of such contacts that an average person in the population would normally have per unit time (κ), and the duration of infectivity of an infected person (D). The formula for R_0 then becomes: $R_{0=} \beta\kappa D$.[137] Household crowding would be expected to increase the number of contacts that household members have over a period of time and potentially the risk of transmission per contact and therefore increase R_0 for infection within that population.

Another reason why the household setting is so important for infectious disease transmission is that we spend the majority of our time in the home environment. Time-activity-microenvironment data for NZ shows we spend about 70% of our lives indoors at home, with even higher proportions for children and the elderly who are more vulnerable to infection.[138]

5.2.2. Consistency with other research

Our results are consistent with the small number of other published literature reviews which highlight the association between crowding and various IDs. This study has been able to go a step further and carry out meta-analysis on all the available literature to produce combined effect estimates.

Systematic reviews particularly relevant to individual meta-analyses are discussed in more detail with the presentation of individual meta-analysis results.[79,114,115]

5.2.3. Lack of intervention studies

Of note, there was a complete absence of randomised controlled trials identified in the systematic review and almost a complete absence of intervention studies. For example, a randomised controlled trial might evaluate the impact of crowding reduction using a staggered intervention approach (as successfully used in NZ to measure the impact of home insulation and home heating[139]).

There was identified, however, one non-randomised study investigating the impact of an intervention using a cohort study design. This recently published study in an Australian aboriginal community evaluated an intervention that aimed to reduce infection disease burden by reducing household crowding.[24] However, the intervention had a limited impact on reducing crowding.

Several systematic reviews of housing interventions have been reported.[140,141] The most recent of these published in 2009 identified a single study that mentioned crowding reduction.[141] This study was a programme to improve housing conditions and reduce overcrowding. It was an uncontrolled US study that aimed at individual owners with families on low incomes. The report was based on a conference abstract (not reviewed).[141]

Our systematic review results are consistent with the findings from evaluation of the HNZC Healthy Housing Programme which show a reduction in acute hospitalisation for younger participants.[130, 132] As has been noted, the Healthy Housing Programme was a mixed intervention with crowding reduction just a part.

5.2.4. Review level limitations

Despite the efforts of the authors, the broad focus of this review has possibly sacrificed a level of depth. Potential limitations of the review are incomplete retrieval of study results, residual confounding and reporting bias.

The review focussed on published papers. This restriction may have limited the identification of relevant articles with non-significant or negative associations. Despite efforts to retrieve all study records, 5/838 full text articles were not obtained for full text screening. Furthermore, articles with insignificant crowding results may not refer to crowding in the abstract or key words, and thus remain undetected by our search. The overall extent or direction to which incomplete retrieval has influenced our results is unclear. However, results from the narrative synthesis are supportive of meta-analysis findings.

Requiring effect measures in the meta-analysis to be adjusted for confounding is important to control confounding bias and is recommended in meta-analyses of observational studies.[21] We attempted to limit confounding by excluding studies unadjusted for age and socioeconomic status from the meta-analysis. Household crowding has a complex link with socioeconomic status and it is possible that the association of CCID with crowding is exaggerated by residual confounding from socioeconomic status.

However, requiring adjusted estimates in this review may also have contributed to selective reporting bias. For example, stepwise regression within studies meant that adjusted estimates were more likely to be available when a crowding exposure contributed significantly to a multivariate model (usually in the positive direction) than when it did not contribute and was discarded from the model. These studies did not report adjusted estimates that could contribute to the meta-analysis although they did contribute to the narrative synthesis.

5.2.5. Burden of disease limitations

The BoD estimates presented here should be taken as broad approximations only. Each of the three components of the individual disease estimations has a degree of measurement error. The limitations of the effect estimations have been described above. The measurement of exposure to household crowding is based on self-reported Census data so is affected by errors in reporting of household size (bedrooms) and occupants (numbers, ages, relationship status). Accurate hospitalisation data depends on the extent of diagnosis and accuracy of disease coding.

The formula used to estimate the BoD makes a number of simplifying assumptions. In particular it dichotomises the population into crowded and not crowded, and study findings have similarly been used to produce effect estimates that compare crowded and not crowded. This simplifying approach was necessary but fails to consider that exposure to household crowding has many gradations. In addition, few of the studies used to produce these pooled estimates will have used similar measures of household crowding to those used to distinguish crowded households in NZ. For example, the American Crowding Index, used by some of the studies included in this systematic review, classified 6.2% of the NZ population as exposed to household crowding (more than one person per room) in the 2006 Census. By contrast, the Canadian National Occupancy Standard used in this BoD analysis identified 10.4% of the population as exposed to household crowding (a bedroom deficit of one or more).[10]

5.3. Implications

This section considers the policy relevance of the findings of this meta-analysis and burden of disease estimation, including potential policy interventions to reduce exposure to household crowding and further research needs.

5.3.1. Policy response to reduce household crowding

A full review of housing policy options to reduce exposure to household crowding is beyond the scope of this report. However, it is important to briefly consider potential policy responses to this threat to public health.

Meta-analysis findings provide evidence for an association between exposure to household crowding and the risk of several important IDs, particularly respiratory and enteric infections. Findings from this report support the need to identify policy and programmes aimed at reducing household crowding for Māori and Pacific households in NZ, particularly those with children. Children under five years of age have the highest rates of hospitalisation of any paediatric age group, and rates are more than

double for Māori (SRR 2.05, CI 2.04–2.07) and Pacific (SRR 2.11, CI 2.09–2.13) compared with European/Other.[1]

A major driver of household crowding is housing affordability. The ratio of housing costs to income is often used as a way of measuring affordability. The Ministry of Social Development (MSD) defines housing affordability based on "the proportion of households and the proportion of people within households spending >30% of their income on housing".[142] From 1988 to 1997 the proportion of households spending >30% of their household income on housing increased from 11% to 25%. This proportion levelling off at 24% in 1998 and 2001, declined slightly to 21% in 2004, then increasing to 26% in 2007 and 27% in 2009.[19] Low housing affordability is concentrated in poorer households, those containing children, and those containing Māori and Pacific families.[19]

Changes in government policy influence housing affordability. Successive governments have tended to develop unique responses to affordability problems and housing need. In the early 1980s, the National Government provided income-related rents for state tenants and income assistance for low-income beneficiaries in the private rental sector. In the mid-1980s, Labour expanded income assistance in the private rental sector to low-income wage earners and the Housing Corporation targeted state housing to those facing serious housing need. In the early 1990s, National introduced market rents for state housing and state tenants could apply for an Accommodation Supplement to assist them with their rent. There was also the sale of some social housing (11,000 state houses). In 1999, Labour reintroduced income-related rents and maintained an Accommodation Supplement for the private rental sector and homeowners.[143]

The size of the state housing stock may have contributed to housing affordability. This stock has varied over time, with increasing sales in the early-1980s and early-1990s.[143] In the early 1980s, the stock declined from 59,500 to 56,100 and subsequently increased to 63,550 by 1991. Over the first half of the 1990s, it reduced again to 52,500 and then increased to 63,070 in the early 2000s. The patterns of sale and constructions has shaped the spatial planning, architecture and demography of state housing.[144] Social housing policies are likely to continue to influence housing affordability going into the future.

A detailed study of the relationship between government housing policy and household crowding in the 1990s[145] concluded that household crowding in that decade was strongly influenced by housing affordability and state housing rents.[145] House prices almost doubled between 2001 and 2007 and it is predicted that household crowding will rise in response to increased rents as demand for private rental housing increases.[146]

Some of the drivers behind housing need are outside the housing sector. They include: demographic changes (patterns of household formation, migration, and greater ethnic diversity); changes in the levels and distribution of employment and unemployment; economic growth and recession; and levels of income inequality.

One additional factor that may contribute specifically to household crowding for Māori and Pacific peoples is racial discrimination in the private rental market. Analysis of the NZ Health Survey has shown that Māori are thirteen times more likely than European/Other to experience self-reported racial discrimination when buying or

renting housing.[147] Observational studies of discrimination in the private rental market have also confirmed racial discrimination by private landlords.[148]

Specific government interventions may reduce levels of household crowding. The HNZC Healthy Housing Programme included this objective as one of its specific goals. Evaluations of the programme show that it has been highly successful at reducing hospitalisations in children, with suggestive evidence of a reduction in CCIDs.[132,149]

Our meta-analysis results highlight the importance of considering interventions to improve health and particularly the health of children living in poverty. A summary of housing policy options was recently published by the Expert Advisory Group on Solutions to Child Poverty.[12]

In summary, interventions to reduce household crowding in NZ might include the following broad strategies:

- Policies and programmes to increase the number of social and affordable houses and their proportion of the total housing stock.
- Policies to refocus and redesign demand side accommodation supplements and income related rent subsidies to ensure there is additional support for low income families and in particular larger families.
- Policies to improve accessibility to affordable housing for those most in need, including Māori and Pacific households. This approach should consider measures to reduce racial discrimination when buying or renting housing.
- Interventions to reduce household crowding, and improve the quality of existing social housing managed by HNZC. Evaluations of the HNZC Healthy Housing Programme, which includes a component aimed at reducing levels of household crowding, showed that it was highly effective at reducing hospitalisation rates in children.

5.3.2. Further research

This analysis has identified several important gaps in research:

- The meta-analysis itself could be further refined and extended. For example, the quality of individual studies that have been included could be further assessed. Currently, some quality assessment is included in the study selection process, notably whether they adjust for key confounders (age, socioeconomic status). Further quality assessment would include study design, ascertainment of outcome, selection of controls, selection of the study population and adjustment for additional confounding. There were studies (n=89) that were eligible for inclusion and which adjusted for key confounders, but which did not report an OR/RR (Figure 2). Authors of these studies could be approached to see if they can provide this analysis. These refinements would change the magnitude of the meta-analysis findings (and the burden of disease estimates) but are very unlikely to alter the overall conclusions of this review.
- Further meta-analyses could explore other dimensions of household crowding excluded from this current review, notably bed sharing. It would also be useful to consider the impact on infectious diseases of crowding in other settings, notably

prisons. New Zealand has a very high rate of imprisonment and there have been publicised outbreaks of infectious diseases in prison. This is an important area that needs further research.

- Intervention studies are required to determine if the findings summarised here from observational studies truly represent causality between household crowding and increased risk of CCID. Randomised controlled trials such as those with staggered interventions would provide the most robust form of evidence. A crowding reduction programme could be randomly allocated to one group and the control group would receive the intervention at a later time. New Zealand is well positioned to conduct such research.
- Meta-analyses highlight the paucity of quality studies investigating the impact of household crowding on some important IDs such as rheumatic fever, influenza and skin infection. Given New Zealand's relatively high rates of these diseases we are well placed to carry out such studies.
- There is no apparent international consensus on household crowding or how to measure it. The value of well-designed observational studies could be improved by standardisation in the measurement of exposure to household crowding, rigorous adjustment for confounding, and longitudinal study designs that incorporate changes in crowding exposures and a wide range of CCID outcomes.
- Findings in this report reinforce the additional research information needs raised in our previous report on the distribution of household crowding in NZ.[10] We need to better understand what household crowding means in practice, for example how crowding is perceived, how rooms are used within households, and how people adapt to higher levels of household crowding. It would be valuable to relate findings on the distribution of household crowding and how this has changed over time to the incidence and distribution of IDs in these same populations. It would also be important to assess the impact of household crowding on well-being more generally, and on the health and social functioning of individuals and families. Previous studies indicate negative effects on education and psychological distress.[150,151] It would also be useful to fully evaluate interventions in NZ that have sought to lower levels of household crowding.

6. Conclusion

The findings of this review support the conclusion that household crowding is an important risk factor for transmission of most major categories of close-contact infectious diseases. Restricting our analysis to the highest quality studies (n=116), and those where there were multiple published works looking at similar outcomes, allowed us to produce combined estimates of the effect of household crowding on 10 infectious diseases outcomes. In nine out of 10 of these outcomes there was a statistically significant positive relationship between household crowding and the risk of disease (and in the remaining one the effect was positive, but not statistically significant).

Meta-analyses reliant on observational studies are considered low quality evidence for causality and may be somewhat overstated by reporting bias and incomplete retrieval. However, narrative review results of a much larger group of studies support the meta-analysis results.

The evidence was most robust (with low to moderate unexplained heterogeneity) for gastroenteritis, hepatitis A, *H. pylori* infection, pneumonia/LRTI, *Hib* disease, RSV bronchiolitis, meningococcal disease, and tuberculosis. These IDs contribute to a significant number of hospitalisations and some deaths in NZ, so even small increases in risk from crowding are likely to represent a significant burden of disease. There were very few high quality studies of several important infectious diseases, notably skin infections and rheumatic fever, so it is not possible to make conclusions about the impact of household crowding on these diseases. These areas would benefit from further research.

Findings of this study are particularly relevant to child health. Several of the diseases covered have particularly high rates in children, notably bronchiolitis, pneumonia, gastroenteritis and meningococcal disease. New Zealand children and young people have higher levels of exposure to household crowding than older age groups. Rates of serious infectious diseases have increased over the last 20 years in NZ for children (as they have across all age groups).

The burden of disease analysis showed that about 10% of hospital admissions a year can be attributed to household crowding for the nine categories of infectious disease included in the analysis. It also showed how the large ethnic difference in exposure to household crowding are contributing to the markedly higher rates of serious infectious diseases seen in Māori and Pacific populations.

Findings from this systematic review support the need to identify policies, programmes and interventions to reduce household crowding, particularly for Māori and Pacific households in NZ and households with children. Evaluation of interventions which aim to reduce household crowding would provide a significant contribution to the research base in this area.

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