

A scoping review of the detection, epidemiology and control of *Cyclospora cayetanensis* with an emphasis on produce, water and soil

Review

Cite this article: Totton SC, O'Connor AM, Naganathan T, Martinez BAF, Vriezen ER, Torrence ME, Sargeant JM (2021). A scoping review of the detection, epidemiology and control of *Cyclospora cayetanensis* with an emphasis on produce, water and soil. *Epidemiology and Infection* **149**, e49, 1–10. <https://doi.org/10.1017/S0950268821000200>

Received: 3 November 2020

Revised: 24 December 2020


Accepted: 25 January 2021

Key words:

Control; *Cyclospora*; epidemiology

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Abstract

Cyclospora cayetanensis is a parasite causing cyclosporiasis (an illness in humans). Produce (fruits, vegetables, herbs), water and soil contaminated with *C. cayetanensis* have been implicated in human infection. The objective was to conduct a scoping review of primary research in English on the detection, epidemiology and control of *C. cayetanensis* with an emphasis on produce, water and soil. MEDLINE® (Web of Science™), Agricola (ProQuest), CABI Global Health, and Food Science and Technology Abstracts (EBSCOhost) were searched from 1979 to February 2020. Of the 349 relevant primary research studies identified, there were 75 detection-method studies, 40 molecular characterisation studies, 38 studies of *Cyclospora* in the environment (33 prevalence studies, 10 studies of factors associated with environmental contamination), 246 human infection studies (212 prevalence/incidence studies, 32 outbreak studies, 60 studies of environmental factors associated with non-outbreak human infection) and eight control studies. There appears to be sufficient literature for a systematic review of prevalence and factors associated with human infection with *C. cayetanensis*. There is a dearth of publicly available detection-method studies in soil ($n=0$) and water ($n=2$), prevalence studies on soil ($n=1$) and studies of the control of *Cyclospora* (particularly on produce prior to retail ($n=0$)).

Introduction

Rationale

Cyclospora cayetanensis was first reported in humans in 1979 [1], but was not fully identified until the early 1990s [2]. *Cyclospora cayetanensis* is a single-celled parasite that causes an illness in humans called cyclosporiasis [3]. *Cyclospora cayetanensis* is shed in the stool of infected people. The organism requires 1–2 weeks in the environment to sporulate (become infective); therefore, direct person-to-person transmission is unlikely [3]. Environmental elements, in particular produce (such as fruits, vegetables and herbs), water and soil can become contaminated with *C. cayetanensis* and have all been implicated as sources of human infection [4]. Since the external environment is an essential component of the *C. cayetanensis* life cycle, an understanding of the detection, epidemiology and control of *Cyclospora* is best focused on the agent/environment and agent/host/environment interfaces, rather than the agent/host interface.

Scoping reviews are a type of literature review used for knowledge synthesis [5, 6]. They use systematic and transparent methods to summarise research on broad topics, map available evidence and identify gaps in current knowledge [6]. Scoping reviews may act as preludes to systematic reviews and/or help direct the focus of future primary research by highlighting areas in which no, or little, research has yet been conducted [5].

Preliminary searches conducted on 12 December 2019 in MEDLINE® (Web of Science™) (1950–date of search), Agricola (ProQuest) (1970–date of search) and CABI Global Health (1973–date of search), and on 3 January 2020 in Food Science and Technology Abstracts (EBSCOhost) (1969–date of search) using the search terms ['*Cyclospora*' AND 'systematic review'] and ['*Cyclospora*' AND 'scoping review'] found no scoping or systematic reviews of *Cyclospora*.

Objectives

The primary objective was to conduct a scoping review of the detection, epidemiology and control of *C. cayetanensis* with emphasis on the environment (produce (fruits, vegetables

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and herbs), water and soil), with the aim of identifying gaps in the literature, areas for future research directions and topics with sufficient evidence base for systematic reviews.

Methods

Protocol and registration

The protocol was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) [6] and was registered on the University of Guelph Atrium on 4 February 2020 (<https://atrium.lib.uoguelph.ca/xmlui/handle/10214/17805>). It can also be accessed at Systematic Reviews in Animal Health and Food (www.syreaf.org).

Eligibility criteria

Studies included in the review had to meet all three of criteria 1–3, and at least one of criteria 4–11:

- (1) studies of *C. cayetanensis*, as this is the only species of *Cyclospora* that causes cyclosporiasis (illness in humans) [3]. Studies that reported only *Cyclospora* species but did not specify that the organisms were *C. cayetanensis* were therefore not eligible; however, a change was made from the protocol to include studies in which the species of *Cyclospora* was not specified, provided the study involved humans, human waste or water that was likely to be contaminated with human waste, because *C. cayetanensis* is the only *Cyclospora* species that infects humans;
- (2) published in English;
- (3) primary research (narrative or non-systematic reviews were not eligible for inclusion, as the absence of reported methods would preclude the assessment of rigour and comprehensiveness. Although the number of systematic reviews, scoping reviews, *in silico* (computer models) and quantitative risk assessments (QRA) captured by the literature search were enumerated, no other information was collected from these studies);
- (4) molecular characterisation studies (e.g. genome sequencing, identification of genotyping markers, prevalence of molecular subtypes, etc.);
- (5) detection-methods studies;
- (6) studies of *C. cayetanensis* prevalence in produce, water or soil;
- (7) studies investigating an association of factors with *C. cayetanensis* contamination of produce, water or soil;
- (8) studies of the incidence or prevalence of *Cyclospora* infection in humans;
- (9) studies of the association of various factors (including consumption of unwashed produce, untreated water or contact with soil) with human infection;
- (10) studies in which causes (produce, water or soil) of cyclosporiasis outbreaks were investigated or
- (11) studies of the control of *Cyclospora* in the environment.

Studies of the diagnosis of human infection (by testing blood or tissue samples), pathogenesis and treatment of cyclosporiasis were not eligible, as the focus of this scoping review was on the agent/environment/host and agent/environment interfaces, not the agent/host interface.

Table 1. Search strategy^a in MEDLINE® (Web of Science™) for a scoping review of the detection, epidemiology and control of *Cyclospora cayetanensis*

Search no.	Search string
1	TS = cyclospora Indexes = MEDLINE Timespan = 1979–2020
2	TS = cyclosporiasis Indexes = MEDLINE Timespan = 1979–2020
3	TS = cayetanensis Indexes = MEDLINE Timespan = 1979–2020
4	#3 OR #2 OR #1

^aThere were no document type or language restrictions.

Animals have not been documented as intermediate or primary hosts of *C. cayetanensis* [3], and therefore studies that looked at *Cyclospora* only in animals were not eligible.

Information sources

The following databases were searched from 1979 to the date of search: MEDLINE® (Web of Science™), Agricola (ProQuest), Food Science and Technology Abstracts (EBSCOhost) (searched 5 February 2020), and CABI Global Health (searched 7 February 2020). Results of the database searches were uploaded into EndNote® X8 Desktop, de-duplicated then uploaded into DistillerSR® (Evidence Partners, Ottawa, Canada) review management software for further de-duplication. Additionally, a manual search was conducted for any remaining duplicates. One reviewer (ST) scanned the reference lists of 11 recently published narrative reviews [7–17] for additional relevant studies. Authors of relevant studies were not contacted to identify additional studies.

Search

As the focus of this scoping review was broad and the topic relatively new, a simple search was conducted (with no restrictions on study design or research focus) that would not require specialised information retrieval knowledge; therefore, the review team (AMOC, JMS, SCT) designed the search. Given the simplicity of the search strategy, it was not submitted for peer review. Searches were conducted by SCT and BAFM. There were no document-type or language restrictions in the search, but publication date was limited to studies published from 1979 to the date of the search, since *C. cayetanensis* was first reported in humans in this year [1].

The search strategy for MEDLINE® is shown in Table 1. Addition of a wildcard (*) term in the search (cyclospor*) was evaluated; however, this was not included in the final search because, while it added to the search results, the majority of new citations were irrelevant studies on the medications Cyclosporine A and cyclosporin. Adding the terms Title (TI), MeSH Heading or MESH Major Topic did not contribute any unique hits to the search.

Selection of sources of evidence

In DistillerSR®, two reviewers independently assessed each record for eligibility, first based on the title/abstract, then, if the record

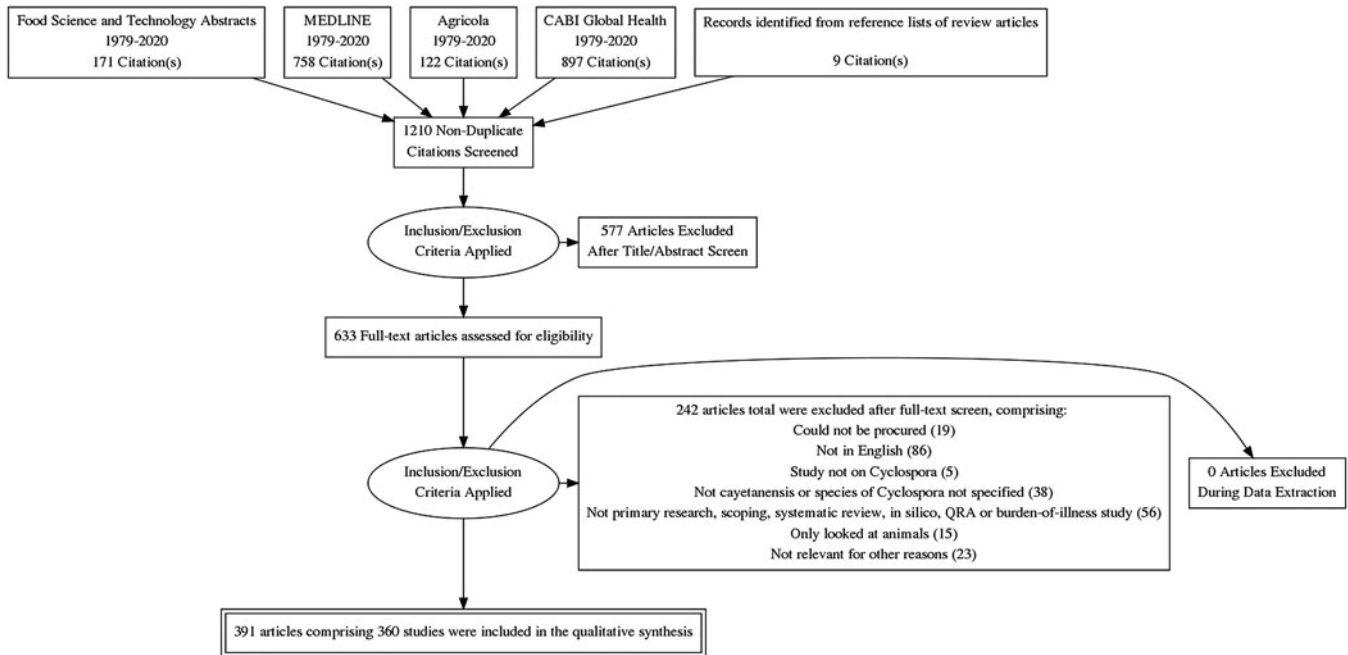


Fig. 1. The total numbers of records originating from each database searched, the number remaining after de-duplication, and the number of studies assessed at title/abstract and full-text screening (with reasons for exclusion) for a scoping review of the detection, epidemiology and control of *Cyclospora cayetanensis* (template from [18]).

was deemed likely to be relevant, on the full text. Conflicts were resolved via discussion or by consulting a third reviewer.

The title/abstract screening form (Supplementary Table S1) was pretested on 100 records, and the full-text screening form (Supplementary Table S2) was pretested on five records, during which, the forms were revised for clarity and consistency. During screening, it was decided to exclude case reports and case series, since they did not report sufficient data to calculate prevalence or to assess factors associated with infection.

Data charting

Data charting was performed in DistillerSR® by two reviewers working independently using a data-charting form designed for this review (by AMOC, JMS and SCT) that was pretested on five studies. The data-charting form allowed response options to be added for certain questions. Conflicts were resolved through discussion or by consulting a third reviewer. Authors of eligible studies were not contacted for clarification or additional information.

Data items

The final version of the data-charting form is shown in Supplementary Table S3. For the purposes of this review, produce was defined as fruits, vegetables and herbs. Soil studies were those in which the authors reported examining soil or compost. Water studies were those in which the authors reported examining water or a watery substance likely to contain *Cyclospora* (i.e. sewage or sludge).

The species of *Cyclospora* can be determined only by using molecular methods [9]. However, if the authors of an article only used microscopy to examine produce, water or soil, but they still reported that they found *C. cayetanensis*, these data

were mapped, but the reviewers noted the lack of confirmation of species by molecular methods. If the authors did not use molecular methods to confirm species for the detection in food, water and soil and did not specify that *C. cayetanensis* was detected, data from these studies were not mapped. The exception to this was if authors tested wastewater/sewage without using molecular methods to confirm the species; data from these studies were mapped as *C. cayetanensis*, because *cayetanensis* is the only species of *Cyclospora* that infects humans [3].

Critical appraisal of individual sources of evidence

As this was a scoping review, a risk-of-bias assessment of the individual studies was not conducted.

Synthesis of results

Results were summarised using a combination of narrative text, tables and figures and are grouped by study type (detection method development and/or validation studies, epidemiological studies (molecular characterisation, human infection, environmental (i.e. produce, water, soil) contamination) and control studies). Frequency of each study type and characteristics of those studies, descriptions of the study populations, detection matrices examined and control methods tested are also reported.

Results

Selection of sources of evidence

The numbers of articles originating from each database searched, the number remaining after de-duplication and the number assessed at title/abstract and full-text screening (with reasons for exclusion of the latter) are presented in a PRISMA flow diagram (Fig. 1). The search results for the MEDLINE® database are shown

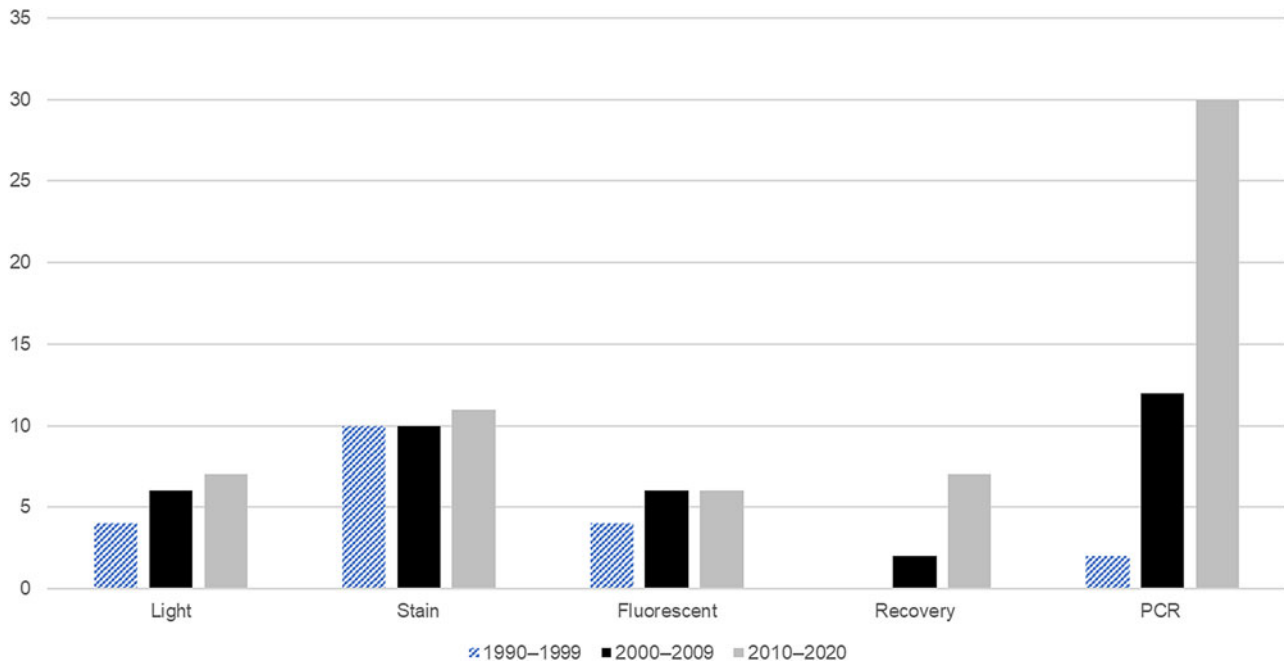


Fig. 2. The number of detection-method studies, by detection method and by decade the study was published, in a scoping review of *Cyclospora cayetanensis*, based on literature published between 1979 and February 2020. Light = light microscopy techniques that do not involve stain(s), Stain = light microscopy with staining, Fluorescent = fluorescent microscopy, Recovery = techniques used to recover *Cyclospora* from the detection matrix.

in Supplementary Table S4. Of the 86 references for which the full text was not in English, 36 were in Spanish, 13 in Turkish, 10 in French, nine in Portuguese, seven in Chinese, five in Japanese and one each were in Czech, Dutch, German, Norwegian, Persian and Polish.

Characteristics of sources of evidence

Of the relevant studies identified, there were:

- seven burden-of-illness studies
- two *in silico* (computer model) studies
- one qualitative risk assessment
- one systematic review (of gastrointestinal parasites, including *Cyclospora*, in Africa)
- 349 primary research studies (based on 380 references (31 records identified as primary research reported data that overlapped with other publications)), which are described in more detail below

Citation information for all of the above studies is given in Supplementary Table S5.

Risk-of-bias assessment within sources of evidence

A risk-of-bias assessment of the literature was not conducted, as this was not relevant to the objectives of this scoping review.

Results of individual sources of evidence

Molecular characterisation studies

There were 40 molecular characterisation studies. Five of these were also detection-method studies and for two of those, the detection method involved molecular characterisation. Twelve

molecular characterisation studies reported the prevalence of molecular subtypes of *Cyclospora* and so were also mapped under the prevalence of human infection and prevalence of *Cyclospora* contamination in the environment, independent of human outbreaks, described below.

Detection method development and/or validation studies

Seventy-five detection-method studies were found. The reviewers did not extract whether the detection method studies were on the development of the detection method, validation or both. All tests were for detection of *Cyclospora* DNA or sporulated and/or non-sporulated oocysts in various matrices. Some studies examined more than one type of matrix. Figure 2 shows the number of detection method studies by detection method and by decade of publication.

Produce. Twenty-one detection-method studies examined produce. Of these, one study used immunofluorescence microscopy on leafy green produce [19], 19 studies evaluated PCR as a detection method (13 tested fruits, seven tested vegetables, 10 tested herbs), and four studies examined techniques to enhance the recovery of *Cyclospora* from the matrices tested (two studies used fruits as a matrix, one used vegetables, four used herbs).

Water. Two detection-method studies evaluated detection in water [20, 21]. Both examined river water, and one [20] also tested lake and drinking water. This latter study evaluated the effectiveness of a continuous separation channel centrifugation for recovering *C. cayetanensis* oocysts from water. Shields and Olson [21] tested a nested-PCR–restriction fragment length polymorphism (RFLP) protocol.

Soil. None of the studies examined detection in soil.

Other matrices. Fifty studies evaluated the detection of *C. cayetanensis* in human stool. Two PCR studies used filter paper and other matrices, and one PCR study did not report the matrix used.

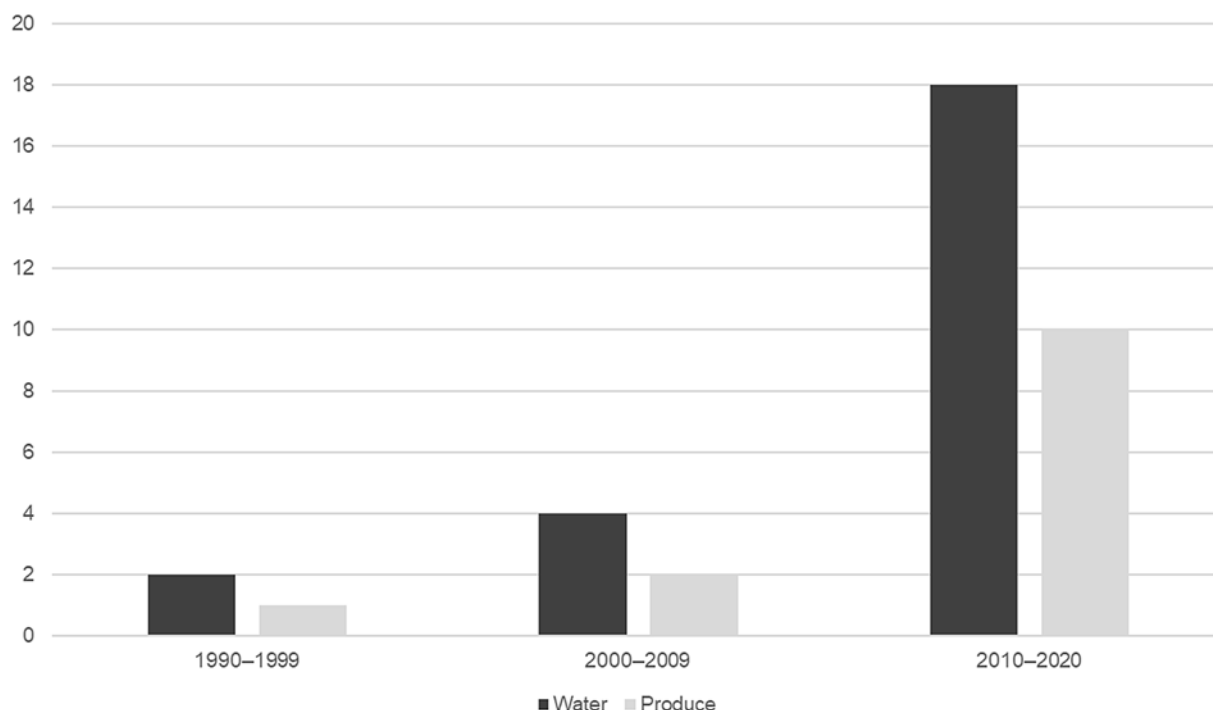


Fig. 3. The number of studies that reported the prevalence of *Cyclospora cayetanensis* in water and produce, by decade of publication, in a scoping review of *Cyclospora*, based on a search of the published literature from 1979 to February 2020.

Table 2. Studies (number of studies) in which the prevalence of *Cyclospora cayetanensis* contamination was reported in produce

Food tested	Condition	Country
Fruits ^a (4)	Fresh (11)	Canada (2)
	Frozen (0)	Italy (2)
Vegetables ^b (15)	Fresh/frozen status not reported (2)	South Korea (1)
Herbs ^c (7)	Domestic (11)	Cambodia (1)
	Imported (3)	China (1)
	Domestic/imported status not reported (2)	Ghana (1)
	Processed (1)	Peru (1)
	Unprocessed (1)	United States (1)
	Processed/unprocessed status not reported (11)	Colombia (1)
	Hand-picked (1)	Nepal (1)
	Mechanically harvested (0)	Nigeria (1)
	Hand-/mechanically-picked status not reported (12)	

^aFruits tested comprised: blueberries (1), watermelon (1), melon (1), banana (1), guava (1), mango (1), tamarillo (1) and tomatoes (incl. cherry tomatoes) (3).

^bVegetables tested comprised: ready-to-eat packaged salad (1), cabbage (5), sprouts (1), carrots (3), onions (1), lettuce (9), sweet peppers (1), water spinach (2), 'leafy green produce' (3), celery (3), baby bok choy (1), crown daisy (1), endive (2), regular (not water) spinach (4), leaf mustard (2), cucumber (3), potato (1), beans (kidney or French) (1), green chilies (2), arugula (2), baby arugula (1), baby spinach (1), spring mix (1), kale (1), Romaine lettuce (2), chard (1), mixture of dandelion, collards, rapini, escarole, mache (1), chicory (1), cauliflower (1), green onions (2), radish (2), leeks (1), broccoli (1), sugar peas (1), packaged blends of leafy vegetables, including iceberg lettuce, romaine lettuce, baby lettuces, leaf lettuce, radicchio, endive, and escarole (1), green leaf (1), water leaf (1), Ugwu leaf (1), bitter leaf (1), Sokoyokoto (1), Igbagba (1), winter-grown cabbages (1).

^cHerbs tested comprised: perilla leaves (1), chives (2), coriander (1), fennel (2), schizonepeta (1), Chinese chives (1), mint (1), basil (2), cilantro (1), parsley (1), huacatay (1), Yerba Buena (1).

Studies of *Cyclospora* contamination of the environment (produce, water and soil)

Studies of prevalence of *C. cayetanensis* contamination in the environment (produce, water and soil), independent of human outbreaks. This is a summary of the number of prevalence studies for each environmental matrix (produce, water and soil). Actual prevalence of *Cyclospora* contamination in each type of matrix (i.e. percentage of positive samples) was not extracted for this review. Figure 3 shows the number of studies that reported the

prevalence of *C. cayetanensis* in water and produce, by decade of publication.

Produce. Thirteen studies reported the prevalence of *C. cayetanensis* in produce (Table 2). For five of these studies, the authors reported testing for *C. cayetanensis*, but did not confirm the species using molecular methods. Two of the prevalence studies were conducted each in Canada and Italy, and one study was conducted in each of Cambodia, China, Colombia, Ghana, Nepal, Nigeria, Peru, South Korea and the USA.

Table 3. Studies (number of studies) in which the prevalence of *Cyclospora cayetanensis* contamination was reported in water

Type of water tested	Country
Natural ^a (9)	United States (3) Colombia (2)
Drinking ^b (10)	Guatemala (2) Italy (2)
Drinking water treatment plants ^c (3)	Brazil (1) China (1)
Well water (3)	Egypt (1) Ghana (1)
Waterworks, water pumps, water tanks (1)	Haiti (1) Mexico (1)
Irrigation (4)	Nepal (1) Nigeria (1)
Wastewater ^c (7)	Peru (1) Romania (1)
Sludge (1)	Rwanda (1) Saudi Arabia (1)
Vegetable processing water (1)	Spain (1) Tunisia (1)
Post-harvest wash water (1)	Vietnam (1) Zimbabwe (1)
Recreational (0)	

^aNatural water also includes pond water, tidal brackish water and canal water.

^bTap water was considered to be drinking water.

^cIncludes pre- and post-treatment samples.

Water. Twenty-four studies examined the prevalence of *Cyclospora* contamination in water (Table 3). For seven of these, the authors reported testing water for *C. cayetanensis*, but they did not confirm the species using molecular methods, and these water samples were not reported to be contaminated with human sewage, so the species could not be assumed to be *C. cayetanensis*. Of the 24 water contamination prevalence studies, three were conducted in the USA, two studies each were conducted in Colombia, Guatemala and Italy, and one study each was conducted in Brazil, China, Egypt, Ghana, Haiti, Mexico, Nepal, Nigeria, Peru, Romania, Rwanda, Saudi Arabia, Spain, Tunisia and Zimbabwe.

Soil. A single study, conducted from spring 2012 to winter 2014 in Italy, described the prevalence of *C. cayetanensis* in agricultural soil samples [22]. The authors used molecular methods to confirm *C. cayetanensis*.

Studies of factors investigated for an association with *Cyclospora* contamination of the environment (produce, water and soil). Reported here are all factors that were investigated for an association with *Cyclospora* contamination, not specifically factors reported to have a significant association, as assessing whether the studies were adequately powered to detect significant associations was beyond the scope of this review.

Produce. Three studies investigated the associations of various factors with *Cyclospora* contamination of produce. Season was examined as a factor in two produce studies: one Italian study [23], which examined ready-to-eat packaged salad, and one Peruvian study [24], which examined cabbage, lettuce, celery, spinach, green chili, green onions, basil, radish, leeks, broccoli, cilantro, parsley, sugar peas, huacatay and yerba buena. Type of market (supermarket vs. open air market) was examined as a possible factor associated with *Cyclospora* contamination in one study in Ghana [25], examining cabbage, carrots, onions, lettuce and sweet peppers.

Water. Seven studies investigated the associations of various factors with *Cyclospora* contamination of water (Table 4).

Soil. No studies were found that examined the association of any factor with *Cyclospora* contamination of soil.

Studies of human infection with *C. cayetanensis*

Studies of prevalence/incidence of human infection by geographic region. There were 212 studies reporting the prevalence or incidence of *C. cayetanensis* infection in humans. Of these, 99 studies were conducted in Asia, 43 in Africa, 31 in North America, 18 in South America, 10 in Europe, five in Central America, one in New Zealand, and five studies did not report the country in which they were conducted.

Studies investigating an association of environmental factors (including produce, water and soil) with human infection that was not associated with outbreaks. One hundred and five studies investigated the association of various factors with human infection not associated with outbreaks. Forty-five of these examined only host (not environmental) factors for an association with human infection (i.e. immunocompetence, age, sex, race/ethnicity, etc.). The remaining 60 studies examined environmental factors. Fourteen of these examined general enteric/protozoal infection (which included *Cyclospora* infection) as an outcome, rather than *Cyclospora* infection specifically. Of the 60 studies investigating environmental factors, 28 were conducted in Asia, 10 in North America, eight in Africa, six in South America, four in Central America, three in Europe, and one study did not report the country in which it was conducted. Table 5 reports a summary of the environmental factors examined. This is a summary of environmental factors examined for an association with human infection, not of environmental factors reported to be significantly associated with human infection, as assessing whether the studies were adequately powered to detect significant differences was not part of this scoping review.

Identified causes (produce, water, soil) of cyclosporiasis outbreaks. Thirty-two studies reported outbreak data on cyclosporiasis. The produce and water factors attributed to the outbreak were mapped.

Produce. Twenty-five studies identified a produce source of a human outbreak. The number of studies by each type of produce implicated is reported in Table 6. Of these 25 studies, 23 were conducted in North America, and one study each was conducted in Australia and Germany.

Water. A single study implicated water as the source of an outbreak. In the summer of 1990 in Chicago, tap water in a physicians' dormitory was identified as the source of a cyclosporiasis outbreak [37].

Soil. No studies identified soil as the cause of a cyclosporiasis outbreak.

Control of *Cyclospora* in the environment (including produce, water and soil)

Produce. Four studies evaluated the control of *Cyclospora* in produce. The interventions tested were: washing with distilled water (with lettuce) [24]; immersion in 0.85% saline or water with 3 min of vigorous shaking (lettuce, cabbage, green pepper, onions, carrots and tomatoes) [25]; 20 min exposure to gaseous chlorine dioxide (basil and lettuce) [38]; and freezing or heating (−70 to 100 °C for 15 min to 7 days) (basil) [39]. Results of these studies were not extracted, as the purpose of this scoping review was to characterise the research, rather than summarise study results. All studies for which a production stage was identified were done at the post-retail stage of production.

Table 4. Summary of studies examining an association of various factors with the contamination of water by *Cyclospora*

Citation	Country	Factors examined for an association with <i>C. cayetanensis</i> contamination	Types of water examined
[26]	Nepal	Source of water	Irrigation water, drinking water, pond water
[27]	Zimbabwe	Source of water	Drinking water
[28]	Egypt	Source of water, season	Natural water, tap water, waterworks, water pumps, water tanks, canal
[29]	Spain	Season	Natural water, drinking water treatment plants, wastewater treatment plants
[30]	Nepal	Season	Sewage
[31]	Not reported	Season	Sewage
[32]	Vietnam	Source of water, season, geographic region	Tap water, water tanks

Table 5. Summary of environmental factors examined for an association with *Cyclospora* infection in humans, independent of outbreaks

Environmental factor categories (number of studies)	Environmental factors evaluated for a possible association (number of studies)
Produce (11)	Eating unwashed fruits or vegetables (4), eating uncooked vegetables, fruits or other food (3), eating fruits or vegetables (1), eating unwashed fruit (1), eating unwashed fruit or herbs abroad (1), source of fruits or vegetables (market vs. backyard garden) (1)
Water (21)	Source of drinking water (19), contact with water via swimming (6)
Soil (4)	Contact with soil (3), contact with soil contaminated with human faeces (1)
Other environmental factors (58)	Season (27), geographic location of residence (15), urban vs. rural residence (1), conditions inside the home (e.g. toilet in house) (11), contact with domestic animals/children (12), recent international travel (8), conditions outside the home (e.g. sewer system, crowding, rodents, livestock) (5), employed on a raspberry farm (2), employment with exposure to solid faecal waste (1), type of school attended (1), contact with/drinking breastmilk (child) (1)

Table 6. Summary of produce significantly associated with outbreak(s) of cyclosporiasis

Produce category associated with a human outbreak (number of studies)	Produce subcategory significantly associated with the outbreak (number of studies)
Fruits (14)	Raspberries (10) ^a , blackberries (3) ^{a,b} , blueberries (2) ^{a,b} , oranges (1) ^b , cantaloupe (1) ^c , strawberries (1) ^a
Vegetables (8)	Green onions (2) ^d , lettuce (2) ^{c,d} , snow peas (1), mesclun lettuce (1), Romaine lettuce (1), sugar snap peas (1), cherry tomatoes (1) ^b
Herbs (8)	Basil (5), cilantro (2), chives (2) ^{c,d} , dill (1) ^d , parsley (1) ^d

^aIn one outbreak [33] consumption of a dessert containing a mixture of raspberries, strawberries, blackberries, blueberries and cream was significantly associated with cyclosporiasis. However, since these components were served mixed together, it was impossible to identify which of these individual elements was responsible for the outbreak.

^bAlthough in one outbreak, a statistically significant association with blueberries, blackberries, oranges and cherry tomatoes was found, the cause of the outbreak could not be definitively determined [34].

^cIn one outbreak, cantaloupes, chives and lettuce were all significantly associated with illness, but the individual food item responsible for the outbreak could not be conclusively identified [35].

^dIn one study, the cause of the outbreak was identified as a salad containing a mixture of lettuce, green onions, dill, chives and parsley. Because the items were mixed, it was impossible to identify the component of the salad that caused the illness [36].

Water. Four studies evaluating control *Cyclospora* in water were found ('water' included distilled water, deionised water and phosphate-buffered saline). Interventions examined included fungicides (captan, benomyl and zineb) and insecticides (malathion and diazinon 4E) [40], microwave heating (10–45 s) [41], freezing and heating (–70 to 100 °C) [39], and magnesium oxide nanoparticles [42].

Soil. No control studies of *Cyclospora* in soil were found.

Other. No control studies of *Cyclospora* on other matrices or surfaces were found.

Synthesis of results

An overall framework mapping the scoping review results for the primary research studies is shown in Table 7.

Table 7. Synthesis of 349 primary research studies (based on 380 references) found in a scoping review of the detection, epidemiology and control of *Cyclospora cayetanensis*, with an emphasis on produce, water and soil

Type of study	Focus of study	Number of studies	Number of studies
Detection method development and/or validation			75
			Produce 21
			Water 2
			Soil 0
			Human stool 50
Epidemiology			301
Molecular characterisation			40
	Prevalence of molecular subtypes	12	Produce 3
			Water 2
			Soil 0
			Human stool 7
Studies of <i>Cyclospora</i> in the environment			38
Prevalence in the environment, independent of human outbreaks	33	Produce 13	
		Water 24	
		Soil 1	
Studies of factors associated with <i>Cyclospora</i> contamination of produce, water or soil	10	Produce 3	
		Water 7	
		Soil 0	
Studies of human infection with <i>Cyclospora</i>			246
Prevalence/incidence of human infection			212
	Studies of the association of environmental factors with human infection in non-outbreak situations	60	Produce 11
			Water 21
			Soil 4
			Other 58
	Studies investigating causes of cyclosporiasis outbreaks	32	Produce ^a 25
			Water 1
Soil 0			
Control of <i>Cyclospora</i> in the environment			8
After retail sale	4	Produce 4	
		Water 4	
		Soil 0	
Not applicable	4	Water 4	
		Soil 0	
		Soil 0	

^aNumber of studies demonstrating a statistically significant association between a type of produce and human illness during an outbreak.

Discussion

Summary of evidence

This scoping review found only one potentially relevant systematic review, and its focus was on gastrointestinal pathogens (not specifically *Cyclospora*) in Sub-Saharan Africa [43].

Additionally, this scoping review revealed an absence of detection-method studies on soil and only two studies on water. In 2019, a validated method for detecting *C. cayetanensis* in water was accepted as a standard method by the FDA [44].

Pertinently, a recent Blue-Ribbon Panel report indicated a need for the development of detection methods for *C. cayetanensis* in environmental samples [45]. We discerned an upward trend of detection-method studies using DNA-based methods (PCR), which allow confirmation of species (*cayetanensis*), as well as a more recent increase (since 2000) in studies of techniques used to enhance the recovery of *Cyclospora* from produce and water samples

There was only one study of the prevalence of *C. cayetanensis* contamination in soil, indicating another potential area for future

primary research. The number of published prevalence studies of *Cyclospora* contamination in both produce and water has been trending upwards over time, indicating, perhaps, a growing interest in transmission pathways and maintenance of this organism in the environment. A systematic review of the prevalence of *Cyclospora* in water is currently being undertaken by some of the authors of this scoping review (protocol available here: <https://atrium.lib.uoguelph.ca/xmlui/handle/10214/18106>). A meta-analysis will also be conducted if sufficient data are available. With the number of published prevalence studies in produce also growing over time, there may, in the near future, be sufficient publicly available data to conduct a systematic review of the prevalence of *Cyclospora* contamination of produce.

Our review revealed that there appears to be a sufficient number of studies to support a systematic review of prevalence/incidence and environmental factors (independent of human outbreaks) associated with *Cyclospora* infection in humans, although the wide geographic range of the studies and consequent heterogeneity may limit the possibility of performing a meta-analysis.

The low number of studies on methods to control *Cyclospora* in the environment precludes conducting a systematic review and meta-analysis of these studies and highlights a potential area for primary research. Interestingly, there were no control studies on soil or on produce at the preharvest or harvest stages of production, indicating further gaps that could be addressed with primary research.

Limitations

Researchers were not contacted to seek unpublished studies on *C. cayetanensis*. It is possible that the gaps in the literature identified by this review are addressed by unpublished studies. Authors of any unpublished studies are strongly encouraged to publish their results so that they are available for use in scoping and systematic reviews, QRAs, or guideline development for *C. cayetanensis* control and also to allow identification of true research gaps. Additionally, the full text for 19 studies could not be obtained, and an additional 86 studies were not in English, therefore, their data were not mapped. A scan of the titles and abstracts of these references revealed that two studies published in French [46, 47] examined the presence of *C. cayetanensis* in natural and drinking water, and one study for which the full text was unavailable [48] searched for *Cyclospora* in water samples, although according to the abstract, molecular methods were not used to confirm the species. A further study whose full text could not be obtained [49] examined the effects of solar disinfection and chlorine on *Cyclospora* in drinking water.

Papers that did not use molecular methods to confirm the species of *Cyclospora* found in produce, soil and in water not contaminated with human stool were excluded from the review. Admittedly, any of these may have detected *C. cayetanensis* (although it was not confirmed).

Conclusions

Our scoping review identified gaps in the literature regarding detection-method studies on soil or water, studies of the prevalence and factors associated with *C. cayetanensis* contamination of soil, and studies of methods for controlling *Cyclospora* in the environment. These gaps could be addressed by conducting primary research and/or finding unpublished studies of these topics.

Sufficient studies are available for a systematic review and possible meta-analysis of the prevalence of *Cyclospora* contamination of water. Such a review is currently underway. Additionally, there may be sufficient studies for a systematic review of the prevalence and factors associated with human *Cyclospora* infection. A systematic review would allow a full evaluation of the information from primary research studies and identification of the most appropriate next steps in the research and decision-making process.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0950268821000200>.

Data. The full set of data generated from this scoping review is available on request from the corresponding author.

Acknowledgements. We thank Makenna Hughes for help with article procurement.

Financial support. This study was funded by the United States Food and Drug Administration.

Conflict of interest. MET is an employee of the FDA. The remaining authors declare that they have no conflicts of interest.

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