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Epidemiology, detection, and intervention/control of Cyclospora cayetanensis: A scoping review protocol

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Epidemiology, detection, and intervention/control of Cyclospora cayetanensis: A scoping review protocol

Abstract

Background: Cyclosporiasis is a food- and waterborne illness in humans caused by the consumption of contaminated food or water. As the causative agent, *Cyclospora cayetanensis*, has only been recently described, the published literature is limited and no scoping reviews on this topic have yet been conducted.

Objectives: Our objective is to conduct a scoping review of the epidemiology, detection in matrix, and intervention/control of *C. cayetanensis* worldwide in humans, plant-based food, and in the environment with the aim of identifying gaps in the literature, potential areas where there may be sufficient literature to warrant a systematic review, and prioritizing future research directions.

Eligibility criteria: All primary research, systematic reviews, scoping reviews and quantitative risk assessments in English, conducted anywhere in the world on the epidemiology, detection in matrix, and intervention/control of *Cyclospora cayetanensis* are eligible. Studies of the pathogenesis, diagnosis of illness in people, and treatment of cyclosporiasis are not eligible.

Sources of evidence: The following databases will be searched: MEDLINE® (Web of ScienceTM), Agricola (ProQuest), CABI Global Health, and Food Science and Technology Abstracts (EBSCOhost) from 1979 to the present.

Charting methods: We will extract information on general study characteristics, study purpose (epidemiology, detection, control) and within each of these categories, the study setting, study design, life cycle stage of *Cyclospora* investigated, and matrices tested. Based on the purpose of the study we will also extract the method of detection evaluated, risk factors for human illness, environmental and food contamination, incidence/prevalence in the environment and on food types, or the control approaches investigated.

Disciplines
Epidemiology | Food Science | Veterinary Preventive Medicine, Epidemiology, and Public Health

1   **Epidemiology, detection, and intervention/control of**

2   *Cyclospora cayetanensis***: A scoping review protocol**

3

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19

20 **Abstract**

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22 consumption of contaminated food or water. As the causative agent, *Cyclospora cayetanensis*,

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40 the study we will also extract the method of detection evaluated, risk factors for human illness,

41 environmental and food contamination, incidence/prevalence in the environment and on food

42 types, or the control approaches investigated.

43   **1. Introduction**

44   *1.1. Rationale*

45   *Cyclospora cayetanensis* is a single-celled parasite that causes an illness called cyclosporiasis in

46   humans when a person consumes water or food contaminated with the organism (CDC, 2019). *C.*

47   *cayetanensis* is shed in the feces by infected people. After 1 to 2 weeks in the environment, the

48   organism reaches the life cycle stage (sporulated oocyst) that is infectious to other people (CDC,

49   2019). Although the disease most commonly occurs in tropical and subtropical regions, people in

50   all parts of the world may become infected via ingestion of contaminated fresh produce imported

51   from those regions, with a recent outbreak occurring in the USA in 2019 linked to basil from

52   Mexico (CDC, 2019).

53

54   Scoping reviews are a type of literature review used for knowledge synthesis (Munn et al., 2018;

55   Tricco et al., 2018). Scoping reviews use systematic and transparent methods to summarize

56   research on broad topics, map the available evidence, and identify gaps in the current knowledge

57   (Tricco et al., 2018). A scoping review may act as a prelude to a systematic review and/or it may

58   help direct the focus of future primary research by highlighting areas where no research has been

59   conducted (Munn et al., 2018).

60

61   *C. cayetanensis* was first reported in humans in 1979 (Ashford, 1979) but it was not fully

62   identified until the early 1990s (Ortega and Sanchez, 2010). The literature base on this organism

63   consequently appears to be relatively limited; preliminary searches for existing scoping reviews

64   and systematic reviews of *Cyclospora* were conducted on December 12th, 2019 in MEDLINE®

65   (Web of Science™) (dates searched: 1950-Present), Agricola (ProQuest) (dates searched: 1970-

66 Present), and CABI Global Health (dates searched: 1973-present) using the search terms

67 ["*Cyclospora*" AND "systematic review"] and ["*Cyclospora*" AND "scoping review"]. The same

68 search was conducted in Food Science and Technology Abstracts (EBSCOhost) on January 3rd

69 2020. No scoping or systematic reviews of *Cyclospora* were found.

70

71 *1.2. Objectives*

72 Our objective is to conduct a scoping review of the epidemiology, intervention/control, and

73 detection in matrix of *Cyclospora cayetanensis* worldwide in humans, plant-based food, and in

74 the growing environment, i.e. water and soil, with the aim of identifying research gaps in the

75 literature and prioritizing future research directions, and identifying topics with sufficient

76 evidence base for systematic reviews.

77

78 2. Methods

79 *2.1. Protocol and registration*

80 This protocol was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-

81 Analyses Extension for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018). This protocol

82 will be registered on the University of Guelph Atrium and can be accessed at SYREAF

83 [www.syreaf.org].

84

85 *2.2. Eligibility criteria*

86 Studies included in the review must be:

87 1) published in English (though studies in English from any part of the world are eligible);

88 2) primary research, systematic reviews, scoping reviews, or quantitative risk assessments

89 (QRA) only. Narrative or non-systematic reviews will not be eligible for inclusion, as the

90 absence of reported methods precludes the assessment of rigor and comprehensiveness;

91   3) studies of *Cyclospora cayetanensis*, as this is the only species of *Cyclospora* that causes

92 cyclosporiasis in humans (CDC, 2019). Studies that report only *Cyclospora* species but do not

93 specify that the organism is *C. cayetanensis* will therefore not be eligible.; 4) studies of any life

94 stage (oocysts, sporocysts, or sporozoites) in any exposure source (soil, water and plants-based

95 food).

96 In humans, direct person-to-person transmission of cyclosporiasis does not occur (CDC, 2019)

97 therefore this is not of interest to the review. According to the CDC, animals have not been

98 documented as an intermediate or primary host of *C. cayetanensis* and therefore animal studies

99 are not of interest. Studies of the diagnosis of human illness, pathogenesis, and treatment of

100 cyclosporiasis are not eligible for this review.

101

102 *2.3. Information sources*

103 To identify relevant studies, the following databases will be searched from 1979 to the present:

104 MEDLINE® (Web of Science™), Agricola (ProQuest), CABI Global Health, and Food Science

105 and Technology Abstracts (EBSCOhost). As the focus of this scoping review is broad and the

106 topic is relatively new, we consider it appropriate to conduct a simple search (with no

107 restrictions on study design or research focus) that will not require specialized information

108 retrieval knowledge; therefore the review team designed the search without input from a library

109 scientist. Results of the database searches will be uploaded into Endnote® X8 Desktop for de-

110 duplication. The resulting de-duplicated results will be imported into DistillerSR® (Evidence

111 Partners, Ottawa, ON, Canada) review management software for further de-duplication. We will

112 also scan the reference lists of ten (subject to availability) of the most recently published

113 narrative reviews for additional relevant studies. We will not be contacting authors to identify

114 additional studies.

115

116 *2.4. Search*

117 The search strategy for MEDLINE® is in Table 1, Agricola (ProQuest) is in Table 2, CABI

118 Global Health is in Table 3, and for Food Science and Technology Abstracts (EBSCOhost) is in

119 Table 4, and will be conducted by members of the review team (AOC and ST). Given the

120 simplicity of the search string we did not submit the search strategy for peer review. There will

121 be no document-type or language restrictions included in the search, but the search will be

122 limited to studies published from 1979 to the date of the search, since *C. cayetanensis* was first

123 reported in humans in this year (Ashford, 1979). We did evaluate the addition of a wildcard (*)

124 term in the search (cyclospor*) however this was not included in the final search because it

125 added tremendously to the search results but the majority of new citations were irrelevant studies

126 on the antibiotic Cyclosporine A, a cyclic nonribosomal peptide, cyclosporin (a polypeptide).

127 Adding the terms Title (TI), MeSH Heading or MESH Major Topic did not add identify any

128 unique hits to the search

129

130 *Table 1: Proposed search strategy[1] in MEDLINE® (Web of Science[TM]) for a scoping review of the epidemiology, detection, and*
131 *intervention/control of Cyclospora cayetanensis.*

132

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

133   [1] There will be no document type or language restrictions.

134

135   *Table 2:Proposed search strategy in Agricola (ProQuest) for a scoping review of the epidemiology, detection, and*
136   *intervention/control of Cyclospora cayetanensis.*

Search no.	Search string
1	cyclospora OR cyclosporiasis OR cayetanensis

137   Search will be from January 1st, 1979 to present.

138   There will be no restrictions on source type, document type, or language.

139

140   *Table 3: Proposed search strategy in CABI Global Health for a scoping review of the epidemiology, detection, and*
141   *intervention/control of Cyclospora cayetanensis.*

Search no.	Search string
1	(cyclospora) OR (cyclosporiasis) OR (cayetanensis) AND yr:[1979 TO 2020]

142   Search will be from 1979 to present with no document type restrictions. Search of "all fields."

143

144   *Table 4: Proposed search strategy in food science and technology abstracts*

Search no.	Search string
1	(cyclospora) OR (cyclosporiasis) OR (cayetanensis) AND yr:[1979 TO 2020]

145

146

147   *2.5. Selection of sources of evidence*

148 In DistillerSR®, two reviewers working independently will assess the retrieved records for

149 eligibility, first based on the title/abstract, then, if they are deemed likely to be relevant, on the

150 full text. For eligibility assessment based on the title/abstract, two reviewers will be required to

151 exclude any record. For eligibility assessment based on the full text, two reviewers will be

152 required to include or exclude any record. Conflicts will be resolved via discussion, and if

153 consensus cannot be reached, by consulting a third reviewer.

154

155 The title/abstract screening form was pre-tested by all reviewers on 100 records and revised as

156 needed for clarity and consistency, before screening begins. This form comprises the following

157 question:

158

159   Q1. Based on the title/abstract, is the study a systematic review, a scoping review, a

160   QRA, a computer model (in silico) study, a burden of illness study, a molecular

161 characterization study or primary

162   research on detection in matrix, epidemiology of the exposure source, epidemiology

163   of human exposure, and/or intervention/control of the exposure source in *Cyclospora*

164   *cayetanensis*?

165   a. Yes (proceed to full-text screening)

166   b. No (exclude)

167   c. Unclear (proceed to full-text screening)

168   d. No, but it may be a relevant narrative review (exclude)

169

170   The full-text screening form was pre-tested by all reviewers on five records and revised for

171   clarity and consistency prior to the beginning of screening. This form comprises the following

172   questions:

173

174   Q1. Is the full text available in English?

175   a. Yes (proceed to Q2)

176   b. No, the full text is not in English (exclude) Specify language _____

177   c. No, the full text is not available (exclude)

178   Q2. Does the full text describe a study on *Cyclospora cayetanensis*?

179   a. Yes (proceed to Q3)

180   b. No (The study is of a different species of *Cyclospora*) (exclude)

181   c. No (The study is not on *Cyclospora* at all) (exclude)

182   Q3. Does the full text describe primary research, a systematic review, a scoping review, a

183   computer model study, a burden of illness studyor a QRA of *Cyclospora*

184   *cayetanensis*?

185   a. Yes (proceed to Q4)

186   b. No (exclude)

187   c. No but this is a potentially relevant narrative review (exclude)

188   Q4. If this is primary research, does the full text describe a study on the detection in

189   matrix, epidemiology of the exposure source, epidemiology of human exposure,

190   and/or intervention/control of the exposure source in *Cyclospora cayetanensis*?

191   a. Yes (proceed to data extraction)

192   b. No (This is a study of cyclosporiasis treatment in humans) (exclude)

193   c. No (This is a study of the pathogenesis of cyclosporiasis) (exclude)

194   d. No (This is an animal study) (specify species tested) (exclude)

195   e. No (This is a study of diagnosis of illness in humans) (exclude)

196   f. No (The study is not relevant for other reasons (exclude)

197   g. This is a computer model study, a burden of illness study or a QRA (include)

198

199   The total number of articles originating from each database searched, the number remaining after

200   de-duplication, and the number of studies assessed at title/abstract and full-text screening (with

201   reasons for exclusion for the latter) will be reported in a PRISMA Flow Diagram.

202

203   *2.6. Data charting process*

204   Data charting will take place in DistillerSR®. Data will be charted from all eligible studies by

205   two reviewers working independently, using a data-charting form designed for this review that

206   was pre-tested by all reviewers on five studies, with subsequent revision for clarity and ease of

207   use before charting begins. Conflicts will be resolved through discussion or, when this is not

208   possible, by consulting a third reviewer. Authors of eligible studies will not be contacted for

209   clarification/additional information.

210

211   *2.7. Data items*

212   Reviewers will extract the following categories of data:

213

214   **Study types:**

215   Primary research

216   Quantitative risk assessment

217   *In silico* model

218   Burden of illness study

219   Systematic review[*]

220   Scoping review[*]

221   * As our preliminary search did not detect any systematic or scoping reviews, we expect that we

222   may not find either of these types of studies in the final database search.

223

224   The following data will be collected for primary research studies only:

225   **General study characteristics:**

226   Year(s) and month(s) of study conduct if reported

227   Location (country) in which the study was conducted

228

229   **What was the purpose of the study?**

230   1.   Epidemiology (incl. transmission to humans, to the environment, to food)

231   1.1. Human infection

232   1.1.1. What was the study population?

233   1.1.1.1. Outbreak

234   1.1.1.2. Non-outbreak

235   1.1.1.2.1 If non-outbreak, specify the population

236   •   Immuno-compromised, organ transplant, HIV, etc.

237   •   Hospital cases (immune state not specified) – retrospective

238   evaluation of cases

239   • Non- hospitalized Non-immunocompromised populations

240   (health workers, agricultural workers, etc.)

241   1.1.1. Prevalence study

242   1.1.1.1.   Prevalence of the organism or some molecular subtype of the organism

243   1.1.1.2.   Demographics of the exposed population

244   1.1.2. Risk Factor study

245   1.1.2.1.   What risk factors were investigated (could include genotype)?

246   1.2. Exposure source

247   1.2.1. Specify exposure source(s) evaluated (berries/food, water, soil)

248   1.2.1.1. If produce, specify the type of produce investigated.

249   1.2.1.1.1. If produce, specify: fresh vs frozen, domestic vs

250   imported, processed vs unprocessed, hand-picked vs

251   mechanically harvested

252   1.2.1.2. If water, specify recreational, irrigation, natural, runoff, sewage

253   1.2.1.3. If soil, specify agricultural, compost, other

254   1.2.2. Specify if this was an Outbreak or a Non-outbreak study.

255   1.2.3. What was the purpose of the study? (Prevalence or Risk Factor study)

256   1.2.3.1. If this was a Prevalence \study, did the authors report the

257   prevalence of the organism and/or molecular subtypes of the

258   organism?

259   1.2.3.2. If this was a Risk Factor study, what factors were investigated?

260

261   1.3. Molecular Characterization of *Cyclospora*

262   2. Detection Method Development and Validation Study

263   2.1. Specify matrix (water, soil, human feces, etc.)

264   2.2. What stage of the life cycle of Cyclospora are they detecting?

265   2.3. Natural or challenge

266   2.4. What detection methods were used (PCR, Light microscopy, UV microscopy, Other)?

267   3. Control (intervention) study

268   3.1. What was the matrix (exposure source or Petri dish) they applied the intervention to?

269   3.1.1. If it's a matrix, at what stage was the intervention applied (pre-harvest, post-

270   harvest, etc.)?

271   3.1.2. What life cycle stage of *Cyclospora* was the control used against?

272   3.1.3. Natural infection vs challenge

273   3.1.4. What was the control (intervention) used? (type, method of application)

274   3.1.5. Describe the comparison group.

275

276   *2.8. Critical appraisal of individual sources of evidence*

277   As this is a scoping review, we will not conduct a critical appraisal of the literature.

278

279   *2.9. Synthesis of results*

280   The results will be summarized with descriptive statistics reporting the frequency of topics

281   investigated using a combination of tables and narrative text. Results of this review will be used

282   to identify knowledge gaps and help prioritize research directions, including areas for potential

283   systematic review for the control of *Cyclospora cayetanensis* in produce.

284

285 **Funding**

287

288 **References**

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