Use of a non-probabilistic online panel as a control group for case-control studies to investigate food and waterborne outbreaks in Lower Saxony, Germany

Delphine Perriat¹,²*, Elke Mertens², Johannes Dreesman²

¹ European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Control and Prevention (ECDC), Solna, Sweden
² Public Health Agency of Lower Saxony, Department for Infectious Disease Epidemiology, Germany

*corresponding author, delphine.perriat@gmail.com

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Introduction

In Germany, infectious disease outbreaks continue to pose a high burden on public health (1). Control measures should be timely and rapidly implemented in order to prevent new infections and protect the health of the public. To decide on the best control measures, it is key to identify the outbreak source. Case-control methodologies are commonly used to achieve this (2). Outbreak cases and controls are questioned about possible risk factors, and their answers are compared (e.g. food exposures during foodborne outbreaks).

Established methods of recruiting controls include case- or physician-nominated controls, random or sequential digit dialing and convenience sampling (2–4). In addition of being resource-intensive, such methods are mostly slow, resulting in delays in identifying the source of infection, which can be vital for stopping severe outbreaks (5). Additionally, those methods can be subject to selection bias, as controls are not representative of the population at risk.

New and innovative methods are required, which are easy and timely to implement and reduce bias (6). Web-surveys are increasingly used to collect data, including in the field of health and in epidemiological surveys as they are cost-effective while maintaining scientific rigor (7–10). Moreover, methods that allow a prior recruitment of controls are promising, because they offer the possibility to improve the timeliness and the representativeness of controls for the population that gave rise to the cases (11).

Recently, commercial online panels have shown encouraging results (12–14). Those panels comprise individuals who have elected to receive internet-based questionnaires and can opt to complete them, usually in return of a reward. They are frequently used by marketing companies or polling organizations to obtain information about a target audience. Commercial online panels have successfully been used to collect epidemiological exposure data in retrospective (15) and prospective case-control studies (16–21). One of the key benefits of this approach is that it allows efficiently and rapidly recruiting many controls, therefore enabling timely investigation of outbreaks.

According to the German law, the primary responsibility of outbreak investigations lies with the local health authorities, and the coordination can be transferred to the state or national health authorities in complex situations (e.g. when the outbreak spread to several localities or regions) (22). Analytic studies are a key component of outbreak investigations (23). However, they are often not conducted as they require human and financial resources beyond typical case investigation and case finding efforts (24). Local health authorities would highly benefit from the availability of online panels to recruit controls. However, such method remains beyond their reach because of their limited public health resources. As part of efforts to strengthen the investigation of food and waterborne outbreaks of infectious gastrointestinal diseases at the local level, we identified the need to explore the use of an online panel as a source of controls for case-control studies as part of outbreak investigations.

The "Hygiene and Health Online Survey (HuGO)" panel consists of 277 adults, who live in the federal state of Lower Saxony, Germany. They accepted to regularly
answer online to health- and hygiene-related questions. We examined the feasibility, suitability and reliability of using the non-probabilistic online HuGO panel as a control group to recruit controls for case-control studies to investigate food and waterborne outbreaks in Lower Saxony, Germany.

Methods

The data sources and data analysis steps are summarized in the Table 1.

Data sources

We used three data sources:

- **The Lower Saxony Microcensus 2018**: The Microcensus contains basic socio-demographic information on a randomly selected sample of the population living in Lower Saxony, Germany (n = 6,537), including gender, nationality, age, household composition, school and postgraduate training and employment status. This sample is considered representative of Lower Saxony (25).

- **Four historical case-control studies**: The four historical studies successfully investigated food and waterborne outbreaks in Lower Saxony and in the neighbouring German federal States between 2001 and 2017, using case-control designs: *Campylobacter jejuni* infection via tap water (study A), *Salmonella enterica Bovismobificans* infection via raw pork (study B), *Salmonella enterica Goldcoast* infection via raw pork (study C) and *Salmonella enterica Oranienburg* via chocolate (study D). Details of the conduction of the studies are given in Table 2. Parallel microbiological investigations to the studies provided microbiological evidence that supported the epidemiological findings.

- **The Hygiene and Health Online Survey (HuGO) panel**: To form the HuGO panel, participants from the Hygiene and Behavior Infectious Diseases Study (HaBIDS) panel were integrated. The HaBIDS panel was a population-based longitudinal panel, created by the Helmholtz Center for Infection Research in 2014. A total of 2,379 participants aged 15 to 69 years were drawn by means of probability sampling from the regional population registries of Lower Saxony (26). They were regularly consulted to answer online to questions on knowledge, attitudes and practices related to infections in Lower Saxony. In 2015, the HaBIDS panel included 1,037 participants aged more than 18 years old (27). In 2018, they were offered to form the HuGO panel, led by the Public Health Agency of Lower Saxony (Niedersächsisches Landesgesundheitsamt, NLGA, https://www.nlga.niedersachsen.de/). The panel aims at supporting the activities of the Public Health Agency, in infection prevention and control. This includes the investigation of outbreaks and the quick assessment of the population perceptions towards infection control measures. A total of 277 members of the HaBIDS panel agreed to form the HuGO panel. On January 17, 2019, the HuGO panelists were asked by email to answer an online survey, in which they were questioned about their socio-demographic characteristics and eating habits of the past week. The socio-demographic
questions were based on the Lower Saxony Microcensus 2018, and the eating habit questions on the four historical case-control studies. A reminder was sent on February 22, 2019. As controls of case-control study should be free of the outcome of interest, panelists with gastrointestinal symptoms in the week prior to answering the questionnaire were filtered out using a dedicated question at the beginning of the online questionnaire.

Data analysis
We explored the use of the panel according to three components:

- Feasibility of using the HuGO panel as a control group in outbreak investigations. We reported the human and financial resources required to conduct the case-control study using panelists as controls, including the creation of the online questionnaire. We reported the response rate among HuGO panelists after receiving the questionnaire: on the same day, after one day, after one week, after receiving a reminder, and in total. When available, we provided information on the time, human and financial resources required to conduct the historical studies.

- Suitability of the HuGO panel for Lower Saxony in terms of basic socio-demographic characteristics. We compared the panelists to the sample of the Lower Saxony Microcensus 2018 on sex, age, nationality, household composition, education level and employment status, using chi2 goodness of fit tests.

- Reliability of using the HuGO panel as a control group in the investigation of four historical outbreaks. We refer as "historical studies" to case-control studies with historical cases and historical controls, and as "HuGO studies" to case-control studies, with historical cases and HuGO panelists as controls. In the HuGO studies, we controlled for the possible confounding effects of sex and age by matching the frequencies between historical cases and panelists on both variables (Supplementary File 1). When the information on sex or age of historical cases was not available, the frequencies of panelists were matched to those of the Lower Saxony Microcensus 2018. Separately in historical and in HuGO studies, we used univariable logistic regression analyses to assess the association between the food and water exposures and the disease. When possible, we performed multivariable logistic regressions. We included in the regression models all exposure variables that were associated with the disease with a p-value less than 0.2 in univariable analyses. We also included in the models the categorical variables for age and sex (as possible confounders) when the controls where not frequency matched to cases on those variables. Odds ratios (OR) were used to determine whether a particular exposure was a risk factor for the occurrence of the disease. The 95% confidence interval (95%CI) was used to estimate the precision of the OR. An exposure was regarded as a risk factor if the OR was >1 and the p-value < 0.05, or as a protective factor if the OR was <1 and the p-value < 0.05. If an exposure was a risk factor or a protective factor in both
historical and HuGO studies, we considered that both studies had similar results.
All analyses were performed using the statistical software R.

Results

Feasibility
One scientist, working for the Public Health Agency of Lower Saxony conducted the study. A working day was required to create the online questionnaire using the Lamapoll® software. Apart from the software cost, no additional financial resource was required. A total of 203/277 (73%) HuGO panelists answered the survey: 76/277 (27%) answered the questionnaire on the day they received it, adding up to 107/277 (39%) on the following day and to 152/203 (54%) within a week. After receiving a reminder, a month later, 30/277 (11%) additional panelists answered.

Suitability
There were statistically significant differences in the distribution of all measured sociodemographic characteristics between the panelists and the population of Lower Saxony (Table 3). For example, the proportion of women participating in the HuGO panel was higher than in the population of Lower Saxony (63% vs. 51%), the proportion of people younger than 30 was lower (7% vs. 17%) and a higher proportion attended university (32% vs. 9%).

Reliability
No panelists experienced gastrointestinal symptoms in the week prior to the survey. The Table 4 summarizes the results of the univariable logistic regression analyses for the food items that were identified as outbreak sources in the historical studies. Results of univariable analyses where controls were frequency matched to cases on sex and age, and results of multivariable analyses for all food items are provided in the Supplementary File 2.

Using panelists as controls to investigate the four historical outbreaks gave consistent results in three instances. In the studies B, C and D, the ORs of the outbreak sources were significant and of similar magnitude to those of the historical studies. In Study A, drinking tap water at home was associated with the disease in the historical study (Odds Ratio in univariable analysis (ORu) = 9.6 [1.8-51]), but not in the HuGO study (ORu = 1.6 [0.33-7.5]). Results were consistent in univariable and multivariable analyses, with or without frequency matching.

Discussion
We investigated the feasibility, suitability and reliability of using panelists as controls in case-control studies to investigate food and waterborne outbreaks. We found that using panelists would lead to the same results as using traditional controls, and the
study would benefit from increased speed of recruitment as well as limited costs for public health action.

**Timely and low-cost outbreak investigation thanks to panel controls**

The majority of panelists responded to the online questionnaire in less than a week, ensuring a higher response rate than traditional methods such as random digit dialing (9,13). The recruitment of panelists as controls also required far less staff and financial resources than other approaches, as it amounts to sending an email rather than conducting numerous face-to-face or telephone interviews (12; 14). In the event of an actual food or waterborne outbreak, the HuGO panel offers a more timely and cost-effective control recruitment and analysis, which would lead to timelier public health actions to limit additional cases (e.g. trace-back investigations, recall of products). It is nevertheless important to consider that the constitution of the HaBIDS panel, from which the HuGO panel stems, did require substantial resources. Indeed, the 2379 panelists were recruited thanks to the dedication of a 1-2 researchers, who drew 16,000 people from the registries of Lower Saxony and send them invitation letters per post therefore reaching an overall response rate of 8.9% (26).

**Suitability of panel controls for outbreak investigation**

The study assessed the suitability of panel controls for case-control studies. Ideally, one would be confident using panelists as controls if these were not more biased than controls used in current best practices. Controls are used to estimate the prevalence of exposures in the population that gave rise to the cases. They are expected to be free of the outcome of interest, representative of the population at risk of the outcome and selected independently of the exposure of interest (28). In the situation of an outbreak investigation, case-control studies aim to estimate a particular exposure-disease association, while appropriately controlling for confounding and avoiding other biases.

Selection bias is a particular problem inherent in case-control studies, where it gives rise to non-comparability between cases and controls, threatening the generalizability of the study results (2). Our study is affected by a sampling bias, as HuGO panelists volunteered to participate in the study. First, HuGO panelists differ from the general population of Lower Saxony in terms of sociodemographic factors such as age, sex and education level. We reduced this bias by matching the frequencies between historical cases and panelists on sex and age, therefore controlling for the possible confounding effects of both variables. Additionally, controls recruited through traditional methods are also rarely representative of the general population (2). It is largely accepted that a lack of representativeness on sociodemographic characteristics does not hamper scientific inference (29,30). Valid scientific inference is achieved if the confounders are controlled for, and there is no reason to believe that control of confounding can be more easily achieved in a randomly-selected control group that in a panel group (29). Second HuGO panelists are significantly more educated than the general population of Lower Saxony. As studies have shown
that a higher education status is associated with healthier eating habits (31), it is likely that HuGO panelists may be more health-conscious than the general population (7,12).

Using the HuGO panelists as controls decreased the likelihood of information bias as compared to using traditional controls, resulting in a greater validity of the food exposure information. First, there is little recall bias as panelists responded within a few days to the questionnaire. As traditional controls are often recruited with days or weeks of delay after the outbreak occurs, they have more difficulties to remember their food exposures at a particular time point. Panelists would then be particularly useful when investigating outbreaks caused by uncommon food exposures, as they are oftentimes more forgotten than common food exposures (32). Additionally, online surveys are less likely to suffer from social desirability bias as other data collection methods, such as phone or face-to-face interviews (26). Panelists are less likely to underreport “bad” food items, and over report “good” food items than traditional controls. They would therefore also be particularly adequate to investigate sensitive exposures, benefitting from the survey anonymity (12,26).

Reliability of control panels to identify outbreak sources

The study explored the circumstances in which using panelists would be reliable to investigate food and waterborne outbreaks. Indeed, investigators expect consistent conclusions regarding the likely outbreak source, regardless of the study design they use for the investigation.

In the present study, three of four outbreak sources could be identified using panelists as controls (studies B, C and D). The differences in the magnitude of the effect estimates (odds ratio) between historical and HuGO studies did not affect the ability of panelists to successfully identify the outbreak sources. As odds ratios measuring associations between contaminated food items and the disease are usually very high during food and waterborne outbreaks (32), we argue that they are not significantly affected by differences in exposure proportions between panelists and traditional controls.

The study shows that in the outbreak A, the association between the consumption of tap water and the gastrointestinal disease could not be identified with a statistical significance by using panelists as controls. We hypothesize that, in this particular situation, panelists did not have the chance of being exposed to the very localized outbreak source (contamination of water supplies with surface water due to a heavy rainfall), and were thus not representative of the population at risk of the outcome. They did not live in the same area as the cases, and were not questioned at the particular time during which the waterborne outbreak occurred. This result furthers the argument that the reliability of panelists is likely to be higher when used as controls in the investigation of region- or nationwide outbreaks (like outbreaks B, C and D) as compared to very local outbreaks (like outbreak A). On the other hand, historical controls were likely to have changed their drinking habits, and drank significantly less tap water than usual, as they were interviewed around 14 days after
the first cases developed symptoms. At that time, information related to the contaminated tap water was already communicated in the news, with a recommendation to rather drink bottled water.

Strengths and limitations

The main strength of this study is that it is a proof of concept for a promising method to recruit controls for case-control studies. Panelists can be asked specific questions about particular products they ate, ways of cooking, places they shopped at etc., as soon as an outbreak occurs, enabling a quick investigation. The present study participates in the efforts to provide local public health professionals with innovative methods to empower them in the conduction of outbreak investigations (33). The study also assesses likely bias of using panelists as controls in the context of outbreak investigations. It supports the findings of other studies that the risk of bias must be assessed anew when a study is conducted to investigate an outbreak (11). Yet overall, the risk of bias when using the HuGO panel should be smaller in situations where the cases seem to resemble the general population (with a tendency of higher education because this is what the panel is composed of). Another strength of the study is the oversampling of the control group. This allows the selection of a subset of more valid controls to match the frequencies of cases in terms of sex and age, thereby addressing confounding and some of the bias introduced by using panelists as controls. Such an approach is here possible given that there is no additional cost per additional questionnaire.

The main limitation of the study concerns the historical studies. Panelists could only be used when population-based controls were used in the historical studies, but not in specific settings (e.g. outbreaks during a party or at a restaurant). This strongly reduced the choice of historical studies for this analysis. The available studies had limited information on some key exposures and multivariable analyses could therefore not always be conducted. Additionally, the panel is affected by a selection bias. As this cannot be controlled via study design, it is therefore important to consider whether the measure of effect for a particular exposure may have been due to such inherent sampling issue. In the situation of a prospective outbreak investigation, socio-demographic data could easily be collected among cases and panelists, and a weighting method could minimize this bias (e.g. frequency matching, propensity scores, quotas) (13).

Perspectives

The study provides encouraging results and warrant further exploration to prove the validity of using panelists as controls in case-control studies. First, we will recruit more panelists (including children), in order to increase the sociodemographic diversity of the panel and its suitability to investigate the upcoming outbreaks. Then, as soon as a likely food or waterborne outbreak occurs in Lower Saxony, we will conduct two parallel case-control studies in which controls would be selected either through a traditional method or from the HuGO panel. The results of both studies will
be compared. Propensity score matching will be used to reduce selection bias (34,35).

Finally, in order to assess in which scenarios or for which hypothesized food and water exposures or behaviours using panelists as controls might be more appropriate than traditional controls, any selection bias introduced by using the panel need to be better understood. A prospect is to compare the reported food and water exposures and behaviours of panelists with that of probability samples from population-based food exposure surveys, such as with the German food exposure survey (36,37) or other sources of such data for which selection biases are minimized or previously characterized (38).

Conclusion
The study shows that using panelists as controls in case-control studies is feasible and suitable to investigate diffuse outbreaks within an adequate time frame, and researchers can benefit from increased speed of recruitment and limited costs. Nevertheless, the circumstances in which panelists are reliable to investigate food and waterborne outbreaks should be further investigated. We therefore recommend the further evaluation of this approach in parallel case-control studies and case-panel studies, especially in the context of food and waterborne outbreak investigations.

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Declaration of interest
Conflicts of Interest: None.

Ethics approval and consent to participate
The recruitment of participants for a panel was approved by the Ethics Committee of Hannover Medical School (No. 2021-2013) and by the Federal Commissioner for Data Protection and Freedom of Information in Germany. All participants provided informed consent before entering the HuGO panel.

Data availability statement.
Data supporting the findings of this study are openly available in Zenodo at https://doi.org/10.5281/zenodo.5243412, reference number [5243412].
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Table 1. Overview of the study methods to investigate the feasibility, suitability and reliability of using the online Hygiene and Health Online Survey (HuGO) panel as a control group for case-control studies to investigate foodborne outbreaks in Lower Saxony, Germany, 2019

| Data sources | Data analysis |
|--------------|---------------|
| **Lower Saxony Microcensus 2018** | **Suitability**: Comparison of the sociodemographic characteristics of the HuGO panelists with participants to the Lower Saxony Microcensus 2018 (chi² goodness of fit test). |
| population sample that is considered representative of Lower Saxony (n= 6537) | **Feasibility**: Computation of response rates among HuGO panelists, and description of the human and financial resources required to conduct the HuGO and historical studies. |
| **Hygiene and Health Online Survey (HuGO) panel** | **Reliability**: Comparison of the strength of the association (using odds ratios) between food exposures and disease, using the four “historical studies” (case-control studies with historical cases and historical controls) vs. the four “HuGO studies” (case-control studies with historical cases and HuGO panelists as controls). |
| non-probabilistic online panel comprised of 277 adults living in Lower Saxony, Germany, who accepted to answer hygiene- and health-related questions, 2019 | |
| **Historical studies** | |
| four case-control studies that successfully investigated foodborne outbreaks in Lower Saxony and neighboring federal states in Germany, 2003-2017 | |

Table 2. Key features of four historical case-control studies that successfully investigated foodborne outbreaks in Germany between 2003 and 2017
| Study identifier | A | B | C | D |
|------------------|---|---|---|---|
| Study period     | July 2017 | February 2005 | June 2004 | September 2001 |
| Study area       | City of Lamspringe, Lower Saxony | Lower Saxony | Saxony Anhalt (neighbouring state of Lower Saxony) | Several German states (including Lower Saxony) |
| Hypothesised exposure | Consumption of contaminated tap water | Consumption of contaminated raw pork | Consumption of contaminated raw pork | Consumption of contaminated chocolate |
| Pathogen (microbiological investigation) | Campylobacter jejuni | Salmonella enterica Bovismobificans | Salmonella enterica Goldcoast | Salmonella enterica Oranienburg |
| Control selection | Random digital dialling among inhabitants of Lamspringe | Random digital dialling among inhabitants of Lower Saxony | Random digital dialling among inhabitants of Saxony Anhalt | Random digital among inhabitants of Germany 1:1 individual matching on sex and age |
| Data collection  | Telephone interviews conducted by 4 staff members of the state health authority during 7 days. Overall 111 persons were called; 46 accepted to participate (41% response rate), among which 35 met the control selection criteria (e.g. presence in Lamspringe during the outbreak period) | Telephone interviews | Telephone interviews | Telephone interviews conducted by a large team of local, state and national health agency staff |
| Number of controls [Number of cases] | 35 [12] | 37 [38] | 54 [14] | 50 [48] |
| Studied exposures | • sex, age • consumption in the last 7 days of unboiled tap water at home, unboiled tap water outside of home | • sex, age • consumption in the last 7 days of raw pork, raw sausage pork, cooked pork, raw beef, raw egg, salad, sprout | • sex, age • consumption in the last 3 days of raw pork, raw sausage pork, cooked pork, raw beef, raw egg | • sex, age • shopping in the last 7 days in the supermarket chain X • consumption in the past 7 days of chocolate bought in the supermarket chain X |
| Available data source | Individual-level data | Individual-level data | Aggregated data | Aggregated data |
Outbreak details

A heavy rainfall led to a contamination of water supplies with surface water in the city of Lamspringe. Interviews of controls were conducted around 14 days after the first cases developed symptoms. At that time, information related to the likely contaminated tap water was communicated in the newspapers, with a recommendation to drink bottled water.

In 2004, Lower Saxony and Saxony Anhalt reported most of the S. Goldcoast cases in Germany (39). A majority of cases included in the case-control study reported having eaten raw pork, which was found to have been supplied by a slaughterhouse in Lower Saxony. S. Goldcoast was found in raw pork as part of self-checks in this slaughterhouse. In Lower Saxony, over 90% of the surveyed cases stated that they had eaten raw pork products in the 3 days before disease onset.

A trace-back analysis of the implicated chocolates along supply chains allowed to identify that they were contaminated prior to their distribution in Germany by the supermarket chain X, and in other European countries (40).

Table 3. Comparison of sociodemographic characteristics between the Hygiene and Health Online Survey (HuGO) panelists (n = 203) and the population of Lower Saxony (Lower Saxony Microcensus 2018)

|                  | HuGO-Panel (n=203) | Lower Saxony Microcensus (n=6537) | chi2 goodness of fit test pvalue |
|------------------|--------------------|----------------------------------|---------------------------------|
|                  | n  | %    | n  | %    |                              |
| sex              |    |      |    |      |                              |
| male             | 74 | 37   | 3232 | 49   | < 0.001                        |
| female           | 129| 63   | 3304 | 51   |                              |
| nationality      |    |      |    |      |                              |
| german           | 201| 99   | 5956 | 91   | < 0.001                        |
| not german       | 2  | 1    | 581  | 9    |                              |
| age group        |    |      |    |      |                              |
| ≥ 18 and <30     | 14 | 7    | 1110 | 17   |                              |
| ≥ 30 and <40     | 24 | 12   | 938  | 14   |                              |
| ≥ 40 and <50     | 41 | 20   | 1054 | 16   |                              |
| ≥ 50 and <60     | 73 | 36   | 1286 | 20   |                              |
| ≥ 60             | 51 | 25   | 2148 | 33   | < 0.001                        |
### Table 4. Comparison of the strength of association between food exposures and disease (odds ratios) in univariable logistic regression analyses between historical and HuGO case-control studies to investigation food- and water-borne outbreaks, Germany 2019

| Study | Outbreak Source | Historical Cases | Historical Controls | Panel Controls | Historical Study | HuGO Study | Historical Study (black) and HuGO Study (blue) | Similar Results in Both Studies |
|-------|-----------------|------------------|---------------------|----------------|-----------------|-----------|-----------------------------------------------|---------------------------------|
|       |                 | n   | %   | n   | %   | n   | %   | OR [95%CI] | p | OR [95%CI] | p | OR [95%CI] | **[95%CI]** |                                  |                                 |
| A     | Tap Water       |      |     |      |     |      |     |          |   |          |   |          |           |                                  |                                 |
|       | Total           | 12  | 100 | 35  | 100 | 203 | 100 |          |   |          |   |          |           |                                  |                                 |
|       | No              | 2   | 17  | 23  | 66  | 49  | 24  |          |   |          |   |          |           |                                  |                                 |
|       | Yes             | 10  | 83  | 12  | 34  | 154 | 76  |          |   |          |   |          |           |                                  |                                 |
| B     | Raw Pork        |      |     |      |     |      |     |          |   |          |   |          |           |                                  |                                 |
|       |                 |      |     |      |     |      |     | 9.2 [2.4-35] |   | 4.3 [2.1-9.1] | |          | |                                  |                                 | yes                             |                                 |

German translations: ¹kein Berufsabschluss, ²Lehre/ Berufsausbildung, ³Fachschulabschluss, ⁴Fachhochschule / Berufsakademie, ⁵Universität / Promotion

**Table 4.** Comparison of the strength of association between food exposures and disease (odds ratios) in univariable logistic regression analyses between historical and HuGO case-control studies to investigation food- and water-borne outbreaks, Germany 2019

- **A** Tap Water
  - Total: 12 cases, 35 controls, 203 panel controls
  - OR: 9.6 [1.8-51], p<0.05 for historical study; 1.6 [0.30-7.5], p=0.70 for HuGO study
- **B** Raw Pork
  - Yes: 10 cases, 12 controls, 154 panel controls
  - OR: 9.2 [2.4-35], p<0.05 for historical study; 4.3 [2.1-9.1], p=0.70 for HuGO study

Similar results in both studies:
- Tap Water: No
- Raw Pork: Yes
**The four historical studies successfully investigated food- and water-borne outbreaks in Lower Saxony and in the neighboring German federal States, using case-control designs:**

- **Campylobacter jejuni** infection via tap water in 2017 (study A),
- **Salmonella enterica Bovismorbificans** infection via raw pork in 2005 (study B),
- **Salmonella enterica Goldcoast** infection via raw pork in 2004 (study C) and
- **Salmonella enterica Oranienburg** via chocolate in 2001 (study D).

### Table: Summary of Study Results

|                | raw pork | chocolate |
|----------------|----------|-----------|
|                | total    | no        | yes       | total    | no        | yes       |
|                | 38       | 21        | 17        | 100      | 37        | 14        |
|                | 100      | 55        | 45        | 100      | 100       | 100       |
|                | p< 0.001 | p< 0.001  | p< 0.001  | 12 [3.1-47] | 9.6 [3.0-30] | p< 0.001 |
|                | yes      | no        | yes       | total    | no        | yes       |
|                | 14       | 5         | 9         | 54       | 36        | 64        |
|                | 100      | 47        | 7         | 100      | 87        | 13        |
|                | p< 0.001 | p< 0.001  | p< 0.001  | 5.0 [1.1-47] | 22 [5.8-83] | p<0.05 |
|                | yes      | no        | yes       | total    | no        | yes       |
|                | 48       | 33        | 11        | 100      | 75        | 25        |
|                | 100      | 96        | 2         | 100      | 98        | 4         |
|                | p< 0.001 | p< 0.001  | p< 0.001  | 5.0 [1.1-47] | 22 [5.8-83] | p<0.05 |

**Notes:**
- **OR:** Odds Ratio, **95%CI:** 95% Confidence Interval, **p:** two-sided p-value from Fisher's Exact test.

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