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# Selective citation in the literature on the hygiene hypothesis: a citation analysis on the association between infections and rhinitis

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## Conflict of Interest

All authors declare to have no conflict of interest.

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**Abstract**

**Objective:** Our objective was to assess the occurrence and determinants of selective citation in scientific publications on Strachan's original hygiene hypothesis. His hypothesis states that lack of exposure to infections in early childhood, increases the risk on rhinitis.

**Setting:** Web of Science Core Collection.

**Participants:** We identified 110 publications in this network, consisting of 5551 potential citations.

**Primary and secondary outcome measures:** The realisation of a potential citation, measured and analysed according to the pre-registered protocol.

**Results:** We found evidence for citation bias in this field: publications with supportive were cited more often than non-supportive publications (odd ratio adjusted for study design [adjOR]: 2.2, 95% confidence interval [CI]: 1.6 - 3.1), and the same was the case for publications with mixed findings (adjOR: 3.1, CI: 2.2 - 4.5). Other relevant determinants for citation were type of exposure, specificity, journal impact factor, authority and self-citation. Surprisingly, prospective cohort studies were cited less often than other empirical studies.

**Conclusions:** There is clear evidence for selective citation in this research field, and particularly for citation bias.

**Strengths and limitations of this study**

- this study assesses how evidence propagates regarding the hygiene hypothesis over time by analysing the likelihood of citation
- it investigates which article characteristics impact citation such as study outcome, journal impact factor, author gender and affiliation, and authority within the field
- we check whether positive studies are cited more often by other studies within the field, and in particular by reviews (which are supposed to give an unbiased overview of the literature)
- limitation: only articles related to the original hygiene hypothesis are included in this analysis

**Background**

The hygiene hypothesis postulates that a high degree of hygiene in early life will increase the risk of developing allergies later in life (1, 2). The underlying mechanism has been the topic of scientific debate. Over time, this debate led to several adaptations and extensions of the hygiene hypothesis, which, as such, provides a good example of how science progresses. Ideally, this progress should be based on all existing evidence, but this is not always the case (3). A citation analysis can help to reveal which part of the available evidence is taken into account, and which evidence is ignored. The current study does not concern the validity of the hygiene hypothesis per se, but rather the citation relations within the scientific literature on this hypothesis.

The hygiene hypothesis was originally proposed to explain the rising prevalence of allergies, with up to 20 to 40 % of the population in developed countries being affected (4). Modern, urbanized life in developed countries generally shows higher levels of hygiene than in previous times or in developing countries. Hygiene limits exposure to infections. Exposure to infections, especially early in life, helps to develop and adapt the immune system to the environment in which we happen to live, in such a way that it learns to discriminate between harmless and harmful intruders. According to the hygiene hypothesis, it is this lack of exposure to relatively harmless intruders early in life, that causes the immune system to malfunction later in life. Hence the rise in allergies.

One of the early mechanisms proposed for this malfunction reasons as follows (5, 6). Allergy-related inflammatory reactions are mediated by Type 2 T helper (Th2) cells of the immune system that is activated by the presence of an allergen. High levels of Th2 cells generally suppress Th1 levels and vice versa. Curiously, however, prevalence of Th1-induced inflammatory bowel disease and auto-immune disease has also increased in developed countries. This suggests that a different process must take place.

The hygiene hypothesis has been amended several times since its early days and gave rise to newer theories such as the '*old friends hypothesis*' (7, 8). This is an adaptation of the original hygiene hypothesis. It states that it is not hygiene per se that is causing the rise in allergy prevalence, but the lack of exposure to *some specific* infections, and also to the gut microbiome and to non-viable intruders from the natural environment, such as endotoxins. Humans have been exposed to these 'old friends' for many centuries and our immune system has co-evolved in their presence. As a result, our immune system has become dependent on the presence of these old friends in order to develop and function properly. Similarly, this adapted hygiene hypothesis states that lack of exposure to these old friends may give rise not only to allergies, but to auto-immune diseases as well.

The original hygiene hypothesis and its later adaptations have a lot in common, and much of the evidence that is supportive for one hypothesis is equally supportive for the others. However, this is not always the case. In our project, publications are classified as either supportive or unsupportive with regards to a hypothesis. For that reason it is important to precisely define the investigated hypothesis.

In our citation network, we focus on the hygiene hypothesis as it was originally stated by Strachan, and not on later modifications (1, 2). This allows us to investigate the development of this hypothesis from the start. Concretely, this means that we focus on the impact of infections and the number of siblings on the development of rhinitis, like in Strachan's original study (2). We included the effects of all viral and bacterial infections. However, we excluded exposure to helminth infections, because different versions of the hygiene hypothesis predict contradictory effects due to their impact on Th2 cells. Indirect proxies for infection that were not part of the original hypothesis, such as growing up on a farm or daycare attendence, were also excluded.

Our main research question is: *Which determinants influence the likelihood of being cited in the scientific literature on the original hygiene hypothesis?* To answer this question, we assessed the impact of a number of determinants that we had investigated earlier in another citation network (9). Of particular importance is the occurrence of citation bias: the phenomenon that supportive, hypothesis-confirming studies have a higher likelihood of being cited than non-supportive or critical studies (10).

## Method

Prior to performing the citation network analysis, we described our methods in a study protocol and stored it at an online repository (11). (Protocol deviations are described in the supplement, Text S1.) In brief, we applied a search strategy to the Web of Science Core Collection (WoSCC), identified relevant literature, downloaded these records with their reference lists, extracted data for each publication, built a dataset with potential citation paths and used specialised software to determine which citations had occurred. These steps will be explained in more detail below. Article selection and data extraction were performed independently by MJEU and BD. Disagreements were resolved in a consensus meeting.

For clarification: we use the words *cited* and *citing* to differentiate between the older publication that may have been cited by a more recent, citing publication. Thus, when we write about cited publications, citing publications, and citation paths, we actually mean *potentially* cited publications, *potentially* citing publications and *potential* citation paths, as these potential citations may or may not be realised.

**Search strategy**

First, we took Strachan's seminal article in which the hygiene hypothesis was launched as point of departure (2). Next, we identified all literature within WoSCC referring to this article. Finally, we limited the output to publications that mentioned hay fever in their title, keywords or abstract (*"hay fever" OR* "*hayfever" OR* "*hay-fever" OR "rhinitis" OR "rhino*"*). The search was performed by BD and updated until 16 August 2017. Only English language publications were included.

The search output was then limited to publications that investigated exposures related to the original hygiene hypothesis. This means that only publications investigating the effect of *number of siblings* and *infection history* were included. Helminths infections were excluded, as their impact is likely to be Th2 rather than Th1 mediated, and different versions of the hygiene hypothesis would make contradictory predictions regarding their impact on allergies. Both empirical and non-empirical publications were included.

**Data extraction**

A range of variables were extracted or derived from each included publication: *content-related publication characteristics* (i.e. type of exposure, publication type and study design, sample size, specificity, study outcome), *content-unrelated publication characteristics* (conclusiveness of the title, funding source, number of authors, number of affiliations, number of references), *journal characteristics* (publisher, journal impact factor), *author characteristics* gender, country, and affiliation of the corresponding author), and *citation characteristics* (within-network authority, self-citation). More details on these characteristics and how we scored them can be found in the supplement (Text S2). In principle, all characteristics were treated as determinant in the statistical analysis.

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**Statistical analysis**

The dataset consisted of all potential citation paths between cited and citing publications. A potential citation path means that the cited publication is published before submission of the citing publication. The underlying assumption is that publications can only refer to other publications up to the date of their submission, and that they can only be cited from their publication date onwards. All analyses were pre-registered in the study protocol unless mentioned otherwise.

**Impact of the cited publication characteristics.** Our dependent variable was citation, or, in other words, whether a potential citation path was realised or not. We used the built-in algorithm of CitNetExplorer to determine whether a citation had occurred (12). This algorithm makes use of reference lists that can be downloaded from the Web of Science Core Collection. The reference lists of all publications in the network were linked by the algorithm with the actual publications in the network. If possible, this linkage was done by DOI, the unique Digital Object Identifier assigned to most present-day publications; otherwise it was based on a combination of first author's surname, first author's first initial, publication year, volume number and first page number. The determinants of citation in our analyses were the characteristics of the cited publication as described above.

Since each publication could refer to multiple other publications, the potential citation paths were related. Therefore we used a multilevel approach in which the potential citations were nested under the citing publication. Specifically, we performed a univariate random-effects logistic regression for each determinant of citation. We repeated these analyses while adjusting for study design, as a proxy for study quality. Another proxy for study quality would be the study sample size. However, as reviews do not have a sample size, this adjusted analysis could only be performed on the sub-selection of cited empirical publications so we did not adjust for sample size in the main analysis.

The outcomes of the logistic regression analyses are reported as odds ratios. The odds ratio may overestimate the true relative risk in studies where the outcome is a common (13). In our network, citation is not a common outcome and consequently the overestimation of the true relative risk will be small.

In addition to the original analysis plan in the protocol, we also calculated the explained variance of the adjusted models, so that these models are easier to compare. For this purpose we calculated McFadden's $R^2$.

**Additional analyses** were performed on sub-selections of the network: a) only cited empirical publications were included (to investigate which empirical evidence is picked up by the rest of the field; explorative analysis); b) only cited empirical publications and citing synthesis publications were included (to investigate which empirical evidence is picked up particularly by reviews and editorials). These analyses were adjusted not only for study design but also for log-transformed sample size because all cited publications had a sample size in these sub-selections.

To check the robustness of our findings we also ran some sensitivity analyses in which the following publications or citation paths were excluded: c) the most cited publications (explorative analysis); d) citation paths with less than one year between publication date of the cited publication and submission date of the citing publication were excluded (to check if a lag time would make a difference as it takes some time before most publications are known and have an impact); e) citing publications that have less than ten potential citations.

**Concordance analysis.** Where applicable, we also calculated whether the cited and the citing publications had the same characteristics (*concordance*). This would for instance be the case if supportive publications would prefer to cite other supportive publications, and if non-supportive publications would prefer to cite other non-supportive publications. If citation would be based on the concordance of study outcome, it would be another measure of citation bias. To test if concordance on several characteristics has an impact on the likelihood of citation, univariate and adjusted (for study design) fixed-effects logistic regression analyses were applied.

**Software**

We used the built-in algorithm of CitNetExplorer 1.0.0 to extract the actual citations between publications (12). We used R 3.2.4 to create a dataset with all potential citation paths, based on the data extraction sheet and the actual citations, and also to calculate the within-network authority, self-citation score, and time to citation for each potential citation path. Finally, we used Stata 13.1 to analyse the results.

**Patient and public involvement**

No patients were involved in this study.

## Results

A total number of 110 publications were identified that fit our criteria, published between 1995 and 2017 (Figure 1, Text S3). Of these, 28 publications focused exclusively on the impact of household size on rhinitis, 48 on the impact of having had infections, and 34 on the impact of both types of exposure. This network of 110 publications comprised a total of 5551 potential citation paths, of which 7% was realised. Their main characteristics are depicted in Table 1 (for more details see Table S1). About two thirds of all publications in the network are empirical studies (39 cross-sectional, 4 case control, 29 cohort studies, and 1 intervention), one third are reviews (27 narrative reviews, 2 systematic reviews, and 8 editorials or leading articles). The study outcome for 35 of the publications was mixed or unclear. Of the remaining publications with a clear study outcome, about 50 % was supportive of the hygiene hypothesis (41 publications with an inverse association between siblings / infection and rhinitis), and about 50 % was non-supportive (34 publications with no association, or with a positive association). The number of citations ranged from 0 (45 publications) to 35, with a median of 1 citation per publication. A ranking of the most cited publications and authors can be found in Table S2.

**Impact of the cited publication characteristics.** The results of the regression analyses are presented in Table 2. Empirical publications were cited more often than non-empirical publications. Compared to empirical studies with a cross-sectional design, prospective cohort studies, narrative reviews and editorials had a lower likelihood of citation, while the two systematic reviews had a higher likelihood of citation. Other determinants that increased the likelihood of citation were specificity, journal impact factor, sample size and within-network authority. Sample size had a modest impact on citation. Publications on only one type of exposure were cited less often than publications on both types of exposure.

Supportive publications had a higher likelihood of being cited than non-supportive publications. This is in line with our hypothesis. However, publications with mixed results were cited even more often. This may be due to our scoring algorithm. After all, if a publication investigated both the number of siblings and the infection history, and it reported dissimilar outcomes for these two exposures, then this publication would have been scored as having mixed results. An explorative chi-square test confirmed that type of exposure and study outcome were related ($\chi^2(4) = 52$, $p < 0.0005$), with 71% of all publications on both types of exposure reporting mixed results, compared to 4% of the publications on only number of siblings and 21% of the publications on only infection history. As double exposure studies are also cited more often compared to the single exposure studies, type of exposure should be considered as a confound of study outcome. To correct for this, we performed an explorative random-effects logistic regression of citation on study outcome, adjusted for both study design and type of exposure. It showed that supportive publications had the highest chance of being cited (adjusted odds ratio [adjOR] 3.1, 95% confidence interval [CI] 2.2-4.3), compared to publications with mixed results (adjOR 2.4, CI 1.5-3.7) and with non-supportive results (reference category; model $R^2 = 0.12$).

Surprisingly, publications with a conclusive title were less likely to receive citations. The format of the title may be prescribed by the journal regulations. We ran some explorative analyses in which we additionally adjusted for the (log-transformed) journal impact factor or publisher on top of study design. The impact of title conclusiveness remained high when additionally adjusted for journal impact factor (adjOR 0.4, CI 0.2-0.6) or publisher (adjOR 0.3, CI 0.2-0.6).

The above results are related to the network as a whole. Of particular importance is how empirical, evidence-generating publications are cited by the rest of the network. We repeated the above analyses on a sub-set of the cited publications, namely the empirical publications; we tested which characteristics of empirical publications were related to their likelihood of being cited. The results (Table S3) are very similar to the analyses on the complete network that include the cited non-empirical publications.

Likewise, we tested how *empirical* publications are cited by *synthesis* publications (Table S4). Again, the direction and magnitudes of the effects were all very similar, except for study outcome. Adjusted for study design, (log-transformed) sample size and type of exposure, supportive empirical publications were much more likely to be cited (adjusted OR 7.3, CI 3.5-15.5) by reviews and editorials, whereas empirical publications with mixed results seemed less likely to be cited (adjusted OR 0.4, CI 0.2-0.9) compared to non-supportive empirical publications (reference category; model $R^2 = 0.12$). As a side note: these analyses are based on a smaller number of cited and citing publications and should be interpreted with caution.

The sensitivity analyses without the four most cited publications showed some dissimilar results (Table S5). The impact of study outcome decreased, the impact of male authors and of North-American authors disappeared, and the impact of case-control studies reversed. The other two sensitivity analyses (with a one year lag time immediately after publication; without citing publications with less than 10 potential citation paths) all showed similar results as the main analyses (Tables S6-S7).

**Concordance analysis.** In addition, we tested whether publications were more likely to be cited by publications with similar characteristics. The results are shown in Table 3. It shows that publications tend to be cited mostly by publications with the same type of exposure, with a similar study outcome, with a corresponding author from the same region, and with one or more authors in common ('self-citation').



## Discussion

Our research aim was to evaluate which determinants influence the likelihood of being cited in the scientific literature on the original hygiene hypothesis stated by David Strachan (2). We found that study outcome, type of exposure, study design, specificity, title conclusiveness, journal impact factor, and the authors' region, affiliation, authority and self-citation all have a substantial impact on the likelihood of citation.

With regard to study outcome, supportive publications are cited more than three times more often than non-supportive publications, while publications with mixed results are cited more than two times as often. Similarly, publications are more likely to refer to other publications with the same study outcome rather than to those that provide counter-evidence to their conclusion. This is a clear sign of citation bias.

The magnitude of citation bias even increases if we focus on how empirical publications, which generate new evidence, are cited by reviews and editorials, which summarise and pass on existing evidence. These reviews and editorials are up to 8 times more likely to cite supportive publications rather than to non-supportive ones. As reviews are generally assumed to give an unbiased summary of the existing evidence, and as such are held in high regard, this is a worrying finding.

In our analyses we consider study design as a proxy for study quality. We believe systematic reviews to be of higher quality than narrative reviews and editorials, and thus to receive more citations. In our network, this is indeed the case. Similarly, we believe that cohort studies outrank cross-sectional and case-control studies but to our surprise they are less likely to be cited. Prospective cohort studies, even though they provide the highest type of evidence in this network, receive the fewest citations of all empirical study designs. This may be due to the fact that these cohort studies tend to focus on multiple risk factors of which only one or two are relevant for the hygiene hypothesis. But the fact that multiple risk factors are investigated in these cohort studies does not imply that their findings on the impact of siblings or infections are of any lesser value or should be ignored.

Another surprising result is related to the title conclusiveness. Publications with titles that state a clear conclusion are cited much less often than publications with vague titles. This seems to be unrelated to the journal, publisher, impact factor, specificity, type of exposure and study outcome. As such, it remains an open question as to why this is the case, and whether this finding is specific for this network or a more general phenomenon.

This study has several limitations. First, it includes two overlapping subnetworks, as is shown by the high odds ratio in the concordance analysis of type of exposure. This makes it difficult to infer for which result a certain publication was cited. Related to this issue, the pre-registered operationalization of study outcome could not be applied because of the hybrid nature of the network, so we developed a scoring system that fits better. Finally, there are different versions of the hygiene hypothesis, and support for one version may not be supportive for another one. We dealt with this issue by limiting ourselves to Strachan's original hygiene hypothesis, and by excluding any determinants with conflicting predictions in different versions. Despite these limitations, sensitivity analyses show that the results seem robust against chance findings.

To conclude, there is evidence for selective citation in this network. Several characteristics of a publication can make it more likely to be cited such as the authority and the region of the author, the impact factor of the journal, the way in which the title was stated, and also study design and study outcome. The fact that positive publications are cited more often than negative ones, particularly if we look at how empirical publications are being picked up by the rest of the network, is a clear sign of citation bias. Finally, this study also shows that particularly narrative reviews may have a preference to refer to supportive evidence.

**Availability of data and material:**

The protocol and the data of this study are available in the dataverse repository, http://hdl.handle.net/10411/ZKGGOG, or by sending an email request to b.duyx@maastrichtuniversity.nl.

**Author Contributions:**

BD developed and performed the search strategy, wrote the R scripts for data transformation and calculation, conducted the analyses and wrote the manuscript. BD and MJEU performed the article selection and data extraction. MPZ and GMHS obtained funding. All authors were involved in the research design and data analysis plan, and read, commented on and approved the final manuscript.

**Transparency declaration**:

The guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained in the supplement.

**Copyright statement:**





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**Table 1. Main characteristics of all 110 publications in hygiene hypothesis network.**

| Characteristic | category | N publications | n potential citations | n realised citations (%) |
|---|---|---|---|---|
| Type of Exposure | only Number of Siblings | 28 | 1512 | 100 (7%) |
| | only Infection History | 48 | 1946 | 144 (7%) |
| | both Siblings & Infections | 34 | 2093 | 148 (7%) |
| Study Outcome Exposure - Rhinitis | supportive | 41 | 2322 | 198 (9%) |
| | mixed results | 35 | 1913 | 129 (7%) |
| | non-supportive | 34 | 1316 | 65 (5%) |
| Publication Type / Study Design | Empirical | 73 | 3517 | 337 (10%) |
| | cross-sectional | 39 | 1697 | 179 (11%) |
| | case-control | 4 | 249 | 36 (14%) |
| | cohort | 29 | 1535 | 121 (8%) |
| | -retrospective | 15 | 817 | 89 (11%) |
| | -prospective | 14 | 718 | 32 (4%) |
| | intervention | 1 | 36 | 1 (3%) |
| | Synthesis | 37 | 2034 | 55 (3%) |
| | narrative review | 27 | 1423 | 16 (1%) |
| | systematic review | 2 | 80 | 20 (25%) |
| | editorial, etc | 8 | 531 | 19 (4%) |
| Sample Size (cat; for empirical publications) | low (1 – 999) | 24 | 909 | 56 (6%) |
| | medium (1000 – 7999) | 25 | 1327 | 143 (11%) |
| | high (>= 8000) | 24 | 1281 | 138 (11%) |
| Journal Impact Factor (cat) | 0 - 2 | 28 | 1275 | 27 (2%) |
| | 2 - 4 | 41 | 2087 | 145 (7%) |
| | >= 4 | 32 | 1671 | 176 (11%) |
| Gender | male | 65 | 3368 | 265 (8%) |
| | female | 42 | 2024 | 123 (6%) |
| | unclear | 3 | 159 | 4 (3%) |
| Affiliation | university | 88 | 4402 | 258 (6%) |
| | government | 9 | 410 | 22 (5%) |
| | industry / other | 13 | 739 | 112 (15%) |
| Country | Europe | 62 | 3903 | 324 (8%) |
| | North-America | 19 | 688 | 38 (6%) |
| | Asia | 21 | 484 | 9 (2%) |
| | Australia / New Zealand | 8 | 476 | 21 (4%) |
| **Total** | | **110** | **5551** | **392 (7%)** |

**Table 2. Odds ratios (95% CIs) for the chance of being cited, all types of publications included, N = 110, n = 5551 )**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.10 |
| only Number of Siblings | 0.8 (0.6 – 1.1) | 0.5 (0.4 – 0.7) | |
| only Infection History | 1.3 (0.97–1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) | | | 0.11 |
| mixed / unclear results | 1.2 (0.9 – 1.7) | 3.1 (2.2 – 4.5) | |
| supportive results | 1.5 (1.1 – 2.0) | 2.2 (1.6 – 3.1) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.3 (3.2 – 5.7) | | 0.04 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.3 (1.8 – 5.8) | | |
| editorial / other | 0.3 (0.2 – 0.4) | | |
| Sample Size (ref: low, n = 3517) | | | 0.02 |
| medium | 1.6 (1.2 – 2.3) | 1.6 (1.0 – 2.6) | |
| high | 1.6 (1.2 – 2.3) | 1.9 (1.2 – 3.0) | |
| Specificity (ref: low) | | | 0.11 |
| medium | 2.5 (1.5 – 4.0) | 2.7 (1.6 – 4.5) | |
| high | 8.8 (5.8 – 13.5) | 5.0 (3.1 – 7.9) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.3 – 0.7) | 0.3 (0.2 – 0.4) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.09 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.2) | 0.8 (0.6 – 1.2) | |
| not reported | 0.4 (0.3 – 0.5) | 0.8 (0.6 – 1.0) | |
| Number of Authors (ref: 1-2) | | | 0.09 |
| 3 - 5 | 1.9 (1.4 – 2.5) | 1.0 (0.7 – 1.5) | |
| >= 6 | 3.6 (2.7 – 4.9) | 1.5 (1.0 – 2.4) | |
| Number of Affiliations (ref: 1) | | | 0.09 |
| 2 | 2.6 (2.0 – 3.5) | 1.8 (1.3 – 2.5) | |
| >= 3 | 2.1 (1.6 – 2.8) | 1.6 (1.1 – 2.2) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.1 (0.8 – 1.3) | 1.0 (0.8 – 1.2) | |
| >= 50 | 0.4 (0.3 – 0.6) | 0.8 (0.5 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 5033) | | | 0.11 |
| 2 – 4 | 3.4 (2.2 – 5.3) | 2.7 (1.7 – 4.2) | |
| >= 4 | 6.0 (4.0 – 9.2) | 4.9 (3.2 – 7.6) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 5392) | 0.8 (0.6 – 1.0) | 0.7 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 0.9 (0.6 – 1.3) | 0.9 (0.5 – 1.4) | |
| Asia | 0.3 (0.1 – 0.6) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.8) | |
| Type of Affiliation (other vs university) | 2.3 (1.8 – 2.9) | 2.0 (1.5 – 2.5) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.4 (1.8 – 3.3) | 1.8 (1.3 – 2.5) | |
| high | 3.7 (2.8 – 4.8) | 2.7 (2.0 – 3.7) | |

* adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

**Table 3. Concordance odds ratios (95% CI's) for the chance of being cited, all types of articles included, N = 110, n = 5551)**

| Content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (conc. vs. not) | 10 (5.6 – 18) | 13 (7.1 – 23) | 0.14 |
| Study Outcome (conc. vs. not, n = 1799)** | 2.9 (1.4 – 6.0) | 3.4 (1.6 – 7.1) | 0.06 |
| **Not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
| Article Type (conc. vs. not) | 1.1 (0.9 – 1.3) | | 0.00 (crude) |
| Funding Source (conc. vs. not, n = 1475)*** | 1.3 (0.8 – 1.9) | 1.2 (0.8 – 1.8) | 0.05 |
| Publisher (conc. vs. not, n = 4971)**** | 0.9 (0.7 – 1.2) | 0.9 (0.7 – 1.2) | 0.08 |
| Author Affiliation (conc. vs. not) | 0.7 (0.6 – 0.9) | 0.8 (0.7 – 1.0) | 0.08 |
| Author Gender (conc. vs. not, n = 5254)***** | 1.0 (0.8 – 1.3) | 1.0 (0.8 – 1.3) | 0.08 |
| Author Region (conc. vs. not) | 1.9 (1.6 – 2.4) | 2.0 (1.6 – 2.5) | 0.09 |
| Self-citation (yes vs no) | 6.1 (3.8 – 9.7) | 6.1 (3.7 – 9.9) | 0.09 |

* adjusted for study design of cited publication; ** publications with mixed results excluded from analysis; *** publications without reported funding source excluded from analysis; **** Three main publishers are differentiated: Wiley-Blackwell, BMJ, and Elsevier. Either the cited or the citing publication should be in one of these categories to be included in the analysis. ***** publications with unclear author's gender excluded from analysis; **N**: number of publication. **n**: number of potential citation paths.

# Supplement

**Text S1.** Protocol deviations

**Text S2.** Data extraction

**Text S3.** References of included literature on Strachan's hygiene hypothesis

**Table S1.** All characteristics of the publications in the hygiene hypothesis network.

**Table S2.** Top 6 of articles and authors within network.

**Table S3.** Odds ratios for the chance of *empirical* publications to be cited within full network.

**Table S4.** Odds ratios for the chance of *empirical* publications to be cited by *synthesis* publications.

**Table S5.** Sensitivity analyses on odds ratios for the chance of being cited, without the four most cited publications.

**Table S6.** Sensitivity analyses on odds ratios for the chance of being cited, with a 1-year time lag between cited and citing publication.

**Table S7.** Sensitivity analyses on odds ratios for the chance of being cited, without citing publications with less than 10 potential citation paths.

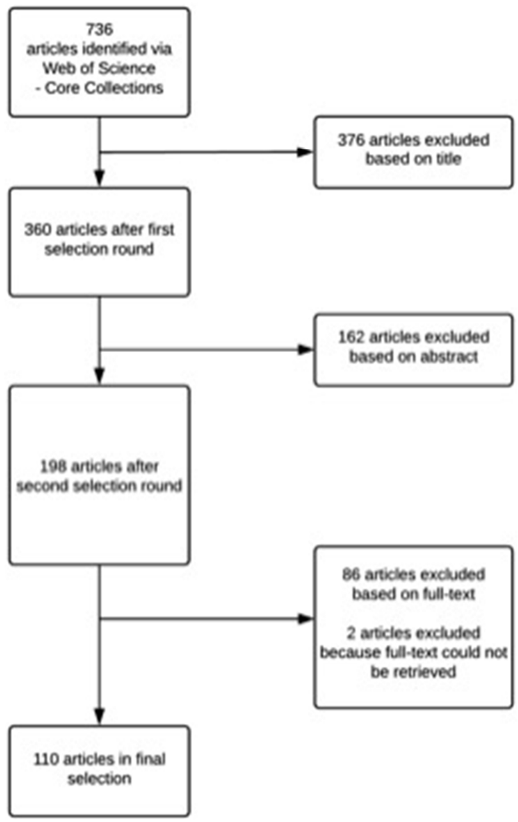


Figure 1. Flow diagram of article selection process.

101x155mm (72 x 72 DPI)

# Selective citation in the literature on the hygiene hypothesis

## Supplement

**Text S1.** Protocol deviations

**Text S2.** Data extraction

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**Text S1. Protocol deviations**

*Search strategy.* We ran some checks of our original search strategy (with '*hygiene hypothesis'* in combination with the pre-specified health outcomes). These checks indicated that many relevant publications in the period 1990 – 2000 were missed. Going through these missed publications we found out that the name for this hygiene hypothesis was not yet accepted or used. Also, we realised that almost all relevant publications within this network referred to Strachan's original study from 1989. We decided to change the search strategy, into *all publications referring to Strachan's original article.* Additionally, we limited the output to those publications that mentioned 'rhinitis' or a similar term in the title, abstract or keywords (see inclusion criteria).

*Inclusion criteria* (regarding the health outcome and types of exposure). Originally, all publications with either health outcome *rhinitis* or *asthma* were to be included. This yielded too many publications in our network, hence we decided to include only publications on rhinitis (or hay fever, or rhinoconjunctivitis). Inclusion solely based on asthma would also have yielded a network that was too large. Also, rhinitis is the original outcome as studied by Strachan. Similarly, we included only publications with exposures *number of siblings* and *infection history.* These are the two most important types of exposure related to the hygiene hypothesis as originally stated by Strachan. Number of siblings was originally studied by Strachan, and infections during childhood (or during pregnancy) was his explanation for the relationship between number of siblings and hay fever.

*Types of health outcome.* We intended to score both *asthma* and *rhinitis* as health outcomes. However, as we included only publications that studied the relationship with rhinitis, and excluded publications that were solely on asthma, we decided to focus on rhinitis. Thus, for the

empirical publications, we scored the relationships Siblings – Rhinitis and Infections – Rhinitis. (We also scored asthma, dermatitis and atopic sensitisation, but only for the sensitivity analyses.) Synthesis publications often did not differentiate between the different allergies in their general conclusion, so for the synthesis publications we scored statements on Siblings – Allergy and Infection – Allergy.

*Types of exposure.* We focused on two exposures: *number of siblings* (or household size or sibling order) and *history of infections* (as assessed by parental questionnaire, serology or medical records). We used this variable also in our analyses; it was scored as a) number of siblings only, b) only infection history, and c) both number of siblings and infection history.

*Study outcome scoring strategy.* There were many empirical publications with contradictory results, especially in the case of Infections where the results seemed to depend on the type of infection. In order to deal with this, we decided to use the *authors' conclusion* on Siblings – Rhinitis and Infections – Rhinitis as leading. We used 5 categories: 0. not measured or reported; 1. effect in line with hygiene hypothesis (inverse relationship); 2. no relationship; 3. effect contrary to hygiene hypothesis (positive relationship); 4. mixed or unclear results. Synthesis publications were scored in a similar way, but then on Siblings – Allergy and Infections – Allergy.

If no clear authors' conclusion was stated in the empirical publications, we used the data that were presented in the tables or the text and scored as follows: 1. statistically significant inverse relationship; 2. no statistically significant relationship; 3. statistically significant positive relationship; 4. mixed or unclear results. If both adjusted analyses and crude analyses were presented we preferred the adjusted ones. There is one exception: adjustment for Infections in

the relationship Siblings – Rhinitis; after all, the hygiene hypothesis states that infection is the mediator between siblings and rhinitis.

In the analyses we used one combined measure for study outcome, with three levels: 1) supportive; 2) mixed results / unclear; 3) non-supportive. Publications were scored as supportive if the exposure or exposures showed an inverse association with rhinitis. Publications were scored as non-supportive if there was no association or a positive association of the exposure with rhinitis. Publications were scored as mixed if the exposure or exposures showed mixed or unclear results, and if two exposures were investigated, and one showed an inverse association and the other showed no or a positive association.

*General conclusion about the hygiene hypothesis*. While studying the literature on the hygiene hypothesis we realised that many related hypotheses reside under this name, all evolved from one another. *The* hygiene hypothesis clearly does not exist. Support for one version of the hypothesis often implied the refutation of another (older) version. As authors assumed different versions, their general conclusion on the hygiene hypothesis would not be compatible. We decided to not score this general conclusion.

*Specificity.* We used 3 outcome categories for publication's specificity instead of 5.

*Study design.* Ecological studies were excluded from the network. Cohort studies were further classified as retrospective and prospective cohort studies. This latter step was data-driven because we realised during the analysis that prospective cohort studies were cited less often.

*Publisher*. In addition to the protocol we also scored the publisher of the journal, based on the information in Journal Citation Reports and in Web of Science. This could be interesting for publisher self-citation concordance analysis.

*Explained variance*. In addition to the original analysis plan in the protocol, we also calculated the explained variance of the adjusted models, so that these models are easier to compare. For this purpose we calculated McFadden's $R^2$ by the following formula: $R^2 = 1 - {LL_M}/{LL_0}$ in which $LL_M$ stands for the log likelihood of the current regression model and $LL_0$ stands for the log likelihood of the empty random-regression model. Both the current and the empty model (without predictors) were nested under the citing publication. Because of missing values for certain determinants (such as sample size), some models could be tested only on a sub-selection of citation paths. If this was the case, then $LL_0$ was calculated on the same sub-selection of citation paths.

**Text S2. Data extraction.**

A range of variables were extracted or derived from each included publication: *content-related publication characteristics* (i.e. type of exposure, publication type and study design, sample size, specificity, study outcome), *content-unrelated publication characteristics* (conclusiveness of the title, funding source, number of authors, number of affiliations, number of references), *journal characteristics* (publisher, journal impact factor), *author characteristics* gender, country, and affiliation of the corresponding author), and *citation characteristics* (within-network authority, self-citation). All characteristics were treated as determinant in the statistical analysis unless stated otherwise.

**Publication characteristics – content-related.** The following variables were in this subcategory: type of exposure, publication type/study design, sample size, specificity, and study outcome. Study outcome is a special content-related characteristic and will be discussed in the next section.

*Type of exposure* refers to the type of exposure that is being studied or reviewed: *only number of siblings*, *only infection history*, or *both*.

*Publication type* was classified into empirical publications, generating their own data, and non-empirical publications. Empirical publications were further classified into the following *study designs*: cross-sectional, case-control, retrospective cohort, prospective cohort, and experimental studies. Non-empirical publications were further classified into: narrative reviews, systematic reviews, and other (editorials, leading articles, commentaries).

*Sample size* concerned the number of participants in the publications. Non-empirical publications had no sample size. The sample size of the empirical publications was classified into three equal categories based on tertiles.

The *specificity* of the publications varied. The higher the specificity of a publication, the better this publication would fit in our network. Some publications may deal only with the statement under investigation, others were broader. Farm, autoimmune diseases, endotoxins, helminths, and animal or mechanistic studies decreased the specificity of a publication, as did publications on other determinants of rhinitis such as air pollution, and mother smoking status. Specificity ranged from 1 (very broad) to 3 (highly specific): 1 - hardly about Strachan's original hygiene hypothesis (associations between siblings / infections – rhinitis); 2 - partly about Strachan's original hygiene hypothesis; 3 - only about Strachan's original hygiene hypothesis.

**Publication characteristics – study outcome.** Study outcome was scored as follows: 1. supportive of the hygiene hypothesis; 2. mixed or unclear results; 3. non-supportive of the hygiene hypothesis. An inverse relationship between past exposure and rhinitis is considered to be supportive for the hygiene hypothesis, while a neutral or positive relationship was scored as non-supportive. The scoring was based on the authors' interpretation of the results, as it was stated in the text of the publication. If the authors' interpretation was unclear, we scored study outcome based on the direction and statistical significance of the data. Non-empirical publications seldom distinguished between allergy subtypes, so we used the stated conclusion on general allergy as outcome measure.

Exposure could be either number of siblings (or order of siblings or household size) or history of bacterial or viral infection (as assessed by parental questionnaire, serology, or medical records). If the impact of number of both siblings and infection history was assessed and they were contradicting each other (with one exposure showing inverse association, the other a neutral or positive association), then study outcome was scored as mixed.

**Publication characteristics - not content-related.** The following variables were in this category: conclusiveness of the title, funding source, number of authors, number of affiliations, and number of references. Title conclusiveness was coded as yes if a clear outcome was stated in the title, including the direction of the relationship (e.g. "Inverse relation between infections and allergies"), otherwise as no (e.g. "Infections, rhinitis, and their relationship"). Funding source was coded as non-profit (e.g. government or university), for-profit, both, or not reported.

**Journal characteristics.** The following variables were in this category: publisher and journal impact factor. Journal impact factor, in the publication year of the potentially cited publication, was retrieved from the Journal Citation Reports (JCR) database. Journal publisher was also retrieved from JCR.

**Author characteristics.** The following variables were in this category: gender of the corresponding author (assessed by first name, with help of www.genderchecker.com; if first name was not given, other articles of the same author were searched, and the profile of the author at the university or at www.researchgate.com was checked), country of the corresponding author, and affiliation of the corresponding author. Affiliation was classified as government, university, industry or other.

**Citation characteristics.** There were some variables that depend on the cited publication as well as the citing publication: time to citation, authority, and self-citation.

*Time to citation* was the number of years between the publication date of the cited publication and the submission date of the citing publication. This variable was not used as determinant of citation, but to determine the dataset of potential citation paths: only citation paths with a positive value for *time to citation* were included in this dataset.

As publication date we used either the online publication date or the paper publication date, depending on which one was earlier. The average duration from submission to publication was nine months in this network. For 57 publications the submission date was not stated. In these cases, it was estimated by subtracting nine months from the publication date.

*Within-network authority* was a measure for the authority of the authors of a cited publication within the network. It was calculated for each author and each year separately, by counting the number of within-network citations to all publications in which the author had been involved. As the number of citations is likely to increase each year, so does the author's authority. Because we were interested in the authority at the moment of citation, the authority value of a cited publication also depends on the publication year of the citing publication. In case of multiple authors, we used the authority value of the author with the highest authority in that year.

A *self-citation* was defined as a citation between two publications that have at least one author in common.

**Text S3. References of included literature on Strachan's hygiene hypothesis**

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**Table S1. All characteristics of the publications in the hygiene hypothesis network.**

| | | N publications | n potential citations | n realised citations (%) |
|---|---|---|---|---|
| **Total** | | 110 | 5551 | 392 (7%) |

| Publication characteristics - content-related | category | N publications | n potential citations | n realised citations (%) |
|---|---|---|---|---|
| Type of Exposure | only Number of Siblings | 28 | 1512 | 100 (7%) |
| | only Infection History | 48 | 1946 | 144 (7%) |
| | both Siblings & Infections | 34 | 2093 | 148 (7%) |
| Study Outcome Exposure - Rhinitis | supportive | 41 | 2322 | 198 (9%) |
| | mixed results | 35 | 1913 | 129 (7%) |
| | non-supportive | 34 | 1316 | 65 (5%) |
| Publication Type / Study Design | Empirical | 73 | 3517 | 337 (10%) |
| | cross-sectional | 39 | 1697 | 179 (11%) |
| | case-control | 4 | 249 | 36 (14%) |
| | cohort | 29 | 1535 | 121 (8%) |
| | -retrospective | 15 | 817 | 89 (11%) |
| | -prospective | 14 | 718 | 32 (4%) |
| | intervention | 1 | 36 | 1 (3%) |
| | Synthesis | 37 | 2034 | 55 (3%) |
| | narrative review | 27 | 1423 | 16 (1%) |
| | systematic review | 2 | 80 | 20 (25%) |
| | -with meta-analysis | 1 | 8 | 1 (13%) |
| | editorial, etc | 8 | 531 | 19 (4%) |
| Sample Size (cat; for empirical publications) | low (1 – 999) | 24 | 909 | 56 (6%) |
| | medium (1000 – 7999) | 25 | 1327 | 143 (11%) |
| | high (>= 8000) | 24 | 1281 | 138 (11%) |
| Specificity | 0 (non-specific) | 27 | 1402 | 25 (2%) |
| | 1 | 39 | 1657 | 65 (4%) |
| | 2 (specific) | 44 | 2492 | 302 (12%) |

| Publication characteristics - not content-related | category | N publications | n potential citations | n realised citations (%) |
|---|---|---|---|---|
| Conclusive Title | not conclusive | 99 | 5026 | 375 (7%) |
| | conclusive | 11 | 525 | 17 (3%) |

| | | | | |
|---|---|---|---|---|
| Funding Source | non-profit | 44 | 2188 | 214 (10%) |
| | for-profit | 1 | 38 | 1 (3%) |
| | both | 12 | 559 | 51 (9%) |
| | not reported / unclear | 53 | 2766 | 126 (5%) |
| Number of Authors | 1 - 2 | 32 | 2017 | 89 (4%) |
| | 3 - 5 | 41 | 2143 | 155 (7%) |
| | >= 6 | 37 | 1391 | 148 (11%) |
| Number of Affiliations | 1 | 36 | 2276 | 111 (5%) |
| | 2 | 24 | 1168 | 108 (9%) |
| | >= 3 | 50 | 2107 | 173 (8%) |
| Number of References | < 30 | 35 | 2307 | 194 (8%) |
| | 30 – 50 | 49 | 2060 | 159 (8%) |
| | >= 50 | 26 | 1184 | 39 (3%) |

| **Journal characteristics** | **category** | **N publications** | **n potential citations** | **n realised citations (%)** |
|---|---|---|---|---|
| Journal Impact Factor (cat) | 0 - 2 | 28 | 1275 | 27 (2%) |
| | 2 - 4 | 41 | 2087 | 145 (7%) |
| | >= 4 | 32 | 1671 | 176 (11%) |
| Publisher | Wiley-Blackwell | 41 | 2107 | 82 (4%) |
| | BMJ | 15 | 1170 | 213 (18%) |
| | Elsevier | 18 | 894 | 43 (5%) |
| | other | 36 | 1380 | 54 (4%) |

| Author characteristics | category | N publications | n potential citations | n realised citations (%) |
|---|---|---|---|---|
| Gender | male | 65 | 3368 | 265 (8%) |
| | female | 42 | 2024 | 123 (6%) |
| | unclear | 3 | 159 | 4 (3%) |
| Affiliation | university | 88 | 4402 | 258 (6%) |
| | government | 9 | 410 | 22 (5%) |
| | industry / other | 13 | 739 | 112 (15%) |
| Country | Europe | 62 | 3903 | 324 (8%) |
| | UK | 26 | 1946 | 165 (8%) |
| | Germany | 11 | 594 | 19 (3%) |
| | Finland | 8 | 516 | 33 (6%) |
| | Italy | 7 | 418 | 85 (20%) |
| | North-America | 19 | 688 | 38 (6%) |
| | USA | 18 | 662 | 36 (5%) |
| | Asia | 21 | 484 | 9 (2%) |
| | Turkey | 9 | 303 | 7 (2%) |
| | Japan | 4 | 60 | 0 (0%) |
| | Australia / New Zealand | 8 | 476 | 21 (4%) |
| | Australia | 7 | 407 | 21 (5%) |

| Citation characteristics | category | n potential citations | n realised citations (%) |
|---|---|---|---|
| Authority | low (0-2) | 2279 | 81 (4%) |
| | medium (2-10) | 1326 | 108 (8%) |
| | high (>= 10) | 1946 | 203 (10%) |
| Time to Citation (in years) | 0 – 1 | 494 | 38 (8%) |
| | 1 – 2 | 521 | 56 (11%) |
| | 2 – 3 | 527 | 50 (9%) |
| | 3 – 4 | 459 | 33 (7%) |
| | 4 – 5 | 456 | 40 (9%) |
| | 5 – 6 | 441 | 35 (8%) |
| | 6 – 7 | 404 | 28 (7%) |
| | 7 – 8 | 372 | 22 (6%) |
| | => 8 | 1877 | 90 (5%) |
| Self-citation | no | 5462 | 365 (7%) |
| | yes | 89 | 27 (30%) |

**Table S2. Top 6 of articles (above) and authors (below) within network, based on the number of received citations up to 2017.**

| Article rank | Article's first author | Title | Year | Nr. of received citations (% of potential citations) |
|---|---|---|---|---|
| 1 | Matricardi | Cross sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus | 1997 | 35 (35 %) |
| 2 | Bodner | Family size, childhood infections and atopic diseases | 1998 | 32 (33 %) |
| 3 | Matricardi | Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study | 2000 | 32 (38 %) |
| 4 | Strachan | Family structure, neonatal infection, and hay fever in adolescence | 1996 | 28 (26 %) |
| 5 | Farooqi | Early childhood infection and atopic disorder | 1998 | 21 (23 %) |
| 6 | Karmaus | Does a higher number of siblings protect against the development of allergy and asthma? A review | 2002 | 19 (26 %) |

| Author rank | Author | Affiliation | Country | Nr. of received citations (= authority) |
|---|---|---|---|---|
| 1 | P. Matricardi | Consiglio Nazionale delle Ricerche, Rome | Italy | 84 |
| 2 | F. Rosmini | Istituto Superiore di Sanita, Rome | Italy | 84 |
| 3 | L. Ferrigno | Istituto Superiore di Sanita, Rome | Italy | 84 |
| 4 | M. Rapicetta | Istituto Superiore di Sanita, Rome | Italy | 67 |
| 5 | D. Strachan | University of London, London | United Kingdom | 57 |
| 6 | S. Bonini | Consiglio Nazionale delle Ricerche, Rome | Italy | 49 |

**Table S3. Odds ratios (95% CIs) for the chance of *empirical* publications to be cited within full network (N = 73, n = 3517).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.04 |
| only Number of Siblings | 0.5 (0.3 – 0.6) | 0.4 (0.3 – 0.5) | |
| only Infection History | 1.0 (0.8 – 1.3) | 0.7 (0.5 – 0.9) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.07 |
| mixed / unclear results | 1.4 (0.9 – 2.3) | 1.1 (0.7 – 1.9) | |
| supportive results | 4.8 (3.2 – 7.0) | 5.1 (3.3 – 7.8) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Study Design (ref: cross-sectional) | | | 0.02 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| Sample Size (ref: low) | | *** | 0.02 |
| medium | 1.6 (1.2 – 2.3) | 1.6 (1.0 – 2.6) | |
| high | 1.6 (1.2 – 2.3) | 1.9 (1.2 – 3.0) | |
| Specificity (ref: low) | | | 0.05 |
| medium | 4.6 (2.6 – 8.2) | 3.5 (1.8 – 6.5) | |
| high | 7.4 (4.5 – 12) | 6.1 (3.5 – 10) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.3 (0.2 – 0.6) | 0.3 (0.1 – 0.5) | 0.03 |
| Funding Source (ref: exclusively non-profit) | | | 0.02 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.2) | 0.8 (0.5 – 1.1) | |
| not reported | 0.8 (0.6 – 1.1) | 0.8 (0.6 – 1.1) | |
| Number of Authors (ref: 1-2) | | | 0.03 |
| 3 - 5 | 1.1 (0.7 – 1.6) | 1.2 (0.7 – 1.8) | |
| >= 6 | 1.7 (1.2 – 2.6) | 1.8 (1.1 – 2.9) | |
| Number of Affiliations (ref: 1) | | | 0.03 |
| 2 | 1.7 (1.2 – 2.4) | 1.8 (1.2 – 2.6) | |
| >= 3 | 1.3 (0.9 – 1.7) | 1.6 (1.2 – 2.4) | |
| Number of References (ref: <30) | | | 0.02 |
| 30 - 50 | 0.9 (0.7 – 1.1) | 1.0 (0.7 – 1.2) | |
| >= 50 | 0.3 (0.1 – 0.7) | 0.3 (0.1 – 0.8) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 3266) | | | 0.06 |
| 2 – 4 | 2.8 (1.7 – 4.5) | 2.6 (1.6 – 4.3) | |
| >= 4 | 5.9 (3.7 – 9.5) | 6.6 (4.0 – 11) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 3457) | 0.6 (0.5 – 0.8) | 0.7 (0.5 – 0.9) | 0.03 |
| Region (ref: Europe) | | | 0.04 |
| North-America | 0.5 (0.3–0.97) | 0.6 (0.3 – 1.1) | |
| Asia | 0.2 (0.1 – 0.4) | 0.1 (0.1 – 0.3) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.9) | |
| Type of Affiliation (other vs university) | 2.4 (1.9 – 3.2) | 2.2 (1.7 – 2.9) | 0.04 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.05 |
| medium | 2.0 (1.4 – 3.0) | 2.1 (1.4 – 3.0) | |
| high | 3.6 (2.6 – 5.1) | 3.8 (2.7 – 5.5) | |

* adjusted for study design and log sample size (if possible). ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited publications; n = number of potential citation paths.

**Table S4. Odds ratios (95% CIs) for the chance of *empirical* publications to be cited by *synthesis* publications (N = 73, n = 1097).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.07 |
| only Number of Siblings | 0.4 (0.2 – 0.7) | 0.3 (0.2 – 0.6) | |
| only Infection History | 1.8 (1.1 – 3.0) | 1.3 (0.7 – 2.3) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 0.5 (0.2 – 1.0) | 0.4 (0.2 – 0.9) | |
| supportive results | 6.0 (3.1 – 12) | 7.3 (3.5 – 15) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Study Design (ref: cross-sectional) | | | 0.04 (crude) |
| case control | 2.1 (1.1 – 4.2) | | |
| retrospective cohort | 1.0 (0.6 – 1.6) | | |
| prospective cohort | 0.3 (0.1 – 0.6) | | |
| Sample Size (ref: low) | | *** | 0.04 |
| medium | 1.6 (0.9 – 2.8) | 1.9 (0.8 – 4.6) | |
| high | 1.3 (0.7 – 2.3) | 1.9 (0.8 – 4.4) | |
| Specificity (ref: low) | | | 0.06 |
| medium | 6.9 (2.8 – 17) | 4.3 (1.6 – 12) | |
| high | 7.6 (3.4 – 17) | 5.6 (2.3 – 13) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.2 – 0.9) | 0.2 (0.1 – 0.6) | 0.05 |
| Funding Source (ref: exclusively non-profit) | | | 0.04 |
| profit or both profit/non-profit | 0.7 (0.4 – 1.2) | 0.7 (0.4 – 1.3) | |
| not reported | 0.6 (0.4 – 1.0) | 0.5 (0.3 – 0.9) | |
| Number of Authors (ref: 1-2) | | | 0.06 |
| 3 - 5 | 0.6 (0.3 – 1.1) | 0.6 (0.3 – 1.2) | |
| >= 6 | 1.5 (0.8 – 2.8) | 1.5 (0.7 – 3.2) | |
| Number of Affiliations (ref: 1) | | | 0.04 |
| 2 | 1.3 (0.7 – 2.4) | 1.6 (0.8 – 3.1) | |
| >= 3 | 1.2 (0.7 – 2.0) | 2.0 (1.1 – 3.6) | |
| Number of References (ref: <30) | | | 0.04 |
| 30 - 50 | 0.7 (0.5 – 1.1) | 0.8 (0.5 – 1.2) | |
| >= 50 | 0.2 (0.04–0.9) | 0.2 (0.04–1.0) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 1015) | | | 0.11 |
| 2 – 4 | 2.6 (1.2 – 5.6) | 2.2 (1.0 – 4.9) | |
| >= 4 | 8.2 (3.8 – 18) | 9.2 (4.1 – 21) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 1079) | 0.5 (0.3 – 0.8) | 0.6 (0.4 – 0.9) | 0.04 |
| Region (ref: Europe) | | | 0.07 |
| North-America | 0.7 (0.2 – 2.2) | 0.9 (0.3 – 2.9) | |
| Asia | 0.2 (0.1 – 0.7) | 0.1 (0.02–0.3) | |
| Australia / New-Zealand | 0.2 (0.1 – 0.6) | 0.2 (0.9 – 0.7) | |
| Type of Affiliation (other vs university) | 3.3 (2.2 – 5.1) | 3.1 (2.0 – 4.8) | 0.07 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.07 |
| medium | 2.6 (1.4 – 4.6) | 2.7 (1.4 – 5.1) | |
| high | 4.0 (2.3 – 7.1) | 4.1 (2.2 – 7.6) | |

* adjusted for study design and log sample size (if possible). ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited (*empirical*) publications; n = number of potential citation paths.

**Table S5. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited within full network, without the four most cited publications. N = 106, n = 5164).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.08 |
| only Number of Siblings | 1.4 (1.0 – 1.9) | 0.9 (0.6 – 1.3) | |
| only Infection History | 1.0 (0.8 – 1.4) | 1.0 (0.7 – 1.4) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.08 |
| mixed / unclear results | 0.8 (0.5 – 1.1) | 1.2 (0.8 – 2.0) | |
| supportive results | 1.0 (0.7 – 1.5) | 1.5 (1.0 – 2.2) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 2.9 (2.1 – 3.9) | | 0.03 (crude) |
| Study Design (ref: cross-sectional) | | | 0.08 (crude) |
| case control | 0.3 (0.1 – 0.8) | | |
| retrospective cohort | 1.1 (0.8 – 1.5) | | |
| prospective cohort | 0.5 (0.3 – 0.8) | | |
| narrative review | 0.1 (0.1 – 0.2) | | |
| systematic review | 4.5 (2.5 – 8.0) | | |
| editorial / other | 0.4 (0.2 – 0.7) | | |
| Sample Size (ref: low, n = 3130) | | *** | 0.02 |
| medium | 2.3 (1.4 – 3.7) | 1.6 (0.9 – 2.9) | |
| high | 3.3 (2.1 – 5.3) | 2.5 (1.5 – 4.2) | |
| Specificity (ref: low) | | | 0.09 |
| medium | 2.4 (1.5 – 3.9) | 3.3 (1.9 – 5.6) | |
| high | 5.6 (3.6 – 8.7) | 3.5 (2.1 – 5.6) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.6 (0.4 – 1.0) | 0.5 (0.3 – 0.9) | 0.08 |
| Funding Source (ref: exclusively non-profit) | | | 0.08 |
| profit or both profit/non-profit | 1.4 (1.0 – 2.0) | 1.4 (0.9 – 2.0) | |
| not reported | 0.5 (0.4 – 0.7) | 1.0 (0.7 – 1.4) | |
| Number of Authors (ref: 1-2) | | | 0.08 |
| 3 - 5 | 1.2 (0.9 – 1.7) | 0.7 (0.5 – 1.1) | |
| >= 6 | 2.0 (1.4 – 2.8) | 0.9 (0.6 – 1.4) | |
| Number of Affiliations (ref: 1) | | | 0.08 |
| 2 | 1.8 (1.3 – 2.5) | 1.1 (0.8 – 1.6) | |
| >= 3 | 1.0 (0.7 – 1.4) | 0.6 (0.4 – 0.9) | |

| | | | |
|---|---|---|---|
| Number of References (ref: <30) | | | 0.08 |
| 30 - 50 | 0.9 (0.7 – 1.2) | 0.7 (0.6 – 1.0) | |
| >= 50 | 0.6 (0.4 – 0.8) | 0.8 (0.5 – 1.3) | |

| **Journal characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4752) | | | 0.09 |
| 2 – 4 | 2.8 (1.8 – 4.3) | 2.5 (1.6 – 3.9) | |
| >= 4 | 4.0 (2.6 – 6.1) | 3.5 (2.2 – 5.5) | |

| **Author characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Gender (female vs male, n = 5005) | 1.4 (1.1 – 1.8) | 1.2 (0.9 – 1.6) | 0.07 |
| Region (ref: Europe) | | | 0.08 |
| North-America | 1.2 (0.8 – 1.8) | 1.0 (0.6 – 1.6) | |
| Asia | 0.4 (0.2 – 0.8) | 0.4 (0.2 – 0.8) | |
| Australia / New-Zealand | 0.8 (0.5 – 1.2) | 0.7 (0.5 – 1.2) | |
| Type of Affiliation (other vs university) | 1.6 (1.2 – 2.2) | 1.4 (1.1 – 2.0) | 0.08 |

| **Citation characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Authority (ref: low) | | | 0.08 |
| medium | 2.1 (1.5 – 2.9) | 1.6 (1.1 – 2.2) | |
| high | 2.2 (1.6 – 3.0) | 1.6 (1.1 – 2.2) | |

In these sensitivity analyses, the four most cited publications shown in Table S2 are excluded as *cited* publications; they are still included as *citing* publications. * adjusted for study design and log sample size (if possible). ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited publications; n = number of potential citation paths.

**Table S6. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited within full network, with a 1-year time lag between cited and citing publication. (N = 110, n = 5057).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.11 |
| only Number of Siblings | 0.7 (0.5 – 1.0) | 0.4 (0.3 – 0.7) | |
| only Infection History | 1.2 (1.0 – 1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 1.2 (0.8 – 1.7) | 2.2 (1.4 – 3.5) | |
| supportive results | 1.7 (1.2 – 2.4) | 3.2 (2.2 – 4.6) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.4 (3.2 – 6.0) | | 0.05 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.4 (1.9 – 6.2) | | |
| editorial / other | 0.3 (0.1 – 0.4) | | |
| Sample Size (ref: low, n = 3199) | | | 0.02 |
| medium | 1.6 (1.1 – 2.2) | 1.4 (0.8 – 2.4) | |
| high | 1.4 (1.0 – 2.1) | 1.6 (0.9 – 2.6) | |
| Specificity (ref: low) | | | 0.12 |
| medium | 2.8 (1.6 – 4.7) | 3.1 (1.7 – 5.6) | |
| high | 10.3 (6.4 – 17) | 6.1 (3.6 – 10) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.5 (0.3 – 0.8) | 0.3 (0.2 – 0.5) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.10 |
| profit or both profit/non-profit | 0.8 (0.6 – 1.2) | 0.8 (0.5 – 1.1) | |
| not reported | 0.4 (0.3 – 0.5) | 0.8 (0.6 – 1.1) | |
| Number of Authors (ref: 1-2) | | | 0.10 |
| 3 - 5 | 2.0 (1.5 – 2.8) | 1.1 (0.7 – 1.8) | |
| >= 6 | 3.7 (2.7 – 5.0) | 1.7 (1.0 – 2.6) | |
| Number of Affiliations (ref: 1) | | | 0.10 |
| 2 | 3.0 (2.2 – 4.1) | 2.1 (1.4 – 3.0) | |
| >= 3 | 2.2 (1.7 – 2.9) | 1.7 (1.2 – 2.3) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.1 (0.9 – 1.4) | 1.0 (0.8 – 1.3) | |
| >= 50 | 0.5 (0.3 – 0.7) | 0.7 (0.4 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4580) | | | 0.12 |
| 2 – 4 | 3.2 (2.0 – 4.9) | 2.5 (1.6 – 4.0) | |
| >= 4 | 5.4 (3.5 – 8.4) | 4.5 (2.9 – 7.1) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 4913) | 0.8 (0.6 – 1.0) | 0.7 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 1.0 (0.7 – 1.5) | 1.0 (0.6 – 1.8) | |
| Asia | 0.3 (0.2 – 0.7) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.9) | 0.5 (0.3 – 0.9) | |
| Type of Affiliation (other vs university) | 2.3 (1.8 – 2.9) | 1.9 (1.5 – 2.5) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.8 (1.9 – 3.9) | 1.9 (1.3 – 2.7) | |
| high | 4.0 (2.9 – 5.5) | 2.8 (2.0 – 4.0) | |

* adjusted for study design. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

**Table S7. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited, without citing publications with less than 10 potential citation paths (N = 110, n = 5507).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.10 |
| only Number of Siblings | 0.8 (0.6 – 1.1) | 0.5 (0.4 – 0.7) | |
| only Infection History | 1.2 (1.0 – 1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 1.2 (0.8 – 1.7) | 2.3 (1.5 – 3.6) | |
| supportive results | 1.7 (1.3 – 2.4) | 3.0 (2.1 – 4.2) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.2 (3.1 – 5.6) | | 0.04 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (1.0 – 2.2) | | |
| retrospective cohort | 0.8 (0.6 – 1.1) | | |
| prospective cohort | 0.4 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.3 (1.8 – 5.8) | | |
| editorial / other | 0.3 (0.2 – 0.4) | | |
| Sample Size (ref: low, n = 3423) | | | 0.02 |
| medium | 1.5 (1.1 – 2.1) | 1.5 (0.9 – 2.5) | |
| high | 1.4 (1.0 – 2.0) | 1.7 (1.1 – 2.8) | |
| Specificity (ref: low) | | | 0.11 |
| medium | 2.2 (1.4 – 3.6) | 2.5 (1.4 – 4.2) | |
| high | 8.6 (5.6 – 13) | 4.9 (3.1 – 7.9) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.3 – 0.7) | 0.3 (0.2 – 0.5) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.09 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.3) | 0.8 (0.6 – 1.2) | |
| not reported | 0.4 (0.3 – 0.5) | 0.7 (0.5 – 1.0) | |
| Number of Authors (ref: 1-2) | | | 0.09 |
| 3 - 5 | 2.0 (1.5 – 2.7) | 1.1 (0.7 – 1.7) | |
| >= 6 | 3.8 (2.8 – 5.2) | 1.7 (1.1 – 2.6) | |
| Number of Affiliations (ref: 1) | | | 0.09 |
| 2 | 2.8 (2.1 – 3.7) | 1.9 (1.3 – 2.6) | |
| >= 3 | 2.2 (1.7 – 2.9) | 1.6 (1.2 – 2.3) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.0 (0.8 – 1.3) | 0.9 (0.7 – 1.2) | |
| >= 50 | 0.4 (0.3 – 0.6) | 0.8 (0.4 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4955) | | | 0.11 |
| 2 – 4 | 3.2 (2.1 – 5.0) | 2.5 (1.6 – 3.9) | |
| >= 4 | 5.7 (3.8 – 8.8) | 4.6 (3.0 – 7.2) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 5350) | 0.8 (0.6 – 1.0) | 0.8 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 0.9 (0.6 – 1.3) | 0.9 (0.5 – 1.4) | |
| Asia | 0.3 (0.2 – 0.6) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.8) | |
| Type of Affiliation (other vs university) | 2.4 (1.9 – 3.0) | 2.0 (1.6 – 2.6) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.4 (1.8 – 3.3) | 1.8 (1.3 – 2.5) | |
| high | 3.8 (2.9 – 5.1) | 2.9 (2.2 – 4.0) | |

* adjusted for study design. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

BMJ Open

# Selective citation in the literature on the hygiene hypothesis: a citation analysis on the association between infections and rhinitis

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| | |

# Selective citation in the literature on the hygiene hypothesis: a citation analysis on the association between infections and rhinitis

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**Conflict of Interest**

All authors declare to have no conflict of interest.

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**Abstract**

**Objective:** Our objective was to assess the occurrence and determinants of selective citation in scientific publications on Strachan's original hygiene hypothesis. His hypothesis states that lack of exposure to infections in early childhood increases the risk of rhinitis.

**Setting:** Web of Science Core Collection.

**Participants:** We identified 110 publications in this network, consisting of 5551 potential citations.

**Primary and secondary outcome measures:** Whether a citation occurs or not, measured and analysed according to the pre-registered protocol.

**Results:** We found evidence for citation bias in this field: publications supportive of the hypothesis were cited more often than non-supportive publications (odds ratio adjusted for study design [adjOR]: 2.2, 95% confidence interval [CI]: 1.6 - 3.1), and the same was the case for publications with mixed findings (adjOR: 3.1, CI: 2.2 - 4.5). Other relevant determinants for citation were type of exposure, specificity, journal impact factor, authority and self-citation. Surprisingly, prospective cohort studies were cited less often than other empirical studies.

**Conclusions:** There is clear evidence for selective citation in this research field, and particularly for citation bias.

## Strengths and limitations of this study

- The study assesses how evidence regarding the hygiene hypothesis propagates over time by analysing the likelihood of citation.
- It investigates which characteristics of a publication – such as study outcome, journal impact factor, author gender and affiliation, and authority within the field – have an impact on citation.
- We check whether supportive studies are cited more often by other studies within the field, and in particular by reviews (which are supposed to give an unbiased overview of the literature).
- Limitation: only articles related to the original hygiene hypothesis are included in this analysis.

## Background

The hygiene hypothesis postulates that a high degree of hygiene in early life will increase the risk of developing allergies later in life (1, 2). The underlying mechanism has been the topic of scientific debate. Over time, this debate led to several adaptations and extensions of the hygiene hypothesis, which, as such, provides a good example of how science progresses. Ideally, this progress should be based on all existing evidence, but this is not always the case (3). A citation analysis can help to reveal which part of the available evidence is taken into account, and which evidence is ignored. The current study does not concern the validity of the hygiene hypothesis per se, but rather the citation relations within the scientific literature on this hypothesis.

The hygiene hypothesis was originally proposed to explain the rising prevalence of allergies, with up to 20% to 40% of the population in developed countries being affected (4). Modern, urbanized life in developed countries generally shows higher levels of hygiene than in previous times or in developing countries. Hygiene limits exposure to infections. Exposure to infections, especially early in life, helps to develop and adapt the immune system to the environment in which we happen to live, in such a way that it learns to discriminate between harmless and harmful intruders. According to the hygiene hypothesis, it is this lack of exposure to relatively harmless intruders early in life, that causes the immune system to malfunction later in life. Hence the rise in allergies.

The hygiene hypothesis has been amended several times since its early days to give rise to newer theories such as the '*old friends hypothesis*' (5, 6). According to this theory, it is not hygiene per se that is causing the rise in allergy prevalence, but the lack of exposure to *some specific* infections, and also to the gut microbiome and to non-viable intruders from the natural environment, such as endotoxins. Humans have been exposed to these 'old friends' for many centuries and our immune system has co-evolved in their presence. As a result, our immune system has become dependent on the presence of these old friends in order to develop and function properly. This adapted hygiene hypothesis states that lack of exposure to these old friends may give rise not only to allergies, but to auto-immune diseases as well.

The original hygiene hypothesis and its later adaptations have a lot in common, and much of the evidence that is supportive for one hypothesis is equally supportive for the others. However, this is not always the case. In our project, publications are classified as either supportive or unsupportive with regards to a hypothesis. For that reason it is important to precisely define the investigated hypothesis. In our citation network, we focus on the hygiene hypothesis as it was originally stated by Strachan, and not on later modifications (1, 2). This allows us to investigate the development of this hypothesis from the start. Concretely, this means that we focus on the impact of infections and the number of siblings on the development of rhinitis, like in Strachan's original study (2).

The number of publications in the research on the hygiene hypothesis is large. It is therefore not feasible for authors to cite every relevant publication in the network and some kind of selection needs to take place. If this selection is based on study outcome, we speak of citation bias (3, 7). The consequences of citation bias can be similar to those of publication bias and reporting bias: disregard of counter-evidence leading to unfounded consensus (8) or polarisation (9), ill-advised research programmes and research waste (8, 10), distorted information in the media (11), and misguided medical decisions (12). Citation bias has been studied in many disciplines. Our systematic review gives an overview of these studies (13) . Many of these studies showed evidence for citation bias in their field, with supportive publications being cited about twice as often as non-supportive ones.

Factors other than study outcome may also have an impact on citation, as was recently shown by Onodera and Yoshikane (14). Measures for journal status (impact factor), author status (number of citations, country of affiliation), and collaboration (number of authors, number of affiliatons) were often found to be related to citation count. The same was consistently found for the number of references of the cited publication. Furthermore, the reporting (15) and source (16, 17) of funding were shown to be related to citation, but the impact of author's affiliation (18) and gender (19-21) is less clear. On the other hand, sample size and study design - both markers of study quality, and as such legimate reasons to base a citation on - often seem unrelated to citation (17, 18, 22-24). In our previous citation networks, we also found associations with self-citation and the specificity of a publication, but not with the title of a publication (25, 26).

In our study, we aimed a) to assess the occurrence of citation bias in the scientific literature on the original hygiene hypothesis; and b) test for other signs of selective citation by assessing the impact of the other factors described above. We will make use of the claim-specific methodology developed by Greenberg (8), but with a modification of the statistical analysis that allows us to test the impact of multiple factors, adjust for study design and take into account the variation in publication time.

## Method

Prior to performing the citation network analysis, we described our methods in a study protocol and stored it at an online repository (27). (Protocol deviations are described in the supplement, Text S1.) In brief, we applied a search strategy to the Web of Science Core Collection (WoSCC), identified relevant literature, downloaded these records with their reference lists, extracted data for each publication, built a dataset with potential citation paths and used specialised software to determine which citations had occurred. These steps will be explained in more detail below. Article selection (first based on title, then on abstract and finally full-text;

Figure 1) and data extraction were performed independently by MJEU and BD. Results were compared after each step, and disagreements were resolved in consensus meetings.

For clarification: a publication in our network can both cite and be cited by other publications in the network, leading to a multitude of citation paths. Not all citation paths are possible as one can only cite articles that were published before. In our study, a citation is considered possible if the cited publication is published before the citing publication is submitted. If such *potential* citation occurred, we call it an *actual* citation. (See also supplementary Text S2.)

**Search strategy**

First, we took Strachan's seminal article in which the hygiene hypothesis was launched as point of departure (2). Next, we identified all literature within WoSCC referring to this article. Finally, we limited the output to publications that mentioned hay fever in their title, keywords or abstract (*"hay fever" OR "hayfever" OR "hay-fever" OR "rhinitis" OR "rhino*"*). The search was performed by BD and updated until 16 August 2017. Only English language publications were included.

The search output was then limited to publications that investigated exposures related to the original hygiene hypothesis. This means that only publications investigating the effect of *number of siblings* and *infection history* were included. Publications on helminths infections were excluded, as different versions of the hygiene hypothesis would make contradictory predictions regarding their impact on allergies. Both empirical and non-empirical publications were included.

**Data extraction**

A range of characteristics were extracted or derived from each included publication. These characteristics are described below and were all tested as determinant of citation in the statistical analysis.

**Publication characteristics – content-related.** The following variables were in this subcategory: type of exposure, publication type, sample size, specificity, and study outcome.

*Type of exposure* refers to the type of exposure that is being studied or reviewed: only number of siblings, only infection history, or both.

*Publication type* was classified into empirical and non-empirical publications. Empirical publications were further classified into the following *study designs*: cross-sectional, case-control, retrospective cohort, prospective cohort, and experimental studies. Non-empirical publications were further classified into: narrative reviews, systematic reviews, and other (editorials, leading articles, commentaries).

*Sample size* concerned the number of participants in the publications. Non-empirical publications had no sample size. The sample size of the empirical publications was classified into three equal categories based on tertiles.

The *specificity* of the publications varied. Some publications only deal with Strachan's hygiene hypothesis, others are broader. Specificity ranges from 1 (very broad) to 3 (very specific). For instance, an empirical publication that only investigates the association between number of siblings and rhinitis would be classified as '3'; if it also investigates the impact of helminth infections and growing up on a farm, and if it also includes other health outcomes such as asthma or auto-immune diseases, it would be classified as '1'.

*Study outcome* was scored as follows: 1. supportive of the hygiene hypothesis; 2. mixed or unclear results; 3. non-supportive of the hygiene hypothesis. An inverse relationship between past exposure and rhinitis is considered to be supportive for the hygiene hypothesis, while a neutral or positive relationship was scored as non-supportive. The scoring was based on the authors' interpretation of the results, as it was stated in the text of the publication. (See also Text S2 for more details.)

**Publication characteristics - not content-related.** The following variables were in this category: conclusiveness of the title, funding source, number of authors, number of affiliations, and number of references. *Title conclusiveness* was coded as yes if in the title a conclusion was stated that included the direction of the relationship (e.g. "Inverse relation between infections and allergies"), otherwise as no (e.g. "Infections, rhinitis, and their relationship"). *Funding source* was coded as non-profit (e.g. government or university), for-profit, both, or not reported.

**Journal characteristics.** The following variables were in this category: publisher and journal impact factor. *Journal impact factor*, in the publication year of the cited publication, was retrieved from the Journal Citation Reports (JCR) database. *Journal publisher* was also retrieved from JCR.

**Author characteristics.** The following variables were in this category: *gender* of the corresponding author (see also Text S2), *country* of the corresponding author, and affiliation of the corresponding author. *Affiliation* was classified as government, university, industry or other.

**Citation characteristics.** There were some variables that depend on the cited publication as well as the citing publication: self-citation and within-network authority. A *self-citation* was defined as a citation between two publications that have at least one author in common.

*Authority* was a measure for the authority of the authors within the network. It was calculated for each author and each year separately, by counting the number of within-network citations to all publications in which the author had been involved. As the number of citations is likely to increase each year, so does the author's authority. Because we were interested in the authority at the moment of citation, the authority value of a cited publication also depends on the publication year of the citing publication. In case of multiple authors, we used the authority value of the author with the highest authority in that year.

**Statistical analysis**

The dataset consisted of all potential citation paths between cited and citing publications. A potential citation path means that the cited publication is published before submission of the citing publication. The underlying assumption is that publications can only cite other publications up to the date of submission of the citing publication, and that publications can only be cited from their publication date onwards. All analyses were pre-registered in the study protocol unless mentioned otherwise.

**Impact of the cited publication characteristics.** Our binary dependent variable was citation within the network (or, more precisely, whether a potential citation had occurred or not). This was determined by the built-in algorithm of CitNetExplorer (28). This algorithm makes use of reference lists that can be downloaded from the Web of Science Core Collection. It links the reference lists of all publications in the network with the actual publications in the network. If possible, this linkage was done by DOI, the unique Digital Object Identifier assigned to most present-day publications; otherwise it was based on a combination of first author's surname, first author's first initial, publication year, volume number and first page number. The determinants of citation in our analyses were the characteristics of the cited publication as described above.

Since each publication could refer to multiple other publications, the potential citation paths were related. Therefore we used a multilevel approach in which the potential citations were nested under the citing publication. Specifically, we performed a univariate random-effects logistic regression for each determinant of citation. We repeated these analyses while adjusting for study design, as a proxy for study quality. Another proxy for study quality would be the study sample size. However, as reviews do not have a sample size, this adjusted analysis could only be performed on the sub-selection of cited empirical publications so we did not adjust for sample size in the main analysis.

In addition to the original analysis plan in the protocol, we also calculated the explained variance of the adjusted models, so that these models are easier to compare. For this purpose we calculated McFadden's $R^2$.

**Additional analyses** were performed on sub-selections of the network: a) only cited empirical publications were included (to investigate which empirical evidence is picked up by the rest of the field; explorative analysis); b) only cited empirical publications and citing synthesis publications were included (to investigate which empirical evidence is picked up particularly by reviews and editorials). These analyses were adjusted not only for study design but also for log-transformed sample size because in these sub-selections all cited publications had a sample size.

To check the robustness of our findings we also ran some sensitivity analyses in which the following publications or citation paths were excluded: c) the most cited publications (explorative analysis); d) citation paths with less than one year between publication date of the cited publication and submission date of the citing publication were excluded (to check if a lag time would make a difference as it takes some time before most publications are known and have an impact); e) citing publications that have less than ten potential citations.

**Concordance analysis.** Where applicable, we also calculated whether the cited and the citing publications had the same characteristics (*concordance*). This would, for instance, be the case if supportive publications would prefer to cite other supportive publications, and if non-supportive publications would prefer to cite other non-supportive publications. If citation would be based on the concordance of study outcome, it would be another measure of citation bias. To test if concordance on several characteristics has an impact on the likelihood of citation, univariate and adjusted (for study design) fixed-effects logistic regression analyses were applied.

**Software**

We used the built-in algorithm of CitNetExplorer 1.0.0 to extract the actual citations between publications (28). We used R 3.2.4 to create a dataset with all potential citation paths, based on the data extraction sheet and the actual citations, and also to calculate the within-network authority and self-citation score for each potential citation path. Finally, we used Stata 13.1 to analyse the results.

**Patient and public involvement**

No patients were involved in this study.

## Results

A total number of 110 publications were identified that fit our criteria, published between 1995 and 2017 (Figure 1, Text S3). Of these, 28 publications focused exclusively on the impact of household size on rhinitis, 48 on the impact of having had infections, and 34 on the impact of both types of exposure. This network of 110 publications had a total of 5551 potential and 392 actual citation paths (7%) between these publications. Their main characteristics are depicted in Table 1 (for more details see Table S1). About two thirds of all publications in the network are empirical studies (39 cross-sectional, 4 case control, 29 cohort studies, and 1 intervention), one third are reviews (27 narrative reviews, 2 systematic reviews, and 8 editorials or leading articles). The study outcome for 35 of the publications was mixed or unclear. Of the remaining publications with a clear study outcome, about 50% was supportive of the hygiene hypothesis (41 publications with an inverse association between siblings / infection and rhinitis), and about

50% was non-supportive (34 publications with no association, or with a positive association). The number of citations ranged from 0 (45 publications) to 35, with a median of 1 citation per publication. A ranking of the most cited publications and authors can be found in Table S2.

**Impact of the cited publication characteristics.** The results of the regression analyses are presented in Table 2. Empirical publications were cited more often than non-empirical publications. Compared to empirical studies with a cross-sectional design, prospective cohort studies, narrative reviews and editorials had a lower likelihood of citation, while the two systematic reviews had a higher likelihood of citation. Other determinants that increased the likelihood of citation were specificity, journal impact factor, sample size and within-network authority. Sample size had a modest impact on citation. Publications on only one type of exposure were cited less often than publications on both types of exposure.

Supportive publications had a higher likelihood of being cited than non-supportive publications. This is in line with our hypothesis. However, publications with mixed results were cited even more often. This may be due to our scoring algorithm. After all, if a publication investigated both the number of siblings and the infection history, and it reported dissimilar outcomes for these two exposures, then this publication would have been scored as having mixed results. An explorative chi-square test confirmed that type of exposure and study outcome were related ($\chi^2(4) = 52$, $p < 0.0005$), with 71% of all publications on both types of exposure reporting mixed results, compared to 4% of the publications on only number of siblings and 21% of the publications on only infection history. As double exposure studies are also cited more often compared to the single exposure studies, type of exposure should be considered as a confounder of study outcome. To correct for this, we performed an explorative random-effects logistic regression of citation on study outcome, adjusted for both study design and type of exposure. It showed that supportive publications had the highest chance of being cited (adjusted odds ratio [adjOR] 3.1, 95% confidence interval [CI] 2.2-4.3), compared to publications with mixed results (adjOR 2.4, CI 1.5-3.7) and with non-supportive results (reference category; model $R^2$ = 0.12).

Surprisingly, publications with a conclusive title were less likely to receive citations. The format of the title may be prescribed by the journal regulations. We ran some explorative analyses in which we additionally adjusted for the (log-transformed) journal impact factor or publisher on top of study design. The impact of title conclusiveness remained high when additionally adjusted for journal impact factor (adjOR 0.4, CI 0.2-0.6) or publisher (adjOR 0.3, CI 0.2-0.6).

The above results are related to the network as a whole. Of particular importance is how empirical, evidence-generating publications were cited by the rest of the network. We repeated the above analyses on a subset of the cited publications, namely the empirical publications, and tested which of their characteristics were related to citation. The results (Table S3) are very similar to the analyses on the complete network that include the cited non-empirical publications.

Likewise, we tested how *empirical* publications were cited by *synthesis* publications (Table S4). Again, the direction and magnitudes of the effects were all very similar, except for study outcome. Adjusted for study design, (log-transformed) sample size and type of exposure, supportive empirical publications were much more likely to be cited (adjusted OR 7.3, CI 3.5-15.5) by reviews and editorials, whereas empirical publications with mixed results seemed less likely to be cited (adjusted OR 0.4, CI 0.2-0.9) compared to non-supportive empirical publications (reference category; model $R^2$ = 0.12). As a side note: these analyses are based on a smaller number of cited and citing publications and should be interpreted with caution.

The sensitivity analyses without the four most cited publications showed some dissimilar results (Table S5). The impact of study outcome decreased, the impact of male authors and of North-American authors disappeared, and the impact of case-control studies reversed. The other two sensitivity analyses (with a one year lag time immediately after publication; without citing publications with less than 10 potential citation paths) all showed similar results as the main analyses (Tables S6-S7).

**Concordance analysis.** In addition, we tested whether publications were more likely to be cited by publications with similar characteristics. The results are shown in Table 3. It shows that publications tended to be cited mostly by publications with the same type of exposure, with a similar study outcome, with a corresponding author from the same region, and with one or more authors in common ('self-citation').

## Discussion

Our research aim was to evaluate the impact of study outcome and other factors on the likelihood of being cited in the scientific literature on the original hygiene hypothesis stated by David Strachan (2). We found that study outcome, type of exposure, study design, specificity, title conclusiveness, journal impact factor, and the authors' region, affiliation, authority and self-citation all have a substantial impact on the likelihood of citation.

With regard to study outcome, supportive publications are cited more than three times more often than non-supportive publications, while publications with mixed results are cited more than two times as often. This is a clear sign of citation bias, and corroborates previous findings (13). Similarly, publications are more likely to refer to other publications with the same study outcome rather than to those that provide counter-evidence to their conclusion. This type of citation bias (based on concordance) has not been studied frequently. In our previous network analyses, on trans fatty acids – cholesterol, and on chlorinated water – asthma, we found no evidence for increased citations between publications with the same study outcomes (25, 26), but three other studies, all related to cardiovascular disease, did find evidence for this type of citation bias (9, 29, 30).

The magnitude of citation bias even increases if we focus on how empirical publications are cited by reviews and editorials. Reviews and editorials in our network are up to 8 times more likely to cite supportive publications rather than non-supportive ones. As reviews are generally assumed to give an unbiased summary of the existing evidence, this is a worrying finding. It confirms the notion that people should be cautious to rely on narrative reviews.

Greenberg states that reviews play an important role in the development and acceptance of belief systems (8). According to him, reviews can amplify the impact of empirical studies because their evidence is propagated when these reviews are cited themselves. Trinquart et al. showed that reviews (including systematic reviews) on the health impact of salt intake display signs of citation bias, and that the conclusions of these reviews were in the same direction as the evidence they include (9). A similar link between the selective citation of supportive evidence and supportive conclusions of reviews was found by Leng (29). This mechanism might explain how reviews can amplify the effect of citation bias. If reviews draw supportive conclusions based on selective citation of supportive evidence, then support for a hypothesis will be propagated while counter-evidence will fade from the literature.

In our analyses we consider study design as a proxy for study quality. We believe systematic reviews to be of higher quality than narrative reviews and editorials, and thus to receive more citations. In our network, this is indeed the case. Similarly, we believe that cohort studies outrank cross-sectional and case-control studies but to our surprise they are less likely to be cited. Prospective cohort studies, even though they provide the highest type of evidence in this network, receive the fewest citations of all empirical study designs. This may be due to the fact that these cohort studies tend to focus on multiple risk factors of which only one or two are relevant for the hygiene hypothesis. But the fact that multiple risk factors are investigated in these cohort studies does not imply that their findings on the impact of siblings or infections are of any lesser value or should be ignored.

This study has several limitations. First, it includes two overlapping sub-networks, as is shown by the high odds ratio in the concordance analysis of type of exposure. This makes it difficult to infer for which result a certain publication was cited. Related to this issue, the pre-registered operationalization of study outcome could not be applied because of the hybrid nature of the network, so we developed a scoring system that fits better. Also, there are different versions of the hygiene hypothesis, and support for one version may not be supportive for another one. We dealt with this issue by limiting ourselves to Strachan's original hygiene hypothesis, and by excluding any determinants with conflicting predictions in different versions. Despite these limitations, sensitivity analyses show that the results seem robust against chance findings. Another limitation is our use of odds ratios to assess the likelihood of citation. The odds ratio may overestimate the true relative risk in studies where the outcome is common (i.e. occurs in more than 5% of all cases, (31)). In our network, citation is not a common outcome (7%) and consequently the overestimation of the true relative risk will be relatively small.

To conclude, there is evidence for selective citation in this network. Several characteristics of a publication can make it more likely to be cited such as the authority and the region of the author, the impact factor of the journal, the way in which the title was stated, and also study design and study outcome. The fact that supportive publications are cited more often than non-supportive ones, particularly if we look at how empirical publications are being picked up by the rest of the network, is a clear sign of citation bias. Finally, this study also shows that particularly narrative reviews may have a preference to refer to supportive evidence.

**Availability of data and material:**

The protocol and the data of this study are available upon request in the DataVerse repository, http://hdl.handle.net/10411/ZKGGOG, or by sending an email to b.duyx@maastrichtuniversity.nl.

**Author Contributions:**

BD was involved in the research design and data analysis plan, prepared the research protocol, developed and performed the search strategy, wrote the R scripts for data transformation and calculation, performed article selection and data extraction, conducted the analyses and wrote the manuscript. MJEU was involved in the research design and data analysis plan, performed the article selection and data extraction, and read, commented on and approved the final manuscript. GMHS obtained funding, was involved in the research design and data analysis plan, and read, commented on and approved the final manuscript. MPZ obtained funding, was involved in the research design and data analysis plan, and read, commented on and approved the final manuscript. LMB was involved in the research design and data analysis plan, and read, commented on and approved the final manuscript.

**Transparency declaration**:

The guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained in the supplement.

**Copyright statement:**

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## **Figure Legends**

Figure 1. Flow diagram of article selection process.

**Table 1. Main characteristics of all 110 publications in hygiene hypothesis network.**

| Characteristic | category | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| Type of Exposure | only Number of Siblings | 28 | 1512 | 100 (7%) |
| | only Infection History | 48 | 1946 | 144 (7%) |
| | both Siblings & Infections | 34 | 2093 | 148 (7%) |
| Study Outcome Exposure - Rhinitis | supportive | 41 | 2322 | 198 (9%) |
| | mixed results | 35 | 1913 | 129 (7%) |
| | non-supportive | 34 | 1316 | 65 (5%) |
| Publication Type / Study Design | Empirical | 73 | 3517 | 337 (10%) |
| | cross-sectional | 39 | 1697 | 179 (11%) |
| | case-control | 4 | 249 | 36 (14%) |
| | cohort | 29 | 1535 | 121 (8%) |
| | -retrospective | 15 | 817 | 89 (11%) |
| | -prospective | 14 | 718 | 32 (4%) |
| | intervention | 1 | 36 | 1 (3%) |
| | Synthesis | 37 | 2034 | 55 (3%) |
| | narrative review | 27 | 1423 | 16 (1%) |
| | systematic review | 2 | 80 | 20 (25%) |
| | editorial, etc | 8 | 531 | 19 (4%) |
| Sample Size (cat; for empirical publications) | low (1 – 999) | 24 | 909 | 56 (6%) |
| | medium (1000 – 7999) | 25 | 1327 | 143 (11%) |
| | high (>= 8000) | 24 | 1281 | 138 (11%) |
| Journal Impact Factor (cat) | 0 - 2 | 28 | 1275 | 27 (2%) |
| | 2 - 4 | 41 | 2087 | 145 (7%) |
| | >= 4 | 32 | 1671 | 176 (11%) |
| Gender | male | 65 | 3368 | 265 (8%) |
| | female | 42 | 2024 | 123 (6%) |
| | unclear | 3 | 159 | 4 (3%) |
| Affiliation | university | 88 | 4402 | 258 (6%) |
| | government | 9 | 410 | 22 (5%) |
| | industry / other | 13 | 739 | 112 (15%) |
| Country | Europe | 62 | 3903 | 324 (8%) |
| | North-America | 19 | 688 | 38 (6%) |
| | Asia | 21 | 484 | 9 (2%) |
| | Australia / New Zealand | 8 | 476 | 21 (4%) |
| **Total** | | **110** | **5551** | **392 (7%)** |

**Table 2. Odds ratios (95% CIs) for the chance of being cited, all types of publications included, N = 110, n = 5551 )**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.10 |
| only Number of Siblings | 0.8 (0.6 – 1.1) | 0.5 (0.4 – 0.7) | |
| only Infection History | 1.3 (0.97–1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) | | | 0.11 |
| mixed / unclear results | 1.2 (0.9 – 1.7) | 3.1 (2.2 – 4.5) | |
| supportive results | 1.5 (1.1 – 2.0) | 2.2 (1.6 – 3.1) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.3 (3.2 – 5.7) | | 0.04 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.3 (1.8 – 5.8) | | |
| editorial / other | 0.3 (0.2 – 0.4) | | |
| Sample Size (ref: low, n = 3517) | | | 0.02 |
| medium | 1.6 (1.2 – 2.3) | 1.6 (1.0 – 2.6) | |
| high | 1.6 (1.2 – 2.3) | 1.9 (1.2 – 3.0) | |
| Specificity (ref: low) | | | 0.11 |
| medium | 2.5 (1.5 – 4.0) | 2.7 (1.6 – 4.5) | |
| high | 8.8 (5.8 – 13.5) | 5.0 (3.1 – 7.9) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.3 – 0.7) | 0.3 (0.2 – 0.4) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.09 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.2) | 0.8 (0.6 – 1.2) | |
| not reported | 0.4 (0.3 – 0.5) | 0.8 (0.6 – 1.0) | |
| Number of Authors (ref: 1-2) | | | 0.09 |
| 3 - 5 | 1.9 (1.4 – 2.5) | 1.0 (0.7 – 1.5) | |
| >= 6 | 3.6 (2.7 – 4.9) | 1.5 (1.0 – 2.4) | |
| Number of Affiliations (ref: 1) | | | 0.09 |
| 2 | 2.6 (2.0 – 3.5) | 1.8 (1.3 – 2.5) | |
| >= 3 | 2.1 (1.6 – 2.8) | 1.6 (1.1 – 2.2) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.1 (0.8 – 1.3) | 1.0 (0.8 – 1.2) | |
| >= 50 | 0.4 (0.3 – 0.6) | 0.8 (0.5 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 5033) | | | 0.11 |
| 2 – 4 | 3.4 (2.2 – 5.3) | 2.7 (1.7 – 4.2) | |
| >= 4 | 6.0 (4.0 – 9.2) | 4.9 (3.2 – 7.6) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 5392) | 0.8 (0.6 – 1.0) | 0.7 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 0.9 (0.6 – 1.3) | 0.9 (0.5 – 1.4) | |
| Asia | 0.3 (0.1 – 0.6) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.8) | |
| Type of Affiliation (other vs university) | 2.3 (1.8 – 2.9) | 2.0 (1.5 – 2.5) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.4 (1.8 – 3.3) | 1.8 (1.3 – 2.5) | |
| high | 3.7 (2.8 – 4.8) | 2.7 (2.0 – 3.7) | |

* adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

**Table 3. Concordance odds ratios (95% CI's) for the chance of being cited, all types of articles included, N = 110, n = 5551)**

| **Content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (conc. vs. not) | 10 (5.6 – 18) | 13 (7.1 – 23) | 0.14 |
| Study Outcome (conc. vs. not, n = 1799)** | 2.9 (1.4 – 6.0) | 3.4 (1.6 – 7.1) | 0.06 |
| **Not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
| Article Type (conc. vs. not) | 1.1 (0.9 – 1.3) | | 0.00 (crude) |
| Funding Source (conc. vs. not, n = 1475)*** | 1.3 (0.8 – 1.9) | 1.2 (0.8 – 1.8) | 0.05 |
| Publisher (conc. vs. not, n = 4971)**** | 0.9 (0.7 – 1.2) | 0.9 (0.7 – 1.2) | 0.08 |
| Author Affiliation (conc. vs. not) | 0.7 (0.6 – 0.9) | 0.8 (0.7 – 1.0) | 0.08 |
| Author Gender (conc. vs. not, n = 5254)***** | 1.0 (0.8 – 1.3) | 1.0 (0.8 – 1.3) | 0.08 |
| Author Region (conc. vs. not) | 1.9 (1.6 – 2.4) | 2.0 (1.6 – 2.5) | 0.09 |
| Self-citation (yes vs no) | 6.1 (3.8 – 9.7) | 6.1 (3.7 – 9.9) | 0.09 |

* adjusted for study design of cited publication; ** publications with mixed results excluded from analysis; *** publications without reported funding source excluded from analysis; **** Three main publishers are differentiated: Wiley-Blackwell, BMJ, and Elsevier. Either the cited or the citing publication should be in one of these categories to be included in the analysis. ***** publications with unclear author's gender excluded from analysis; **N**: number of publication. **n**: number of potential citation paths.

# <u>Supplement</u>

**Text S1.** Protocol deviations

**Text S2.** Data extraction

**Text S3.** References of included literature on Strachan's hygiene hypothesis

**Table S1.** All characteristics of the publications in the hygiene hypothesis network.

**Table S2.** Top 6 of articles and authors within network.

**Table S3.** Odds ratios for the chance of *empirical* publications to be cited within full network.

**Table S4.** Odds ratios for the chance of *empirical* publications to be cited by *synthesis* publications.

**Table S5.** Sensitivity analyses on odds ratios for the chance of being cited, without the four most cited publications.

**Table S6.** Sensitivity analyses on odds ratios for the chance of being cited, with a 1-year time lag between cited and citing publication.

**Table S7.** Sensitivity analyses on odds ratios for the chance of being cited, without citing publications with less than 10 potential citation paths.

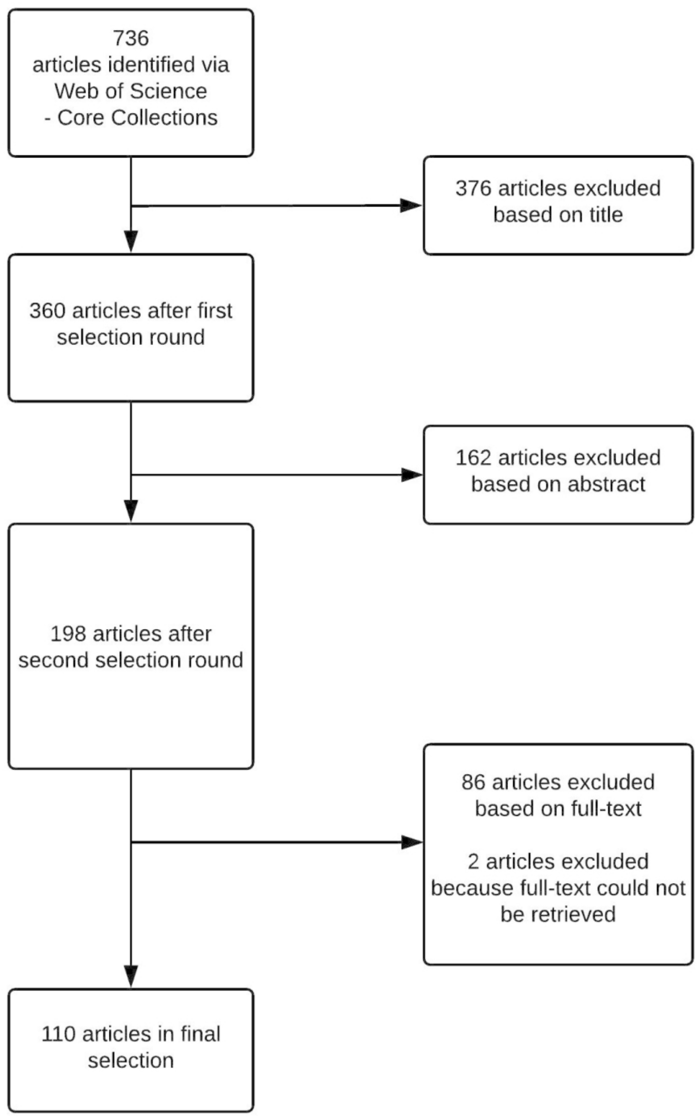


Figure 1. Flow diagram of article selection process.

101x155mm (300 x 300 DPI)

# Selective citation in the literature on the hygiene hypothesis

## Supplement

**Text S1.** Protocol deviations

**Text S2.** Data extraction

**Text S3.** References of included literature on Strachan's hygiene hypothesis

**Table S1.** All characteristics of the publications in the hygiene hypothesis network.

**Table S2.** Top 6 of articles and authors within network.

**Table S3.** Odds ratios for the chance of *empirical* publications to be cited within full network.

**Table S4.** Odds ratios for the chance of *empirical* publications to be cited by *synthesis* publications.

**Table S5.** Sensitivity analyses on odds ratios for the chance of being cited, without the four most cited publications.

**Table S6.** Sensitivity analyses on odds ratios for the chance of being cited, with a 1-year time lag between cited and citing publication.

**Table S7.** Sensitivity analyses on odds ratios for the chance of being cited, without citing publications with less than 10 potential citation paths.

**Text S1. Protocol deviations**

*Search strategy.* We ran some checks of our original search strategy (with '*hygiene hypothesis'* in combination with the pre-specified health outcomes). These checks indicated that many relevant publications in the period 1990 – 2000 were missed. Going through these missed publications we found out that the name for this hygiene hypothesis was not yet accepted or used. Also, we realised that almost all relevant publications within this network referred to Strachan's original study from 1989. We decided to change the search strategy, into *all publications referring to Strachan's original article.* Additionally, we limited the output to those publications that mentioned 'rhinitis' or a similar term in the title, abstract or keywords (see inclusion criteria).

*Inclusion criteria* (regarding the health outcome and types of exposure). Originally, all publications with either health outcome *rhinitis* or *asthma* were to be included. This yielded too many publications in our network, hence we decided to include only publications on rhinitis (or hay fever, or rhinoconjunctivitis). Inclusion solely based on asthma would also have yielded a network that was too large. Also, rhinitis is the original outcome as studied by Strachan. Similarly, we included only publications with exposures *number of siblings* and *infection history.* These are the two most important types of exposure related to the hygiene hypothesis as originally stated by Strachan. Number of siblings was originally studied by Strachan, and infections during childhood (or during pregnancy) was his explanation for the relationship between number of siblings and hay fever.

*Types of health outcome.* We intended to score both *asthma* and *rhinitis* as health outcomes. However, as we included only publications that studied the relationship with rhinitis, and excluded publications that were solely on asthma, we decided to focus on rhinitis. Thus, for the

empirical publications, we scored the relationships Siblings – Rhinitis and Infections – Rhinitis. (We also scored asthma, dermatitis and atopic sensitisation, but only for the sensitivity analyses.) Synthesis publications often did not differentiate between the different allergies in their general conclusion, so for the synthesis publications we scored statements on Siblings – Allergy and Infection – Allergy.

*Types of exposure.* We focused on two exposures: *number of siblings* (or household size or sibling order) and *history of infections* (as assessed by parental questionnaire, serology or medical records). We used this variable also in our analyses; it was scored as a) number of siblings only, b) only infection history, and c) both number of siblings and infection history.

*Study outcome scoring strategy.* There were many empirical publications with contradictory results, especially in the case of Infections where the results seemed to depend on the type of infection. In order to deal with this, we decided to use the *authors' conclusion* on Siblings – Rhinitis and Infections – Rhinitis as leading. We used 5 categories: 0. not measured or reported; 1. effect in line with hygiene hypothesis (inverse relationship); 2. no relationship; 3. effect contrary to hygiene hypothesis (positive relationship); 4. mixed or unclear results. Synthesis publications were scored in a similar way, but then on Siblings – Allergy and Infections – Allergy.

If no clear authors' conclusion was stated in the empirical publications, we used the data that were presented in the tables or the text and scored as follows: 1. statistically significant inverse relationship; 2. no statistically significant relationship; 3. statistically significant positive relationship; 4. mixed or unclear results. If both adjusted analyses and crude analyses were presented we preferred the adjusted ones. There is one exception: adjustment for Infections in

the relationship Siblings – Rhinitis; after all, the hygiene hypothesis states that infection is the mediator between siblings and rhinitis.

In the analyses we used one combined measure for study outcome, with three levels: 1) supportive; 2) mixed results / unclear; 3) non-supportive. Publications were scored as supportive if the exposure or exposures showed an inverse association with rhinitis. Publications were scored as non-supportive if there was no association or a positive association of the exposure with rhinitis. Publications were scored as mixed if the exposure or exposures showed mixed or unclear results, or if two exposures were investigated, and one showed an inverse association and the other showed no or a positive association.

*General conclusion about the hygiene hypothesis*. While studying the literature on the hygiene hypothesis we realised that many related hypotheses reside under this name, all evolved from one another. *The* hygiene hypothesis clearly does not exist. Support for one version of the hypothesis often implied the refutation of another (older) version. As authors assumed different versions, their general conclusion on the hygiene hypothesis would not be compatible. We decided to not score this general conclusion.

*Specificity.* We used 3 outcome categories for publication's specificity instead of 5.

*Study design.* Ecological studies were excluded from the network. Cohort studies were further classified as retrospective and prospective cohort studies. This latter step was data-driven because we realised during the analysis that prospective cohort studies were cited less often. During exploration of the data, we noticed a big different in the citation behaviour of retrospective and prospective cohorts studies. We therefore decided to amend our preregistered data analysis plan (http://hdl.handle.net/10411/ZKGGOG). We differentiated between these research designs (by assigning them a different categorical value), and take this difference into account in our analyses with study design as determinant or as covariate.

*Publisher*. In addition to the protocol we also scored the publisher of the journal, based on the information in Journal Citation Reports and in Web of Science. This could be interesting for publisher self-citation concordance analysis.

*Explained variance.* In addition to the original analysis plan in the protocol, we also calculated the explained variance of the adjusted models, so that these models are easier to compare. For this purpose we calculated McFadden's $R^2$ by the following formula: $R^2 = 1 - {LL_M}/{LL_0}$ in which $LL_M$ stands for the log likelihood of the current regression model and $LL_0$ stands for the log likelihood of the empty random-regression model. Both the current and the empty model (without predictors) were nested under the citing publication. Because of missing values for certain determinants (such as sample size), some models could be tested only on a sub-selection of citation paths. If this was the case, then $LL_0$ was calculated on the same sub-selection of citation paths.

**Text S2. Data extraction**

Most variables are described in the main document. Here follows some additional information for some of the variables.

**Study outcome** was scored as follows: 1. supportive of the hygiene hypothesis; 2. mixed or unclear results; 3. non-supportive of the hygiene hypothesis. An inverse relationship between past exposure and rhinitis is considered to be supportive for the hygiene hypothesis, while a neutral or positive relationship was scored as non-supportive. The scoring was based on the authors' interpretation of the results, as it was stated in the text of the publication. If the authors' interpretation was unclear, we scored study outcome based on the direction and statistical significance of the data. Non-empirical publications seldom distinguished between allergy subtypes, so we used the stated conclusion on general allergy as outcome measure.

Exposure could be either number of siblings (or order of siblings or household size) or history of bacterial or viral infection (as assessed by parental questionnaire, serology, or medical records). If the impact of number of both siblings and infection history was assessed and they were contradicting each other (with one exposure showing inverse association, the other a neutral or positive association), then study outcome was scored as mixed.

**Gender of the corresponding author** was assessed by first name, with help of www.genderchecker.com; if first name was not given, other articles of the same author were searched, and the profile of the author at the university or at www.researchgate.com was checked.

**Time to citation** was the number of years between the publication date of the cited publication and the submission date of the citing publication. This variable was not used as determinant of citation, but to determine the dataset of potential citation paths: only citation paths with a positive value for *time to citation* were considered a potential citation, and only potential citations were included in our dataset.

As *publication date* we used either the online publication date or the paper publication date, whichever was first. The average duration from submission to publication was nine months in this network. For 57 publications the *submission date* was not stated. In these cases, it was estimated by subtracting nine months from the publication date.

**Text S3. References of included literature on Strachan's hygiene hypothesis**


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**Table S1. All characteristics of the publications in the hygiene hypothesis network.**

| | | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| **Total** | | 110 | 5551 | 392 (7%) |

| **Publication characteristics - content-related** | **category** | **N publications** | **n potential citations** | **n actual citations (%)** |
|---|---|---|---|---|
| Type of Exposure | only Number of Siblings | 28 | 1512 | 100 (7%) |
| | only Infection History | 48 | 1946 | 144 (7%) |
| | both Siblings & Infections | 34 | 2093 | 148 (7%) |
| Study Outcome Exposure - Rhinitis | supportive | 41 | 2322 | 198 (9%) |
| | mixed results | 35 | 1913 | 129 (7%) |
| | non-supportive | 34 | 1316 | 65 (5%) |
| Publication Type / Study Design | Empirical | 73 | 3517 | 337 (10%) |
| | cross-sectional | 39 | 1697 | 179 (11%) |
| | case-control | 4 | 249 | 36 (14%) |
| | cohort | 29 | 1535 | 121 (8%) |
| | -retrospective | 15 | 817 | 89 (11%) |
| | -prospective | 14 | 718 | 32 (4%) |
| | intervention | 1 | 36 | 1 (3%) |
| | Synthesis | 37 | 2034 | 55 (3%) |
| | narrative review | 27 | 1423 | 16 (1%) |
| | systematic review | 2 | 80 | 20 (25%) |
| | -with meta-analysis | 1 | 8 | 1 (13%) |
| | editorial, etc | 8 | 531 | 19 (4%) |
| Sample Size (cat; for empirical publications) | low (1 – 999) | 24 | 909 | 56 (6%) |
| | medium (1000 – 7999) | 25 | 1327 | 143 (11%) |
| | high (>= 8000) | 24 | 1281 | 138 (11%) |
| Specificity | 0 (non-specific) | 27 | 1402 | 25 (2%) |
| | 1 | 39 | 1657 | 65 (4%) |
| | 2 (specific) | 44 | 2492 | 302 (12%) |

| **Publication characteristics - not content-related** | **category** | **N publications** | **n potential citations** | **n actual citations (%)** |
|---|---|---|---|---|
| Conclusive Title | not conclusive | 99 | 5026 | 375 (7%) |
| | conclusive | 11 | 525 | 17 (3%) |

| | | | | |
|---|---|---|---|---|
| Funding Source | non-profit | 44 | 2188 | 214 (10%) |
| | for-profit | 1 | 38 | 1 (3%) |
| | both | 12 | 559 | 51 (9%) |
| | not reported / unclear | 53 | 2766 | 126 (5%) |
| Number of Authors | 1 - 2 | 32 | 2017 | 89 (4%) |
| | 3 - 5 | 41 | 2143 | 155 (7%) |
| | >= 6 | 37 | 1391 | 148 (11%) |
| Number of Affiliations | 1 | 36 | 2276 | 111 (5%) |
| | 2 | 24 | 1168 | 108 (9%) |
| | >= 3 | 50 | 2107 | 173 (8%) |
| Number of References | < 30 | 35 | 2307 | 194 (8%) |
| | 30 – 50 | 49 | 2060 | 159 (8%) |
| | >= 50 | 26 | 1184 | 39 (3%) |

| **Journal characteristics** | **category** | **N publications** | **n potential citations** | **n actual citations (%)** |
|---|---|---|---|---|
| Journal Impact Factor (cat) | 0 - 2 | 28 | 1275 | 27 (2%) |
| | 2 - 4 | 41 | 2087 | 145 (7%) |
| | >= 4 | 32 | 1671 | 176 (11%) |
| Publisher | Wiley-Blackwell | 41 | 2107 | 82 (4%) |
| | BMJ | 15 | 1170 | 213 (18%) |
| | Elsevier | 18 | 894 | 43 (5%) |
| | other | 36 | 1380 | 54 (4%) |

| Author characteristics | category | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| Gender | male | 65 | 3368 | 265 (8%) |
| | female | 42 | 2024 | 123 (6%) |
| | unclear | 3 | 159 | 4 (3%) |
| Affiliation | university | 88 | 4402 | 258 (6%) |
| | government | 9 | 410 | 22 (5%) |
| | industry / other | 13 | 739 | 112 (15%) |
| Country | Europe | 62 | 3903 | 324 (8%) |
| | UK | 26 | 1946 | 165 (8%) |
| | Germany | 11 | 594 | 19 (3%) |
| | Finland | 8 | 516 | 33 (6%) |
| | Italy | 7 | 418 | 85 (20%) |
| | North-America | 19 | 688 | 38 (6%) |
| | USA | 18 | 662 | 36 (5%) |
| | Asia | 21 | 484 | 9 (2%) |
| | Turkey | 9 | 303 | 7 (2%) |
| | Japan | 4 | 60 | 0 (0%) |
| | Australia / New Zealand | 8 | 476 | 21 (4%) |
| | Australia | 7 | 407 | 21 (5%) |

| Citation characteristics | category | n potential citations | n actual citations (%) |
|---|---|---|---|
| Authority | low (0-2) | 2279 | 81 (4%) |
| | medium (2-10) | 1326 | 108 (8%) |
| | high (>= 10) | 1946 | 203 (10%) |
| Time to Citation (in years) | 0 – 1 | 494 | 38 (8%) |
| | 1 – 2 | 521 | 56 (11%) |
| | 2 – 3 | 527 | 50 (9%) |
| | 3 – 4 | 459 | 33 (7%) |
| | 4 – 5 | 456 | 40 (9%) |
| | 5 – 6 | 441 | 35 (8%) |
| | 6 – 7 | 404 | 28 (7%) |
| | 7 – 8 | 372 | 22 (6%) |
| | => 8 | 1877 | 90 (5%) |
| Self-citation | no | 5462 | 365 (7%) |
| | yes | 89 | 27 (30%) |

**Table S2. Top 6 of articles (above) and authors (below) within network, based on the number of received citations up to 2017.**

| Article rank | Article's first author | Title | Year | Nr. of received citations (% of potential citations) |
|---|---|---|---|---|
| 1 | Matricardi | Cross sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus | 1997 | 35 (35 %) |
| 2 | Bodner | Family size, childhood infections and atopic diseases | 1998 | 32 (33 %) |
| 3 | Matricardi | Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study | 2000 | 32 (38 %) |
| 4 | Strachan | Family structure, neonatal infection, and hay fever in adolescence | 1996 | 28 (26 %) |
| 5 | Farooqi | Early childhood infection and atopic disorder | 1998 | 21 (23 %) |
| 6 | Karmaus | Does a higher number of siblings protect against the development of allergy and asthma? A review | 2002 | 19 (26 %) |

| Author rank | Author | Affiliation | Country | Nr. of received citations (= authority) |
|---|---|---|---|---|
| 1 | P. Matricardi | Consiglio Nazionale delle Ricerche, Rome | Italy | 84 |
| 2 | F. Rosmini | Istituto Superiore di Sanita, Rome | Italy | 84 |
| 3 | L. Ferrigno | Istituto Superiore di Sanita, Rome | Italy | 84 |
| 4 | M. Rapicetta | Istituto Superiore di Sanita, Rome | Italy | 67 |
| 5 | D. Strachan | University of London, London | United Kingdom | 57 |
| 6 | S. Bonini | Consiglio Nazionale delle Ricerche, Rome | Italy | 49 |

**Table S3. Odds ratios (95% CIs) for the chance of *empirical* publications to be cited within full network (N = 73, n = 3517).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.04 |
| only Number of Siblings | 0.5 (0.3 – 0.6) | 0.4 (0.3 – 0.5) | |
| only Infection History | 1.0 (0.8 – 1.3) | 0.7 (0.5 – 0.9) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.07 |
| mixed / unclear results | 1.4 (0.9 – 2.3) | 1.1 (0.7 – 1.9) | |
| supportive results | 4.8 (3.2 – 7.0) | 5.1 (3.3 – 7.8) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Study Design (ref: cross-sectional) | | | 0.02 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| Sample Size (ref: low) | | *** | 0.02 |
| medium | 1.6 (1.2 – 2.3) | 1.6 (1.0 – 2.6) | |
| high | 1.6 (1.2 – 2.3) | 1.9 (1.2 – 3.0) | |
| Specificity (ref: low) | | | 0.05 |
| medium | 4.6 (2.6 – 8.2) | 3.5 (1.8 – 6.5) | |
| high | 7.4 (4.5 – 12) | 6.1 (3.5 – 10) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.3 (0.2 – 0.6) | 0.3 (0.1 – 0.5) | 0.03 |
| Funding Source (ref: exclusively non-profit) | | | 0.02 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.2) | 0.8 (0.5 – 1.1) | |
| not reported | 0.8 (0.6 – 1.1) | 0.8 (0.6 – 1.1) | |
| Number of Authors (ref: 1-2) | | | 0.03 |
| 3 - 5 | 1.1 (0.7 – 1.6) | 1.2 (0.7 – 1.8) | |
| >= 6 | 1.7 (1.2 – 2.6) | 1.8 (1.1 – 2.9) | |
| Number of Affiliations (ref: 1) | | | 0.03 |
| 2 | 1.7 (1.2 – 2.4) | 1.8 (1.2 – 2.6) | |
| >= 3 | 1.3 (0.9 – 1.7) | 1.6 (1.2 – 2.4) | |
| Number of References (ref: <30) | | | 0.02 |
| 30 - 50 | 0.9 (0.7 – 1.1) | 1.0 (0.7 – 1.2) | |
| >= 50 | 0.3 (0.1 – 0.7) | 0.3 (0.1 – 0.8) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 3266) | | | 0.06 |
| 2 – 4 | 2.8 (1.7 – 4.5) | 2.6 (1.6 – 4.3) | |
| >= 4 | 5.9 (3.7 – 9.5) | 6.6 (4.0 – 11) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 3457) | 0.6 (0.5 – 0.8) | 0.7 (0.5 – 0.9) | 0.03 |
| Region (ref: Europe) | | | 0.04 |
| North-America | 0.5 (0.3–0.97) | 0.6 (0.3 – 1.1) | |
| Asia | 0.2 (0.1 – 0.4) | 0.1 (0.1 – 0.3) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.9) | |
| Type of Affiliation (other vs university) | 2.4 (1.9 – 3.2) | 2.2 (1.7 – 2.9) | 0.04 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.05 |
| medium | 2.0 (1.4 – 3.0) | 2.1 (1.4 – 3.0) | |
| high | 3.6 (2.6 – 5.1) | 3.8 (2.7 – 5.5) | |

* adjusted for study design and log sample size. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited publications; n = number of potential citation paths.

**Table S4. Odds ratios (95% CIs) for the chance of *empirical* publications to be cited by *synthesis* publications (N = 73, n = 1097).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.07 |
| only Number of Siblings | 0.4 (0.2 – 0.7) | 0.3 (0.2 – 0.6) | |
| only Infection History | 1.8 (1.1 – 3.0) | 1.3 (0.7 – 2.3) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 0.5 (0.2 – 1.0) | 0.4 (0.2 – 0.9) | |
| supportive results | 6.0 (3.1 – 12) | 7.3 (3.5 – 15) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Study Design (ref: cross-sectional) | | | 0.04 (crude) |
| case control | 2.1 (1.1 – 4.2) | | |
| retrospective cohort | 1.0 (0.6 – 1.6) | | |
| prospective cohort | 0.3 (0.1 – 0.6) | | |
| Sample Size (ref: low) | | *** | 0.04 |
| medium | 1.6 (0.9 – 2.8) | 1.9 (0.8 – 4.6) | |
| high | 1.3 (0.7 – 2.3) | 1.9 (0.8 – 4.4) | |
| Specificity (ref: low) | | | 0.06 |
| medium | 6.9 (2.8 – 17) | 4.3 (1.6 – 12) | |
| high | 7.6 (3.4 – 17) | 5.6 (2.3 – 13) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.2 – 0.9) | 0.2 (0.1 – 0.6) | 0.05 |
| Funding Source (ref: exclusively non-profit) | | | 0.04 |
| profit or both profit/non-profit | 0.7 (0.4 – 1.2) | 0.7 (0.4 – 1.3) | |
| not reported | 0.6 (0.4 – 1.0) | 0.5 (0.3 – 0.9) | |
| Number of Authors (ref: 1-2) | | | 0.06 |
| 3 - 5 | 0.6 (0.3 – 1.1) | 0.6 (0.3 – 1.2) | |
| >= 6 | 1.5 (0.8 – 2.8) | 1.5 (0.7 – 3.2) | |
| Number of Affiliations (ref: 1) | | | 0.04 |
| 2 | 1.3 (0.7 – 2.4) | 1.6 (0.8 – 3.1) | |
| >= 3 | 1.2 (0.7 – 2.0) | 2.0 (1.1 – 3.6) | |
| Number of References (ref: <30) | | | 0.04 |
| 30 - 50 | 0.7 (0.5 – 1.1) | 0.8 (0.5 – 1.2) | |
| >= 50 | 0.2 (0.04–0.9) | 0.2 (0.04–1.0) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 1015) | | | 0.11 |
| 2 – 4 | 2.6 (1.2 – 5.6) | 2.2 (1.0 – 4.9) | |
| >= 4 | 8.2 (3.8 – 18) | 9.2 (4.1 – 21) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 1079) | 0.5 (0.3 – 0.8) | 0.6 (0.4 – 0.9) | 0.04 |
| Region (ref: Europe) | | | 0.07 |
| North-America | 0.7 (0.2 – 2.2) | 0.9 (0.3 – 2.9) | |
| Asia | 0.2 (0.1 – 0.7) | 0.1 (0.02–0.3) | |
| Australia / New-Zealand | 0.2 (0.1 – 0.6) | 0.2 (0.9 – 0.7) | |
| Type of Affiliation (other vs university) | 3.3 (2.2 – 5.1) | 3.1 (2.0 – 4.8) | 0.07 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.07 |
| medium | 2.6 (1.4 – 4.6) | 2.7 (1.4 – 5.1) | |
| high | 4.0 (2.3 – 7.1) | 4.1 (2.2 – 7.6) | |

* adjusted for study design and log sample size. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited (*empirical*) publications; n = number of potential citation paths.

**Table S5. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited within full network, without the four most cited publications. N = 106, n = 5164).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.08 |
| only Number of Siblings | 1.4 (1.0 – 1.9) | 0.9 (0.6 – 1.3) | |
| only Infection History | 1.0 (0.8 – 1.4) | 1.0 (0.7 – 1.4) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.08 |
| mixed / unclear results | 0.8 (0.5 – 1.1) | 1.2 (0.8 – 2.0) | |
| supportive results | 1.0 (0.7 – 1.5) | 1.5 (1.0 – 2.2) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 2.9 (2.1 – 3.9) | | 0.03 (crude) |
| Study Design (ref: cross-sectional) | | | 0.08 (crude) |
| case control | 0.3 (0.1 – 0.8) | | |
| retrospective cohort | 1.1 (0.8 – 1.5) | | |
| prospective cohort | 0.5 (0.3 – 0.8) | | |
| narrative review | 0.1 (0.1 – 0.2) | | |
| systematic review | 4.5 (2.5 – 8.0) | | |
| editorial / other | 0.4 (0.2 – 0.7) | | |
| Sample Size (ref: low, n = 3130) | | *** | 0.02 |
| medium | 2.3 (1.4 – 3.7) | 1.6 (0.9 – 2.9) | |
| high | 3.3 (2.1 – 5.3) | 2.5 (1.5 – 4.2) | |
| Specificity (ref: low) | | | 0.09 |
| medium | 2.4 (1.5 – 3.9) | 3.3 (1.9 – 5.6) | |
| high | 5.6 (3.6 – 8.7) | 3.5 (2.1 – 5.6) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.6 (0.4 – 1.0) | 0.5 (0.3 – 0.9) | 0.08 |
| Funding Source (ref: exclusively non-profit) | | | 0.08 |
| profit or both profit/non-profit | 1.4 (1.0 – 2.0) | 1.4 (0.9 – 2.0) | |
| not reported | 0.5 (0.4 – 0.7) | 1.0 (0.7 – 1.4) | |
| Number of Authors (ref: 1-2) | | | 0.08 |
| 3 - 5 | 1.2 (0.9 – 1.7) | 0.7 (0.5 – 1.1) | |
| >= 6 | 2.0 (1.4 – 2.8) | 0.9 (0.6 – 1.4) | |
| Number of Affiliations (ref: 1) | | | 0.08 |
| 2 | 1.8 (1.3 – 2.5) | 1.1 (0.8 – 1.6) | |
| >= 3 | 1.0 (0.7 – 1.4) | 0.6 (0.4 – 0.9) | |

| | | | |
|---|---|---|---|
| Number of References (ref: <30) | | | 0.08 |
| 30 - 50 | 0.9 (0.7 – 1.2) | 0.7 (0.6 – 1.0) | |
| >= 50 | 0.6 (0.4 – 0.8) | 0.8 (0.5 – 1.3) | |

| **Journal characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4752) | | | 0.09 |
| 2 – 4 | 2.8 (1.8 – 4.3) | 2.5 (1.6 – 3.9) | |
| >= 4 | 4.0 (2.6 – 6.1) | 3.5 (2.2 – 5.5) | |

| **Author characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Gender (female vs male, n = 5005) | 1.4 (1.1 – 1.8) | 1.2 (0.9 – 1.6) | 0.07 |
| Region (ref: Europe) | | | 0.08 |
| North-America | 1.2 (0.8 – 1.8) | 1.0 (0.6 – 1.6) | |
| Asia | 0.4 (0.2 – 0.8) | 0.4 (0.2 – 0.8) | |
| Australia / New-Zealand | 0.8 (0.5 – 1.2) | 0.7 (0.5 – 1.2) | |
| Type of Affiliation (other vs university) | 1.6 (1.2 – 2.2) | 1.4 (1.1 – 2.0) | 0.08 |

| **Citation characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Authority (ref: low) | | | 0.08 |
| medium | 2.1 (1.5 – 2.9) | 1.6 (1.1 – 2.2) | |
| high | 2.2 (1.6 – 3.0) | 1.6 (1.1 – 2.2) | |

In these sensitivity analyses, the four most cited publications shown in Table S2 are excluded as *cited* publications; they are still included as *citing* publications. * adjusted for study design and log sample size. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited publications; n = number of potential citation paths.

**Table S6. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited within full network, with a 1-year time lag between cited and citing publication. (N = 110, n = 5057).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.11 |
| only Number of Siblings | 0.7 (0.5 – 1.0) | 0.4 (0.3 – 0.7) | |
| only Infection History | 1.2 (1.0 – 1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 1.2 (0.8 – 1.7) | 2.2 (1.4 – 3.5) | |
| supportive results | 1.7 (1.2 – 2.4) | 3.2 (2.2 – 4.6) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.4 (3.2 – 6.0) | | 0.05 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.4 (1.9 – 6.2) | | |
| editorial / other | 0.3 (0.1 – 0.4) | | |
| Sample Size (ref: low, n = 3199) | | | 0.02 |
| medium | 1.6 (1.1 – 2.2) | 1.4 (0.8 – 2.4) | |
| high | 1.4 (1.0 – 2.1) | 1.6 (0.9 – 2.6) | |
| Specificity (ref: low) | | | 0.12 |
| medium | 2.8 (1.6 – 4.7) | 3.1 (1.7 – 5.6) | |
| high | 10.3 (6.4 – 17) | 6.1 (3.6 – 10) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.5 (0.3 – 0.8) | 0.3 (0.2 – 0.5) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.10 |
| profit or both profit/non-profit | 0.8 (0.6 – 1.2) | 0.8 (0.5 – 1.1) | |
| not reported | 0.4 (0.3 – 0.5) | 0.8 (0.6 – 1.1) | |
| Number of Authors (ref: 1-2) | | | 0.10 |
| 3 - 5 | 2.0 (1.5 – 2.8) | 1.1 (0.7 – 1.8) | |
| >= 6 | 3.7 (2.7 – 5.0) | 1.7 (1.0 – 2.6) | |
| Number of Affiliations (ref: 1) | | | 0.10 |
| 2 | 3.0 (2.2 – 4.1) | 2.1 (1.4 – 3.0) | |
| >= 3 | 2.2 (1.7 – 2.9) | 1.7 (1.2 – 2.3) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.1 (0.9 – 1.4) | 1.0 (0.8 – 1.3) | |
| >= 50 | 0.5 (0.3 – 0.7) | 0.7 (0.4 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4580) | | | 0.12 |
| 2 – 4 | 3.2 (2.0 – 4.9) | 2.5 (1.6 – 4.0) | |
| >= 4 | 5.4 (3.5 – 8.4) | 4.5 (2.9 – 7.1) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 4913) | 0.8 (0.6 – 1.0) | 0.7 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 1.0 (0.7 – 1.5) | 1.0 (0.6 – 1.8) | |
| Asia | 0.3 (0.2 – 0.7) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.9) | 0.5 (0.3 – 0.9) | |
| Type of Affiliation (other vs university) | 2.3 (1.8 – 2.9) | 1.9 (1.5 – 2.5) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.8 (1.9 – 3.9) | 1.9 (1.3 – 2.7) | |
| high | 4.0 (2.9 – 5.5) | 2.8 (2.0 – 4.0) | |

* adjusted for study design. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

**Table S7. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited, without citing publications with less than 10 potential citation paths (N = 110, n = 5507).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.10 |
| only Number of Siblings | 0.8 (0.6 – 1.1) | 0.5 (0.4 – 0.7) | |
| only Infection History | 1.2 (1.0 – 1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 1.2 (0.8 – 1.7) | 2.3 (1.5 – 3.6) | |
| supportive results | 1.7 (1.3 – 2.4) | 3.0 (2.1 – 4.2) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.2 (3.1 – 5.6) | | 0.04 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (1.0 – 2.2) | | |
| retrospective cohort | 0.8 (0.6 – 1.1) | | |
| prospective cohort | 0.4 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.3 (1.8 – 5.8) | | |
| editorial / other | 0.3 (0.2 – 0.4) | | |
| Sample Size (ref: low, n = 3423) | | | 0.02 |
| medium | 1.5 (1.1 – 2.1) | 1.5 (0.9 – 2.5) | |
| high | 1.4 (1.0 – 2.0) | 1.7 (1.1 – 2.8) | |
| Specificity (ref: low) | | | 0.11 |
| medium | 2.2 (1.4 – 3.6) | 2.5 (1.4 – 4.2) | |
| high | 8.6 (5.6 – 13) | 4.9 (3.1 – 7.9) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.3 – 0.7) | 0.3 (0.2 – 0.5) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.09 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.3) | 0.8 (0.6 – 1.2) | |
| not reported | 0.4 (0.3 – 0.5) | 0.7 (0.5 – 1.0) | |
| Number of Authors (ref: 1-2) | | | 0.09 |
| 3 - 5 | 2.0 (1.5 – 2.7) | 1.1 (0.7 – 1.7) | |
| >= 6 | 3.8 (2.8 – 5.2) | 1.7 (1.1 – 2.6) | |
| Number of Affiliations (ref: 1) | | | 0.09 |
| 2 | 2.8 (2.1 – 3.7) | 1.9 (1.3 – 2.6) | |
| >= 3 | 2.2 (1.7 – 2.9) | 1.6 (1.2 – 2.3) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.0 (0.8 – 1.3) | 0.9 (0.7 – 1.2) | |
| >= 50 | 0.4 (0.3 – 0.6) | 0.8 (0.4 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4955) | | | 0.11 |
| 2 – 4 | 3.2 (2.1 – 5.0) | 2.5 (1.6 – 3.9) | |
| >= 4 | 5.7 (3.8 – 8.8) | 4.6 (3.0 – 7.2) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 5350) | 0.8 (0.6 – 1.0) | 0.8 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 0.9 (0.6 – 1.3) | 0.9 (0.5 – 1.4) | |
| Asia | 0.3 (0.2 – 0.6) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.8) | |
| Type of Affiliation (other vs university) | 2.4 (1.9 – 3.0) | 2.0 (1.6 – 2.6) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.4 (1.8 – 3.3) | 1.8 (1.3 – 2.5) | |
| high | 3.8 (2.9 – 5.1) | 2.9 (2.2 – 4.0) | |

* adjusted for study design. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

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# Selective citation in the literature on the hygiene hypothesis: a citation analysis on the association between infections and rhinitis

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| | |

# Selective citation in the literature on the hygiene hypothesis: a citation analysis on the association between infections and rhinitis

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## Conflict of Interest

All authors declare to have no conflict of interest.

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## Abstract

**Objective:** Our objective was to assess the occurrence and determinants of selective citation in scientific publications on Strachan's original hygiene hypothesis. His hypothesis states that lack of exposure to infections in early childhood increases the risk of rhinitis.

**Setting:** Web of Science Core Collection.

**Participants:** We identified 110 publications in this network, consisting of 5551 potential citations.

**Primary and secondary outcome measures:** Whether a citation occurs or not, measured and analysed according to the pre-registered protocol.

**Results:** We found evidence for citation bias in this field: publications supportive of the hypothesis were cited more often than non-supportive publications (odds ratio adjusted for study design [adjOR]: 2.2, 95% confidence interval [CI]: 1.6 - 3.1), and the same was the case for publications with mixed findings (adjOR: 3.1, CI: 2.2 - 4.5). Other relevant determinants for citation were type of exposure, specificity, journal impact factor, authority and self-citation. Surprisingly, prospective cohort studies were cited less often than other empirical studies.

**Conclusions:** There is clear evidence for selective citation in this research field, and particularly for citation bias.

## Strengths and limitations of this study

- The study assesses how evidence regarding the hygiene hypothesis propagates over time by analysing the likelihood of citation.
- It investigates which characteristics of a publication – such as study outcome, journal impact factor, author gender and affiliation, and authority within the field – have an impact on citation.
- We check whether supportive studies are cited more often by other studies within the field, and in particular by reviews (which are supposed to give an unbiased overview of the literature).
- Limitation: only articles related to the original hygiene hypothesis are included in this analysis.

## Background

The hygiene hypothesis postulates that a high degree of hygiene in early life will increase the risk of developing allergies later in life (1, 2). The underlying mechanism has been the topic of scientific debate. Over time, this debate led to several adaptations and extensions of the hygiene hypothesis, which, as such, provides a good example of how science progresses. Ideally, this progress should be based on all existing evidence, but this is not always the case (3). A citation analysis can help to reveal which part of the available evidence is taken into account, and which evidence is ignored. The current study does not concern the validity of the hygiene hypothesis per se, but rather the citation relations within the scientific literature on this hypothesis.

The hygiene hypothesis was originally proposed to explain the rising prevalence of allergies, with up to 20% to 40% of the population in developed countries being affected (4). Modern, urbanized life in developed countries generally shows higher levels of hygiene than in previous times or in developing countries. Hygiene limits exposure to infections. Exposure to infections, especially early in life, helps to develop and adapt the immune system to the environment in which we happen to live, in such a way that it learns to discriminate between harmless and harmful intruders. According to the hygiene hypothesis, it is this lack of exposure to relatively harmless intruders early in life, that causes the immune system to malfunction later in life. Hence the rise in allergies.

The hygiene hypothesis has been amended several times since its early days to give rise to newer theories such as the '*old friends hypothesis*' (5, 6). According to this theory, it is not hygiene per se that is causing the rise in allergy prevalence, but the lack of exposure to *some specific* infections, and also to the gut microbiome and to non-viable intruders from the natural environment, such as endotoxins. Humans have been exposed to these 'old friends' for many centuries and our immune system has co-evolved in their presence. As a result, our immune system has become dependent on the presence of these old friends in order to develop and function properly. This adapted hygiene hypothesis states that lack of exposure to these old friends may give rise not only to allergies, but to auto-immune diseases as well.

The original hygiene hypothesis and its later adaptations have a lot in common, and much of the evidence that is supportive for one hypothesis is equally supportive for the others. However, this is not always the case. In our project, publications are classified as either supportive or unsupportive with regards to a hypothesis. For that reason it is important to precisely define the investigated hypothesis. In our citation network, we focus on the hygiene hypothesis as it was originally stated by Strachan, and not on later modifications (1, 2). This allows us to investigate the development of this hypothesis from the start. Concretely, this means that we focus on the impact of infections and the number of siblings on the development of rhinitis, like in Strachan's original study (2).

The number of publications in the research on the hygiene hypothesis is large. It is therefore not feasible for authors to cite every relevant publication in the network and some kind of selection needs to take place. If this selection is based on study outcome, we speak of citation bias (3, 7). The consequences of citation bias can be similar to those of publication bias and reporting bias: disregard of counter-evidence leading to unfounded consensus (8) or polarisation (9), ill-advised research programmes and research waste (8, 10), distorted information in the media (11), and misguided medical decisions (12). Citation bias has been studied in many disciplines. Our systematic review gives an overview of these studies (13) . Many of these studies showed evidence for citation bias in their field, with supportive publications being cited about twice as often as non-supportive ones.

Factors other than study outcome may also have an impact on citation, as was recently shown by Onodera and Yoshikane (14). Measures for journal status (impact factor), author status (number of citations, country of affiliation), and collaboration (number of authors, number of affiliatons) were often found to be related to citation count. The same was consistently found for the number of references of the cited publication. Furthermore, the reporting (15) and source (16, 17) of funding were shown to be related to citation, but the impact of author's affiliation (18) and gender (19-21) is less clear. On the other hand, sample size and study design - both markers of study quality, and as such legimate reasons to base a citation on - often seem unrelated to citation (17, 18, 22-24). In our previous citation networks, we also found associations with self-citation and the specificity of a publication, but not with the title of a publication (25, 26).

In our study, we aimed a) to assess the occurrence of citation bias in the scientific literature on the original hygiene hypothesis; and b) test for other signs of selective citation by assessing the impact of the other factors described above. We will make use of the claim-specific methodology developed by Greenberg (8), but with a modification of the statistical analysis that allows us to test the impact of multiple factors, adjust for study design and take into account the variation in publication time.

## Method

Prior to performing the citation network analysis, we described our methods in a study protocol and stored it at an online repository (27). (Protocol deviations are described in the supplement, Text S1.) In brief, we applied a search strategy to the Web of Science Core Collection (WoSCC), identified relevant literature, downloaded these records with their reference lists, extracted data for each publication, built a dataset with potential citation paths and used specialised software to determine which citations had occurred. These steps will be explained in more detail below. Article selection (first based on title, then on abstract and finally full-text;

Figure 1) and data extraction were performed independently by MJEU and BD. Results were compared after each step, and disagreements were resolved in consensus meetings.

For clarification: a publication in our network can both cite and be cited by other publications in the network, leading to a multitude of citation paths. Not all citation paths are possible as one can only cite articles that were published before. In our study, a citation is considered possible if the cited publication is published before the citing publication is submitted. If such *potential* citation occurred, we call it an *actual* citation. (See also supplementary Text S2.)

**Search strategy**

First, we took Strachan's seminal article in which the hygiene hypothesis was launched as point of departure (2). Next, we identified all literature within WoSCC referring to this article. Finally, we limited the output to publications that mentioned hay fever in their title, keywords or abstract (*"hay fever" OR* "*hayfever" OR* "*hay-fever" OR "rhinitis" OR "rhino*"*). The search was performed by BD and updated until 16 August 2017. Only English language publications were included.

The search output was then limited to publications that investigated exposures related to the original hygiene hypothesis. This means that only publications investigating the effect of *number of siblings* and *infection history* were included. Publications on helminths infections were excluded, as different versions of the hygiene hypothesis would make contradictory predictions regarding their impact on allergies. Both empirical and non-empirical publications were included.

**Data extraction**

A range of characteristics were extracted or derived from each included publication. These characteristics are described below and were all tested as determinant of citation in the statistical analysis.

**Publication characteristics – content-related.** The following variables were in this subcategory: type of exposure, publication type, sample size, specificity, and study outcome.

*Type of exposure* refers to the type of exposure that is being studied or reviewed: only number of siblings, only infection history, or both.

*Publication type* was classified into empirical and non-empirical publications. Empirical publications were further classified into the following *study designs*: cross-sectional, case-control, retrospective cohort, prospective cohort, and experimental studies. Non-empirical publications were further classified into: narrative reviews, systematic reviews, and other (editorials, leading articles, commentaries).

*Sample size* concerned the number of participants in the publications. Non-empirical publications had no sample size. The sample size of the empirical publications was classified into three equal categories based on tertiles.

The *specificity* of the publications varied. Some publications only deal with Strachan's hygiene hypothesis, others are broader. Specificity ranges from 1 (very broad) to 3 (very specific). For instance, an empirical publication that only investigates the association between number of siblings and rhinitis would be classified as '3'; if it also investigates the impact of helminth infections and growing up on a farm, and if it also includes other health outcomes such as asthma or auto-immune diseases, it would be classified as '1'.

*Study outcome* was scored as follows: 1. supportive of the hygiene hypothesis; 2. mixed or unclear results; 3. non-supportive of the hygiene hypothesis. An inverse relationship between past exposure and rhinitis is considered to be supportive for the hygiene hypothesis, while a neutral or positive relationship was scored as non-supportive. The scoring was based on the authors' interpretation of the results, as it was stated in the text of the publication. (See also Text S2 for more details.)

**Publication characteristics - not content-related.** The following variables were in this category: conclusiveness of the title, funding source, number of authors, number of affiliations, and number of references. *Title conclusiveness* was coded as yes if in the title a conclusion was stated that included the direction of the relationship (e.g. "Inverse relation between infections and allergies"), otherwise as no (e.g. "Infections, rhinitis, and their relationship"). *Funding source* was coded as non-profit (e.g. government or university), for-profit, both, or not reported.

**Journal characteristics.** The following variables were in this category: publisher and journal impact factor. *Journal impact factor*, in the publication year of the cited publication, was retrieved from the Journal Citation Reports (JCR) database. *Journal publisher* was also retrieved from JCR.

**Author characteristics.** The following variables were in this category: *gender* of the corresponding author (see also Text S2), *country* of the corresponding author, and affiliation of the corresponding author. *Affiliation* was classified as government, university, industry or other.

**Citation characteristics.** There were some variables that depend on the cited publication as well as the citing publication: self-citation and within-network authority. A *self-citation* was defined as a citation between two publications that have at least one author in common.

*Authority* was a measure for the authority of the authors within the network. It was calculated for each author and each year separately, by counting the number of within-network citations to all publications in which the author had been involved. As the number of citations is likely to increase each year, so does the author's authority. Because we were interested in the authority at the moment of citation, the authority value of a cited publication also depends on the publication year of the citing publication. In case of multiple authors, we used the authority value of the author with the highest authority in that year.

## Statistical analysis

The dataset consisted of all potential citation paths between cited and citing publications. A potential citation path means that the cited publication is published before submission of the citing publication. The underlying assumption is that publications can only cite other publications up to the date of submission of the citing publication, and that publications can only be cited from their publication date onwards. All analyses were pre-registered in the study protocol unless mentioned otherwise.

**Impact of the cited publication characteristics.** Our binary dependent variable was citation within the network (or, more precisely, whether a potential citation had occurred or not). This was determined by the built-in algorithm of CitNetExplorer (28). This algorithm makes use of reference lists that can be downloaded from the Web of Science Core Collection. It links the reference lists of all publications in the network with the actual publications in the network. If possible, this linkage was done by DOI, the unique Digital Object Identifier assigned to most present-day publications; otherwise it was based on a combination of first author's surname, first author's first initial, publication year, volume number and first page number. The determinants of citation in our analyses were the characteristics of the cited publication as described above.

Since each publication could refer to multiple other publications, the potential citation paths were related. Therefore we used a multilevel approach in which the potential citations were nested under the citing publication. Specifically, we performed a univariate random-effects logistic regression for each determinant of citation. We repeated these analyses while adjusting for study design, as a proxy for study quality. Another proxy for study quality would be the study sample size. However, as reviews do not have a sample size, this adjusted analysis could only be performed on the sub-selection of cited empirical publications so we did not adjust for sample size in the main analysis.

In addition to the original analysis plan in the protocol, we also calculated the explained variance of the adjusted models, so that these models are easier to compare. For this purpose we calculated McFadden's $R^2$.

**Additional analyses** were performed on sub-selections of the network: a) only cited empirical publications were included (to investigate which empirical evidence is picked up by the rest of the field; explorative analysis); b) only cited empirical publications and citing synthesis publications were included (to investigate which empirical evidence is picked up particularly by reviews and editorials). These analyses were adjusted not only for study design but also for log-transformed sample size because in these sub-selections all cited publications had a sample size.

To check the robustness of our findings we also ran some sensitivity analyses in which the following publications or citation paths were excluded: c) the most cited publications (explorative analysis); d) citation paths with less than one year between publication date of the cited publication and submission date of the citing publication were excluded (to check if a lag time would make a difference as it takes some time before most publications are known and have an impact); e) citing publications that have less than ten potential citations.

**Concordance analysis.** Where applicable, we also calculated whether the cited and the citing publications had the same characteristics (*concordance*). This would, for instance, be the case if supportive publications would prefer to cite other supportive publications, and if non-supportive publications would prefer to cite other non-supportive publications. If citation would be based on the concordance of study outcome, it would be another measure of citation bias. To test if concordance on several characteristics has an impact on the likelihood of citation, univariate and adjusted (for study design) fixed-effects logistic regression analyses were applied.

### Software

We used the built-in algorithm of CitNetExplorer 1.0.0 to extract the actual citations between publications (28). We used R 3.2.4 to create a dataset with all potential citation paths, based on the data extraction sheet and the actual citations, and also to calculate the within-network authority and self-citation score for each potential citation path. Finally, we used Stata 13.1 to analyse the results.

### Patient and public involvement

No patients were involved in this study.

## Results

A total number of 110 publications were identified that fit our criteria, published between 1995 and 2017 (Figure 1, Text S3). Of these, 28 publications focused exclusively on the impact of household size on rhinitis, 48 on the impact of having had infections, and 34 on the impact of both types of exposure. This network of 110 publications had a total of 5551 potential and 392 actual citation paths (7%) between these publications. Their main characteristics are depicted in Table 1 (for more details see Table S1). About two thirds of all publications in the network are empirical studies (39 cross-sectional, 4 case control, 29 cohort studies, and 1 intervention), one third are reviews (27 narrative reviews, 2 systematic reviews, and 8 editorials or leading articles). The study outcome for 35 of the publications was mixed or unclear. Of the remaining publications with a clear study outcome, about 50% was supportive of the hygiene hypothesis (41 publications with an inverse association between siblings / infection and rhinitis), and about

50% was non-supportive (34 publications with no association, or with a positive association). The number of citations ranged from 0 (45 publications) to 35, with a median of 1 citation per publication. A ranking of the most cited publications and authors can be found in Table S2.

**Impact of the cited publication characteristics.** The results of the regression analyses are presented in Table 2. Empirical publications were cited more often than non-empirical publications. Compared to empirical studies with a cross-sectional design, prospective cohort studies, narrative reviews and editorials had a lower likelihood of citation, while the two systematic reviews had a higher likelihood of citation. Other determinants that increased the likelihood of citation were specificity, journal impact factor, sample size and within-network authority. Sample size had a modest impact on citation. Publications on only one type of exposure were cited less often than publications on both types of exposure.

Supportive publications had a higher likelihood of being cited than non-supportive publications. This is in line with our hypothesis. However, publications with mixed results were cited even more often. This may be due to our scoring algorithm. After all, if a publication investigated both the number of siblings and the infection history, and it reported dissimilar outcomes for these two exposures, then this publication would have been scored as having mixed results. An explorative chi-square test confirmed that type of exposure and study outcome were related ($\chi^2(4) = 52$, $p < 0.0005$), with 71% of all publications on both types of exposure reporting mixed results, compared to 4% of the publications on only number of siblings and 21% of the publications on only infection history. As double exposure studies are also cited more often compared to the single exposure studies, type of exposure should be considered as a confounder of study outcome. To correct for this, we performed an explorative random-effects logistic regression of citation on study outcome, adjusted for both study design and type of exposure. It showed that supportive publications had the highest chance of being cited (adjusted odds ratio [adjOR] 3.1, 95% confidence interval [CI] 2.2-4.3), compared to publications with mixed results (adjOR 2.4, CI 1.5-3.7) and with non-supportive results (reference category; model $R^2$ = 0.12).

Surprisingly, publications with a conclusive title were less likely to receive citations. The format of the title may be prescribed by the journal regulations. We ran some explorative analyses in which we additionally adjusted for the (log-transformed) journal impact factor or publisher on top of study design. The impact of title conclusiveness remained high when additionally adjusted for journal impact factor (adjOR 0.4, CI 0.2-0.6) or publisher (adjOR 0.3, CI 0.2-0.6).

The above results are related to the network as a whole. Of particular importance is how empirical, evidence-generating publications were cited by the rest of the network. We repeated the above analyses on a subset of the cited publications, namely the empirical publications, and tested which of their characteristics were related to citation. The results (Table S3) are very similar to the analyses on the complete network that include the cited non-empirical publications.

Likewise, we tested how *empirical* publications were cited by *synthesis* publications (Table S4). Again, the direction and magnitudes of the effects were all very similar, except for study outcome. Adjusted for study design, (log-transformed) sample size and type of exposure, supportive empirical publications were much more likely to be cited (adjusted OR 7.3, CI 3.5-15.5) by reviews and editorials, whereas empirical publications with mixed results seemed less likely to be cited (adjusted OR 0.4, CI 0.2-0.9) compared to non-supportive empirical publications (reference category; model $R^2$ = 0.12). As a side note: these analyses are based on a smaller number of cited and citing publications and should be interpreted with caution.

The sensitivity analyses without the four most cited publications showed some dissimilar results (Table S5). The impact of study outcome decreased, the impact of male authors and of North-American authors disappeared, and the impact of case-control studies reversed. The other two sensitivity analyses (with a one year lag time immediately after publication; without citing publications with less than 10 potential citation paths) all showed similar results as the main analyses (Tables S6-S7).

**Concordance analysis.** In addition, we tested whether publications were more likely to be cited by publications with similar characteristics. The results are shown in Table 3. It shows that publications tended to be cited mostly by publications with the same type of exposure, with a similar study outcome, with a corresponding author from the same region, and with one or more authors in common ('self-citation').

## Discussion

Our research aim was to evaluate the impact of study outcome and other factors on the likelihood of being cited in the scientific literature on the original hygiene hypothesis stated by David Strachan (2). We found that study outcome, type of exposure, study design, specificity, title conclusiveness, journal impact factor, and the authors' region, affiliation, authority and self-citation all have a substantial impact on the likelihood of citation.

With regard to study outcome, supportive publications are cited more than three times more often than non-supportive publications, while publications with mixed results are cited more than two times as often. This is a clear sign of citation bias, and corroborates previous findings (13). Similarly, publications are more likely to refer to other publications with the same study outcome rather than to those that provide counter-evidence to their conclusion. This type of citation bias (based on concordance) has not been studied frequently. In our previous network analyses, on trans fatty acids – cholesterol, and on chlorinated water – asthma, we found no evidence for increased citations between publications with the same study outcomes (25, 26), but three other studies, all related to cardiovascular disease, did find evidence for this type of citation bias (9, 29, 30).

The magnitude of citation bias even increases if we focus on how empirical publications are cited by reviews and editorials. Reviews and editorials in our network are up to 8 times more likely to cite supportive publications rather than non-supportive ones. As reviews are generally assumed to give an unbiased summary of the existing evidence, this is a worrying finding. It confirms the notion that people should be cautious to rely on narrative reviews.

Greenberg states that reviews play an important role in the development and acceptance of belief systems (8). According to him, reviews can amplify the impact of empirical studies because their evidence is propagated when these reviews are cited themselves. Trinquart et al. showed that reviews (including systematic reviews) on the health impact of salt intake display signs of citation bias, and that the conclusions of these reviews were in the same direction as the evidence they include (9). A similar link between the selective citation of supportive evidence and supportive conclusions of reviews was found by Leng (29). This mechanism might explain how reviews can amplify the effect of citation bias. If reviews draw supportive conclusions based on selective citation of supportive evidence, then support for a hypothesis will be propagated while counter-evidence will fade from the literature.

In our analyses we consider study design as a proxy for study quality. We believe systematic reviews to be of higher quality than narrative reviews and editorials, and thus to receive more citations. In our network, this is indeed the case. Similarly, we believe that cohort studies outrank cross-sectional and case-control studies but to our surprise they are less likely to be cited. Prospective cohort studies, even though they provide the highest type of evidence in this network, receive the fewest citations of all empirical study designs. This may be due to the fact that these cohort studies tend to focus on multiple risk factors of which only one or two are relevant for the hygiene hypothesis. But the fact that multiple risk factors are investigated in these cohort studies does not imply that their findings on the impact of siblings or infections are of any lesser value or should be ignored.

This study has several limitations. First, it includes two overlapping sub-networks, as is shown by the high odds ratio in the concordance analysis of type of exposure. This makes it difficult to infer for which result a certain publication was cited. Related to this issue, the pre-registered operationalization of study outcome could not be applied because of the hybrid nature of the network, so we developed a scoring system that fits better. Also, there are different versions of the hygiene hypothesis, and support for one version may not be supportive for another one. We dealt with this issue by limiting ourselves to Strachan's original hygiene hypothesis, and by excluding any determinants with conflicting predictions in different versions. Despite these limitations, sensitivity analyses show that the results seem robust against chance findings. Another limitation is our use of odds ratios to assess the likelihood of citation. The odds ratio may overestimate the true relative risk in studies where the outcome is common (i.e. occurs in more than 5% of all cases, (31)). In our network, citation is not a common outcome (7%) and consequently the overestimation of the true relative risk will be relatively small.

To conclude, there is evidence for selective citation in this network. Several characteristics of a publication can make it more likely to be cited such as the authority and the region of the author, the impact factor of the journal, the way in which the title was stated, and also study design and study outcome. The fact that supportive publications are cited more often than non-supportive ones, particularly if we look at how empirical publications are being picked up by the rest of the network, is a clear sign of citation bias. Finally, this study also shows that particularly narrative reviews may have a preference to refer to supportive evidence.

**Availability of data and material:**

The protocol and the data of this study are available upon request in the DataVerse repository, http://hdl.handle.net/10411/ZKGGOG, or by sending an email to b.duyx@maastrichtuniversity.nl.

**Author Contributions:**

BD was involved in the research design and data analysis plan, prepared the research protocol, developed and performed the search strategy, wrote the R scripts for data transformation and calculation, performed article selection and data extraction, conducted the analyses and wrote the manuscript. MJEU was involved in the research design and data analysis plan, performed the article selection and data extraction, and read, commented on and approved the final manuscript. GMHS obtained funding, was involved in the research design and data analysis plan, and read, commented on and approved the final manuscript. MPZ obtained funding, was involved in the research design and data analysis plan, and read, commented on and approved the final manuscript. LMB was involved in the research design and data analysis plan, and read, commented on and approved the final manuscript.

**Transparency declaration**:

The guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned and registered have been explained in the supplement.

**Copyright statement:**

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**Figure Legends**

Figure 1. Flow diagram of article selection process.

**Table 1. Main characteristics of all 110 publications in hygiene hypothesis network.**

| Characteristic | category | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| Type of Exposure | only Number of Siblings | 28 | 1512 | 100 (7%) |
| | only Infection History | 48 | 1946 | 144 (7%) |
| | both Siblings & Infections | 34 | 2093 | 148 (7%) |
| Study Outcome Exposure - Rhinitis | supportive | 41 | 2322 | 198 (9%) |
| | mixed results | 35 | 1913 | 129 (7%) |
| | non-supportive | 34 | 1316 | 65 (5%) |
| Publication Type / Study Design | Empirical | 73 | 3517 | 337 (10%) |
| | cross-sectional | 39 | 1697 | 179 (11%) |
| | case-control | 4 | 249 | 36 (14%) |
| | cohort | 29 | 1535 | 121 (8%) |
| | -retrospective | 15 | 817 | 89 (11%) |
| | -prospective | 14 | 718 | 32 (4%) |
| | intervention | 1 | 36 | 1 (3%) |
| | Synthesis | 37 | 2034 | 55 (3%) |
| | narrative review | 27 | 1423 | 16 (1%) |
| | systematic review | 2 | 80 | 20 (25%) |
| | editorial, etc | 8 | 531 | 19 (4%) |
| Sample Size (cat; for empirical publications) | low (1 – 999) | 24 | 909 | 56 (6%) |
| | medium (1000 – 7999) | 25 | 1327 | 143 (11%) |
| | high (>= 8000) | 24 | 1281 | 138 (11%) |
| Journal Impact Factor (cat) | 0 - 2 | 28 | 1275 | 27 (2%) |
| | 2 - 4 | 41 | 2087 | 145 (7%) |
| | >= 4 | 32 | 1671 | 176 (11%) |
| Gender | male | 65 | 3368 | 265 (8%) |
| | female | 42 | 2024 | 123 (6%) |
| | unclear | 3 | 159 | 4 (3%) |
| Affiliation | university | 88 | 4402 | 258 (6%) |
| | government | 9 | 410 | 22 (5%) |
| | industry / other | 13 | 739 | 112 (15%) |
| Country | Europe | 62 | 3903 | 324 (8%) |
| | North-America | 19 | 688 | 38 (6%) |
| | Asia | 21 | 484 | 9 (2%) |
| | Australia / New Zealand | 8 | 476 | 21 (4%) |
| **Total** | | **110** | **5551** | **392 (7%)** |

**Table 2. Odds ratios (95% CIs) for the chance of being cited, all types of publications included, N = 110, n = 5551 )**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.10 |
| only Number of Siblings | 0.8 (0.6 – 1.1) | 0.5 (0.4 – 0.7) | |
| only Infection History | 1.3 (0.97–1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) | | | 0.11 |
| mixed / unclear results | 1.2 (0.9 – 1.7) | 3.1 (2.2 – 4.5) | |
| supportive results | 1.5 (1.1 – 2.0) | 2.2 (1.6 – 3.1) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.3 (3.2 – 5.7) | | 0.04 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.3 (1.8 – 5.8) | | |
| editorial / other | 0.3 (0.2 – 0.4) | | |
| Sample Size (ref: low, n = 3517) | | | 0.02 |
| medium | 1.6 (1.2 – 2.3) | 1.6 (1.0 – 2.6) | |
| high | 1.6 (1.2 – 2.3) | 1.9 (1.2 – 3.0) | |
| Specificity (ref: low) | | | 0.11 |
| medium | 2.5 (1.5 – 4.0) | 2.7 (1.6 – 4.5) | |
| high | 8.8 (5.8 – 13.5) | 5.0 (3.1 – 7.9) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.3 – 0.7) | 0.3 (0.2 – 0.4) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.09 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.2) | 0.8 (0.6 – 1.2) | |
| not reported | 0.4 (0.3 – 0.5) | 0.8 (0.6 – 1.0) | |
| Number of Authors (ref: 1-2) | | | 0.09 |
| 3 - 5 | 1.9 (1.4 – 2.5) | 1.0 (0.7 – 1.5) | |
| >= 6 | 3.6 (2.7 – 4.9) | 1.5 (1.0 – 2.4) | |
| Number of Affiliations (ref: 1) | | | 0.09 |
| 2 | 2.6 (2.0 – 3.5) | 1.8 (1.3 – 2.5) | |
| >= 3 | 2.1 (1.6 – 2.8) | 1.6 (1.1 – 2.2) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.1 (0.8 – 1.3) | 1.0 (0.8 – 1.2) | |
| >= 50 | 0.4 (0.3 – 0.6) | 0.8 (0.5 – 1.3) | |

| **Journal characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 5033) | | | 0.11 |
| 2 – 4 | 3.4 (2.2 – 5.3) | 2.7 (1.7 – 4.2) | |
| >= 4 | 6.0 (4.0 – 9.2) | 4.9 (3.2 – 7.6) | |

| **Author characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Gender (female vs male, n = 5392) | 0.8 (0.6 – 1.0) | 0.7 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 0.9 (0.6 – 1.3) | 0.9 (0.5 – 1.4) | |
| Asia | 0.3 (0.1 – 0.6) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.8) | |
| Type of Affiliation (other vs university) | 2.3 (1.8 – 2.9) | 2.0 (1.5 – 2.5) | 0.10 |

| **Citation characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.4 (1.8 – 3.3) | 1.8 (1.3 – 2.5) | |
| high | 3.7 (2.8 – 4.8) | 2.7 (2.0 – 3.7) | |

* adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

**Table 3. Concordance odds ratios (95% CI's) for the chance of being cited, all types of articles included, N = 110, n = 5551)**

| Content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (conc. vs. not) | 10 (5.6 – 18) | 13 (7.1 – 23) | 0.14 |
| Study Outcome (conc. vs. not, n = 1799)** | 2.9 (1.4 – 6.0) | 3.4 (1.6 – 7.1) | 0.06 |
| **Not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
| Article Type (conc. vs. not) | 1.1 (0.9 – 1.3) | | 0.00 (crude) |
| Funding Source (conc. vs. not, n = 1475)*** | 1.3 (0.8 – 1.9) | 1.2 (0.8 – 1.8) | 0.05 |
| Publisher (conc. vs. not, n = 4971)**** | 0.9 (0.7 – 1.2) | 0.9 (0.7 – 1.2) | 0.08 |
| Author Affiliation (conc. vs. not) | 0.7 (0.6 – 0.9) | 0.8 (0.7 – 1.0) | 0.08 |
| Author Gender (conc. vs. not, n = 5254)***** | 1.0 (0.8 – 1.3) | 1.0 (0.8 – 1.3) | 0.08 |
| Author Region (conc. vs. not) | 1.9 (1.6 – 2.4) | 2.0 (1.6 – 2.5) | 0.09 |
| Self-citation (yes vs no) | 6.1 (3.8 – 9.7) | 6.1 (3.7 – 9.9) | 0.09 |

* adjusted for study design of cited publication; ** publications with mixed results excluded from analysis; *** publications without reported funding source excluded from analysis; **** Three main publishers are differentiated: Wiley-Blackwell, BMJ, and Elsevier. Either the cited or the citing publication should be in one of these categories to be included in the analysis. ***** publications with unclear author's gender excluded from analysis; **N**: number of publication. **n**: number of potential citation paths.

# Supplement

**Text S1.** Protocol deviations

**Text S2.** Data extraction

**Text S3.** References of included literature on Strachan's hygiene hypothesis

**Table S1.** All characteristics of the publications in the hygiene hypothesis network.

**Table S2.** Top 6 of articles and authors within network.

**Table S3.** Odds ratios for the chance of *empirical* publications to be cited within full network.

**Table S4.** Odds ratios for the chance of *empirical* publications to be cited by *synthesis* publications.

**Table S5.** Sensitivity analyses on odds ratios for the chance of being cited, without the four most cited publications.

**Table S6.** Sensitivity analyses on odds ratios for the chance of being cited, with a 1-year time lag between cited and citing publication.

**Table S7.** Sensitivity analyses on odds ratios for the chance of being cited, without citing publications with less than 10 potential citation paths.

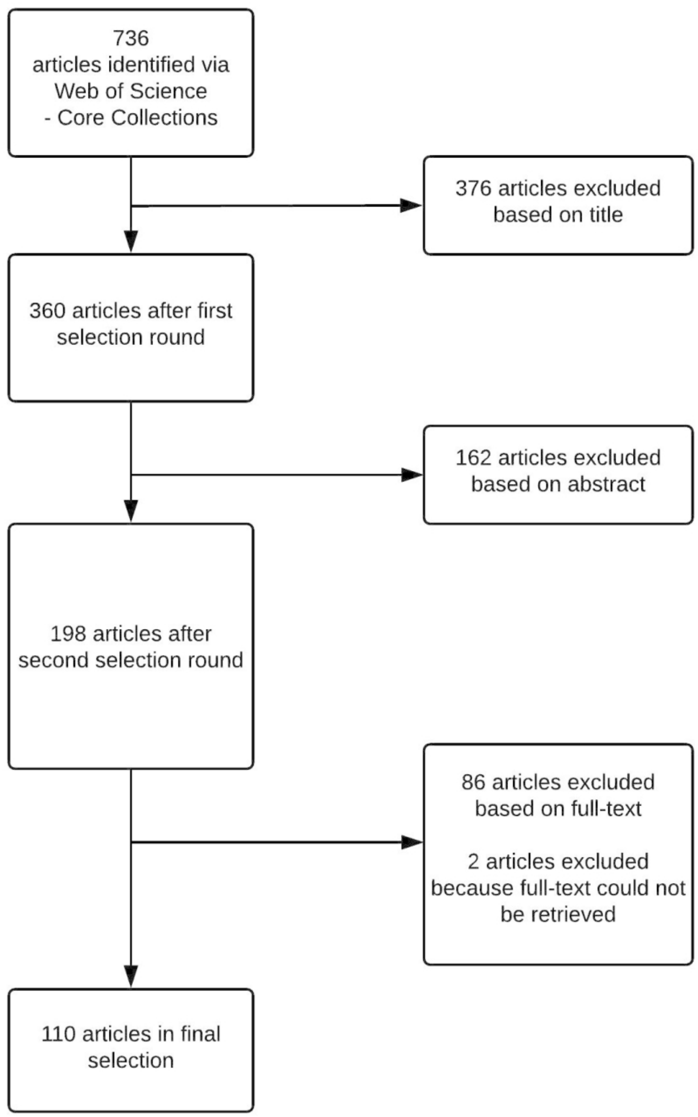


Figure 1. Flow diagram of article selection process.

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# Selective citation in the literature on the hygiene hypothesis

## Supplement

**Text S1.** Protocol deviations

**Text S2.** Data extraction

**Text S3.** References of included literature on Strachan's hygiene hypothesis

**Table S1.** All characteristics of the publications in the hygiene hypothesis network.

**Table S2.** Top 6 of articles and authors within network.

**Table S3.** Odds ratios for the chance of *empirical* publications to be cited within full network.

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**Table S5.** Sensitivity analyses on odds ratios for the chance of being cited, without the four most cited publications.

**Table S6.** Sensitivity analyses on odds ratios for the chance of being cited, with a 1-year time lag between cited and citing publication.

**Table S7.** Sensitivity analyses on odds ratios for the chance of being cited, without citing publications with less than 10 potential citation paths.

**Text S1. Protocol deviations**

*Search strategy.* We ran some checks of our original search strategy (with '*hygiene hypothesis'* in combination with the pre-specified health outcomes). These checks indicated that many relevant publications in the period 1990 – 2000 were missed. Going through these missed publications we found out that the name for this hygiene hypothesis was not yet accepted or used. Also, we realised that almost all relevant publications within this network referred to Strachan's original study from 1989. We decided to change the search strategy, into *all publications referring to Strachan's original article.* Additionally, we limited the output to those publications that mentioned 'rhinitis' or a similar term in the title, abstract or keywords (see inclusion criteria).

*Inclusion criteria* (regarding the health outcome and types of exposure). Originally, all publications with either health outcome *rhinitis* or *asthma* were to be included. This yielded too many publications in our network, hence we decided to include only publications on rhinitis (or hay fever, or rhinoconjunctivitis). Inclusion solely based on asthma would also have yielded a network that was too large. Also, rhinitis is the original outcome as studied by Strachan. Similarly, we included only publications with exposures *number of siblings* and *infection history.* These are the two most important types of exposure related to the hygiene hypothesis as originally stated by Strachan. Number of siblings was originally studied by Strachan, and infections during childhood (or during pregnancy) was his explanation for the relationship between number of siblings and hay fever.

*Types of health outcome.* We intended to score both *asthma* and *rhinitis* as health outcomes. However, as we included only publications that studied the relationship with rhinitis, and excluded publications that were solely on asthma, we decided to focus on rhinitis. Thus, for the

empirical publications, we scored the relationships Siblings – Rhinitis and Infections – Rhinitis. (We also scored asthma, dermatitis and atopic sensitisation, but only for the sensitivity analyses.) Synthesis publications often did not differentiate between the different allergies in their general conclusion, so for the synthesis publications we scored statements on Siblings – Allergy and Infection – Allergy.

*Types of exposure.* We focused on two exposures: *number of siblings* (or household size or sibling order) and *history of infections* (as assessed by parental questionnaire, serology or medical records). We used this variable also in our analyses; it was scored as a) number of siblings only, b) only infection history, and c) both number of siblings and infection history.

*Study outcome scoring strategy.* There were many empirical publications with contradictory results, especially in the case of Infections where the results seemed to depend on the type of infection. In order to deal with this, we decided to use the *authors' conclusion* on Siblings – Rhinitis and Infections – Rhinitis as leading. We used 5 categories: 0. not measured or reported; 1. effect in line with hygiene hypothesis (inverse relationship); 2. no relationship; 3. effect contrary to hygiene hypothesis (positive relationship); 4. mixed or unclear results. Synthesis publications were scored in a similar way, but then on Siblings – Allergy and Infections – Allergy.

If no clear authors' conclusion was stated in the empirical publications, we used the data that were presented in the tables or the text and scored as follows: 1. statistically significant inverse relationship; 2. no statistically significant relationship; 3. statistically significant positive relationship; 4. mixed or unclear results. If both adjusted analyses and crude analyses were presented we preferred the adjusted ones. There is one exception: adjustment for Infections in

the relationship Siblings – Rhinitis; after all, the hygiene hypothesis states that infection is the mediator between siblings and rhinitis.

In the analyses we used one combined measure for study outcome, with three levels: 1) supportive; 2) mixed results / unclear; 3) non-supportive. Publications were scored as supportive if the exposure or exposures showed an inverse association with rhinitis. Publications were scored as non-supportive if there was no association or a positive association of the exposure with rhinitis. Publications were scored as mixed if the exposure or exposures showed mixed or unclear results, or if two exposures were investigated, and one showed an inverse association and the other showed no or a positive association.

*General conclusion about the hygiene hypothesis*. While studying the literature on the hygiene hypothesis we realised that many related hypotheses reside under this name, all evolved from one another. *The* hygiene hypothesis clearly does not exist. Support for one version of the hypothesis often implied the refutation of another (older) version. As authors assumed different versions, their general conclusion on the hygiene hypothesis would not be compatible. We decided to not score this general conclusion.

*Specificity.* We used 3 outcome categories for publication's specificity instead of 5.

*Study design.* Ecological studies were excluded from the network. Cohort studies were further classified as retrospective and prospective cohort studies. This latter step was data-driven because we realised during the analysis that prospective cohort studies were cited less often. During exploration of the data, we noticed a big difference in the citation behaviour of retrospective and prospective cohorts studies. We therefore decided to amend our preregistered data analysis plan (http://hdl.handle.net/10411/ZKGGOG). We differentiated between these research designs (by assigning them a different categorical value), and take this difference into account in our analyses with study design as determinant or as covariate.

*Publisher*. In addition to the protocol we also scored the publisher of the journal, based on the information in Journal Citation Reports and in Web of Science. This could be interesting for publisher self-citation concordance analysis.

*Explained variance.* In addition to the original analysis plan in the protocol, we also calculated the explained variance of the adjusted models, so that these models are easier to compare. For this purpose we calculated McFadden's $R^2$ by the following formula: $R^2 = 1 - {}^{LL_M}/_{LL_0}$ in which $LL_M$ stands for the log likelihood of the current regression model and $LL_0$ stands for the log likelihood of the empty random-regression model. Both the current and the empty model (without predictors) were nested under the citing publication. Because of missing values for certain determinants (such as sample size), some models could be tested only on a sub-selection of citation paths. If this was the case, then $LL_0$ was calculated on the same sub-selection of citation paths.

**Text S2. Data extraction**

Most variables are described in the main document. Here follows some additional information for some of the variables.

**Study outcome** was scored as follows: 1. supportive of the hygiene hypothesis; 2. mixed or unclear results; 3. non-supportive of the hygiene hypothesis. An inverse relationship between past exposure and rhinitis is considered to be supportive for the hygiene hypothesis, while a neutral or positive relationship was scored as non-supportive. The scoring was based on the authors' interpretation of the results, as it was stated in the text of the publication. If the authors' interpretation was unclear, we scored study outcome based on the direction and statistical significance of the data. Non-empirical publications seldom distinguished between allergy subtypes, so we used the stated conclusion on general allergy as outcome measure.

Exposure could be either number of siblings (or order of siblings or household size) or history of bacterial or viral infection (as assessed by parental questionnaire, serology, or medical records). If the impact of number of both siblings and infection history was assessed and they were contradicting each other (with one exposure showing inverse association, the other a neutral or positive association), then study outcome was scored as mixed.

**Gender of the corresponding author** was assessed by first name, with help of www.genderchecker.com; if first name was not given, other articles of the same author were searched, and the profile of the author at the university or at www.researchgate.com was checked.

We performed a validity check of the gender assessment on a random sample of 20 publications. We checked our original assessment (described above) against the results from another gender assessment tool: Gender-API.com. This tool takes into account the person's country while assessing gender based on his or her first name Additionally, it gives an accuracy score for each assessment. The results can be found in the Table below. Our reference assessment reached the same results as the original one, with a 100% accuracy.

**Table. Validity check for gender assessment on random sample (N=20).**

| ID [1] | First Name of Corresponding Author | Country of Corresponding Author | Genderchecker Assessment | Our Data-extraction Assessment | Gender-API Assessment [2] (validity check) | Accuracy of Gender-API Assessment [2] |
|---|---|---|---|---|---|---|
| 1 | David | UK | male | male | male | 99% |
| 5 | Barbara | UK | female | female | female | 98% |
| 13 | Nick [3] | UK | male | male | male | 98% |
| 14 | Sarah [3] | UK | female | female | female | 98% |
| 18 | Juha | Finland | unisex | male [4] | male | 100% |
| 24 | Anthony | UK | male | male | male | 99% |
| 25 | Erika | Germany | female | female | female | 98% |
| 26 | Mustafa | Turkey | male | male | male | 100% |
| 31 | Johannes | Germany | male | male | male | 99% |
| 35 | Paolo | Italy | male | male | male | 99% |
| 73 | Anne-Louise [5] | Australia | no match | female | female | 100% |
| | Anne | | unisex | | | |
| | Louise | | female | | | |
| 75 | Keiko | Japan | female | female | female | 99% |
| 78 | Aarif | Turkey | male | male | male | 75% |
| 79 | Sharad | India | male | male | male | 100% |
| 87 | Woei Kang [5] | Singapore | no match | male | | |
| | Woei | | male | | male | 67% |
| | Kang | | unisex | | male | 88% |
| 94 | Jonathan | USA | male | male | male | 99% |
| 95 | Ahmet | Turkey | male | male | male | 100% |
| 97 | Chun-Yuh [5] | Taiwan | no match | male [4] | | |
| | Chun | | unisex | | male | 53% |
| | Yuh | | no match | | male | 60% |
| 103 | David | UK | male | male | male | 99% |
| 109 | Katherine | USA | female | female | female | 99% |

**Notes**. 1. See Text S3 for the references. 2. Based on combination of first name and country. 3. First name was not stated in publication, but retrieved via ResearchGate.net; match between profile and correpsonding author based on surname, initials, affiliation and research topic. 4. Web search revealed a man with same name and afflilation. 5. Composite names that could not be assessed as a whole were assessed by its composites.

**Time to citation** was the number of years between the publication date of the cited publication and the submission date of the citing publication. This variable was not used as determinant of citation, but to determine the dataset of potential citation paths: only citation paths with a positive value for *time to citation* were considered a potential citation, and only potential citations were included in our dataset.

As *publication date* we used either the online publication date or the paper publication date, whichever was first. The average duration from submission to publication was nine months in this network. For 57 publications the *submission date* was not stated. In these cases, it was estimated by subtracting nine months from the publication date.

**Text S3. References of included literature on Strachan's hygiene hypothesis**


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**Table S1. All characteristics of the publications in the hygiene hypothesis network.**

| | | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| **Total** | | 110 | 5551 | 392 (7%) |

| Publication characteristics - content-related | category | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| Type of Exposure | only Number of Siblings | 28 | 1512 | 100 (7%) |
| | only Infection History | 48 | 1946 | 144 (7%) |
| | both Siblings & Infections | 34 | 2093 | 148 (7%) |
| Study Outcome Exposure - Rhinitis | supportive | 41 | 2322 | 198 (9%) |
| | mixed results | 35 | 1913 | 129 (7%) |
| | non-supportive | 34 | 1316 | 65 (5%) |
| Publication Type / Study Design | Empirical | 73 | 3517 | 337 (10%) |
| | cross-sectional | 39 | 1697 | 179 (11%) |
| | case-control | 4 | 249 | 36 (14%) |
| | cohort | 29 | 1535 | 121 (8%) |
| | -retrospective | 15 | 817 | 89 (11%) |
| | -prospective | 14 | 718 | 32 (4%) |
| | intervention | 1 | 36 | 1 (3%) |
| | Synthesis | 37 | 2034 | 55 (3%) |
| | narrative review | 27 | 1423 | 16 (1%) |
| | systematic review | 2 | 80 | 20 (25%) |
| | -with meta-analysis | 1 | 8 | 1 (13%) |
| | editorial, etc | 8 | 531 | 19 (4%) |
| Sample Size (cat; for empirical publications) | low (1 – 999) | 24 | 909 | 56 (6%) |
| | medium (1000 – 7999) | 25 | 1327 | 143 (11%) |
| | high (>= 8000) | 24 | 1281 | 138 (11%) |
| Specificity | 0 (non-specific) | 27 | 1402 | 25 (2%) |
| | 1 | 39 | 1657 | 65 (4%) |
| | 2 (specific) | 44 | 2492 | 302 (12%) |

| Publication characteristics - not content-related | category | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| Conclusive Title | not conclusive | 99 | 5026 | 375 (7%) |
| | conclusive | 11 | 525 | 17 (3%) |

| | | | | |
|---|---|---|---|---|
| Funding Source | non-profit | 44 | 2188 | 214 (10%) |
| | for-profit | 1 | 38 | 1 (3%) |
| | both | 12 | 559 | 51 (9%) |
| | not reported / unclear | 53 | 2766 | 126 (5%) |
| Number of Authors | 1 - 2 | 32 | 2017 | 89 (4%) |
| | 3 - 5 | 41 | 2143 | 155 (7%) |
| | >= 6 | 37 | 1391 | 148 (11%) |
| Number of Affiliations | 1 | 36 | 2276 | 111 (5%) |
| | 2 | 24 | 1168 | 108 (9%) |
| | >= 3 | 50 | 2107 | 173 (8%) |
| Number of References | < 30 | 35 | 2307 | 194 (8%) |
| | 30 – 50 | 49 | 2060 | 159 (8%) |
| | >= 50 | 26 | 1184 | 39 (3%) |

| **Journal characteristics** | **category** | **N publications** | **n potential citations** | **n actual citations (%)** |
|---|---|---|---|---|
| Journal Impact Factor (cat) | 0 - 2 | 28 | 1275 | 27 (2%) |
| | 2 - 4 | 41 | 2087 | 145 (7%) |
| | >= 4 | 32 | 1671 | 176 (11%) |
| Publisher | Wiley-Blackwell | 41 | 2107 | 82 (4%) |
| | BMJ | 15 | 1170 | 213 (18%) |
| | Elsevier | 18 | 894 | 43 (5%) |
| | other | 36 | 1380 | 54 (4%) |

| Author characteristics | category | N publications | n potential citations | n actual citations (%) |
|---|---|---|---|---|
| Gender | male | 65 | 3368 | 265 (8%) |
| | female | 42 | 2024 | 123 (6%) |
| | unclear | 3 | 159 | 4 (3%) |
| Affiliation | university | 88 | 4402 | 258 (6%) |
| | government | 9 | 410 | 22 (5%) |
| | industry / other | 13 | 739 | 112 (15%) |
| Country | Europe | 62 | 3903 | 324 (8%) |
| | UK | 26 | 1946 | 165 (8%) |
| | Germany | 11 | 594 | 19 (3%) |
| | Finland | 8 | 516 | 33 (6%) |
| | Italy | 7 | 418 | 85 (20%) |
| | North-America | 19 | 688 | 38 (6%) |
| | USA | 18 | 662 | 36 (5%) |
| | Asia | 21 | 484 | 9 (2%) |
| | Turkey | 9 | 303 | 7 (2%) |
| | Japan | 4 | 60 | 0 (0%) |
| | Australia / New Zealand | 8 | 476 | 21 (4%) |
| | Australia | 7 | 407 | 21 (5%) |

| Citation characteristics | category | n potential citations | n actual citations (%) |
|---|---|---|---|
| Authority | low (0-2) | 2279 | 81 (4%) |
| | medium (2-10) | 1326 | 108 (8%) |
| | high (>= 10) | 1946 | 203 (10%) |
| Time to Citation (in years) | 0 – 1 | 494 | 38 (8%) |
| | 1 – 2 | 521 | 56 (11%) |
| | 2 – 3 | 527 | 50 (9%) |
| | 3 – 4 | 459 | 33 (7%) |
| | 4 – 5 | 456 | 40 (9%) |
| | 5 – 6 | 441 | 35 (8%) |
| | 6 – 7 | 404 | 28 (7%) |
| | 7 – 8 | 372 | 22 (6%) |
| | => 8 | 1877 | 90 (5%) |
| Self-citation | no | 5462 | 365 (7%) |
| | yes | 89 | 27 (30%) |

**Table S2.** Top 6 of articles (above) and authors (below) within network, based on the number of received citations up to 2017.

| Article rank | Article's first author | Title | Year | Nr. of received citations (% of potential citations) |
|---|---|---|---|---|
| 1 | Matricardi | Cross sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus | 1997 | 35 (35 %) |
| 2 | Bodner | Family size, childhood infections and atopic diseases | 1998 | 32 (33 %) |
| 3 | Matricardi | Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study | 2000 | 32 (38 %) |
| 4 | Strachan | Family structure, neonatal infection, and hay fever in adolescence | 1996 | 28 (26 %) |
| 5 | Farooqi | Early childhood infection and atopic disorder | 1998 | 21 (23 %) |
| 6 | Karmaus | Does a higher number of siblings protect against the development of allergy and asthma? A review | 2002 | 19 (26 %) |

| Author rank | Author | Affiliation | Country | Nr. of received citations (= authority) |
|---|---|---|---|---|
| 1 | P. Matricardi | Consiglio Nazionale delle Ricerche, Rome | Italy | 84 |
| 2 | F. Rosmini | Istituto Superiore di Sanita, Rome | Italy | 84 |
| 3 | L. Ferrigno | Istituto Superiore di Sanita, Rome | Italy | 84 |
| 4 | M. Rapicetta | Istituto Superiore di Sanita, Rome | Italy | 67 |
| 5 | D. Strachan | University of London, London | United Kingdom | 57 |
| 6 | S. Bonini | Consiglio Nazionale delle Ricerche, Rome | Italy | 49 |

**Table S3. Odds ratios (95% CIs) for the chance of *empirical* publications to be cited within full network (N = 73, n = 3517).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.04 |
| only Number of Siblings | 0.5 (0.3 – 0.6) | 0.4 (0.3 – 0.5) | |
| only Infection History | 1.0 (0.8 – 1.3) | 0.7 (0.5 – 0.9) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.07 |
| mixed / unclear results | 1.4 (0.9 – 2.3) | 1.1 (0.7 – 1.9) | |
| supportive results | 4.8 (3.2 – 7.0) | 5.1 (3.3 – 7.8) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Study Design (ref: cross-sectional) | | | 0.02 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| Sample Size (ref: low) | | *** | 0.02 |
| medium | 1.6 (1.2 – 2.3) | 1.6 (1.0 – 2.6) | |
| high | 1.6 (1.2 – 2.3) | 1.9 (1.2 – 3.0) | |
| Specificity (ref: low) | | | 0.05 |
| medium | 4.6 (2.6 – 8.2) | 3.5 (1.8 – 6.5) | |
| high | 7.4 (4.5 – 12) | 6.1 (3.5 – 10) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.3 (0.2 – 0.6) | 0.3 (0.1 – 0.5) | 0.03 |
| Funding Source (ref: exclusively non-profit) | | | 0.02 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.2) | 0.8 (0.5 – 1.1) | |
| not reported | 0.8 (0.6 – 1.1) | 0.8 (0.6 – 1.1) | |
| Number of Authors (ref: 1-2) | | | 0.03 |
| 3 - 5 | 1.1 (0.7 – 1.6) | 1.2 (0.7 – 1.8) | |
| >= 6 | 1.7 (1.2 – 2.6) | 1.8 (1.1 – 2.9) | |
| Number of Affiliations (ref: 1) | | | 0.03 |
| 2 | 1.7 (1.2 – 2.4) | 1.8 (1.2 – 2.6) | |
| >= 3 | 1.3 (0.9 – 1.7) | 1.6 (1.2 – 2.4) | |
| Number of References (ref: <30) | | | 0.02 |
| 30 - 50 | 0.9 (0.7 – 1.1) | 1.0 (0.7 – 1.2) | |
| >= 50 | 0.3 (0.1 – 0.7) | 0.3 (0.1 – 0.8) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 3266) | | | 0.06 |
| 2 – 4 | 2.8 (1.7 – 4.5) | 2.6 (1.6 – 4.3) | |
| >= 4 | 5.9 (3.7 – 9.5) | 6.6 (4.0 – 11) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 3457) | 0.6 (0.5 – 0.8) | 0.7 (0.5 – 0.9) | 0.03 |
| Region (ref: Europe) | | | 0.04 |
| North-America | 0.5 (0.3–0.97) | 0.6 (0.3 – 1.1) | |
| Asia | 0.2 (0.1 – 0.4) | 0.1 (0.1 – 0.3) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.9) | |
| Type of Affiliation (other vs university) | 2.4 (1.9 – 3.2) | 2.2 (1.7 – 2.9) | 0.04 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.05 |
| medium | 2.0 (1.4 – 3.0) | 2.1 (1.4 – 3.0) | |
| high | 3.6 (2.6 – 5.1) | 3.8 (2.7 – 5.5) | |

* adjusted for study design and log sample size. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited publications; n = number of potential citation paths.

**Table S4. Odds ratios (95% CIs) for the chance of *empirical* publications to be cited by *synthesis* publications (N = 73, n = 1097).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.07 |
| only Number of Siblings | 0.4 (0.2 – 0.7) | 0.3 (0.2 – 0.6) | |
| only Infection History | 1.8 (1.1 – 3.0) | 1.3 (0.7 – 2.3) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 0.5 (0.2 – 1.0) | 0.4 (0.2 – 0.9) | |
| supportive results | 6.0 (3.1 – 12) | 7.3 (3.5 – 15) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Study Design (ref: cross-sectional) | | | 0.04 (crude) |
| case control | 2.1 (1.1 – 4.2) | | |
| retrospective cohort | 1.0 (0.6 – 1.6) | | |
| prospective cohort | 0.3 (0.1 – 0.6) | | |
| Sample Size (ref: low) | | *** | 0.04 |
| medium | 1.6 (0.9 – 2.8) | 1.9 (0.8 – 4.6) | |
| high | 1.3 (0.7 – 2.3) | 1.9 (0.8 – 4.4) | |
| Specificity (ref: low) | | | 0.06 |
| medium | 6.9 (2.8 – 17) | 4.3 (1.6 – 12) | |
| high | 7.6 (3.4 – 17) | 5.6 (2.3 – 13) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.2 – 0.9) | 0.2 (0.1 – 0.6) | 0.05 |
| Funding Source (ref: exclusively non-profit) | | | 0.04 |
| profit or both profit/non-profit | 0.7 (0.4 – 1.2) | 0.7 (0.4 – 1.3) | |
| not reported | 0.6 (0.4 – 1.0) | 0.5 (0.3 – 0.9) | |
| Number of Authors (ref: 1-2) | | | 0.06 |
| 3 - 5 | 0.6 (0.3 – 1.1) | 0.6 (0.3 – 1.2) | |
| >= 6 | 1.5 (0.8 – 2.8) | 1.5 (0.7 – 3.2) | |
| Number of Affiliations (ref: 1) | | | 0.04 |
| 2 | 1.3 (0.7 – 2.4) | 1.6 (0.8 – 3.1) | |
| >= 3 | 1.2 (0.7 – 2.0) | 2.0 (1.1 – 3.6) | |
| Number of References (ref: <30) | | | 0.04 |
| 30 - 50 | 0.7 (0.5 – 1.1) | 0.8 (0.5 – 1.2) | |
| >= 50 | 0.2 (0.04–0.9) | 0.2 (0.04–1.0) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 1015) | | | 0.11 |
| 2 – 4 | 2.6 (1.2 – 5.6) | 2.2 (1.0 – 4.9) | |
| >= 4 | 8.2 (3.8 – 18) | 9.2 (4.1 – 21) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 1079) | 0.5 (0.3 – 0.8) | 0.6 (0.4 – 0.9) | 0.04 |
| Region (ref: Europe) | | | 0.07 |
| North-America | 0.7 (0.2 – 2.2) | 0.9 (0.3 – 2.9) | |
| Asia | 0.2 (0.1 – 0.7) | 0.1 (0.02–0.3) | |
| Australia / New-Zealand | 0.2 (0.1 – 0.6) | 0.2 (0.9 – 0.7) | |
| Type of Affiliation (other vs university) | 3.3 (2.2 – 5.1) | 3.1 (2.0 – 4.8) | 0.07 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.07 |
| medium | 2.6 (1.4 – 4.6) | 2.7 (1.4 – 5.1) | |
| high | 4.0 (2.3 – 7.1) | 4.1 (2.2 – 7.6) | |

* adjusted for study design and log sample size. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited (*empirical*) publications; n = number of potential citation paths.

**Table S5. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited within full network, without the four most cited publications. N = 106, n = 5164).**

| **Publication characteristics, content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.08 |
| only Number of Siblings | 1.4 (1.0 – 1.9) | 0.9 (0.6 – 1.3) | |
| only Infection History | 1.0 (0.8 – 1.4) | 1.0 (0.7 – 1.4) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.08 |
| mixed / unclear results | 0.8 (0.5 – 1.1) | 1.2 (0.8 – 2.0) | |
| supportive results | 1.0 (0.7 – 1.5) | 1.5 (1.0 – 2.2) | |

| **Publication characteristics, other content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 2.9 (2.1 – 3.9) | | 0.03 (crude) |
| Study Design (ref: cross-sectional) | | | 0.08 (crude) |
| case control | 0.3 (0.1 – 0.8) | | |
| retrospective cohort | 1.1 (0.8 – 1.5) | | |
| prospective cohort | 0.5 (0.3 – 0.8) | | |
| narrative review | 0.1 (0.1 – 0.2) | | |
| systematic review | 4.5 (2.5 – 8.0) | | |
| editorial / other | 0.4 (0.2 – 0.7) | | |
| Sample Size (ref: low, n = 3130) | | *** | 0.02 |
| medium | 2.3 (1.4 – 3.7) | 1.6 (0.9 – 2.9) | |
| high | 3.3 (2.1 – 5.3) | 2.5 (1.5 – 4.2) | |
| Specificity (ref: low) | | | 0.09 |
| medium | 2.4 (1.5 – 3.9) | 3.3 (1.9 – 5.6) | |
| high | 5.6 (3.6 – 8.7) | 3.5 (2.1 – 5.6) | |

| **Publication characteristics, not content-related** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.6 (0.4 – 1.0) | 0.5 (0.3 – 0.9) | 0.08 |
| Funding Source (ref: exclusively non-profit) | | | 0.08 |
| profit or both profit/non-profit | 1.4 (1.0 – 2.0) | 1.4 (0.9 – 2.0) | |
| not reported | 0.5 (0.4 – 0.7) | 1.0 (0.7 – 1.4) | |
| Number of Authors (ref: 1-2) | | | 0.08 |
| 3 - 5 | 1.2 (0.9 – 1.7) | 0.7 (0.5 – 1.1) | |
| >= 6 | 2.0 (1.4 – 2.8) | 0.9 (0.6 – 1.4) | |
| Number of Affiliations (ref: 1) | | | 0.08 |
| 2 | 1.8 (1.3 – 2.5) | 1.1 (0.8 – 1.6) | |
| >= 3 | 1.0 (0.7 – 1.4) | 0.6 (0.4 – 0.9) | |

| | | | |
|---|---|---|---|
| Number of References (ref: <30) | | | 0.08 |
| 30 - 50 | 0.9 (0.7 – 1.2) | 0.7 (0.6 – 1.0) | |
| >= 50 | 0.6 (0.4 – 0.8) | 0.8 (0.5 – 1.3) | |

| **Journal characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4752) | | | 0.09 |
| 2 – 4 | 2.8 (1.8 – 4.3) | 2.5 (1.6 – 3.9) | |
| >= 4 | 4.0 (2.6 – 6.1) | 3.5 (2.2 – 5.5) | |

| **Author characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Gender (female vs male, n = 5005) | 1.4 (1.1 – 1.8) | 1.2 (0.9 – 1.6) | 0.07 |
| Region (ref: Europe) | | | 0.08 |
| North-America | 1.2 (0.8 – 1.8) | 1.0 (0.6 – 1.6) | |
| Asia | 0.4 (0.2 – 0.8) | 0.4 (0.2 – 0.8) | |
| Australia / New-Zealand | 0.8 (0.5 – 1.2) | 0.7 (0.5 – 1.2) | |
| Type of Affiliation (other vs university) | 1.6 (1.2 – 2.2) | 1.4 (1.1 – 2.0) | 0.08 |

| **Citation characteristics** | **Crude OR** | **Adjusted OR *** | **$R^2$ *** |
|---|---|---|---|
| Authority (ref: low) | | | 0.08 |
| medium | 2.1 (1.5 – 2.9) | 1.6 (1.1 – 2.2) | |
| high | 2.2 (1.6 – 3.0) | 1.6 (1.1 – 2.2) | |

In these sensitivity analyses, the four most cited publications shown in Table S2 are excluded as *cited* publications; they are still included as *citing* publications. * adjusted for study design and log sample size. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. *** only adjusted for study design. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. N = number of potentially cited publications; n = number of potential citation paths.

**Table S6. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited within full network, with a 1-year time lag between cited and citing publication. (N = 110, n = 5057).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.11 |
| only Number of Siblings | 0.7 (0.5 – 1.0) | 0.4 (0.3 – 0.7) | |
| only Infection History | 1.2 (1.0 – 1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 1.2 (0.8 – 1.7) | 2.2 (1.4 – 3.5) | |
| supportive results | 1.7 (1.2 – 2.4) | 3.2 (2.2 – 4.6) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.4 (3.2 – 6.0) | | 0.05 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (0.9 – 2.2) | | |
| retrospective cohort | 0.9 (0.7 – 1.2) | | |
| prospective cohort | 0.3 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.4 (1.9 – 6.2) | | |
| editorial / other | 0.3 (0.1 – 0.4) | | |
| Sample Size (ref: low, n = 3199) | | | 0.02 |
| medium | 1.6 (1.1 – 2.2) | 1.4 (0.8 – 2.4) | |
| high | 1.4 (1.0 – 2.1) | 1.6 (0.9 – 2.6) | |
| Specificity (ref: low) | | | 0.12 |
| medium | 2.8 (1.6 – 4.7) | 3.1 (1.7 – 5.6) | |
| high | 10.3 (6.4 – 17) | 6.1 (3.6 – 10) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.5 (0.3 – 0.8) | 0.3 (0.2 – 0.5) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.10 |
| profit or both profit/non-profit | 0.8 (0.6 – 1.2) | 0.8 (0.5 – 1.1) | |
| not reported | 0.4 (0.3 – 0.5) | 0.8 (0.6 – 1.1) | |
| Number of Authors (ref: 1-2) | | | 0.10 |
| 3 - 5 | 2.0 (1.5 – 2.8) | 1.1 (0.7 – 1.8) | |
| >= 6 | 3.7 (2.7 – 5.0) | 1.7 (1.0 – 2.6) | |
| Number of Affiliations (ref: 1) | | | 0.10 |
| 2 | 3.0 (2.2 – 4.1) | 2.1 (1.4 – 3.0) | |
| >= 3 | 2.2 (1.7 – 2.9) | 1.7 (1.2 – 2.3) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.1 (0.9 – 1.4) | 1.0 (0.8 – 1.3) | |
| >= 50 | 0.5 (0.3 – 0.7) | 0.7 (0.4 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4580) | | | 0.12 |
| 2 – 4 | 3.2 (2.0 – 4.9) | 2.5 (1.6 – 4.0) | |
| >= 4 | 5.4 (3.5 – 8.4) | 4.5 (2.9 – 7.1) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 4913) | 0.8 (0.6 – 1.0) | 0.7 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 1.0 (0.7 – 1.5) | 1.0 (0.6 – 1.8) | |
| Asia | 0.3 (0.2 – 0.7) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.9) | 0.5 (0.3 – 0.9) | |
| Type of Affiliation (other vs university) | 2.3 (1.8 – 2.9) | 1.9 (1.5 – 2.5) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.8 (1.9 – 3.9) | 1.9 (1.3 – 2.7) | |
| high | 4.0 (2.9 – 5.5) | 2.8 (2.0 – 4.0) | |

* adjusted for study design. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.

**Table S7. Sensitivity analyses on odds ratios (95% CIs) for the chance of being cited, without citing publications with less than 10 potential citation paths (N = 110, n = 5507).**

| Publication characteristics, content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Type of Exposure (ref: both Siblings & Infections) | | | 0.10 |
| only Number of Siblings | 0.8 (0.6 – 1.1) | 0.5 (0.4 – 0.7) | |
| only Infection History | 1.2 (1.0 – 1.6) | 0.8 (0.6 – 1.1) | |
| Study Outcome (ref: non-supportive results) ** | | | 0.12 |
| mixed / unclear results | 1.2 (0.8 – 1.7) | 2.3 (1.5 – 3.6) | |
| supportive results | 1.7 (1.3 – 2.4) | 3.0 (2.1 – 4.2) | |

| Publication characteristics, other content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Publication Type (empirical vs synthesis) | 4.2 (3.1 – 5.6) | | 0.04 (crude) |
| Study Design (ref: cross-sectional) | | | 0.09 (crude) |
| case control | 1.4 (1.0 – 2.2) | | |
| retrospective cohort | 0.8 (0.6 – 1.1) | | |
| prospective cohort | 0.4 (0.2 – 0.5) | | |
| narrative review | 0.1 (0.0 – 0.1) | | |
| systematic review | 3.3 (1.8 – 5.8) | | |
| editorial / other | 0.3 (0.2 – 0.4) | | |
| Sample Size (ref: low, n = 3423) | | | 0.02 |
| medium | 1.5 (1.1 – 2.1) | 1.5 (0.9 – 2.5) | |
| high | 1.4 (1.0 – 2.0) | 1.7 (1.1 – 2.8) | |
| Specificity (ref: low) | | | 0.11 |
| medium | 2.2 (1.4 – 3.6) | 2.5 (1.4 – 4.2) | |
| high | 8.6 (5.6 – 13) | 4.9 (3.1 – 7.9) | |

| Publication characteristics, not content-related | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Conclusive Title (yes vs no) | 0.4 (0.3 – 0.7) | 0.3 (0.2 – 0.5) | 0.10 |
| Funding Source (ref: exclusively non-profit) | | | 0.09 |
| profit or both profit/non-profit | 0.9 (0.6 – 1.3) | 0.8 (0.6 – 1.2) | |
| not reported | 0.4 (0.3 – 0.5) | 0.7 (0.5 – 1.0) | |
| Number of Authors (ref: 1-2) | | | 0.09 |
| 3 - 5 | 2.0 (1.5 – 2.7) | 1.1 (0.7 – 1.7) | |
| >= 6 | 3.8 (2.8 – 5.2) | 1.7 (1.1 – 2.6) | |
| Number of Affiliations (ref: 1) | | | 0.09 |
| 2 | 2.8 (2.1 – 3.7) | 1.9 (1.3 – 2.6) | |
| >= 3 | 2.2 (1.7 – 2.9) | 1.6 (1.2 – 2.3) | |
| Number of References (ref: <30) | | | 0.09 |
| 30 - 50 | 1.0 (0.8 – 1.3) | 0.9 (0.7 – 1.2) | |
| >= 50 | 0.4 (0.3 – 0.6) | 0.8 (0.4 – 1.3) | |

| Journal characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Journal Impact Factor (ref: 0-2, n = 4955) | | | 0.11 |
| 2 – 4 | 3.2 (2.1 – 5.0) | 2.5 (1.6 – 3.9) | |
| >= 4 | 5.7 (3.8 – 8.8) | 4.6 (3.0 – 7.2) | |

| Author characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Gender (female vs male, n = 5350) | 0.8 (0.6 – 1.0) | 0.8 (0.6 – 1.0) | 0.09 |
| Region (ref: Europe) | | | 0.11 |
| North-America | 0.9 (0.6 – 1.3) | 0.9 (0.5 – 1.4) | |
| Asia | 0.3 (0.2 – 0.6) | 0.2 (0.1 – 0.4) | |
| Australia / New-Zealand | 0.5 (0.3 – 0.8) | 0.5 (0.3 – 0.8) | |
| Type of Affiliation (other vs university) | 2.4 (1.9 – 3.0) | 2.0 (1.6 – 2.6) | 0.10 |

| Citation characteristics | Crude OR | Adjusted OR * | $R^2$ * |
|---|---|---|---|
| Authority (ref: low) | | | 0.11 |
| medium | 2.4 (1.8 – 3.3) | 1.8 (1.3 – 2.5) | |
| high | 3.8 (2.9 – 5.1) | 2.9 (2.2 – 4.0) | |

* adjusted for study design. ** both the 'crude' and adjusted analyses are (additionally) adjusted for type of exposure. **supportive:** supportive for Strachan's original hygiene hypothesis, i.e. inverse association between siblings/infections and allergy. **non-supportive:** no association or positive association between siblings/infections and allergy. **N**: number of publications. **n**: number of potential citation paths.