Cryptosporidium Reference Unit for England and Wales

Annual report of referrals and *Cryptosporidium* genotyping, England and Wales, 2022

National report for England and Wales

Cryptosporidium Reference Unit

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Acknowledgements

Public Health Wales would like to thank all the laboratory staff who sent *Cryptosporidium* positive faeces for genotyping and thus contributed to the information presented in this report.

Report prepared by the national Cryptosporidium Reference Unit and the Communicable Disease Surveillance Centre.

https://phw.nhs.wales/services-and-teams/cryptosporidium-reference-unit/

UKAS Accredited medical laboratory 9510

Suggested citation: Public Health Wales Microbiology 2023. Annual report of referrals and Cryptosporidium genotyping, England and Wales, 2022.

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Summary

- Diagnostic laboratories may refer stools for confirmation of equivocal findings or specialist testing of high-risk patients.
- All diagnostic laboratories in England and Wales are asked to send all *Cryptosporidium* positive stools for genotyping.
- In 2022, a total of 2913 specimens were referred to the national *Cryptosporidium* Reference Unit from 103 laboratories.
- The region (by location of referring laboratory) that referred the highest number of specimens was the North West (n = 569), followed by Yorkshire and the Humber (n = 429).
- The region that referred the lowest number of specimens was London (n = 63).
- Of the 2913 specimens referred nationally, 215 were either not confirmed (n = 108) or not typable by current methods (n = 107).
- Of the 2698 genotyped specimens, 1694 (63%) were identified as *Cryptosporidium parvum* and 919 (34%) were identified as *Cryptosporidium hominis.* 19 were both *C. parvum* and *C. hominis*, and 66 were other *Cryptosporidium* species.
- Of the genotyped specimens, 440 (16%) reported international travel and 65% of these were *C. hominis.*
- A multilocus variable number of tandem repeats analysis (MLVA) scheme provided evidence to strengthen links between cases and exposures / settings, and identified outbreaks more rapidly than disease surveillance alone.

Part 1. Referrals to the National *Cryptosporidium* Reference Unit from England and Wales

Diagnostic laboratories may refer stools for confirmation of equivocal findings or specialist testing of high-risk patients.

All diagnostic laboratories in England and Wales are asked to send all *Cryptosporidium* positive stools for genotyping. This is actively encouraged; there is no charge and our aim is to achieve unbiased molecular surveillance as well as to support cluster / outbreak identification and investigations; please see the section "Subtyping, clusters and outbreak investigations".

If individual laboratories have trouble sending specimens, please talk to the reference unit about facilitating this.

Our submission form can be found here:

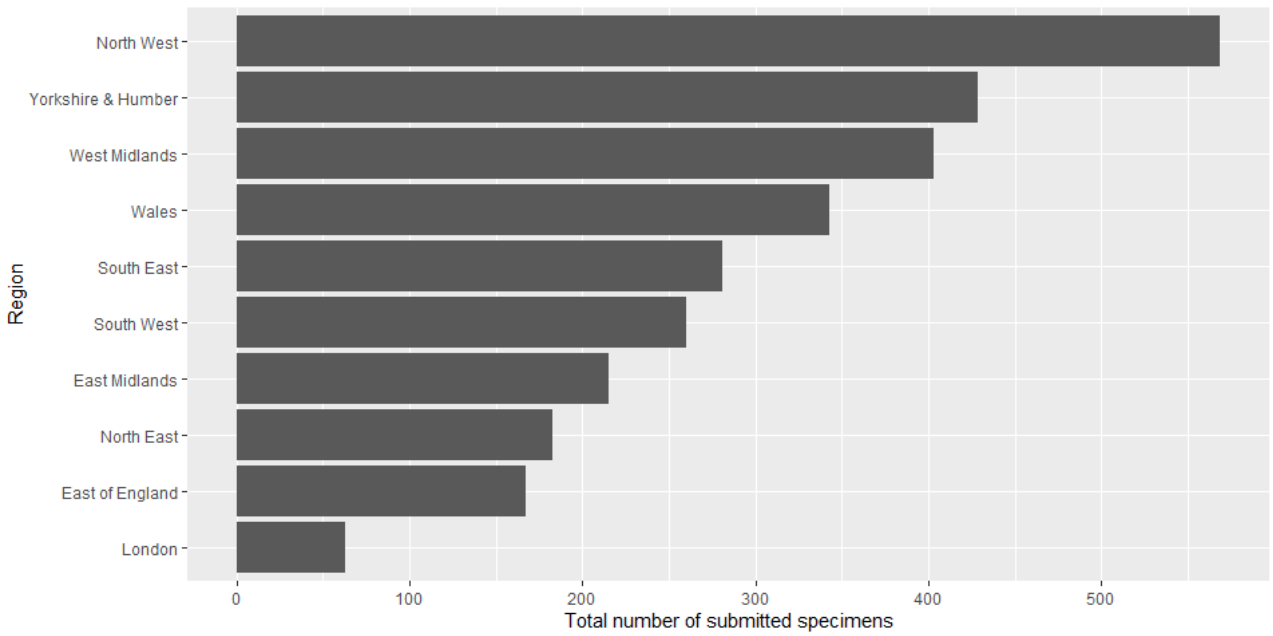
https://phw.nhs.wales/services-and-teams/cryptosporidium-reference-unit/specimen-submission-form/

In 2022, a total of 2913 specimens were referred to the national Cryptosporidium Reference Unit from 103 laboratories.

Summary of referrals by region and laboratory

The region (by location of laboratory as resident postcode data is not always provided) with the highest number of specimens submitted was the North West (n = 569), followed by the Yorkshire and Humber region (n = 429). The region that referred the lowest number of specimens submitted was London (n = 63). Providing postcode information is helpful for spatial analysis as well as liaising with Health Protection Teams and there is space on our submission form for this.

***Cryptosporidium* specimens referred to the reference unit by region, 2022**



Summary of referrals by region and month

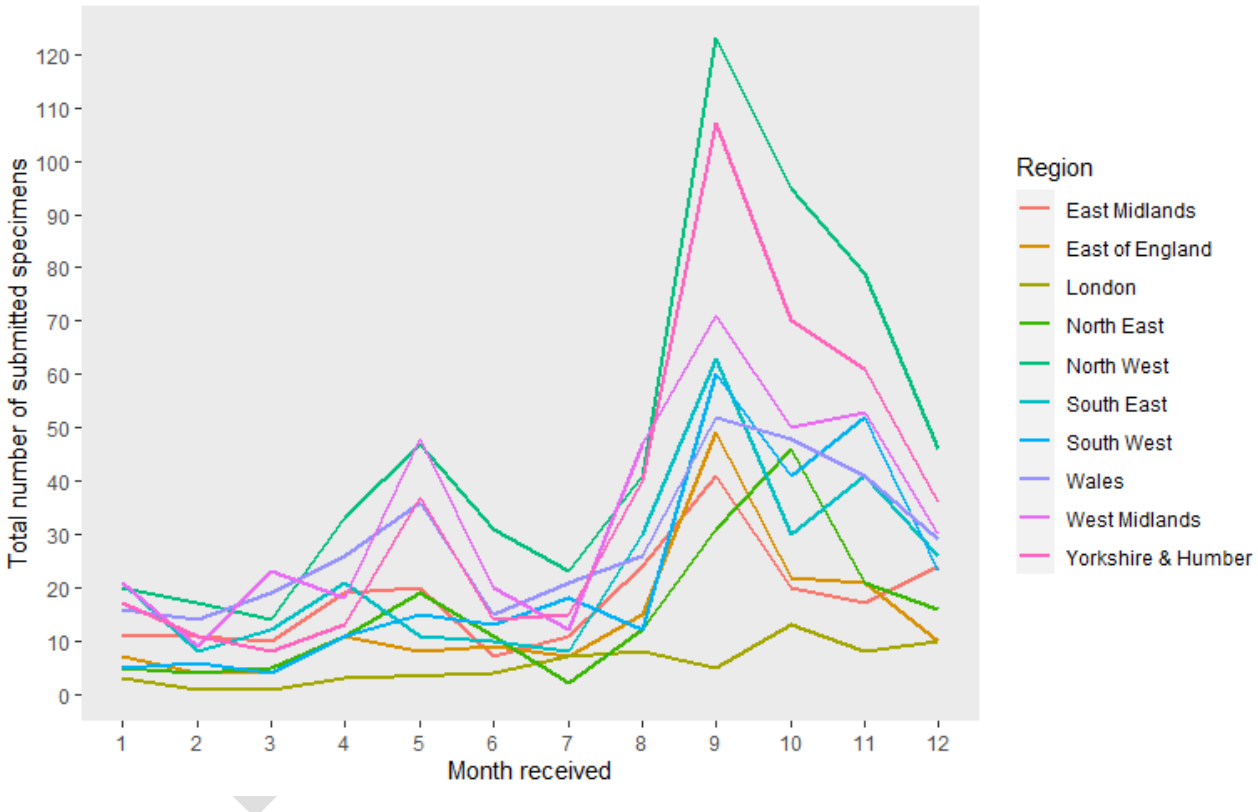
Temporal data are analysed here by month of specimen receipt, as specimen dates are not always provided. There is a place for this information on our submission form.

Most regions experienced a small peak in the number of specimens referred in May and their highest peak in September. The region with the highest monthly number of specimens referred was the North West in September (n = 123).

The trend in the North East and London differed with their highest number of specimens referred in October (North East = 46, London = 13).

There is usually a small spring peak and a larger autumn peak in *Cryptosporidium* cases, so this pattern was not unexpected.

Total number of specimens referred per month by region, 2022



Part 2: *Cryptosporidium* genotyping of referred specimens from England and Wales, 2022

Genotyping to identify *Cryptosporidium* species helps to understand the epidemiology and transmission of *Cryptosporidium*, and thus interventions.

C. hominis is host-adapted to humans and transmission is anthroponotic. *C. parvum*, in addition to humans, has a wide range of animal hosts and zoonotic transmission is especially linked to young livestock.

At the national reference unit, genotyping is undertaken in the first instance by duplex real-time PCR to detect *C. parvum* and *C. hominis*. If these predominant species are not detected, a real-time PCR that detects all *Cryptosporidium* species is used and the amplicon is sequenced to confirm which species is present.

These methods are described in Robinson *et al*., 2020 and Elwin *et al*., 2022.

Summary of *Cryptosporidium* species identified

Of the 2913 referred specimens in 2022, 215 were either not confirmed (n = 108) or not typable by current methods (n = 107).

Of the 2698 genotyped specimens, 1694 (63%) were identified as *C. parvum* and 919 (34%) were identified as *C. hominis*. This is a higher proportion of *C. parvum* than seen in most years previously, but may be influenced by COVID-19 pandemic interventions which had a significant effect on the species distribution in 2020-2021 as shown in a time-series analysis by Adamson *et al*., 2023.

Both *C. parvum* and *C. hominis* were detected in 19 specimens.

Other *Cryptosporidium* species were detected in 66 (2%) specimens:

Other *Cryptosporidium* species

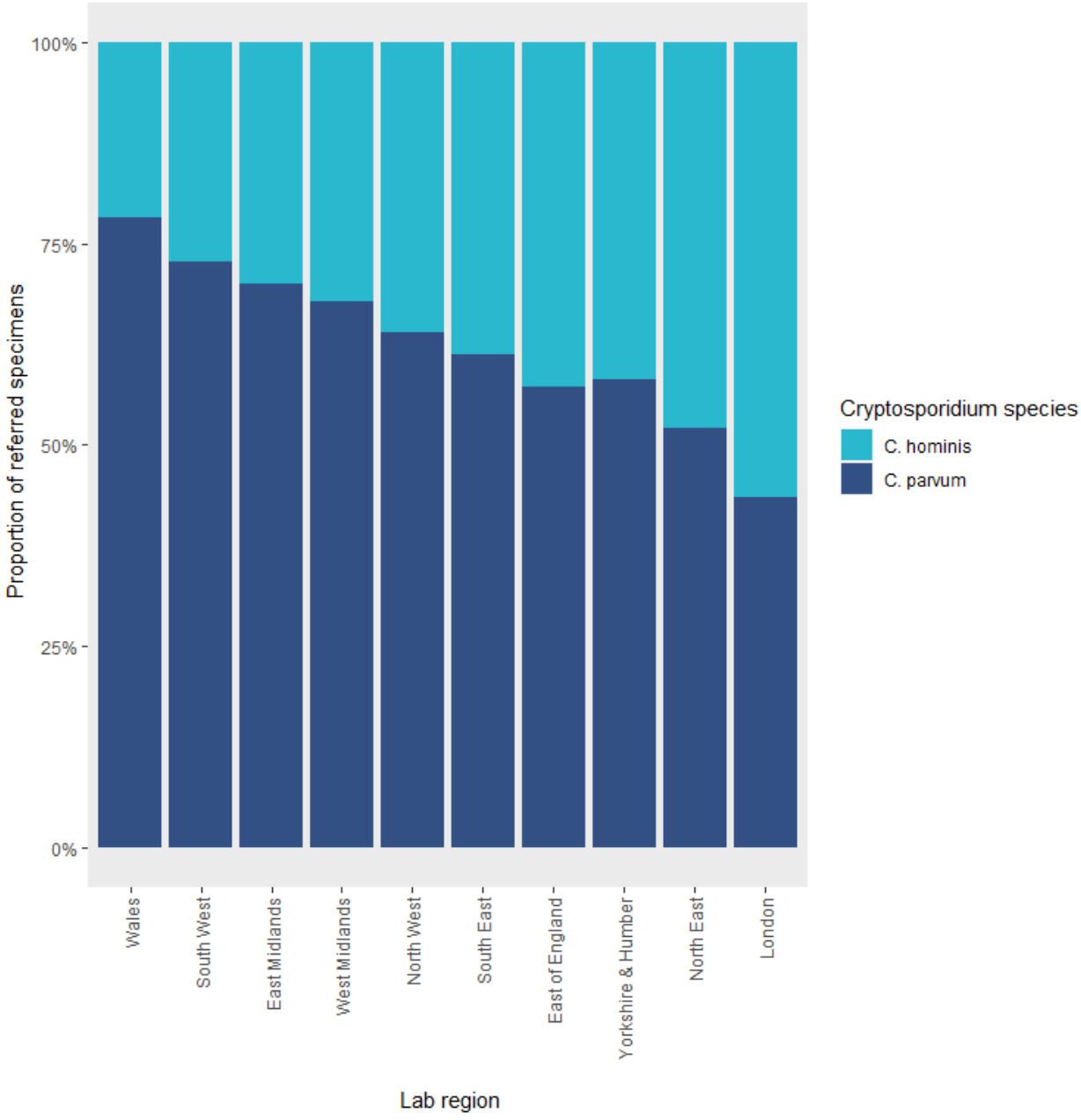
***Cryptosporidium* species (number detected in 2022)**	**Main reservoir hosts**
C. cuniculus (20)	Rabbits
C. ubiquitum (15)	Ruminants, rodents, carnivores, primates
C. felis (13)	Cats
C. meleagridis (10)	Birds
C. occultus (3)	Rodents
C. canis (2)	Dogs
C. ditrichi (1)	Rodents
C. tyzzeri (1)	Rodents
Deer mouse genotype III (1)	Rodents

Spatial distribution of *Cryptosporidium* species, 2022

The spatial distribution of *C. parvum* and *C. hominis* is influenced by socio-economic and environmental risk factors. For *C. hominis* these include living in an urban area where high population density facilitates person-to-person spread. For *C. parvum* these include living in a rural area, or where ruminant livestock density is high.

The occurrence of *C. parvum* and *C. hominis* differed between regions. Wales had the highest frequency of *C. parvum* specimens (78%) compared to *C. hominis* (22%), whereas London reported the lowest frequency of *C. parvum* specimens (44%) compared to *C. hominis* (56%).

Proportion of *C. hominis* / *C. parvum* by region of referring laboratory, England and Wales, 2022



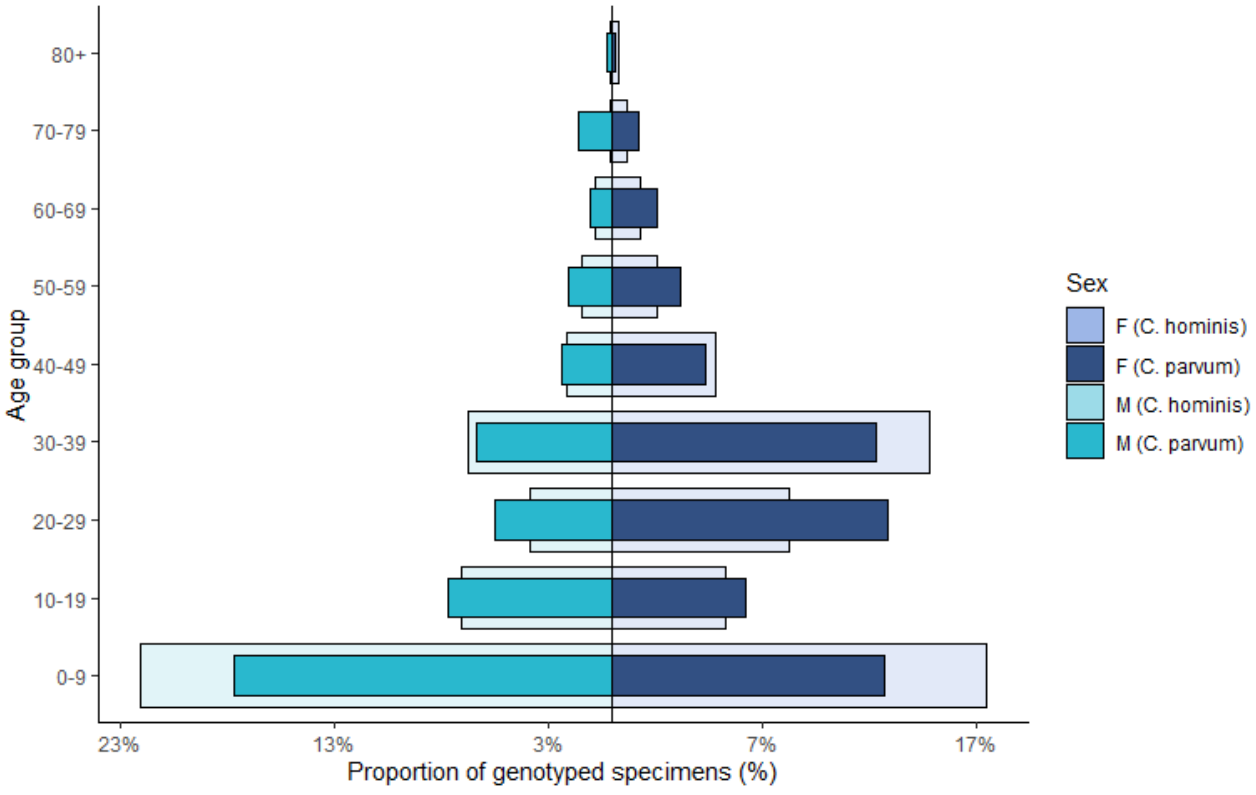
Age-sex distribution of *C. parvum* and *C. hominis*, 2022

Age and sex information was available for 2596/2613 (99%) *C. parvum* and *C. hominis* specimens. Most were from the 0-9 age group (n = 872) and 30-39 age group (n = 511).

There was no difference overall between the sex distribution of *C. parvum* where 938/1688 (56%) specimens were from females and 750 (44%) from males, and *C. hominis* where 505/908 (56%) were from females and 403 (44%) from males.

The age and sex distribution differed; there were more specimens from boys under 10 years of age, and from women aged 20-39 years. *C. hominis* predominated in young children. Interestingly, a predominance of *C. hominis* in women of childbearing age usually seen was not so evident in 2022 and in the 20-29 age group there was a greater proportion of *C. parvum*.

Age and Sex of *C. parvum* and *C. hominis* cases, England and Wales, 2022

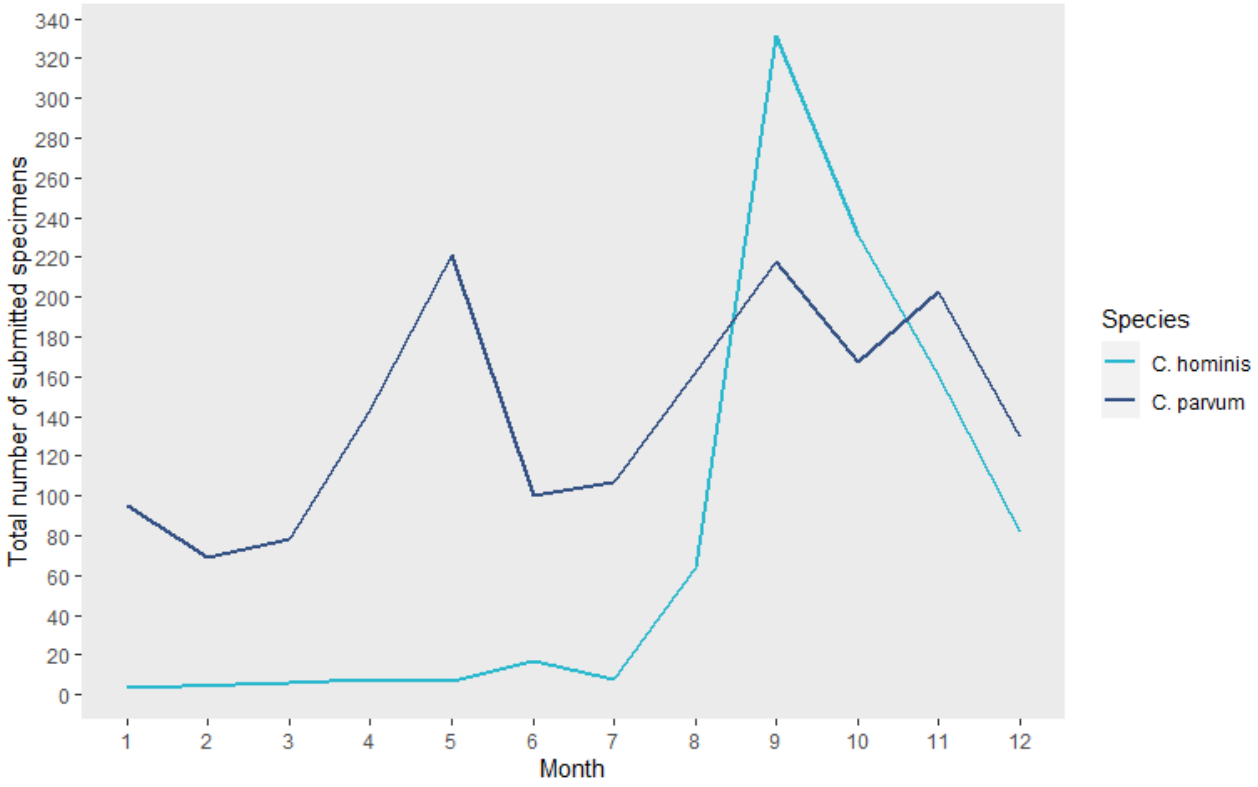


Temporal distribution of *Cryptosporidium* species, 2022

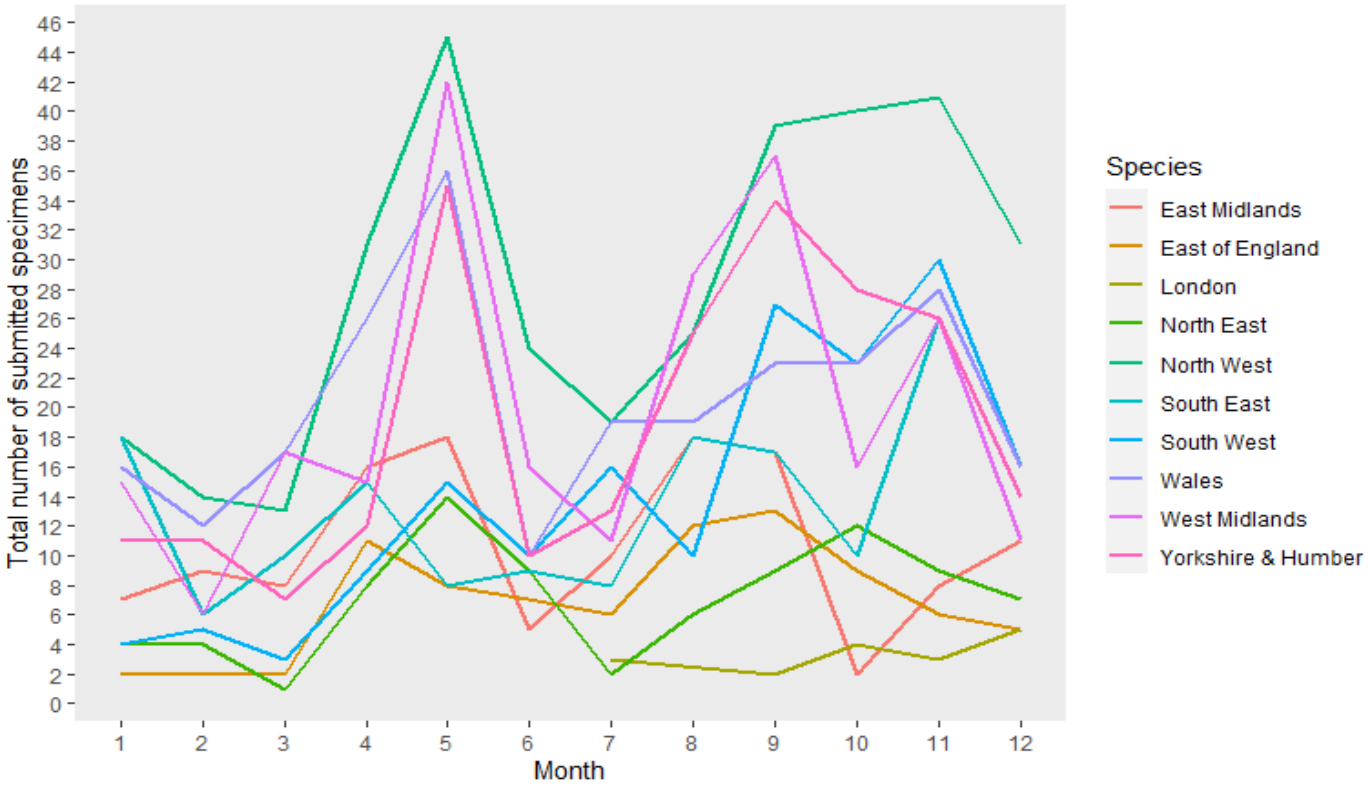
The temporal distribution of *Cryptosporidium* species is influenced by environmental factors and human behaviour such as seasonal visits to open farms and international travel to see friends and family or for holidays.

The number of *C. parvum* specimens peaked in May (n = 221) and again in September (n = 218). The number of submitted *C. hominis* specimens stayed consistently low across the first eight months of the year, peaking sharply in September (n = 331), when 160 of these reported foreign travel (see below).

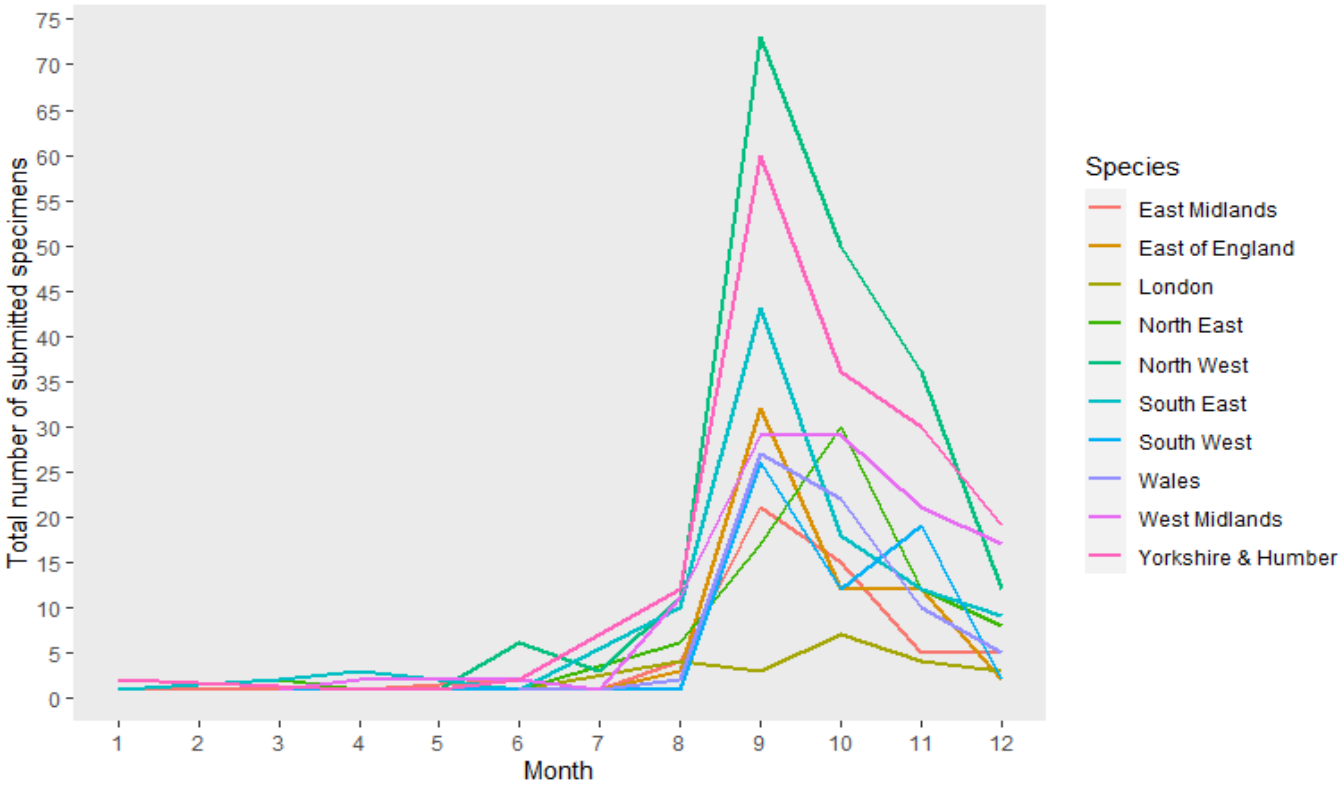
C. parvum and *C. hominis* specimens by month of receipt, England and Wales, 2022



C. parvum specimens by month of receipt by region in England and Wales, 2022



C. hominis specimens per month of receipt by region in England and Wales, 2022

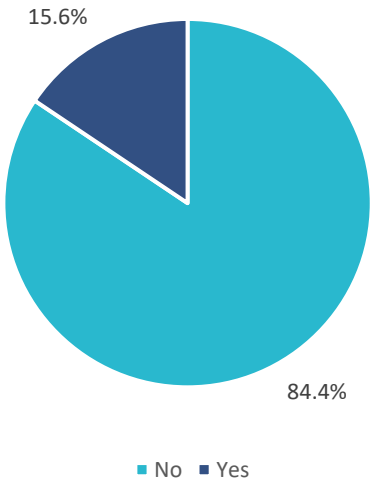


Travel history and *Cryptosporidium* species

A history of international travel is often associated with *Cryptosporidium* infection, but can be underestimated if the history is not recorded. This is why we include a space to record this on our submission form.

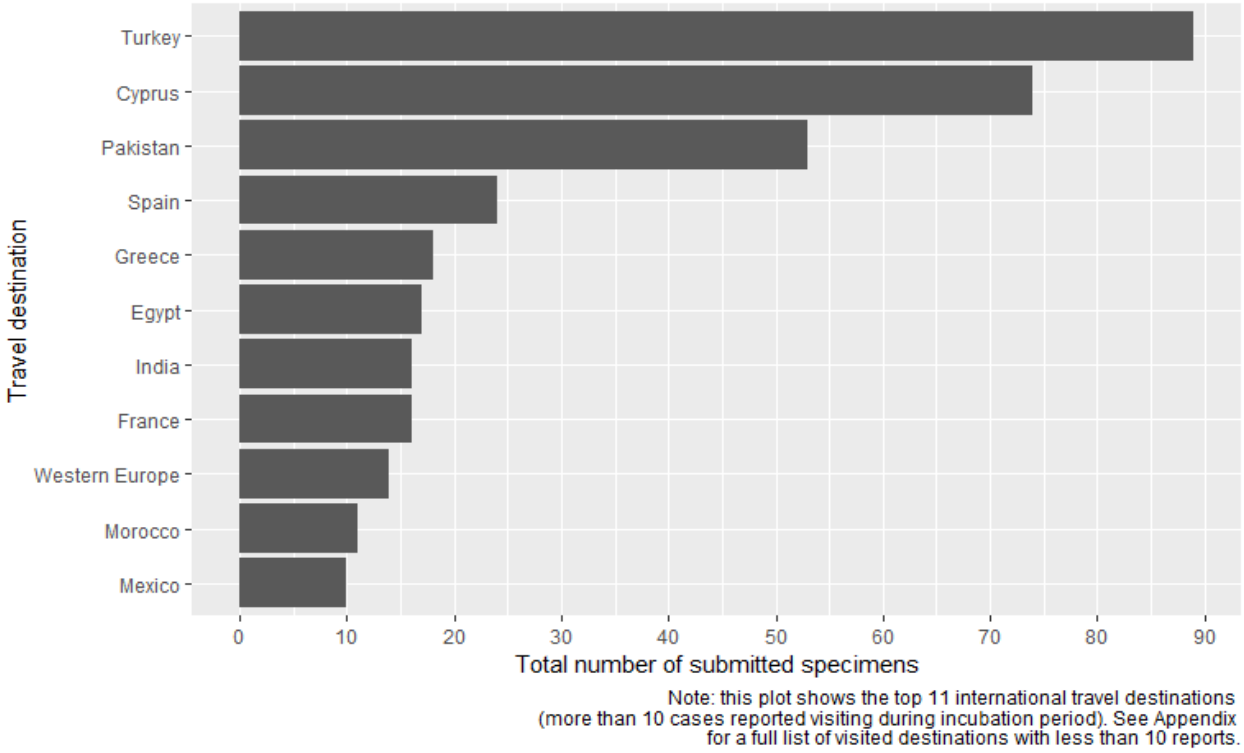
In 2022, 440/2698 (16%) of genotyped *Cryptosporidium* specimens reported international travel within the incubation period of their infection.

Proportion of genotyped specimens, England and Wales, with an international travel report, 2022



The top three travel destinations were Turkey (n = 89), Cyprus (n = 74) and Pakistan (n = 53). Cyprus does not normally feature strongly among *Cryptosporidium* cases and was investigated further (see the section on subtypes, clusters and outbreaks).

International travel destinations of *Cryptosporidium* cases genotyped from England and Wales, 2022 (see Appendix for destinations with <10 reports)



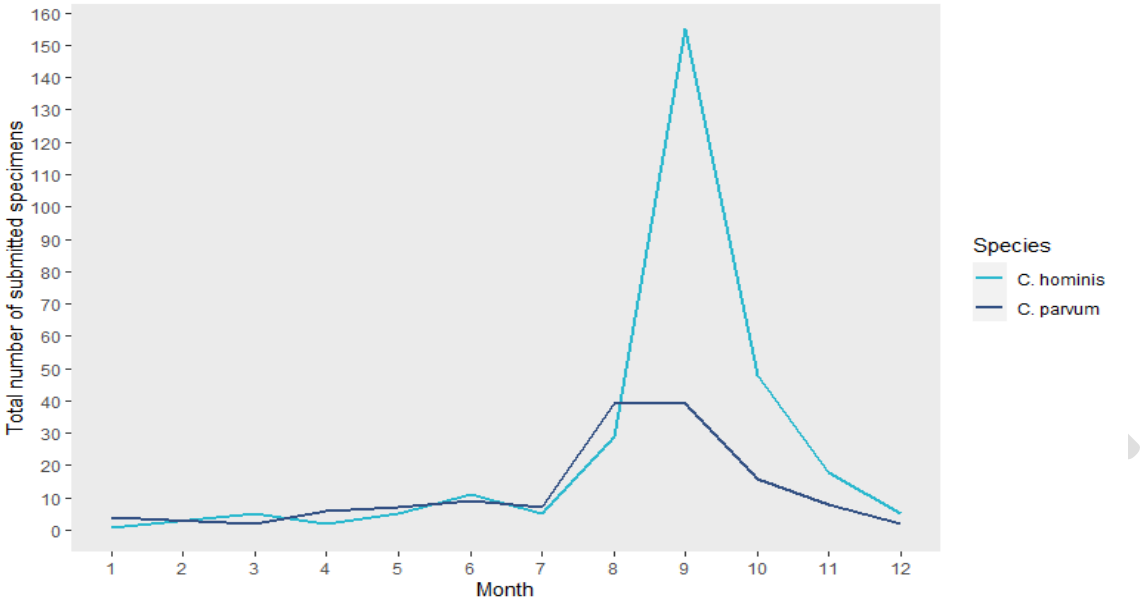
Of the 440 genotyped specimens that reported foreign travel, more were C. *hominis* (65%) than *C. parvum* (32%). Most (14/19) of the co-infections *C. hominis* and *C. parvum* had reported international travel.

International travel destinations and *Cryptosporidium* species, 2022

Cryptosporidium species	Total among travellers	Turkey	Cyprus	Pakistan	Other countries
C. hominis	284	71	51	37	125
C. parvum	139	15	14	13	97
C. hominis & *C. parvum*	14	0	9	1	4
C. ubiquitum	1	0	0	0	1
C. meleagridis	1	0	0	0	1
C. canis	1	0	0	1	0

The majority (n = 155) of *C. hominis* specimens with international travel history were received in September, whereas the months with the highest frequency of international travel for *C. parvum* specimens were August and September (n = 39).

***C. parvum* and *C. hominis* case reporting international travel by month of receipt from England and Wales, 2022**



Subtyping, clusters and outbreak investigations in England and Wales, 2022

One of the main values of *Cryptosporidium* genotyping and subtyping is for identifying and investigating outbreaks. Without the specimens you refer for genotyping, this would not be possible and the public health response would be compromised.

Traditionally, the CRU has used gp60 subtyping by sequencing a hypervariable region of the *gp60* gene to investigate outbreaks. More explanation of the gp60 nomenclature and outbreak investigations can be found in Chalmers *et al*., 2019.

In 2022, nine outbreaks benefitted from gp60 subtyping.

Four outbreaks were caused by *C. hominis*, all linked to swimming pools in September, October and November. The gp60 subtypes in three outbreaks were IdA16 and in one outbreak it was IfA12G1R5. Although swimming pool-related Cryptosporidium outbreaks are usually caused by *C. hominis* and are more common in the autumn, there were no outbreaks at all reported in 2020 and 2021 (probably because of COVID-19 restrictions) and now the distribution of gp60 subtypes is very different compared to before the pandemic, when most *C. hominis* outbreaks were IbA10G2. This is indicative of a need to look more closely at the variation in *C. hominis* that seems to have arisen and whether the development of a multilocus genotyping scheme for *C. hominis* is needed.

For *C. parvum*, which was known to be more variable than *C. hominis*, a multilocus genotyping scheme (using variable number of tandem repeats analysis, or MLVA) was implemented in 2021. You can read more about it in Gopfert *et al*., 2022 and in Robinson *et al*., 2022.

As well as investigating outbreaks by MLVA, we also piloted the routine testing of all *C. parvum* cases in Wales and the north west of England by MLVA. This pilot study was supported by pump priming funding from the National Institute for Health and Care Research (NIHR) Health Protection Research Unit in Gastrointestinal Infections. The final report can be found on our website, here: https://phw.nhs.wales/services-and-teams/cryptosporidium-reference-unit/hpru-gi-pump-priming-project-2022/

In 2022, six outbreaks were caused by *C. parvum*, five linked to open farms and one to a day care nursery. The open farm outbreaks were in February to May and the nursery outbreak was in December.

In the nursery outbreak, in the south east of England, all five cases had the same MLVA profile. In a small outbreak of three cases linked to an open farm in south east Wales, all three cases shared a MLVA profile. The finding of the same MLVA profiles in small outbreaks strengthened the epidemiological links between the cases.

In one larger outbreak at an open farm in Hertfordshire, there were two MLVA profiles and cases either had one or the other profile, or a mix of the two.

In an outbreak in north Wales, there was one main outbreak profile and two additional cases were linked by their MLVA profile and subsequently discovered to have visited the farm and included in the outbreak investigation.

A cluster of cases with the same MLVA profile in Greater Manchester was highlighted to the Health Protection Team. On investigation, a common exposure was found and an open farm inspected. Failures to comply with guidance were identified and improvements made. Additionally, as a result of raising awareness of this farm, cases of STEC were linked to it, re-enforcing the importance of the public health actions taken.

In summary, MLVA provided evidence to strengthen the links between cases and exposures / settings and can identify outbreaks more rapidly than disease surveillance. This is only possible if laboratories send us specimens; thank you for doing this.

Genotyping plans for 2023

- Prepare for testing all *C. parvum* specimens by MLVA from all of England and Wales by establishing the infrastructure for cluster communication and management.
- Work with the Animal and Plant Health Agency to improve sampling and testing of animals on premises linked to human outbreaks.
- Work with UKHSA to audit and improve Cryptosporidium genotyping and subtyping data capture in SGSS.
- Improve specimen referrals for genotyping to provide unbiased molecular surveillance.
- Initiate implementation of electronic reporting via NPEX. This will be on a lab-by-lab basis.

Appendix

Full list of international travel destinations with fewer than 10 reports from referred specimens (number of specimens) from England and Wales, 2022:

Africa (4)	Indonesia (1)
Algeria (1)	Iraq (3)
Bangladesh (2)	Israel (2)
Botswana (1)	Italy (7)
Bulgaria (3)	Kenya (1)
Cambodia (1)	Lanzarote (2)
Canary Islands (1)	Majorca (6)
Cape Verde (1)	Malaysia (1)
Caribbean Islands (1)	Malta (3)
Central African Republic (1)	Mauritius (1)
Central America (2)	Menorca (3)
Colombia (1)	Middle East (1)
Costa Rica (2)	Nepal (1)
Cote d'Ivoire (1)	Nigeria (1)
Crete (3)	Peru (2)
Croatia (3)	Portugal (6)
Cuba (1)	Qatar (1)
Dominican Republic (1)	Somalia (2)
Dubai (3)	South Africa (4)
Eastern Europe (3)	South America (1)
Eritrea (1)	Southeast Asia (1)
Ethiopia (1)	Sri Lanka (1)
Fiji (1)	Sudan (4)
French Guiana (1)	Syria (1)
Germany (1)	Tanzania (1)
Ghana (1)	Tenerife (2)
Gran Canaria (1)	Tunisia (2)
Guinea (1)	USA (1)
Hungary (1)	Uganda (1)
Ibiza (1)	Zimbabwe (1)

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Acknowledgements

We thank all the laboratories who sent, continue to send, and that have stated to send, *Cryptosporidium* positive faeces for genotyping. Without your help, improved understanding of the occurrence, distribution, epidemiology and transmission of *Cryptosporidium* would not be possible. This also enables timely public health actions and targeted interventions. THANK YOU!

Thanks are extended to our colleagues Oghogho Orife and Kerry Metters at the Public Health Wales Communicable Disease Surveillance Centre for data analysis and presentation.

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