

BHIVA guidelines for the treatment of opportunistic infections: gastrointestinal chapter

Public consultation comments

Compilation of all comments received via BHIVA website. The writing group thanks everyone who replied to the consultation. All comments were considered by the writing group and amendments have been made where appropriate.
14 July 2019

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1.	Laura Waters	Mortimer Market Centre, London	Thank you for this well-written update. I have a few comments that I hope are helpful: 1) Please avoid 'HIV-infected' e.g. 'non-HIV-infected' in the the general overview (replace with HIV-negative or without HIV?) 2) Reference 1 advocates considering OI as a cause of GI Sx even if CD4 >200 so I wonder if worth including that point 3) Some of the numbering appears disordered 4) '4.4.2.5 Prevention and impact of cART' gives a grade 1B recommendation but then no discussion or references 5) Suggest signposting to NICE guidance on diarrhoea for people with good CD4: https://cks.nice.org.uk/diarrhoea-adults-assessment	Agreed, HIV-infected replaced Reference numbering corrected The evidence in the references in the text below this statement are, we believe, sufficient to give this recommendation and grade NICE reference not included as due for revision
2.	R D Mehta		Great venture!Welcome	Thank you
3.	Alastair Duncan	Guy's and St Thomas' NHS Foundation	I think there should be more reference to nutrition support within this section, as GI OIs can lead to weight loss and wasting.	Additional paragraph on nutritional support inserted in section 4.4.2

		Trust, London	<p>I suggest: 4.3.4: Add a sentence such as "Odynophagia can lead to reduced nutritional intake requiring referral to a dietitian. In cases of severe oesophageal pain, local analgesia may be required to facilitate passing nasogastric feeding tubes."</p> <p>4.4.4.2: In the "Treatment" section here I recommend replacing "nutritional support" with "referral to a dietitian for nutrition support".</p>	
4.	Andy Winter	NHS Greater Glasgow and Clyde	<p>Thank you for a comprehensive guideline . Under 4.4.2.3. I don't think it is reasonable to ask for blood cultures in all presentations of diarrhoea, at least not unless there are systemic features.</p> <p>I think you have got here as you have split the approach into pathological categories and wonder if you could consider summarising a more practical clinician-focussed and patient centered approach to diagnostics based on symptoms signs and risk factors? then proceed into the causative agents?</p> <p>At present the guideline is a list of agents with associated tests and treatments but usually we are faced with someone who may have a GI condition which may or may not be infection. it may help to expand 4.2 to talk about the role of faecal elastase, calprotectin, exclusion of coeliac disease, and drug side effects as differentials. And iwth older population with bowel habit change bowel cancer is also increasing.</p> <p>Thanks</p>	<p>Blood cultures retained as most of writing group felt they were useful in many presentations</p> <p>Thank you for your other suggestions – we decided to keep the general format of the guidelines</p>
5.	Yvonne Gilleece	Brighton and Sussex University Hospitals NHS Trust	<p>these guidelines are very welcome and well done to the writing group for the clarity of each topic.</p> <p>My comments are suggested to enhance toe document.</p> <p>Bacterial diarrhoea -Suggest the paragraphs regarding causative organisms are reversed to be more relevant to a UK audience (starts with US). -Table would be more useful if in alphabetical name order of organism and this should may also be applicable to all subsequent tables. -Treatment section should reference BASSH treatment for enteric STIs more clearly with a weblink.</p> <p>Many thanks for the opportunity to comment on these guidelines</p>	<p>Thank you for the comments – we decided to keep the original format of the guidelines</p>
6.	Brendan Payne	Royal Victoria Infirmary,	<p>Table 4.3. I find the 'diagnosis' column of Table 4.3 to be confusing. The use of</p>	<p>The term molecular test has been substituted in the</p>

		Newcastle	<p>NAAT / PCR / RT-PCR / qRT-PCR terminology seems a bit arbitrary. Why not just say 'molecular' testing as a coverall for these? Specifically for CMV saying 'PCR (preferred)' is confusing and contradicts the subsequent text. For CMV colitis IHC on biopsy is the gold standard. Whereas CMV PCR has a relatively minor role to play in diagnosing CMV colitis. I would omit mention of pp65 Ag as this is rarely, if ever, done these days. I would also omit CMV-specific T-cell assays as these are still really research tools, and are certainly not used to make a diagnosis of CMV colitis.</p> <p>For adenovirus I would omit mention of viral culture and of serology. I don't feel these have any role in contemporary practice. Adenovirus qPCR on blood might however be considered in an immunocompromised person with evidence of adenovirus in stool.</p> <p>Table 4.4. Giardia. PHE now prefers use of molecular testing for Giardia owing to higher sensitivity (in general population). This is not however available everywhere. Entamoeba. Diloxanide is now very difficult to source. Paromomycin is an alternative for luminal clearance.</p>	<p>table as suggested</p> <p>Pp65 omitted</p> <p>Culture and serology have been omitted</p> <p>Molecular test included</p> <p>Diloxanide included</p>
7.	Adele Wolujewicz	Southmead Hospital, Bristol	<p>Dear writing group,</p> <p>In the context of rising syphilis diagnoses, it would be useful to add a line to the section on oropharyngeal infections e.g.</p> <p>Primary syphilis can present with oral ulcers as well as causing genital and perianal ulceration. Individuals at risk should be screened in line with national guidelines.</p> <p>Reference: British Association of Sexual Health and HIV 2015: UK national guidelines on the management of syphilis. Available at: https://www.bashguidelines.org/media/1148/uk-syphilis-guidelines-2015.pdf</p> <p>Many thanks, Adele</p>	<p>Has been included in section 3.2</p>
8.	Public Health	Public Health England	<p>1. <i>Shigella</i> is a sexually transmissible enteric infection that can result in severe dysentery.</p>	<p>We believe these points are adequately covered in the guidelines</p>

	<p>England</p>		<ul style="list-style-type: none"> ○ <i>S. sonnei</i> and <i>S. flexneri</i> are endemic in the United Kingdom (UK), although they can also be travel associated. Over the past 10 years in England and Wales, non-travel associated cases in adults aged 16 to 60 years-old have risen and now account for most of all cases reported ○ Outbreaks of <i>S. sonnei</i> and <i>S. flexneri</i> in the UK have been linked to person-to-person spread among gay, bisexual and other men who have sex with men (MSM), including those living with HIV (1). <ol style="list-style-type: none"> 2. <i>Shigella</i> spp are becoming increasingly resistant to antimicrobials, and fluoroquinolone-resistant <i>Shigella</i> spp (2) are recognised by the World Health Organisation as priority antimicrobial drug resistant gram-negative bacteria (3). 3. Advice should be sought from microbiologists for the treatment of infection with <i>Shigella</i> spp, and laboratories should follow the European Committee on Antimicrobial Susceptibility Testing (EUCAST) protocols for antimicrobial susceptibility testing (4). 4. <i>Shigella</i> spp are notifiable organisms and infectious bloody diarrhoea is a notifiable disease; therefore, clinicians should notify their local Health Protection Team (HPT) of cases. <ul style="list-style-type: none"> ○ Laboratories report these cases directly to Public Health England, so the case may be contacted by the Environmental Health Office or HPT to conduct a public health risk assessment to identify any transmission risks (for example food handlers, healthcare workers etc.) and to provide appropriate advice on reducing the risks of transmission. 5. Further information on the management of MSM with symptoms of sexually transmissible enteritis and proctitis are provided in the British Association fo Sexual Health and HIV (BASHH) 2016 UK national guideline on the sexual health care of MSM (5). <p>1. https://www.gov.uk/government/collections/shigella-guidance-data-</p>	
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			<p>and-analysis</p> <p>2. https://www.nature.com/articles/s41467-018-03949-8</p> <p>3. https://www.who.int/medicines/areas/rational_use/prioritization-of-pathogens/en/</p> <p>4. https://www.gov.uk/government/publications/multi-drug-resistant-shigella-sonnei-cluster-2018-to-2019</p> <p>5. https://www.bashhguidelines.org/media/1162/msm-2016.pdf</p>	
9.	Heather Leake Date	Brighton and Sussex University Hospitals NHS Trust	<p>1. Generally very clear and well-presented.</p> <p>2. Candidiasis - no dose or duration given for fluconazole. Suggest tabulate treatments as per some of the other OIs. All sections would benefit from a summary table of drug, dose, duration etc.</p> <p>3. Give greater prominence to the presentation of STIs as causes of diarrhoea, and link to BASHH guidelines.</p>	<p>Doses/duration now included</p> <p>See comments above</p>
10.	British Infection Association	British Infection Association	<p>Our organisation broadly supports these new guidelines.</p> <p>We expected a fuller methods in the document appendix- how many papers were reviewed and what was the basis of inclusion/rejection from the evidence? Please could this be included or linked to.</p> <p>Stool and blood cultures should be included in the routine diagnostic work-up of diarrhoea in PLWH- should this statement be qualified with CD4 counts that are low? Are all those with diarrhoea living with HIV even when immune system is good going to have blood cultures? This will have an impact on false positive results and we would not advise this.</p> <p>In the table 4.2 if stating 'as per national guidelines' a link should be included to the reference in case they change? Some trusts no longer use metronidazole and these guidelines are from 2013 suggesting a change in practice since then. Listing all diagnostic methods e.g. for C.diff can be confusing to the reader who may not understand which are used in which setting. C.diff testing differs by hospital so perhaps 'according to local protocol' is the best way of stating this.</p> <p>Is the association of MAI and HIV really 'indeterminate'-Is this not established at low CD4 and would treatment of HIV not then reduce the risk of future infection?</p>	<p>Appendix 1 shows search strategy, however the other information is not normally included</p> <p>See statement above about blood cultures</p> <p>Given anticipated change in national guidelines it was felt not helpful to provide a link given it would likely be out of date by the time of publication of these guidelines</p> <p>Agreed, changed to 'yes'</p>

			<p>The section on strongyloides makes no mention of the risk of giving ivermectin when the patient in fact has filariasis (the serology can cross-react) inducing encephalopathy. It is usual to refer to a specialist as a result. The statement ivermectin is better than albendazole is missing a reference.</p> <p>The section on giardia needs some mention of recurrence/persistence. And mention of the need for hygiene to prevent re-infection from a partner. And some mention of onward referral if recurs.</p>	<p>A sentence has been added to cover this issue. A reference has now been added to cover this</p> <p>These issues are now covered</p>
11.	British Infection Association	British Infection Association	<p>Further comments from our members as I queried the use of metronidazole for C.diff in this guideline and received this specialist response:</p> <p>Inclusion of metronidazole for treatment of CDI as an oral agent is outdated</p> <p>The recommendation is based on the PHE guidelines which are 6 years old and a Cochrane review published in 2017. Both sources do not take into account more contemporary literature that confirms metronidazole as an inferior agent to vancomycin and fidaxomicin both for severe and non-severe episodes. See:</p> <p>1Sarna et al. Annals Pharmacotherapy 2019 1-9</p> <p>2Igarashi et al. J Infect Chemother 2019 24:11, 907-914</p> <p>3Beinortas et al. Lancet Infect Dis 2018 18:9, 1035-1044</p> <p>4Stevens et al. JAMA Intern Med. 2017;177:546-553</p> <p>5Nguyen et al . Transpl Infect Dis. 2018;20:e12867</p> <p>The PHE guidelines are being reviewed.</p> <p>Metronidazole should probably only be used as an iv agent where oral drugs are contraindicated.</p>	<p>See above comments</p> <p>Agreed, hence reference to national guidelines</p>

			The guideline does not mention bezlotoxumab which may be useful in preventing recurrence (particularly in cases where FMT is not available or where there are contraindications)	Not currently in national guidelines to our knowledge
12.	British Infection Association	British Infection Association	<p>Hello,</p> <p>Thank you for inviting us to comment on the BHIVA OI guideline gastrointestinal chapter. To put my feedback into context I am an SHO level doctor currently working in infectious diseases and probably have had less experience than other people giving feedback. Furthermore, my experience is biased as my only experience caring for PLWH are those who are unwell enough to be admitted to hospital (often with a new HIV diagnosis and not yet taking cART). I have therefore reviewed this guideline from the perspective of management of a potentially medically unstable patient with a lot of diagnostic uncertainty. I hope that you find my perspective as a junior member of a medical team helpful in developing these guidelines.</p> <p>Declaration of Conflict of Interest: I am a NIHR funded research fellow working on a randomised control trial assessing the impact of rapid multiplex PCR testing on patients presenting with acute gastroenteritis. I have received travel grants and a speaker honorarium from BioFire (bioMérieux) who develop and produce equipment that tests for an wide array of gastrointestinal pathogens. The views expressed below are my own and do not necessary represent the BIA Guideline committee nor the NIHR.</p> <p>Section 4.3</p> <p>I struggled finding specific information in the section and I wonder if it might be due to the format/structure of the subheadings. This might be improved by a restructuring with a section on oral symptoms followed by a separate section on oesophageal symptoms.</p> <p>In the oral symptoms section I would advise again further subheadings for oral ulceration and oral candidiasis. In the oral ulceration section I would mention testing for HSV (?and syphilis) via PCR (this can then be removed from 4.3.3). I would consider expanding the oral candidiasis section and include differentials including hairy leukoplakia. Herpetic gingivostomatitis might also be worth a mention?</p> <p>Section 4.3.3</p>	<p>Thank you for these comments</p> <p>The writing group preferred the formatting as it is</p> <p>See comments about STIs above</p>

		<p>Having read the referenced RCT I still feel that the in some situations it is reasonable to proceed straight to endoscopic evaluation in conjunction with empirical fluconazole. Firstly, for those patients in whom an additional/alternative oesophageal condition is suspected. Secondly for patients in which a delay in the treatment of an alternative cause of oesophageal symptoms carries a risk of overall clinical deterioration (i.e. patients with a poor physiological/nutritional status). I worry that the current wording of the guideline discourages this.</p> <p>Therefore I would propose adding:</p> <p>If an additional/alternative diagnosis is suspected, or, if a delay in the treatment of an alternative cause of oesophageal symptoms carries a risk of clinical deterioration it is recommended to request endoscopy at the time of starting empirical Fluconazole (Grade 1D, low-quality evidence).</p> <p>4.4.1 Definition of acute diarrhoea. “Diarrhoea is normally defined as having more than two bowel movements per day, with acute diarrhoea occurring for less than 4 weeks and chronic diarrhoea for more than 4 weeks” Be careful – I’m not sure this is accurate. The conventional classification of diarrhoea is acute (less than 14 days), persistent (greater than 14 days) and chronic (greater than 4 weeks). These definitions are supported by the world health organisation, NICE and American College of Gastroenterology. https://cks.nice.org.uk/diarrhoea-adults-assessment#!topicSummary https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease https://gi.org/topics/diarrhea-acute-and-chronic/ However I acknowledge that the British Society for Gastroenterologists state: “There is no consensus on the duration of symptoms that define chronic as opposed to acute diarrhoea. However, most groups including this GDG accept that symptoms persisting for longer than 4 weeks suggest a non-infectious aetiology and merit further investigation” (Arasaradnam RP, Brown S, Forbes A, et al. Gut 2018;67:1380–1399). But this framework is obviously less applicable to PLWH as often chronic diarrhoea can also be caused by an opportunistic infection! Therefore I would advocate changing this definition to adopt the WHO definition of acute diarrhoea and propose that this sentence is changed to:</p>	<p>In the COVID era this plan is not easy, and the current wording will fit better with practice</p> <p>The writing group preferred the original definition</p>
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			<p>further information.</p> <p>Kind Regards,</p> <p>Dr Samuel Mills – Junior member of the BIA guidelines committee.</p>	
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