The prevalence of polycystic ovary syndrome in reproductive-aged women of different ethnicity: a systematic review and meta-analysis

SUPPLEMENTARY MATERIALS

The model includes several modules. Suppose there are I studies in total for the White, and for each studies $i = 1,...,I$ we observed the number of PCOS cases out of the total unselected female population. A Binomial distribution was used to model these studies:

$$x_i \sim Binomial(\beta_i, m_i) \quad (1)$$

β_i represents the probability of developing PCOS for White in study. *i.* Because the outcome is binary, which means that individuals can either be a PCOS case or not, we used logistic regression to model the pooled mean probability of developing PCOS for the White population (study-specific probability). We further assumed that random variables obtained after logit scale transformation follows a normal distribution:

$$logit(\beta_i) = \gamma_i\ Normal(\mu_\gamma, \sigma_\gamma^2) \quad (2)$$

μ_γ represents the pooled mean probability of developing PCOS on the logit scale for White population. In order to calculate the probability of PCOS, we need to rescale it to estimate:

$$p = \frac{\exp(\mu_\gamma)}{1+\exp(\mu_\gamma)} \quad (3)$$

where p is the pooled mean probability of PCOS for White population as a whole

This module is completed by including some reasonable prior distributions to μ_γ and σ_γ Markov Chain Monte Carlo methods were then performed in JAGS (interfaced with R) so the prior distributions can be updated by the observed data to generate some posterior distributions from which random samples of parameters of interest (i.e. prevalence of PCOS) can be drawn.

We tested several versions of prior distributions for this model by attempting a range of values for p and k in the following formula:

$$\mu_\gamma \sim Normal(p\ , \sigma_\gamma^2) \quad (4)$$

$$\sigma_\gamma \sim Uniform(0, k) \quad (5)$$

The prior distribution we included are based on some reasonable subjective belief. Given thatwe do not expect very high risk of developing PCOS for women, i.e. >20% in the general population. The values of were chosen to be within a reasonable range, i.e. 2-20% and different values were tested in a descending order (from largest value to smallest value). For example, we may start from 15% and go down to 12%, 9%, 6%, 3% to see which values of p produce better model fit statistics. It should be noted that μ_γ and σ_γ are on a logit scale, so even k= 2 represents a large variance.

However, as previously, we assumed that σ_γ follows a uniform distribution, it potentially indicates a problem that the simulation processes tend to be largely influenced by k where k is the upper bound of the uniform distribution, i.e.*Uniform* (0, k) Therefore, we decided to attempt half-Cauchy distribution for :

$$\mu_\gamma \sim Normal(p, \sigma_\gamma^2) \quad (6)$$

$$\sigma_\gamma = \frac{|Z_r|}{\sqrt{\varepsilon_r}} \quad (7)$$

$$Z_r \sim Normal(0, \sigma_{z_r}^2) \quad (8)$$

$$\varepsilon_r \sim Gamma(0.5, 0.5) \quad (9)$$

$$\sigma_{z_r}^2 = \frac{1}{B_r^2} \quad B_r \sim Uniform(0, 0.5) \quad (10)$$

The half-Cauchy distribution is advantageous in terms of allowing for outliers and accommodating small variances close to zero.

The statistical software provided deviance information criterion (DIC) of each model, which is a measurement of the goodness of fit of the model to the data, with lower values indicating a better fit. We attempted different versions of priors and then integrated results from various models by model averaging. Models with smaller DIC were weighted up while models with larger DIC were weighted down. The following formula was used to compute the weight of each model we included after statistical reasoning:

$$w_h = \frac{exp(-0.5\Delta DIC_h)}{\sum_{h=1}^{H} exp(-0.5\Delta DIC_h)} \quad (11)$$

where $\Delta DIC_h = min_h(DIC_h) - DIC_h$ and $h = 1,...H$, indicating the set of models

The same statistical principles were applied to obtain estimates of prevalence for other ethnic groups.

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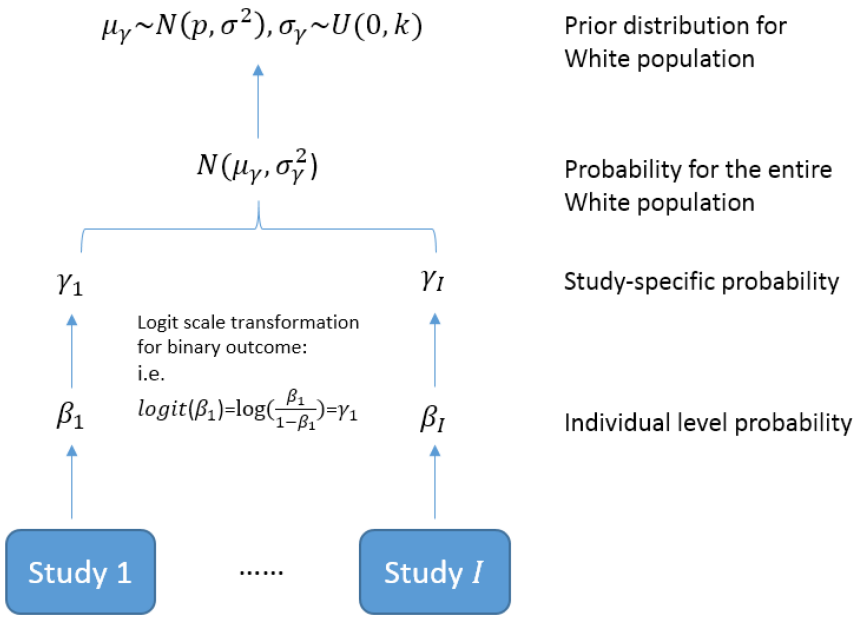
Supplementary Table 1: Results of prevalence studies (42 studies in total). See Supplementary_ Table_1

Supplementary Table 2: Evaluation of methodological quality of the 42 prevalence studies (score equals the total number of stars). See Supplementary_Table_2



Supplementary Figure 1: The modelling approach is discussed by using an explicit example of the White (Caucasian) population. The results of the rest of ethnic groups were estimated based on the same method. The graphic representation of this model is shown in Figure 1.

Supplementary Table 1. Results of prevalence studies (42 studies in total)

Article (ref.)	Country	Sample size	Age	Estimated Prevalence of PCOS in female population (%)			
				1990 NIH Criteria	2003 Rotterdam Consensus	2006 Androgen Excess Society	Other Criteria
Americas							
Knochenhauer *et al*[1]*	US	277	18-45yrs	4.0	-	-	-
Azziz *et al* [2]*	US	400	18-45yrs	6.6	-	-	
Goodarzi *et al*[3]	US	156	34.0+/- 8.6 yrs	-	-	-	13 (Self-reported irregular menses and clinical signs of hyperandrogenism)
Lo *et al* [4]	US	644166	15-44yrs	-	-	-	2.2
Okoroh *et al*[5]	US	12171830	18-45yrs	1.11	1.59	1.20	-
Christensen *et al*[6]	US	137502	15-19yrs	0.56 1.14 (include undiagnosed)	-	-	-
Sirman *et al[7]*	US	143413	15-45yrs	-	-	-	0.88 (ICD-9 code of oligo-menorrhea/amenorrhea plus hirsutism)
Moran *et al*[8]	Mexico	150	20-45yrs	6.0 (95% CI: 1.9-10.1)	6.6 (95% CI: 2.3-10.9)	-	-
Gabrielli *et al*[9]*	Brazil	859	18-45yrs	8.03	8.5	-	-
Faria *et al* [10]	Brazil	485	15-18yrs	-	-	-	6.2 (medical diagnosed PCOS)

Europe							
Michelmore *et al*[11]	UK	230	18-25yrs	8.0	-	-	-
Ding *et al*[12]	UK	2,087,107	15-45yrs	-	-	-	2.27 (95% CI 2.23% to 2.31%) (Readcode defined diagnosis)
Diamanti-Kandarakis *et al*[13]*	Greece	192	17-45yrs	6.8	-	-	-
Asuncion *et al*[14]*	Spain	154	18-45yrs	6.5	-	-	-
Sanchón *et al* [15]*	Spain	592	≥ 18yrs Median: 27~33* IQR: 9~13*	5.4% (95% CI: 3.6-7.2)	-	-	-
Lindholm *et al* [16]	Sweden	147	25-40yrs	-	-	-	4.8 (self-reported 1990 NIH)
Lauritsen *et al*[17]	Denmark	447	20-40yrs	-	16.6	-	-
Asia							
Chen *et al* [18]*	China	915	19-45yrs	-	2.4	2.2	-
Ma *et al* [19]*	China	2111	19-45yrs	-	6.11	-	-
Li *et al* [20]*	China	15924	19-45yrs	-	5.6	-	-
Jiao*et al* [21]*	China	1600	19-45yrs	-	8.25	-	-
Zhuang*et al* [22]	China	1645	12-44yrs	7.1	11.2	7.4	-
Sung *et al* [23]	Korea	8080 (target)	16-39yrs	4.4	6.3	5.1	-
Nidhi *et al*	India	460	15-18yrs	-	9.13	-	-

[24]					10.97 (imputation)		
Gill *et al* [25]	India	1520	18-25yrs	3.7	-	-	-
Joshi *et al* [26]	India	600	15-24yrs	-	22.5	10.7	-
Kumarapeli *et al*[27]	Sri Lanka	2915	15-39yrs	-	6.3 (95% CI: 5.9-6.8)	-	-
Vutyavanich et al [28]	Thailand	1095	18-40yrs	5.7	-	-	-
Middle East							
Musmar *et al*[29]	Palestine	137	18-24yrs	7.3	-	-	-
Hashemipour *et al*[30]	Iran	1000	14-18yrs	-	-	-	3 (clinical PCOS)
Mehrabian *et al*[31]	Iran	820	17-34yrs	7.0	15.2	7.92	-
Asgharnia *et al*[32]	Iran	1850	17-18yrs	11.34	-	-	-
Tehrani *et al*[33]*	Iran	929	18-45yrs	7.1 (95% CI: 5.4-8.8)	14.6 (95% CI: 12.3-16.9)	11.7 (95% CI: 9.5-13.7)	-
Esmaeilzadeh *et al*[34]	Iran	1549	16-20yrs	-	-	-	8.3 (95% CI: 4.0-12.0, criteria of PCOS not stated)
Rashidi *et al*[35]*	Iran	602	18-45yrs	4.8 (95% CI: 3.1-6.5)	14.1 (95% CI: 11.3-16.9)	12.0 (95% CI: 9.3-14.5)	-
Yildiz *et al[36]**	Turkey	392	18-45yrs	6.1	19.9	15.3	-

Khaduri *et al* [37]	Oman	3644	12-45yrs	-	7.0	-	2.8 (95% CI: 0.7-9.6, per 1000 in 2010).
Attlee *et al* [38]	United Arab Emirates	50	17-23yrs	-	-	-	20 (criteria of PCOS not stated)
Oceania							
Lowe *et al* [39]	Australia	100	-	-	12	-	-
March *et al*[40]	Australia	728	27-34yrs	8.7+/-2.0 (95% CI)	11.9 +/- 2.4 17.8 +/- 2.8 (imputation for non-consenting group included)	10.2 +/- 2.2 12.0+/- 2.4 (imputation for non-consenting group included)	-
Boyle*et al*[41]	Australia	248	15-44yrs	15.3 (95% CI, 10.8–19.8)	-	-	-
Joham *et al* [42]	Australia	8612	28-33yrs	-	-	-	5.8 (95% CI: 5.3-6.3, self-reported PCOS).

Supplementary Table 2: Evaluation of methodological quality of the 42 prevalence studies (score equals the total number of stars)

Study	Appropriate sampling †	PCOS measured reliably and objectively ‡	Response rate ◊	Sample size Δ	Crude number of cases $	Age range§	Ethnicity ƨ	Score
Knochenhauer et al (1998)[1]	×	*	*	*	*	*	*	6
Michelmore et al (1999)[11]	×	*	×	*	×	×	*	3
Diamanti-Kandarakis et al (1999)[13]	×	*	*	*	*	*	*	6
Asuncion et al (2000)[14]	×	*	*	*	*	*	*	6
Azziz et al(2004)[2]	×	*	×	*	*	*	*	5
Hashemipour et al (2004)[30]	*	*	*	*	*	×	*	6
Goodarzi et al (2005)[3]	×	×	*	*	*	*	*	5
Lowe et al (2005)[39]	×	×	*	*	*	×	×	3
Lo et al (2006)[4]	×	×	×	×	×	*	×	1
Vutyavanich et al (2007)[28]	×	*	*	*	*	*	*	6
Chen et al (2008)[18]	×	*	*	*	*	*	*	6
Kumarapeli et al (2008)[27]	*	*	*	*	*	*	*	7
Lindholm et al (2008)[16]	*	*	*	*	*	×	*	6
Yildiz et al (2012)[36]	×	*	*	*	*	*	*	6
March et al (2010)[40]	×	*	×	*	*	×	*	4
Ma et al (2010)[19]	*	*	*	*	*	*	*	7
Moran et al (2010)[8]	×	*	*	*	*	*	*	6
Sung et al (2010)[23]	×	*	×	×	×	*	×	2
Asgharnia et al (2011)[32]	*	*	*	*	*	×	*	6
Mehrabian et al (2011)[31]	×	*	×	*	*	×	*	4
Nidhi et al (2011)[24]	×	*	*	*	*	×	*	5
Tehrani et al (2011)[33]	*	*	*	*	*	*	*	7
Boyle et al (2012)[41]	×	*	*	*	*	*	*	6

Gabrielli et al (2012)[9]	*	*	*	*	*	*	*	7
Gill et al (2012)[25]	×	*	×	*	*	×	*	4
Okorohet al (2012) [5]	×	×	×	*	×	*	×	2
Sanchón et al (2012)[15]	×	*	*	*	*	*	×	5
Christensen et al (2013)[6]	×	×	×	*	*	×	×	2
Esmaeilzadeh et al (2014)[34]	*	*	*	*	*	×	*	6
Faria et al (2013)[10]	×	×	×	*	*	×	×	2
Joham et al (2014)[42]	*	×	×	*	*	×	*	4
Khaduri et al (2013)[37]	×	×	×	*	*	*	×	3
Li et al (2013)[20]	*	*	*	*	*	*	*	7
Musmar et al (2013)[29]	×	*	*	*	*	×	*	5
Attlee et al (2014)[38]	×	×	*	*	*	×	*	4
Lauritsen et al (2014)[17]	×	*	×	*	*	*	*	5
Jiao et al (2014)[21]	×	*	×	*	*	*	*	5
Joshi et al (2014)[26]	*	*	*	*	*	×	*	6
Rashidiet al (2014)[35]	*	*	*	*	*	*	*	7
Sirman et al (2014)[7]	×	×	×	*	*	*	*	4
Zhuang et al (2014)[22]	*	*	*	*	*	×	*	6
Ding et al (2016)[12]	×	×	×	*	*	*	×	3

† (a) Appropriate sampling (target population clearly defined and probability sampling applied) (awarded one star)

(b) Inappropriate sampling (i.e. convenient sampling) **OR** cases based on medical records where sampling frame was not applied **OR** not stated/unknown (cross)

‡ (a) Systematic screening performed for sample population and PCOS was strictly defined (awarded one star)

(b) Medical records based studies where no systematic screening was performed **OR** studies which used self-reported (i.e. based on questionnaire) PCOS cases

◊(a)Low non-participant rate (≤30%) of the initial target sample population for further study (i.e. systematic screening) **OR** low non-response rate (≤30%) of a deliberated-designed questionnaire (awarded one star)

(b) High non-response rate or refusal rate to further study (≥30%) of the initial target sample population **OR** high non-response rate (≥30%) of a deliberated-designed questionnaire OR studies based on electronic medical record where incomplete patient information (i.e. missing data) is a routine problem, leading to incomplete ascertainment of cases **OR** not stated/unknown (cross)

Δ (a) Sample size clearly stated (awarded one star) (b) Not stated/unknown (cross)

$ (a) Crude number of cases clearly stated (awarded one star) (b) Not stated/unknown (cross)

§ (a) Age range of the sample population is approximately same as the reproductive age, i.e. 15~45 years, 18~45 years, 17~45 years (awarded one star)

(b) Otherwise (narrower age range **OR** upper/lower bound of age range lying outside the limit, i.e. 18~24 years, 12~44 years **OR** not stated/unknown) (cross)

ƨ (a) Ethnicity of PCOS cases and sample population clearly stated (awarded one star)

(b) Ethnicity not clearly stated/unknown (cross)