United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease (2019 Interim Update)

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What is new in the 2019 interim update?

- the European Medicines Agency has released new guidance highlighting the potential for disabling and permanent side effects following the use of fluoroquinolone antibiotics. The guidance recommends that fluoroquinolones should not be used for mild to moderate bacterial infections when alternative antibiotic therapy is available. The PID guideline has therefore been updated to move fluoroquinolones from first to second-line use, except for women with *M genitalium* associated PID.
- the UK national treatment guideline for gonorrhoea has been updated to recommend the use of an increased dose of 1g ceftriaxone. The PID guideline has been updated to also recommend this increased dose.
- advice on the use of antibiotics in very early pregnancy (before a pregnancy test becomes positive) has been updated following advice from the UK Teratology Information Service. The benefits of therapy would outweigh the risks in this situation.

Introduction and methodology

Objectives

This guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of pelvic inflammatory disease (PID) covering the management of the initial presentation, as well as how to reduce transmission, complications and future repeat infection.

It is aimed primarily at women aged 16 years or older (see specific guidelines for those under 16) presenting to health care professionals working in departments offering specialist care in STI management within the United Kingdom. However, the principles of the recommendations should be adopted across all providers – non-specialist providers may need to develop local care pathways where appropriate.

Included in the guideline is a patient information leaflet.

Search strategy

The following reference sources were used to provide a comprehensive basis for the guideline:

1. **Medline Search**

Medline was searched using the search terms: (oophoritis or salpingitis or endometritis or pelvic inflammatory disease or PID or adnexitis or parametritis or adnexal disease) NOT primary immunodeficiency; the search was limited to humans and English language papers. The search was from 1st January 2010 to 1st August 2017 and identified 12 947 titles. Article titles and abstracts were reviewed and if relevant the full text article obtained. Priority was given to randomised controlled trial and systematic review evidence.

2. **2015 CDC STD Treatment Guidelines (www.cdc.gov/std/tg2015/default.htm)**

3. **Cochrane Collaboration Databases (www.cochrane.org)**

A number of limitations were recognised in the evidence base:

- a gold standard for the accurate diagnosis of PID is not available therefore a pragmatic approach to diagnosis and treatment is applied in many clinical trials
- the evidence base for PID treatment mostly comes from studies from several years ago which may not reflect recent changes in antimicrobial sensitivity patterns or newer diagnostic

tests, particularly for gonorrhoea. The management recommendations have therefore been adapted to reflect this.

- there are relatively less data available on the long term effectiveness of therapy compared to short term resolution of symptoms

Methods

Article titles and abstracts were reviewed and if relevant the full text article obtained. Priority was given to randomised controlled trial and systematic review evidence, and recommendations made and graded on the basis of best available evidence. The evidence was compiled by an external information specialist and reviewed by the authors before being incorporated into the guideline using the BASHH framework for guideline development. Successive drafts of the guideline were informed by feedback from the guideline authors. The final draft guideline was used for piloting and external review as outlined below.

An Equality Impact Assessment was undertaken to assess the relevance of the guideline recommendations in relation to age, disability, gender, gender reassignment, pregnancy, race, religion/belief and sexual orientation (Appendix 1).

A lay representative reviewed the guideline and contributed to the development of a patient information leaflet, with the support of co-author CE. This resulted in a number of changes to improve the clarity of both documents. The guideline was also reviewed by the BASHH Public Panel.

Piloting and feedback

Health professional and patient views were further sought by piloting a draft of the guideline with a sample of target users. This was coordinated by the BASHH Clinical Effectiveness Group (CEG) using health care professionals independent from the writing committee who adopt the guideline into their clinical practice in a virtual fashion for a period of time and then provide an evaluation using a standard feedback form.

Aetiology

- pelvic inflammatory disease (PID) is usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abcess and/or pelvic peritonitis.
- *Neisseria gonorrhoeae* and *Chlamydia trachomatis* have been identified as causative agents[1-3]. *C. trachomatis* is the commonest identified cause accounting for 14-35% of cases[4,5], whilst *Gardnerella vaginalis*, anaerobes (including *Prevotella*, *Atopobium* and *Leptotrichia*) and other organisms commonly found in the vagina may also be implicated. *Mycoplasma genitalium* has been associated with upper genital tract infection in women and is a very likely cause of PID[6-8]. Pathogen negative PID is common[9].
- *N. gonorrhoeae* and *C. trachomatis* are detected less commonly in older women with PID
- the insertion of an intrauterine device (IUD) increases the risk of developing PID but only for 4-6 weeks after insertion. This risk is probably highest in women with pre-existing gonorrhoea or *C. trachomatis*.

Clinical Features

Symptoms

The following features are suggestive of a diagnosis of PID[2,3,10,11]

- lower abdominal pain which is typically bilateral (but can be unilateral)
- abnormal vaginal or cervical discharge which is often purulent
- deep dyspareunia
- abnormal vaginal bleeding, including post coital bleeding, inter-menstrual bleeding and menorrhagia
- secondary dysmenorrhoea

Signs

- lower abdominal tenderness which is usually bilateral
- adnexal tenderness on bimanual vaginal examination – a tender mass is sometimes present
- cervical motion tenderness on bimanual vaginal examination
- fever (>38°C) in moderate to severe disease

A diagnosis of PID should be considered, and usually empirical antibiotic treatment offered, in any sexually active woman who has recent onset, lower abdominal pain associated with local tenderness on bimanual vaginal examination, in whom pregnancy has been excluded and no other cause for the pain has been identified. The risk of PID is highest in women aged under 25[5] not using barrier contraception and with a history of a new sexual partner. The diagnosis of PID based only on positive examination findings, in the absence of lower abdominal pain, should only be made with caution[12].

Complications

- women with immunosuppression secondary to HIV may have more severe symptoms associated with PID but respond well to standard antibiotic therapy[13]. No change in treatment recommendations compared to HIV uninfected patients is required[14-16]. (Grade 1B)
- the Fitz-Hugh Curtis syndrome comprises right upper quadrant pain associated with perihepatitis which occurs in some women with PID, especially by *C. trachomatis*. Although laparoscopic division of hepatic adhesions has been performed, there is insufficient clinical trial evidence to make specific recommendations for additional treatment beyond that for uncomplicated PID.
- a tubo-ovarian abscess should be suspected in patients who are systemically unwell and/or have severe pelvic pain. The palpation of an adnexal mass, or lack of response to therapy, should prompt pelvic imaging with ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI). Tubo-ovarian abscess is an indication for hospital admission for parenteral antimicrobial therapy, with appropriate anaerobic cover, and to monitor for signs of rupture or sepsis.
- the randomised controlled trial evidence for whether an intrauterine contraceptive device should be left in situ or removed in women presenting with PID is limited[17-19]. In women with mild to moderate PID the IUD may be left in situ but a review should be performed after 48-72 hours and the IUD removed if significant clinical improvement has not occurred. The decision to remove the IUD needs to be balanced against the risk of pregnancy in those who have had otherwise unprotected intercourse in the preceding 7 days. Emergency hormonal contraception following removal of an IUD may be appropriate for some women in this situation.

Diagnosis

- PID may be symptomatic or asymptomatic. Even when present, clinical symptoms and signs lack sensitivity and specificity (the positive predictive value of a clinical diagnosis is 65-90% compared to laparoscopic diagnosis[3,10,11])
- Testing for gonorrhoea, *C. trachomatis* and *M. genitalium* in the lower genital tract is recommended since a positive result supports the diagnosis of PID and may alter subsequent therapy (Grade 1B). The absence of infection at this site does not exclude PID however[3,10,11].
    - Local availability of *M. genitalium* testing currently varies but implementation of testing is strongly recommended to guide the choice of appropriate therapy
- An elevated ESR or C reactive protein, or high blood white cell count, also supports the diagnosis but is non-specific[20] and usually only abnormal in moderate or severe PID.
- The **absence** of endocervical or vaginal pus cells on Gram-stained examination of a vaginal smear has a good negative predictive value (95%) for a diagnosis of PID but their **presence** is non-specific (poor positive predictive value – 17%)[21].
- Ultrasound scanning is of limited value for uncomplicated PID but is helpful if an abscess or hydrosalpix is suspected[22]. Doppler ultrasound can detect increased blood flow associated with pelvic infection and may be useful, but it cannot differentiate between PID and other causes of increased vascularity such as endometriosis[23,24].
- MRI or CT scanning of the pelvis may be helpful in differentiating PID from alternative diagnoses[25-27] but are not indicated routinely. MRI, when available, is preferable since it provides high resolution images and avoids ionising radiation in women of reproductive age.

The differential diagnosis of lower abdominal pain in a young woman includes:

- ectopic pregnancy – pregnancy should be excluded in all women suspected of having PID
- acute appendicitis – nausea and vomiting occurs in most patients with appendicitis but only 50% of those with PID. Cervical movement pain will occur in about a quarter of women with appendicitis[28,29].
- endometriosis – the relationship between symptoms and the menstrual cycle may be helpful in establishing a diagnosis
- complications of an ovarian cyst e.g. torsion or rupture – symptoms are often of sudden onset

- urinary tract infection – often associated with dysuria and/or urinary frequency
- irritable bowel syndrome – disturbance in bowel habit and persistence of symptoms over a prolonged time period are common. Acute bowel infection or diverticular disease can also cause lower abdominal pain usually in association with other gastrointestinal symptoms.
- functional pain (pain of unknown aetiology) – may be associated with longstanding symptoms

Management

It is likely that delaying treatment increases the risk of long term sequelae such as ectopic pregnancy, infertility and pelvic pain[30,31]. Because of this, and the lack of definitive diagnostic criteria, a low threshold for empiric treatment of PID is recommended (Grade 1B). Broad spectrum antibiotic therapy is required to cover the wide range of aerobic and anaerobic bacteria commonly isolated from the upper genital tract in women with PID[2,3].

Some of the best evidence for the effectiveness of antibiotic treatment in preventing the long term complications of PID comes from the PEACH study where women were treated with cefoxitin followed by doxycycline – pregnancy rates after 3 years were similar or higher than those in the general population[32,33]. More recent mathematical modelling also supports a low rate of infertility and ectopic pregnancy following effective treatment of PID[34].

The choice of which of the recommended treatment regimens to use may be influenced by:

- robust evidence on local antimicrobial sensitivity patterns
- robust evidence on the local epidemiology of specific infections in this setting
- cost
- patient preference and compliance
- severity of disease
- patient age – sexually transmitted pathogens are less likely to be the cause of PID in older women[5]
- local antibiotic stewardship guidelines

General Advice

Rest is advised for those with severe disease. (Grade 1D)

Appropriate analgesia should be provided. (Grade 1D)

Intravenous therapy is recommended for patients with more severe clinical disease (Grade 1D) e.g. pyrexia > 38^{o}C, clinical signs of tubo-ovarian abscess, signs of pelvic peritonitis.

To avoid reinfection, patients should be advised to avoid oral or genital intercourse until they, and their partner(s), have completed their treatment (Grade 1D).

A detailed explanation of their condition with particular emphasis on the long term implications for the health of themselves and their partner(s) should be provided, reinforced with clear and accurate written information (Grade 1D). A patient information leaflet is included in Appendix 2 of this guideline.

When giving information to patients, the clinician should consider the following:

- an explanation of what treatment is being given and its possible adverse effects
- that following treatment fertility is usually maintained but there remains a risk of future infertility, chronic pelvic pain or ectopic pregnancy
- clinically more severe disease is associated with a greater risk of sequelae
- repeat episodes of PID are associated with an exponential increase in the risk of infertility
- the earlier treatment is given the lower the risk of future fertility problems
- future use of barrier contraception will significantly reduce the risk of PID
- the need to screen sexual contacts for infection to prevent re-infection

Outpatient therapy is as effective as inpatient treatment for patients with clinically mild to moderate PID[32]. Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations (Grade 1D):

- a surgical emergency cannot be excluded
- lack of response to oral therapy
- clinically severe disease
- presence of a tubo-ovarian abscess
- intolerance to oral therapy
- pregnancy

Further Investigation

All sexually active women who are potentially fertile should be offered a pregnancy test to exclude ectopic pregnancy (Grade 1D).

Treatment

The following antibiotic regimens are evidence based.

Recommended Regimens

All the recommended regimens are of similar efficacy.

Outpatient Regimens

First Line Therapy

i.m. ceftriaxone* 1g single dose followed by oral doxycycline 100mg twice daily *plus* metronidazole 400mg twice daily for 14 days

Grade 1A[35-37]

*Clinical trial data support the use of cefoxitin for the treatment of PID but this agent is not easily available in the UK so ceftriaxone, which has a similar spectrum of activity, is recommended.

Second Line Therapy

oral ofloxacin 400mg twice daily *plus* oral metronidazole 400mg twice daily for 14 days

Grade 1A[37-41]

oral moxifloxacin 400mg once daily for 14 days

Grade 1A[42-44]

Metronidazole is included in some regimens to improve coverage for anaerobic bacteria. Anaerobes are of relatively greater importance in patients with severe PID and metronidazole may be discontinued in those patients with mild or moderate PID who are unable to tolerate it.

Ofloxacin and moxifloxacin should be avoided in patients who are at high risk of gonococcal PID (e.g. when the patient's partner has gonorrhoea, in clinically severe disease, following sexual contact abroad) because of high levels of quinolone resistance [45]. *N. gonorrhoeae* is, however, an uncommon cause of PID in the UK (< 3%) and in those not at high risk of gonorrhoea quinolones can be used as second line empirical treatment, with therapy being adjusted subsequently if testing reveals quinolone resistant *N. gonorrhoeae*.

Levofloxacin is the L isomer of ofloxacin[46] and has the advantage of once daily dosing (500mg OD for 14 days). It may be used as a more convenient alternative to ofloxacin[42].

Three large RCTs support the efficacy of moxifloxacin for PID. There is a potential risk of serious liver reactions occurring with this agent but they are uncommon (12 cases reported in the UK from 2003-16 with no deaths) and moxifloxacin is generally well tolerated[47] (Grade 1D). Of the three recommended PID treatment regimens, moxifloxacin provides the highest microbiological activity against *M. genitalium*[8].

Ofloxacin, levofloxacin and moxifloxacin are effective for the treatment of *C. trachomatis.* Quinolones (ofloxacin, levofloxacin and moxifloxacin) can cause disabling and potentially permanent side-effects involving tendons. muscles, joints and the nervous system[48], and are therefore only recommended as second line therapy except for the treatment of *M genitalium* associated PID where no alternative therapy is available. Quinolones are also not licensed for use in patients aged under 18.

Replacing intramuscular ceftriaxone with an oral cephalosporin (e.g. cefixime) is not recommended because there is no clinical trial evidence to support its use, and tissue levels are likely to be lower which might impact on efficacy. Reports of decreasing susceptibility of *N. gonorrhoeae* to cephalosporins also supports the use of parenteral based regimens when gonococcal PID is suspected (to maximise tissue levels and overcome decreased susceptibility).

Azithromycin is recommended in some guidelines as additional treatment for uncomplicated gonorrhoea. It is not recommended for gonococcal PID for the following reasons:

- azithromycin is used to 'protect' cephalosporin therapy to try slow down the development of *N. gonorrhoeae* resistance but the number of cases of gonococcal PID in the UK is very small (2-3% of all PID). Therefore its use is unlikely to affect the public health control of antibiotic resistance.
- use of the 'non-azithromycin containing' regimens listed above is clinically effective
- adherence rates for existing two week PID treatment regimens are poor[49] and the addition of azithromycin has the potential to cause early discontinuation of medication due to gastrointestinal side effects.

Ceftriaxone provides microbiological cover for *N. gonorrhoeae* but also other aerobic and anaerobic bacteria associated with PID. The use of doxycycline plus metronidazole, in the absence of ceftriaxone, is not recommended because the evidence base is limited, previous trials have reported significant rates of treatment failure[50,51] and the addition of ceftriaxone improves treatment outcome[52].

Alternative Regimens

intramuscular ceftriaxone 1g immediately, followed by azithromycin 1 g/week for 2 weeks

Grade 2B[53,54]

Clinical trial evidence for this regimen is limited but it may be used when the treatments above are not appropriate e.g. allergy, intolerance. Single doses of azithromycin have the potential to induce macrolide resistance in *M. genitalium* and, if possible, use should be restricted to women who are known to be *M. genitalium* negative.

Inpatient Regimens

i.v. ceftriaxone 2g daily *plus* i.v. doxycycline 100mg twice daily (oral doxycycline may be used if tolerated) followed by oral doxycycline 100mg twice daily *plus* oral metronidazole 400mg twice daily for a total of 14 days

Grade 1A[36,37]

i.v. clindamycin 900mg 3 times daily *plus* i.v. gentamicin (2mg/kg loading dose) followed by 1.5mg/kg 3 times daily [a single daily dose of 7mg/kg may be substituted]) followed by either oral clindamycin 450mg 4 times daily or oral doxycycline 100mg twice daily plus oral metronidazole 400mg twice daily to complete 14 days

Grade 1A[36]

Gentamicin levels should be monitored if this regimen is used.

Intravenous therapy should be continued until 24 hours after clinical improvement and then switched to oral (Grade 2D). Intravenous doxycycline is not currently licensed in the UK but is available from IDIS world medicines (tel. 01932 824100).

Alternative Regimens

Clinical trial evidence for the following regimens is more limited but they may be used when the treatments above are not appropriate e.g. allergy, intolerance:

i.v. ofloxacin 400mg BD *plus* i.v. metronidazole 500mg TID for 14 days

Grade 1B[37-39]

i.v. ciprofloxacin 200mg BD plus i.v. (or oral) doxycycline 100mg BD plus i.v. metronidazole 500mg TID for 14 days

Grade 1B[38,55]

Allergy

There is no clear evidence of the superiority of any one of the recommended regimens over the others. Therefore patients known to be allergic to one of the suggested regimens should be treated with an alternative.

Pregnancy and Breastfeeding

- PID in pregnancy is uncommon but associated with an increase in both maternal and fetal morbidity, therefore parenteral therapy is advised although none of the suggested evidence based regimens are of proven safety in this situation.
- there are insufficient data from clinical trials to recommend a specific regimen and empirical therapy with agents effective against gonorrhoea, *C. trachomatis* and anaerobic infections should be considered taking into account local antibiotic sensitivity patterns (e.g. i.v. ceftriaxone, i.v. erythromycin and i.v. metronidazole switching to oral therapy following clinical response and completing 2 weeks of treatment) (Grade 2D).
- use of the recommended antibiotic regimens (listed above for non-pregnant women) in very early pregnancy (prior to a pregnancy test becoming positive) is justified by the benefits of treatment of PID at any stage of pregnancy being likely to outweigh any possible risks (personal communication, UK National Teratology Information Service – 15th October 2018).

Surgical Management

- laparoscopy may help early resolution of severe disease by dividing adhesions and draining pelvic abscesses[56] but ultrasound guided aspiration of pelvic fluid collections is less invasive and may be equally effective[57,58]
- laparotomy may be required to assess and treat clinically severe pelvic infection
- it is possible to perform adhesiolysis in cases of perihepatitis but there is no evidence on whether this is superior to only using antibiotic therapy

Follow Up

Review at 72 hours is recommended[11] for those with moderate or severe symptoms or signs (Grade 2D). Failure to improve suggests the need for further investigation, parenteral therapy and/or surgical intervention.

Further review, either in clinic or by phone, 2-4 weeks after therapy is recommended (Grade 1D) to ensure:

- adequate clinical response to treatment
- compliance with oral antibiotics
- screening and treatment of sexual contacts
- awareness of the significance of PID and its sequelae
- repeat pregnancy test, if clinically indicated

If initial testing for gonorrhoea was positive, repeat testing should be routinely performed after 2 to 4 weeks. If initial testing for *C. trachomatis* was positive, repeat testing after 3 to 5 weeks is appropriate for women who have persisting symptoms or where compliance with antibiotics and/or tracing of sexual contacts indicate the possibility of persisting or recurrent infection.

The following are recommended if the initial test for *M. genitalium* is positive:

- treatment with moxifloxacin. This agent currently has good microbiological activity against *M. genitalium* (Grade 1D)
- repeat testing for *M. genitalium* following treatment to ensure microbiological clearance. Treatment failure following the use of any of the recommended regimens has been reported but is least likely following treatment with moxifloxacin. The optimal time for testing after starting treatment is not known but 4 weeks is recommended based on expert opinion[59,60] (Grade 1D).

Partner Notification and Treatment of Sexual Partners

- current male partners of women with PID should be contacted and offered health advice and screening for gonorrhoea and *C. trachomatis* (Grade 1D). Other recent sexual partners may also be offered screening - tracing of contacts within a 6 month period since onset of symptoms is recommended but this time period may be influenced by the sexual history (Grade 2D).
- gonorrhoea or *C. trachomatis* diagnosed in the male partner should be treated appropriately and concurrently with the index patient according to the relevant BASHH guideline at www.bashh.org (Grade 1D).
- in women with confirmed *M. genitalium* infection, their male partner(s) should be offered testing for *M. genitalium* and, if positive, treated appropriately and concurrently with the index case (for appropriate treatment regimens see the BASHH Non-specific Urethritis Guideline – www.bashh.org)
- because many cases of PID are not associated with gonorrhoea, *C. trachomatis* or *M. genitalium*, broad spectrum empirical therapy should also be offered to male partners e.g. doxycycline 100mg twice daily for 1 week (Grade 2D).
- partners should be advised to avoid oral or vaginal intercourse until they and the index patient have completed their treatment course (Grade 1D).

Auditable Outcome Measures

Appropriate short term audit outcomes include:

- proportion of women receiving treatment with a recommended regimen – target 95%
- proportion of women with suspected PID tested for *M. genitalium* - target 90%
- proportion of women who are reviewed (face to face, by telephone or online) within 4 weeks of initiating treatment for PID – target 60%

Recommendations for future research

- assessment of the utility of metronidazole as an adjunctive therapy for patients with mild to moderate PID

- development of sensitive and specific diagnostic tests
- assessment of efficacy of a single dose versus multiple doses of ceftriaxone within treatment regimens for the management of PID

Qualifying statement

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources.

All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

Editorial independence

This guideline was commissioned, edited and endorsed by the BASHH CEG. The group receives funding from BASHH for external researcher support which was used in the production of this guideline.

Declarations of interest

All members of the guideline writing committee completed the BASHH conflict of interest declaration detailed below at the time the guideline's final draft was submitted to the CEG. JR has received consultancy fees from BD Diagnostics and GSK pharma, and sponsorship to attend a medical conference from Janssen pharma.

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Timescale for next revision

An author group will be invited by the BASHH CEG to review and revise the guideline in 2022 using the BASHH framework for guideline development.

Acknowledgements

The group wishes to thank our public panel member for their hard work throughout the development of the guideline. In addition, the group wishes to thank the external researcher Dr. Jacoby Patterson for her help in the production of this guideline.

Appendix 1: Equality Impact Assessment

Topic suggestion: impact assessment				
Guidance title: BASHH Guidelines for the Management of Pelvic Inflammatory Disease 2016. Completed by Dr Darren Cousins				
How relevant is the topic to equality?	Inequalities in health impact of the condition or public health issue	Potential of guidance to add value	Priority for NHS or other government department	Topic relevance: conclusions and outcome
	- Prevalence and impact of condition or public health problem - Prevalence of risk factors	- Inequalities in access, uptake or impact - Timeliness - Equality issues identified by proposers of this topic - Equality issues identified by patient or lay organisations	- Department of Health - DCLG, DCSF. DoT, Home Office, etc. - Other agency or ALB - Agencies in devolved nations	- High/medium/low/ none - Not known/inconclusive - Reasons for rating - Recommendation
Gender - Women - Men	This disease does not present in men	Clear guidance on treatment of male contact of patients with this condition	Society of Sexual Health Advisers (SSHA)	Low
Race - Asian or Asian British - Black or Black British - People of mixed race - Irish - White British - Chinese - Other minority groups not listed	The highest rates of STI diagnoses at sexual health clinics are found among people of black ethnicity in deprived areas. This is most likely seen as a consequence of a complex interplay of cultural, economic and behavioural factors.	Accurate diagnosis and better tolerated treatments should improve the burden of disease in the community	Dept of Health	Medium
Disability - Sensory - Learning disability - Mental health - Cognitive - Mobility - Other impairment	There are no data to suggest any link between this condition and disability status, although people with mental health problems are at disproportionate risk of STIs in general	None identified although use of clinical tests in guideline may improve diagnostic accuracy in non verbalising patients	Dept of Health	Low

Age - Older people - Children and young people - Young adults	Young woman are disproportionately at greater risk of this condition in common with other sexually transmitted infections	Accurate diagnosis and better tolerated treatments should improve the burden of disease in the community.	Dept of Health	Medium
Sexual orientation and gender identity - Lesbians - Gay men - Bisexual people - Transgender people	This disease does not present in men. There are little data on the prevalence of this condition in gay or bisexual women	None identified	Dept of Health Commissioners of local sexual health services	Low
Religion / belief	There are no data to suggest any link between religion or belief and this condition	None identified	None identified	Low
Socioeconomic status	There are no specific data to suggest any link between this condition and socioeconomic status, although people of low socioeconomic status are disproportionately higher risk of STIs in general	Accurate diagnosis and better tolerated treatments should improve the burden of disease in the community	Commissioners of local sexual health services National public health agencies that consider data collection in sexual health (e.g. Public Health England)	Medium
Other categories - Gypsy travellers - Refugees and asylum seekers - Migrant workers - Looked after children - Homeless people	There are no data to suggest any link between this condition and these categories although some people in these categories may not be identified by sexual health services	None identified	Commissioners of local sexual health services National public health agencies that consider data collection in sexual health (e.g. Public Health England)	Low

Appendix 2: Patient information leaflet on PID

See attached document

References

- 1. Goller J, Fairley C, Guy R, Bradshaw C, Chen M, Hocking J. Aetiology of infections associated with 1228 cases of pelvic inflammatory disease in an urban Australian sexual health clinic setting. *Sexually Transmitted Diseases* 2014; **41**: S59.
- 2. Recommendations arising from the 31st Study Group: The Prevention of Pelvic Infection. In: Templeton A, ed. The Prevention of Pelvic Infection. London: RCOG Press; 1996: 267-70.
- 3. Bevan CD, Johal BJ, Mumtaz G, Ridgway GL, Siddle NC. Clinical, laparoscopic and microbiological findings in acute salpingitis: report on a United Kingdom cohort. *British Journal of Obstetrics & Gynaecology* 1995; **102**(5): 407-14.
- 4. Goller JL, De Livera AM, Fairley CK, et al. Population attributable fraction of pelvic inflammatory disease associated with chlamydia and gonorrhoea: a cross-sectional analysis of Australian sexual health clinic data. *Sexually Transmitted Infections* 2016; **18**: 18.
- 5. Price MJ, Ades AE, Welton NJ, Simms I, Macleod J, Horner PJ. Proportion of Pelvic Inflammatory Disease Cases Caused by Chlamydia trachomatis: Consistent Picture From Different Methods. *J Infect Dis* 2016; **214**(4): 617-24.
- 6. Manhart LE. Mycoplasma genitalium: An emergent sexually transmitted disease? *Infect Dis Clin North Am* 2013; **27**(4): 779-92.
- 7. Lis R, Rowhani-Rahbar A, Manhart LE. Mycoplasma genitalium Infection and Female Reproductive Tract Disease: A Meta-analysis. *Clinical Infectious Diseases* 2015; **61**(3): 418-26.
- 8. Dean G, Whetham J, Soni S, Pitt R, Alexander S. Pelvic Inflammatory Disease (PID), Mycoplasma genitalium and macrolide resistance in England. *Sexually Transmitted Infections* 2016; **92**(Suppl 1): A12-A.
- 9. Goller JL, De Livera AM, Fairley CK, et al. Characteristics of pelvic inflammatory disease where no sexually transmitted infection is identified: a cross-sectional analysis of routinely collected sexual health clinic data. *Sexually Transmitted Infections* 2017; **93**(1): 68-70.
- 10. Morcos R, Frost N, Hnat M, Petrunak A, Caldito G. Laparoscopic versus clinical diagnosis of acute pelvic inflammatory disease. *Journal of Reproductive Medicine* 1993; **38**(1): 53-6.
- 11. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines 2015. 2015 2015. http://www.cdc.gov/std/tg2015/default.htm (accessed 15.11.17 2016).
- 12. Morris GC, Stewart CMW, Schoeman SA, Wilson JD. A cross-sectional study showing differences in the clinical diagnosis of pelvic inflammatory disease according to the experience of clinicians: Implications for training and audit. *Sexually Transmitted Infections* 2014; **90**(6): 445-51.
- 13. Kamenga MC, De Cock KM, St.Louis ME, et al. The impact of human immunodeficiency virus infection on pelvic inflammatory disease: a case-control study in Abidjan, Ivory Coast. *American Journal of Obstetrics & Gynecology* 1995; **172**(3): 919-25.
- 14. Cohen CR, Sinei S, Reilly M, et al. Effect of human immunodeficiency virus type 1 infection upon acute salpingitis: a laparoscopic study. *Journal of Infectious Diseases* 1998; **178**(5): 1352-8.

- 15. Bukusi EA, Cohen CR, Stevens CE, et al. Effects of human immunodeficiency virus 1 infection on microbial origins of pelvic inflammatory disease and on efficacy of ambulatory oral therapy. *American Journal of Obstetrics & Gynecology* 1999; **181**(6): 1374-81.
- 16. Irwin KL, Moorman AC, O'Sullivan MJ, et al. Influence of human immunodeficiency virus infection on pelvic inflammatory disease. *Obstetrics & Gynecology* 2000; **95**(4): 525-34.
- 17. Altunyurt S, Demir N, Posaci C. A randomized controlled trial of coil removal prior to treatment of pelvic inflammatory disease. *European Journal of Obstetrics Gynecology and Reproductive Biology* 2003; **107**: 81-4.
- 18. Soderberg G, Lindgren S. Influence of an intrauterine device on the course of an acute salpingitis. *Contraception* 1981; **24**(2): 137-43.
- 19. Tepper NK, Steenland MW, Gaffield ME, Marchbanks PA, Curtis KM. Retention of intrauterine devices in women who acquire pelvic inflammatory disease: a systematic review. *Contraception* 2013; **87**(5): 655-60.
- 20. Miettinen AK, Heinonen PK, Laippala P, Paavonen J. Test performance of erythrocyte sedimentation rate and C- reactive protein in assessing the severity of acute pelvic inflammatory disease. *American Journal of Obstetrics & Gynecology* 1993; **169**(5): 1143-9.
- 21. Yudin MH, Hillier SL, Wiesenfeld HC, Krohn MA, Amortegui AA, Sweet RL. Vaginal polymorphonuclear leukocytes and bacterial vaginosis as markers for histologic endometritis among women without symptoms of pelvic inflammatory disease. *American Journal of Obstetrics and Gynecology* 2003; **188(2)**: 318-23.
- 22. Romosan G, Valentin L. The sensitivity and specificity of transvaginal ultrasound with regard to acute pelvic inflammatory disease: A review of the literature. *Archives of Gynecology and Obstetrics* 2014; **289**(4): 705-14.
- 23. Romosan G, Bjartling C, Skoog L, Valentin L. Ultrasound for diagnosing acute salpingitis: a prospective observational diagnostic study. *Human Reproduction* 2013; **28**(6): 1569-79.
- 24. Molander P, Sjoberg J, Paavonen J, Cacciatore B. Transvaginal power Doppler findings in laparoscopically proven acute pelvic inflammatory disease. *Ultrasound in Obstetrics & Gynecology* 2001; **17**(3): 233-8.
- 25. Lee MH, Moon MH, Sung CK, Woo H, Oh S. CT findings of acute pelvic inflammatory disease. *Abdominal Imaging* 2014; **39**(6): 1350-5.
- 26. Fahmy HS, Swamy N, Elshahat HM. Revisiting the role of MRI in gynecological emergencies - An institutional experience. *Egyptian Journal of Radiology and Nuclear Medicine* 2015; **46**(3): 769-79.
- 27. Wongwaisayawan S, Kaewlai R, Dattwyler M, Abujudeh HH, Singh AK. Magnetic Resonance of Pelvic and Gastrointestinal Emergencies. *Magn Reson Imaging Clin N Am* 2016; **24**(2): 419-31.
- 28. Bongard F, Landers DV, Lewis F. Differential diagnosis of appendicitis and pelvic inflammatory disease. A prospective analysis. *American Journal of Surgery* 1985; **150**(1): 90-6.
- 29. Lewis FR, Holcroft JW, Boey J, Dunphy JE. Appendicitis: a critical review of diagnosis and treatment in 1000 cases. *Archives of Surgery* 1975; **110**: 677-84.

- 30. Hillis SD, Joesoef R, Marchbanks PA, et al. Delayed care of pelvic inflammatory disease as a risk factor for impaired fertility. *American Journal of Obstetrics & Gynecology* 1993; **168**(5): 1503-9.
- 31. Taylor BD, Ness RB, Darville T, Haggerty CL. Microbial correlates of delayed care for pelvic inflammatory disease. *Sex Transm Dis* 2011; **38**(5): 434-8.
- 32. Ness RB, Soper DE, Holley RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) Randomized Trial. *American Journal of Obstetrics & Gynecology* 2002; **186**(5): 929-37.
- 33. Haggerty CL, Ness RB, Amortegui A, et al. Endometritis does not predict reproductive morbidity after pelvic inflammatory disease. *American Journal of Obstetrics & Gynecology* 2003; **188**(1): 141-8.
- 34. Price MJ, Ades AE, Soldan K, et al. The natural history of Chlamydia trachomatis infection in women: a multi-parameter evidence synthesis. *Health Technol Assess* 2016; **20**(22): 1-250.
- 35. Arredondo JL, Diaz V, Gaitan H, et al. Oral clindamycin and ciprofloxacin versus intramuscular ceftriaxone and oral doxycycline in the treatment of mild-to- moderate pelvic inflammatory disease in outpatients. *Clinical Infectious Diseases* 1997; **24**(2): 170-8.
- 36. Hemsell DL, Little BB, Faro S, et al. Comparison of three regimens recommended by the Centers for Disease Control and Prevention for the treatment of women hospitalized with acute pelvic inflammatory disease. *Clinical Infectious Diseases* 1994; **19**(4): 720-7.
- 37. Martens MG, Gordon S, Yarborough DR, Faro S, Binder D, Berkeley A. Multicenter randomized trial of ofloxacin versus cefoxitin and doxycycline in outpatient treatment of pelvic inflammatory disease. Ambulatory PID Research Group. *Southern Medical Journal* 1993; **86**: 604-10.
- 38. Walker CK, Kahn JG, Washington AE, Peterson HB, Sweet RL. Pelvic inflammatory disease: metaanalysis of antimicrobial regimen efficacy. *Journal of Infectious Diseases* 1993; **168**: 969-78.
- 39. Wendel GD, Jr., Cox SM, Bawdon RE, Theriot SK, Heard MC, Nobles BJ. A randomized trial of ofloxacin versus cefoxitin and doxycycline in the outpatient treatment of acute salpingitis. *Am J Obstet Gynecol* 1991; **164**: 1390-6.
- 40. Soper DE, Brockwell NJ, Dalton HP. Microbial etiology of urban emergency department acute salpingitis: treatment with ofloxacin. *American Journal of Obstetrics & Gynecology* 1992; **167**: 653-60.
- 41. Peipert JF, Sweet RL, Walker CK, Kahn J, Rielly-Gauvin K. Evaluation of ofloxacin in the treatment of laparoscopically documented acute pelvic inflammatory disease (salpingitis). *Infectious Diseases in Obstetrics & Gynecology* 1999; **7**(3): 138-44.
- 42. Judlin P, Liao Q, Liu Z, Reimnitz P, Hampel B, Arvis P. Efficacy and safety of moxifloxacin in uncomplicated pelvic inflammatory disease: the MONALISA study. *BJOG* 2010; **117**(12): 1475-84.
- 43. Heystek MJ, Ross JDC, Group PS. A randomised double-blind comparison of moxifloxacin and doxycycline/metronidazole/ciprofloxacin in the treatment of acute, uncomplicated pelvic inflammatory disease. *International Journal of STD & AIDS* 2009; **20**: 690-5.

- 44. Ross JD, Cronje HS, Paszkowski T, et al. Moxifloxacin versus ofloxacin plus metronidazole in uncomplicated pelvic inflammatory disease: results of a multicentre, double blind, randomised trial. *Sex Transm Infect* 2006; **82**(6): 446-51.
- 45. Public Health England. Surveillance of antimicrobial resistance in Neisseria gonorrhoeae - GRASP 2014 Report. London, 2015.
- 46. Isaacson DM, Fernadez JA, Frosco M, et al. Levofloxacin: A review of its antibacterial activity. *Recent Res Devel in Antimicrob Agents & Chemotherapy* 1996; **1**: 391-439.
- 47. Raz-Pasteur A, Shasha D, Paul M. Fluoroquinolones or macrolides alone versus combined with beta-lactams for adults with community-acquired pneumonia: Systematic review and meta-analysis. *International Journal of Antimicrobial Agents* 2015; **46**(3): 242-8.
- 48. European Medicines Agency. Disabling and potentially permanent side effects lead to suspension or restrictions of quinolone and fluoroquinolone antibiotics. 2018. https://www.ema.europa.eu/documents/referral/quinolone-fluoroquinolone-article-31-referral-disabling-potentially-permanent-side-effects-lead_en.pdf.
- 49. Dunbar-Jacob J, Sereika SM, Foley SM, Bass DC, Ness RB. Adherence to oral therapies in pelvic inflammatory disease. *Journal of Women's Health* 2004; **13**(3): 285-91.
- 50. Witte EH, Peters AA, Smit IB, et al. A comparison of pefloxacin/metronidazole and doxycycline/metronidazole in the treatment of laparoscopically confirmed acute pelvic inflammatory disease. *European Journal of Obstetrics, Gynecology, & Reproductive Biology* 1993; **50**(2): 153-8.
- 51. Heinonen PK, Teisala K, Punnonen R, et al. Treating pelvic inflammatory disease with doxycycline and metronidazole or penicillin and metronidazole. *Genitourinary Medicine* 1986; **62**(4): 235-9.
- 52. Piyadigamage A, Wilson J. Improvement in the clinical cure rate of outpatient management of pelvic inflammatory disease following a change in therapy. *Sex Transm Infect* 2005; **81**(3): 233-5.
- 53. Savaris RF, Teixeira LM, Torres TG, Edelweiss MI, Moncada J, Schachter J. Comparing ceftriaxone plus azithromycin or doxycycline for pelvic inflammatory disease: a randomized controlled trial. *Obstetrics & Gynecology* 2007; **110**(1): 53-60.
- 54. Bevan CD, Ridgway GL, Rothermel CD. Efficacy and safety of azithromycin as monotherapy or combined with metronidazole compared with two standard multidrug regimens for the treatment of acute pelvic inflammatory disease. *Journal of International Medical Research* 2003; **31**(1): 45-54.
- 55. Heinonen PK, Teisala K, Miettinen A, Aine R, Punnonen R, Gronroos P. A comparison of ciprofloxacin with doxycycline plus metronidazole in the treatment of acute pelvic inflammatory disease. *Scandinavian Journal of Infectious Diseases - Supplementum* 1989; **60**: 66-73.
- 56. Reich H, McGlynn F. Laparoscopic treatment of tuboovarian and pelvic abscess. *Journal of Reproductive Medicine* 1987; **32**(10): 747-52.
- 57. Aboulghar MA, Mansour RT, Serour GI. Ultrasonographically guided transvaginal aspiration of tuboovarian abscesses and pyosalpinges: an optional treatment for acute pelvic inflammatory disease. *American Journal of Obstetrics & Gynecology* 1995; **172**(5): 1501-3.

- 58. Corsi PJ, Johnson SC, Gonik B, Hendrix SL, McNeeley SG, Jr., Diamond MP. Transvaginal ultrasound-guided aspiration of pelvic abscesses. *Infectious Disease in Obstetrics and Gynecology* 1999; **7**(5): 216-21.
- 59. Jensen Jo S, Cusini M, Gomberg M. 2016 European guideline on Mycoplasma genitalium infections. 2016. http://www.iusti.org/regions/europe/pdf/2016/2016EuropeanMycoplasmaGuidelines.pdf.
- 60. Falk L, Enger M, Jensen JS. Time to eradication of Mycoplasma genitalium after antibiotic treatment in men and women. *Journal of Antimicrobial Chemotherapy* 2015; **70**(11): 3134-40.