

Is Letrozole more effective than Clomiphene Citrate at stimulating ovulation in women with PCOS struggling with infertility?

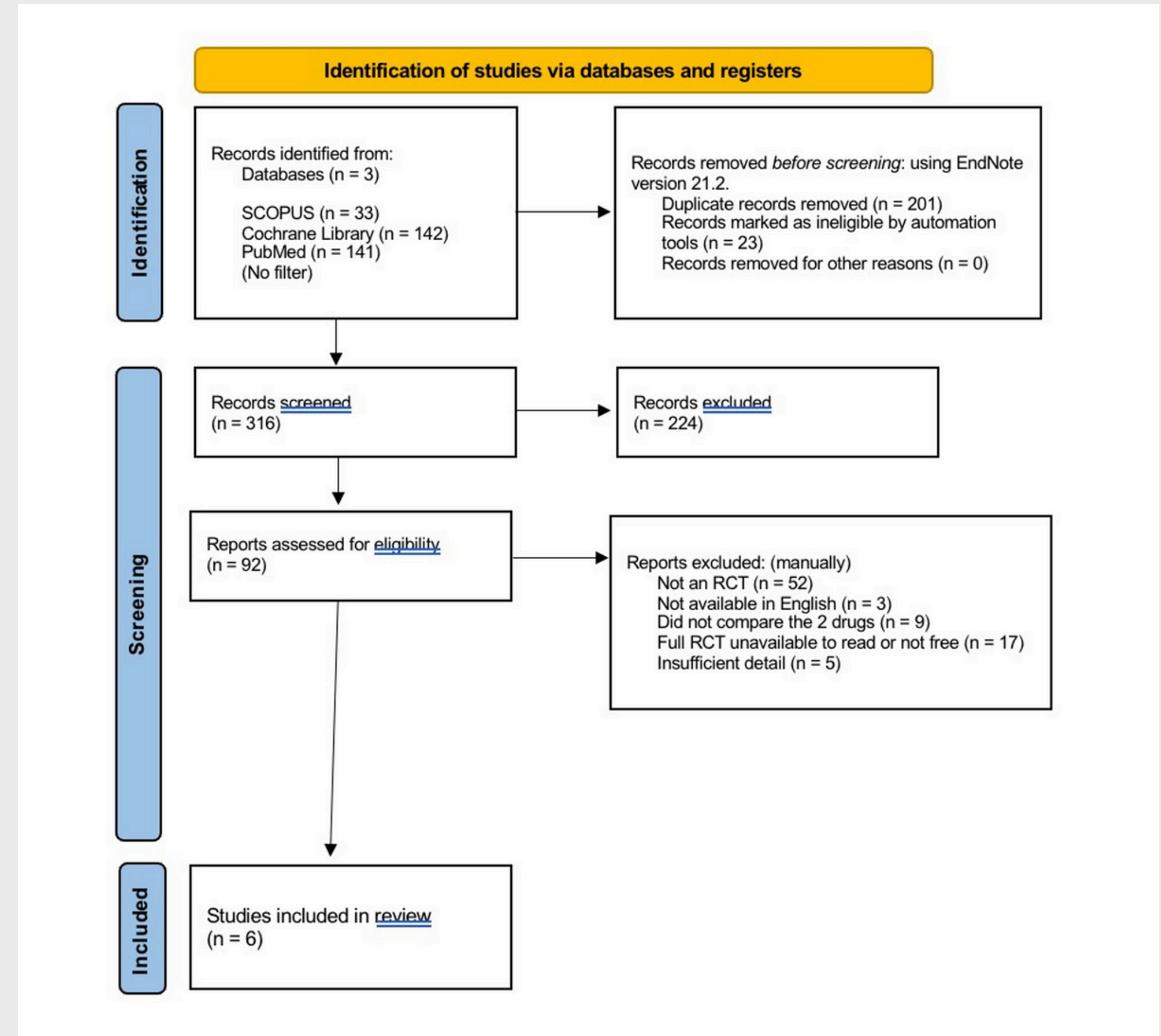
INTRODUCTION

1 in 10 women in the UK have PCOS. In short, 1 in 10 women are likely to struggle when trying to conceive. Unable to ovulate due to cystic ovaries. Clomiphene Citrate is currently the 1st line medication given to women with PCOS planning on having a child. But studies have tilted their narrative towards Letrozole which may have a higher rate of ovulation and thereby pregnancy in these women. Letrozole is currently a breast cancer drug, but it is now proving to be used for more than just breast cancer.

AIMS

To provide a comprehensive overview on trials that have looked at how Letrozole works better than CC to stimulate ovulation and in result reduce rates of infertility amongst women with PCOS.

SEARCH METHOD



REFERENCES

1. Dante G, Vaccaro V, Facchinetti F. Use of progestagens during early pregnancy [Internet]. U.S. National Library of Medicine; 2013 [cited 2024 Mar 16]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3987350/>
2. Cable JK. Physiology, progesterone [Internet]. U.S. National Library of Medicine; 2023 [cited 2024 Mar 16]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK558960/#:~:text=Progesterone%20is%20also%20secreted%20by,generally%20occurs%20after%20week%20ten>

METHODS

The trials included are all RCTs through a database search through SCOPUS, PubMed and Cochrane Library. All the trials have the following in common;

- Women were split into the Letrozole and CC group
- Ovulation rates were measured
- Pregnancy rates were followed up

The eligibility criteria for the systematic review included being available in English, available for free, comparing the two drugs, had to be a RCT and had sufficient detail for comparison. Data on ovulation and pregnancy was provided in all trials included.

RESULTS WITH ADDITIONAL DETAIL

Endometrial thickness - 6 out of the 6 trials included in the systemic review reported a thicker endometrial thickness in the Letrozole group than CC. Making it more hospitable for implantation.

Progesterone levels on day 21 - Trials reported higher levels in the Letrozole group - increasing chances of implantation and maintenance of pregnancy in the first 8 weeks [1,2].

Oestrogen levels - Letrozole did not decrease oestrogen levels unlike CC, allowing smaller follicles to degenerate and larger to survive - having higher chances of fertilisation.

Single mature follicle - Although Letrozole does not increase the number of follicles released on ovulation, it allows the survival of a single but mature follicle.

More FSH release - Prior to ovulation, an oestrogen deficient environment is created with Letrozole - allowing an FSH surge just after ovulation, initiating the maturation of the follicles on ovulation.

Half-life of Letrozole is shorter than CC - Less adverse effects due to staying in the system for a shorter duration.

Quality of cervical mucus - Due to the longer half-life of CC, there is a higher amount of cervical mucus build up - although this is usually a sign of ovulation and aiding of the sperm to the egg - higher levels can also be detrimental to the fertilisation.

CONCLUSION

Although CC remains the first-line medication provided for infertility in hopes of conceiving in women with PCOS, the systematic review proves that Letrozole is a strong alternative. This is not only supported by clinical trials but also a multitude of research which has highlighted higher fertilisation rates in comparison to CC.

AUTHORS

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RESULTS

Table 1

Trial year	Location of trial	Patients on Clomiphene Citrate (CC)	Patients on Letrozole (Femara)	Clomiphene Citrate (CC) Ovulation rate (%)	Letrozole Ovulation rate (%)	Ovulation Statistical significance (P value <0.05)	Clomiphene citrate (CC) Pregnancy rate (%)	Letrozole Pregnancy rate (%)	Pregnancy Statistical significance (P value <0.05)
2006	Istanbul Türkiye	55	51	63.6%	82.4%	0.016	9.1%	21.6%	0.037
2009	Dhaka, Bangladesh	32	32	37.5%	62.5%	<0.05	18.75%	40.62%	>0.05
2011	Kolkata, India	78	69	61.5%	86.9%	<0.05	17.9%	28.9%	<0.05
2014	Massachusetts, United States	376	374	76.6%	88.5	<0.001	21.5%	31.3%	0.003
2017	Nottingham and Derby, United Kingdom	79	80	79.7	83.8%	0.513	43.0%	61.2%	0.022
2018	Iowa, United States	N/A	Letrozole only: 35 Letrozole + CC: 35	Letrozole + CC: 77.1%	42.9%	0.007	Letrozole + CC: 12.1%	8.8%	0.709

Table 2a

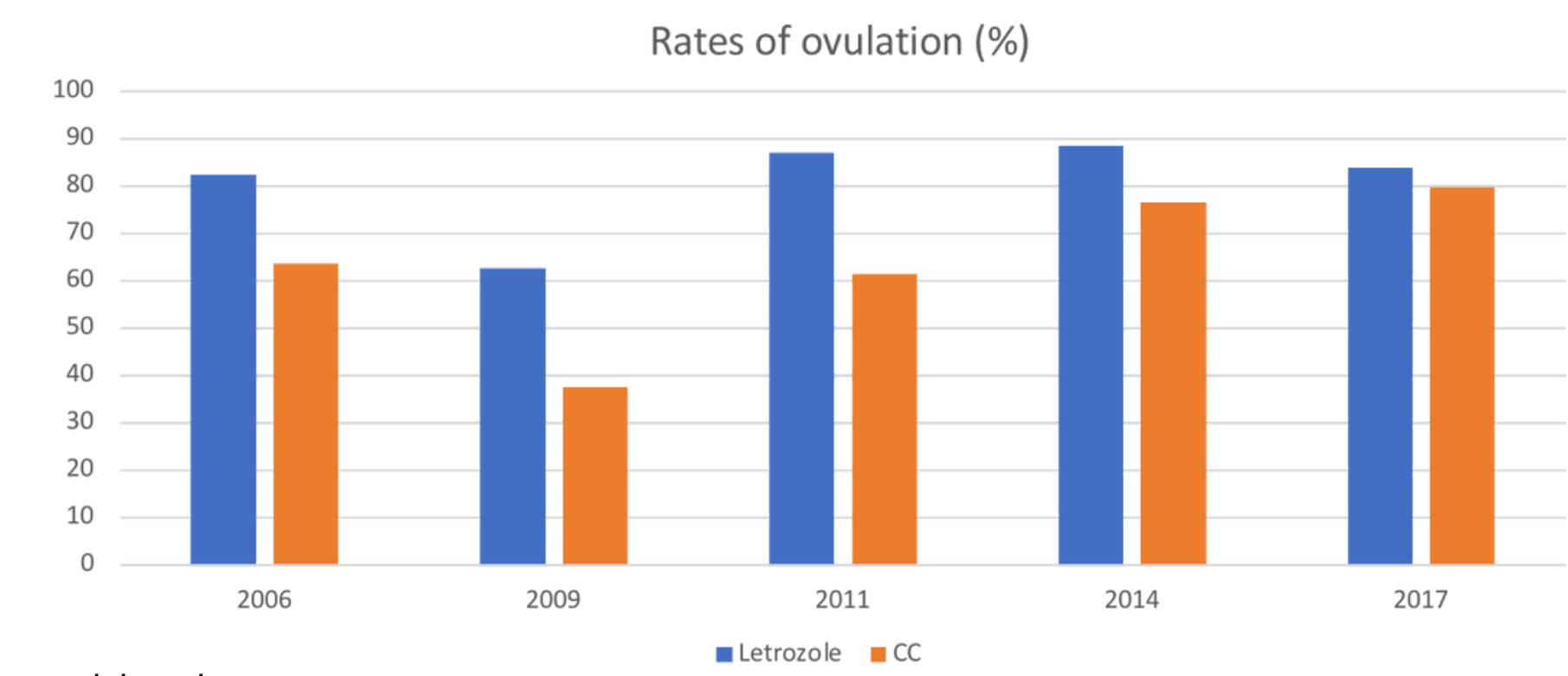


Table 2b

