# Supplementary Data

## Supplementary Technical Appendix S2: Description of Inputs and Approach for Laboratory Testing and Test Sensitivity by Pathogen

For those pathogens where laboratory-confirmed illnesses were scaled up to the Canadian population, laboratory testing and test sensitivity values were required. Supplementary Technical Appendix S2 Table S1 presents estimated laboratory testing and test sensitivity values by pathogen.

#### Laboratory Testing

Laboratory testing was divided into those pathogens that are routinely tested and those for which a laboratory test needs to be specifically requested. ''Routinely tested'' therefore refers to the proportion of Canadian laboratories testing for the specified pathogen in a routine stool test (e.g., 97% of laboratories will routinely test a stool sample for Campylobacter spp.). ''Test requested'' refers to the proportion of cases for which a physician requests a laboratory test for the disease-causing pathogen (e.g., 80% of those with brucellosis who submit a sample to a laboratory will be tested for Brucella spp.). It is assumed that if a specific test is requested by a physician, it will be completed by the laboratory.

The values for those pathogens that are routinely tested were based on the 2001 National Studies on Acute Gastrointestinal Illness (NSAGI) Laboratory Survey (Government of Canada, 2002) and a review by Canadian Public Health Laboratory Network (CPHLN) directors. For those pathogens for which a test needs to be requested, values were derived from the 2001 NSAGI Laboratory Survey, the U.S.-CDC estimates (Scallan et al., 2011), other literature, and the CPHLN directors' review. All of the laboratory testing values are general ranges chosen to encompass pathogens that were deemed to have similar testing practices as well as uncertainty in the values.

The 2001 NSAGI Laboratory Survey was designed to examine public health reporting within the Canadian enteric disease surveillance system at the laboratory interface (Government of Canada, 2002). It was administered to 470 microbiology laboratories across Canada, of which 408 (87%) responded (Government of Canada, 2002). Respondents answered questions pertaining to the two aims of the survey: ''1) quantify the proportion of stool specimens that are positive for an enteric pathogen; and 2) examine inter-laboratory variations in key factors influencing whether an etiological agent is identified as it passes through the laboratory interface and understand how such variations may affect the interpretation of surveillance data'' (Government of Canada, 2002).

The CPHLN was established in 2001 and is a national association of public health laboratory professionals (The Canadian Public Health Laboratory Network, 2012). The network acts as a unified voice for federal and provincial laboratory directors (The Canadian Public Health Laboratory Network, 2012). Suggested values for laboratory testing for each of the pathogens were sent out to 10 CPHLN directors representing 10 different provinces. The directors were asked to provide a yes/no answer to whether they thought that the suggested value was reasonable and to provide any comments. Responses were received from 8 (80%) of the directors. Once the completed surveys were received, the suggested values were revised based on the directors' comments. These revised values were then sent out to the CPHLN directors once again for a final review.

A slight modification of the data sources used applies to Cryptosporidium spp., Cyclospora cayetanensis, and Giardia spp. For these pathogens, the laboratory testing values were based on two different sources. This included proportion of stool samples positive for parasites from the 2001 NSAGI Laboratory Survey (Government of Canada, 2002) and second, on a value from a British Columbia, Canada study, reporting that 56% of physicians ''always or often'' request tests for parasites from patients with acute gastrointestinal illness (Edge et al., 2007).

## Test Sensitivity

Test sensitivity refers to the probability that a diseased person will be identified as diseased (positive) by a given test. The test or laboratory method was chosen to be the one most commonly used to identify the pathogen in Canada, as indicated in the 2001 NSAGI Laboratory Survey (Government of Canada, 2002) and the literature. Values for test sensitivity for each of the pathogens were then derived from the literature and the CPHLN directors' review. As for laboratory testing, these values are general ranges chosen to encompass values from the literature and pathogens using similar testing methods as well as uncertainty. A minimum of 50% test sensitivity was chosen as a conservative estimate (i.e., the lower the test sensitivity, the greater the underdiagnosis of a pathogen).

Studies from the literature were assessed, with preference given to those evaluating a diagnostic test (versus, for example, an outbreak), using human clinical samples, having an appropriate reference standard, having a larger sample size, and being more recent. For the review by CPHLN directors, as with laboratory testing, the suggested laboratory method and values for test sensitivity were provided to the directors, and the laboratory method and/or values were revised based on comments received.

For some of the pathogens, more specific factors were also considered. For Vibrio spp., other, the test sensitivity value was assumed to be the same as that for Vibrio parahaemolyticus due to similar pathogen characteristics and laboratory methods used for identification. For Salmonella Typhi, due to low and varying values in the literature, more emphasis was placed on having a test sensitivity value similar to that of other pathogens using blood culture (a minimum value greater than 50%).



<sup>a</sup>The proportion of laboratories testing for the specified pathogen in a routine stool test.<br><sup>b</sup>The proportion of cases for which a physician requests a laboratory test for the disease-causing pathogen (assumes that the l

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cValue assumed to be the same as for Vibrio parahaemolyticus.

ELISA, enzyme-linked immunosorbent assay; EIA, enzyme immunoassay.

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### Supplementary Technical Appendix S3: Description of Inputs and Approach for Proportion Travel-Related and Proportion Foodborne by Pathogen

Values for proportion travel-related and proportion foodborne were required for all pathogens. Supplementary Technical Appendix S3 Table S1 presents the proportion travelrelated and proportion foodborne values for the 30 pathogens included in this study. To estimate these values, preference was given to nationally representative data for Canada, followed by provincial data and Canadian-based published literature. If there was a gap in the Canadian-based data, the values and references used by the U.S.-Centers for Disease Control and Prevention (CDC) estimates (Scallan et al., 2011) were typically used as a proxy. Data from the U.S.-CDC estimates used in the Canadian estimates for proportion travelrelated and proportion foodborne were derived from U.S. surveillance systems (Cholera and Other Vibrio Illness Surveillance System, Foodborne Disease Outbreak Surveillance System, and National Notifiable Disease Surveillance System and available literature) (Scallan et al., 2011).

Inputs for proportion of cases that are travel-related were derived from C-EnterNet surveillance (2005–2010) and the British Columbia reportable disease systems' (2008–2010) (Government of Canada, 2012a; Taylor et al., 2010) data for pathogens under surveillance in these programs. C-EnterNet surveillance data were based on one sentinel site, as only one site was fully implemented for the time period of interest for this study. The proportion of travel-related cases from this single sentinel site and province of British Columbia may not be representative of the rest of the Canadian population. The definition of being a travel-related case varied between systems for a few pathogens (detailed in Supplementary Technical Appendix S1). Data from the Enhanced National Listeriosis Surveillance Program were also used for proportion travel-related for cases of Listeria monocytogenes. For the remaining pathogens, values and references used by the U.S.-CDC estimates (Scallan et al., 2011) were used as a proxy for a Canadian-based input.

Inputs for proportion foodborne were based on a Canadian expert elicitation as the primary source (Ravel et al., 2010). In this expert elicitation, participants were asked to provide their best estimate (5<sup>th</sup> and 95<sup>th</sup> percentile) of the percentage of foodborne illness relative to total cases for nine pathogens. They were asked to disregard travel-related illness and were not required to account for proportion from nonfoodborne sources of illness. For some pathogens, experts' responses were clustered and bimodal results were observed. To explore this phenomenon, Ravel et al. reviewed other relevant literature sources and compared their elicitation results with those of the literature. On the basis of these comparisons, the estimates clustered closest to those reported in the literature were selected to inform the proportion foodborne used in our model. For the remaining pathogens, values from U.S.-CDC estimates (Scallan et al., 2011) were used to determine proportion acquired through a foodborne route. Exceptions to



"Based on reporting of foodborne outbreaks (US FDOSS).<br>"Based on foodborne botulism only.<br>"Based on U.S. Cholera and other *Vibrio* Illness Surveillance System (COVIS).<br>"Based on outbreaks reported to U.S. Centers for Dis aBased on reporting of foodborne outbreaks (US FDOSS).

bBased on foodborne botulism only.

"Based on U.S. Cholera and other Vibrio Illness Surveillance System (COVIS).<br>"Based on outbreaks reported to U.S. Centers for Disease Control and Prevention (unpublished data).

eBased on U.S. National Notifiable Diseases Surveillance System (NNDSS).

VTEC, verotoxigenic E. coli; ETEC, enterotoxigenic E. coli; n/a, not applicable.

this include the value for Salmonella Typhi (value based on the Canadian expert elicitation value for nontyphoidal Salmonella) and adenovirus (value based on those for other similar viruses in U.S.-CDC estimates [Scallan et al., 2011]), where no value was available from either of these sources.

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### Supplementary Technical Appendix S4: Estimate of Foodborne Illness Caused by Unspecified Agents

A proportion of foodborne illnesses are caused by less understood agents (Supplementary Fig. S1). To determine the total number of foodborne illnesses in Canada, an estimate of unspecified agents causing foodborne illness was required. Unspecified agents causing foodborne illness were defined based on the U.S.-Centers for Disease Control and Prevention (CDC) definition, as: ''known agents with insufficient data for estimating agent-specific episodes of illness; known agents not yet recognized as causing food-borne illness; microbes,



SUPPLEMENTARY FIG. S1. Agents that cause foodborne illness. ETEC, enterotoxigenic Escherichia coli; VTEC, verotoxigenic Escherichia coli.

chemicals or other substances known to be in food but for which pathogenicity is unproven; and agents not yet described" (Scallan et al., 2011).

An approach, similar to that used by the US-CDC estimate for unspecified agents causing foodborne illness was employed (Scallan et al., 2011). To estimate the number of foodborne illnesses annually related to unspecified agents, the total number of cases of acute gastrointestinal illness (AGI) occurring annually in Canada was estimated, from which the total number of estimated cases for known pathogens that cause AGI was subtracted and then the proportion domestically acquired and foodborne related was applied to the remainder (Supplementary Fig. S2). Estimates of illness were not made for unspecified agents that do not typically result in symptoms of AGI.

To estimate the number of cases of AGI, data from the National Studies on Acute Gastrointestinal Illness population surveys completed in 2001–2002 (0.56 episodes per person per year), 2002–2003 (0.76 episodes per person per year), and 2005–2006 (0.53 episodes per person per year) were used (Majowicz et al., 2004; Thomas et al., 2006; Sargeant et al., 2008). The proportion of individuals with AGI was estimated

to be those who experienced three or more loose stools in 24 hours or any vomiting in the past 28 days excluding those with chronic conditions, or concurrent symptoms of coughing, sneezing, sore throat, or runny nose. Data were standardized by gender and 5-year age categories to the 2006 Canadian census population (Statistics Canada, 2008), with an estimated rate of 0.630 (95% confidence interval 0.574–0.689) episodes per person-year. This incidence rate was applied to the approximated 2006 Canadian population to estimate the total annual number of episodes of AGI.

For 25 of the 30 major known pathogens of foodborne illness, AGI was considered either a major symptom (e.g., Campylobacter spp., nontyphoidal Salmonella spp.) or the illness can initially manifest as AGI (i.e., Salmonella serotype Typhi, Trichinella spp., and Vibrio vulnificus). Five pathogens were considered to have major symptoms that do not typically include AGI, even if diarrhea and vomiting can occur with some of these (e.g., Clostridium botulinum and hepatitis A virus) (Supplementary Fig. S1).

To estimate the total number of cases attributed to the 25 pathogens known to cause symptoms of vomiting or diarrhea, both domestic and travel-related cases and all transmission



SUPPLEMENTARY FIG. S2. Schematic of estimates of illness caused by unspecified acute gastrointestinal illness (AGI) agents. The number of illnesses caused by 25 known AGI pathogens was subtracted from the overall estimate of AGI to estimate the number of illnesses caused by unspecified agents. To estimate the proportion domestically acquired and foodborne, we estimated for those 25 known AGI pathogens the proportion domestically acquired and proportion foodborne. These proportions were applied to the estimate of the total number of cases of AGI related to unspecified agents to estimate the total number of domestically acquired. CrI, credible intervals.



Supplementary Technical Appendix S4 Table S4. Model Inputs for Estimating Domestically Acquired Foodborne Illness due to Unspecified<br>Acute Gastromytestinal Lilness Agents Supplementary Technical Appendix S4 Table S4. Model Inputs for Estimating Domestically Acquired Foodborne Illness due to Unspecified Acute Gastrointestinal Illness Agents

routes were included (i.e., did not exclude those that were not foodborne). The under-reporting and underdiagnosis multipliers related to the domestically acquired cases were applied to the number of laboratory-confirmed cases related to travel. These travel cases were excluded from the main pathogen specific estimates, with the assumption that the under-reporting and under-diagnosis may differ for travel-related cases compared with domestically acquired cases. The sum of the total estimated illness for the 25 pathogens was then subtracted from the estimated total number of episodes of AGI to generate an estimate of the total number of cases of AGI related to unspecified agents. For the 25 known pathogens that cause symptoms of AGI, the proportion domestically acquired (97.3%) and the proportion foodborne (20.1%) were then applied to the total number of cases of AGI related to unspecified agents, to estimate the total number of domestically acquired, foodborne cases of AGI related to unspecified agents.

To account for uncertainty, probability distributions were used to describe the range of plausible values for all model inputs. The modeling approach used and parameters of these probability distributions are detailed in Supplementary Technical Appendix S4 Table S1. Model outputs are in the form of probability distributions summarized by a mean estimate with 90% credible intervals (90%CrI).

We estimate that 2.4 million (90% credible intervals: 1.8–3.0 million) episodes of domestically acquired foodborne acute gastrointestinal illness were caused by unspecified agents, circa 2006 (Supplementary Fig. S2). We estimate that 20.5 million acute gastrointestinal illnesses occur each year in Canada. Subtracting 8.2 million estimated illnesses caused by the 25 known AGI pathogens leaves 12.2 million acute gastrointestinal illnesses caused by unspecified agents. The proportion of these unspecified agents acquired through domestic foodborne transmission is unknown; however, applying the distribution of the proportion of illnesses from the 25 known AGI pathogens that were domestically acquired (97.3%) and foodborne (20.1%) yields an estimate of 2.4 million domestically acquired foodborne illnesses caused by unspecified agents.

Unspecified agents are the largest contributor (60%) to the total number of episodes of foodborne illness currently estimated in Canada. The proportion of illnesses estimated to be foodborne was a main driver of the estimate of illness caused by unspecified foodborne agents. Because no data existed with which to directly estimate the proportion of unspecified agents that were domestically acquired and foodborne, distributions of these proportions were estimated to be similar to those of the 25 known AGI pathogens. Viral illnesses account for approximately 88% of illnesses caused by the 25 known AGI pathogens; thus, they have a large influence on the foodborne proportion. As a result, the mean proportion of unspecified agents that were estimated to be transmitted by food was 20.1%, which is lower than 26% used for the U.S.-CDC estimate (Scallan et al., 2011). The specified pathogens method for estimating the viruses incorporated the total population; therefore, our results estimated more viruses being domestically acquired and foodborne compared to the U.S.-CDC approach, which only included children less than 5 years of age in the estimate. Viruses occurring in the U.S. adult population would have been captured in the unspecified agents estimate. Therefore, our proportion of total domestic, foodborne illness due to unspecified agents is lower (60%) than the U.S.- CDC estimate (80%) (Scallan et al., 2011).

Although the number of episodes of foodborne illness caused by unspecified agents is substantial, the statement that 60% of foodborne illnesses are unspecified must be treated with caution. We may have under- or overestimated the number of episodes of illness caused by the 25 known AGI pathogens, which would impact the results for the unspecified agents. The proportion of illnesses transmitted by food and domestically acquired for unspecified agents may differ from that for the 25 known gastrointestinal pathogens.

#### Disclosure Statement

No competing financial interests exist.

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