**Supplementary material 2: *Parameter estimation***

We describe the data sources and statistical methods used to estimate the model parameters. Further details about the data-sources and likelihood functions have been previously published[1](#_ENREF_1).

*Estimation of*  (used in models 1-3)

No data sources are available that directly inform . However, routine data on the rate of PID diagnosed in the general population in England () are available: Hospital Episode Statistics (HES),[2](#_ENREF_2) General Practice Research Database (GPRD)[3](#_ENREF_3), and KC-60, the routine returns from STI clinics[4](#_ENREF_4). Data for 2002 from each of these sources by age-group along with census population estimates[5](#_ENREF_5) for women are presented in table WA2.1. There is a degree of overlap between the three sources. After consultation with experts we take the total of the STI, GPRD, and HES data, within each age group to provide information (with a Binomial likelihood) on an upper bound for the number of diagnosed PID and we take the number of STI clinic cases plus the largest from GPRD or HES cases to provide information (with a Binomial likelihood) on a lower bound. We assume the true PID incidence rate is uniformly distributed between these bounds. A more direct estimate of the PID incidence is the control arm of the POPI chlamydia screening trial[6](#_ENREF_6). Participants were alerted to the risks of PID as part of the consenting process and knew they would be followed up at the end of the study. As such it’s likely that all or most PID for which symptoms developed would have been detected so the data provide an estimate of the incidence rate of symptomatic PID . To map these estimates to  we identified one study providing estimates of the proportion of PID that is symptomatic, and diagnosed.[7](#_ENREF_7) This is a cross-sectional study of 36 women with TFI. 11 reported a previous diagnosis of PID, 21 reported a history of symptoms but no diagnosis, and 4 reported no history of symptoms or diagnosis. We used Bayesian multi-parameter evidence synthesis methods[8](#_ENREF_8)[9](#_ENREF_9) to assess the consistency of all of these data sources and to jointly synthesise them to calculate pooled estimates of all the parameters using the relationship:



Where  is the proportion of episodes that are symptomatic. Estimates obtained for  and are given in table WA2.2.

*Estimation of*  (used in models 1-3)

We could not find any data that directly inform  or any function of  and  that allows them to be identified. Instead we use an estimate of the ratio of infection and re-infection rates for *Chlamydia trachomatis* from a recent evidence synthesis of data on the incidence, prevalence and duration of CT infection in women in England[10](#_ENREF_10). The re-infection rate could not be estimated for the general population so we use the estimate for the GP setting of 7.08 (95%CrI; 3.97,11.6) and there was no evidence that this ratio varies by age. Follow-up was only for an 18-month period[11](#_ENREF_11) but we assume it is valid for 2 years.

*Estimation of*  (used in models 1-2)

Laparoscopic examination of clinical PID cases is no longer performed. However, several epidemiological studies provide relevant data. The Lund study[12](#_ENREF_12) analysis relates to hospital-diagnosed PID that has been laparoscopically confirmed. The proportion of all those referred with clinical PID who were confirmed by laparoscopy fell systematically from 80% in those recruited 1960-64 and 1965-69, to 78% in 1970-74, to 70% in 1975-79, and to 60% in 1980-84[13](#_ENREF_13). A 2003 paper by Simms[14](#_ENREF_14) reviews 7 studies reporting between 31% and 79% confirmation rates, with the lowest figure coming from the most recent study published in 2003. A continuing decrease in the proportion of clinical PID that is confirmed on laparoscopy is probably to be expected in view of the fact that it is now recognised that acute PID is difficult to diagnose because of the wide variation in the symptoms and signs. Many women with PID have subtle or mild symptoms[15-17](#_ENREF_15). Because of the difficulty of diagnosis and the potential for damage to the reproductive health of women (even by apparently mild or subclinical PID), health-care providers are now advised to maintain a low threshold for the diagnosis of PID[15](#_ENREF_15)[16](#_ENREF_16). So the most relevant evidence likely comes from a recently published UK study on a cohort of women with abdominal pain[18](#_ENREF_18). 112 women were graded as “almost certain”, “probable”, or “possible” PID, or were “very unlikely” to have PID on the basis of their symptoms. 42.9% (12/28) of those with grades as having at least probable PID were confirmed on laparoscopy, and 87% of these had high titres of specific IgG antibody to CT. If a grading of “possible PID” is included, 19/56 (33.9%) were confirmed. The definition of “probable” here accords with the definitions used in our analyses of routine UK data above. From these data we assign an informative prior to  of the form:

#### 

Note that we could have jointly estimated the model parameters using the same data we used as well as the Lund data using MPES methods[8](#_ENREF_8)[9](#_ENREF_9). However, as we do not have a clear idea of the proportion likely to have been diagnosed we decided against this.

**Table S2.1**. Number of incident cases of diagnosed Pelvic Inflammatory Disease in England, 2002.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Age | Hospital Episode Statistivs  A | General Practice Research Databasea  B | Genitorurinary Medicine Clinicsb  C | Min  C+Max(B,A) | Max  A+B+C | Female Population |
| 16-19 | 1233 | 5083 | 3212 | 8295 | 9528 | 1199600 |
| 20-24 | 3101 | 8842 | 4399 | 13241 | 16342 | 1519100 |
| 25-34 | 9756 | 14932 | 3919 | 18851 | 28607 | 3502100 |
| 35-44 | 10526 | 9609 | 1388 | 11914 | 21523 | 3795600 |

a Definite and probable PID as defined in French et al[3](#_ENREF_3)

b Data by age not available for 2002 so we assume the age distribution for these data were the same as in 2009

**Table S2.2**. Results of the synthesis of evidence on the incidence of all-cause PID in England from a multi-parameter evidence synthesiss of incidence, prevalence, and duration data[1](#_ENREF_1)

|  |  |  |
| --- | --- | --- |
| Parameters | Age | model |
| PID incidence, % per year | 16-19 | 2.1 (1.5, 2.9) |
|  | 20-24 | 2.8 (2.0, 2.8) |
|  | 25-34 | 1.9 (1.3, 2.8) |
|  | 35-44 | 1.3 (0.78,1.9) |
|  |  |  |
|  | 16-24 | 2.5 (1.8, 3.4) |
|  | 25-44 | 1.6 (1.1, 2.2) |
|  | 16-44 | 1.8 (1.3, 2.5) |
|  |  |  |
| % of PID diagnosed | 16-44 | 36.0 (26, 48) |
| % of symptomatic PID undiagnosed | 16-44 | 51.4 (39, 63) |
| % of PID that’s asymptomatic | 16-44 | 12.6 (4.3, 25) |

**REFERENCES**

1. Price M, Ades A, Soldan S, Welton N, Macleod J, Simms I, et al. The natural history of Chlamydia trachomatis infection in women: a multi-parameter evidence synthesis. *Health Technology Assessment Methodology report* 2016;in press.

2. The Health and Social Care information Centre. Hospital Episode Statistics. , 2012.

3. French CE, Hughes G, Nicholson A, Yung M, Ross JD, Williams T, et al. Estimation of the rate of pelvic inflammatory disease diagnoses: trends in England, 2000-2008. *Sexually Transmitted Diseases* 2011;38(3):158-62.

4. Health Protection Agency. All new STI episodes seen at GUM clinics in the UK: 1998 - 2007. London, 2008.

5. Office for National Statistics. Population estimates for years 2000-2010, <http://www.ons.gov.uk/ons/datasets-and-tables/index.html>. London: Office for National Statistics, 2014.

6. Oakeshott P, Kerry S, Aghaizu A, Atherton H, Hay S, Taylor-Robinson D, et al. Randomised controlled trial of screening for Chlamydia trachomatis to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. *British Medical Journal* 2010;340(:c1642).

7. Wolner-Hanssen P. Silent pelvic inflammatory disease - is it overstated? *Obstetrics and Gynecology* 1995;86(3):321-25.

8. Ades AE, Sutton AJ. Multiparameter evidence synthesis in epidemiology and medical decision making: current appoaches. *Statistics in Society, JRSS(A)* 2006;169(1):5-35.

9. Ades AE, Welton N, Caldwell D, Price M, Goubar A, Lu G. Multiparameter evidence synthesis in epidemiology and medical decision-making. *Journal of Health Services & Research Policy* 2008;13(S3):12-22.

10. Price M, Ades A, De Angelis D, Welton N, Macleod J, Soldan K, et al. Incidence of Chlamydia trachomatis infection in England: two methods of estimation. *Epidemiology and Infection* 2014;142(3):562-67.

11. LaMontagne DS, Baster K, Emmett L, Nichols T, Randall S, McLean L, et al. Incidence and reinfection rates of genital chlamydial infection among women aged 16-24 years attending general practice, family planning and genitourinary medicine clinics in England: a prospective cohort study by the Chlamydia Recall Study Advisory Group. *Sexually Transmitted Infections* 2007;83(4).

12. Westrom L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility - a cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. *Sexually Transmitted Diseases* 1992;19(4):185-92.

13. Westrom L, Bengtsson LP, Mardh PA. Incidence, trends, and risks of ectopic pregnancy in a population of women. *British Medical Journal* 1981;282(6257):15-18.

14. Simms I, Warburton F, Westrom L. Diagnosis of pelvic inflammatory disease: time for a rethink. *Sexually Transmitted Infections* 2003;79(6):491-94.

15. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. *Morbidity and Mortality Weekly Report* 2010;59(RR-12):1-116.

16. Ross JMG. UK National Guideline for the Management of Pelvic Inflammatory Disease, 2011.

17. Brunham RC, Gottlieb SL, Paavonen J. Pelvic Inflammatory Disease. *New England Journal of Medicine* 2015;372(21):2039-48.

18. Taylor-Robinson D, Jensen JS, Svenstrup HF, Stacey CM. Difficulties experienced in defining the microbial cause of pelvic inflammatory disease. *International Journal of STD & AIDS* 2012;23:18-24.