Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Effect of semen collection location on semen parameters and fertility outcomes and implications for practice in the COVID-19 era: a systematic review and metaanalysis of randomized and observational studies

Pakapong Kerdtawee, MD; Lingling Salang, MD; Jen Sothornwit, MD

OBJECTIVE: During the COVID-19 era, semen collection at infertility centers might increase the risk of spreading SARS-CoV-2. Seminal fluid collection at home is an alternative method for preventing this spread. However, there is no conclusion about the effect of home vs clinic semen collection on semen parameters and assisted reproductive technology outcomes. This systematic review and metaanalysis aimed to assess the effect of semen collection location on semen parameters and fertility outcomes.

DATA SOURCES: A literature search was conducted using the major electronic databases including MEDLINE via Ovid, EMBASE, Scopus, CINAHL, OpenGrey, and CENTRAL from their inception to September 2021. ClinicalTrials.gov was searched to identify the ongoing registered clinical trials.

STUDY ELIGIBILITY CRITERIA: We included all human randomized controlled trials and observational studies that investigated the effect of at-home semen collection vs in-clinic semen collection on semen parameters and fertility outcomes.

METHODS: We pooled the mean difference and risk ratio using Review Manager software version 5.4.1 (The Cochrane Collaboration, 2022). The Grading of Recommendations, Assessment, Development and Evaluations approach was applied to assess the quality of evidence.

RESULTS: Seven studies (3018 semen samples) were included. Overall, at-home semen collection results made little to no difference in semen volume (mean difference, 0.37; 95% confidence interval, −0.10 to 0.85; low-quality evidence), sperm count (mean difference, −6.02; 95% confidence interval, −27.26 to 15.22; very low-quality evidence), and sperm motility (mean difference, 0.76; 95% confidence interval, −4.39 to 5.92; very low-quality evidence) compared with in-clinic semen collection. There was no difference in fertilization rate (risk ratio, 1.00; 95% confidence interval, 0.97—1.03; very low-quality evidence) and pregnancy rate in in vitro fertilization (risk ratio, 1.04; 95% confidence interval, 0.86—1.25; very low-quality evidence).

CONCLUSION: At-home semen collection had no adverse effects on semen parameters or fertility outcomes compared with in-clinic collection. However, higher-quality evidence is needed.

Key words: collection location, fertility outcomes, semen analysis, semen parameters

Introduction

COVID-19, which is caused by SARS-CoV-2, remains a serious threat to public health. Its rapid transmission has led to worldwide spread of the disease over the last 2 years. The World Health Organization (WHO) declared COVID-19 a global pandemic with widespread implications for the healthcare system.[1] Inevitably, infertility management is affected by avoidance of human physical contact and decreased clinic visits, as cited by the American Society for Reproductive Medicine, European Society of Human Reproduction and Embryology, and International Federation of Fertility Societies.[2–4]

There is inconclusive evidence regarding the effect of COVID-19 infection on the male reproductive organs in the short and long term. Focusing on semen parameters, Guo et al reported no impact of COVID infection on sperm concentration, motility, and morphology,[5] whereas other studies showed a negative effect trend on some seminal parameters.[6–8]

Generally, males are assigned to an infertility center for semen collection, which might increase the risk of spreading SARS-CoV-2. Collecting semen at home is an alternative strategy to prevent the spread of SARS-CoV-2. The WHO manual recommends that in exceptional cases, semen can be collected at home within an hour of analysis.[9–12] Gao et al[13] reported on the benefits of home semen collection, stating that males who collected semen at home were more relaxed and reached orgasm more easily than males who collected semen in clinics. There is no conclusion about the effect of home vs clinic semen collection on semen parameters and assisted reproductive technology (ART) outcomes.

Various studies have reported the effects of semen collection location on

From the Faculty of Medicine, Department of Obstetrics and Gynecology, Khon Kaen University, Khon Kaen, Thailand.

Received April 21, 2022; revised Aug. 20, 2022; accepted Sept. 2, 2022.

The authors report no conflict of interest.

Corresponding author: Lingling Salang, MD. Slingling@kku.ac.th

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2022.09.009

AJOG at a Glance

Why was this study conducted?

This review was conducted to assess the effects of semen collection location on semen parameters and fertility outcomes.

Key findings

This metaanalysis showed that at-home semen collection had no adverse effects on semen parameters or fertility outcomes compared with at-clinic semen collection.

What does this add to what is known?

This is one of the earliest systematic reviews and metaanalyses conducted with all currently available data and large samples comparing the effect of at-home vs at-clinic semen collection on semen parameters and clinical outcomes, which showed comparable results. High-quality evidence from randomized controlled trials is needed to strengthen evidence for future practice.

semen parameters and infertility treatment outcomes. For example, several studies reported that home semen collection significantly increased the mean time to semen processing compared with in-clinic collection. However, semen parameters and pregnancy rates in intrauterine insemination (IUI) and in vitro fertilization (IVF) outcomes were not significantly different between groups.[13–15] In contrast, Yavas and Selub[16] reported differences in IUI cycle outcomes, ie, the pregnancy rate was significantly higher with in-clinic semen collection than with at-home collection with the menopausal gonadotropin stimulation procedure (44% vs 18%; *P* value=.03). However, the differences with the clomiphene citrate stimulation procedure were not statistically significant.[16]

During the pandemic, at-home semen collection could be a satisfactory alternative, whether for work-up, IUI, or ART. The current review was undertaken to assess the effects of semen collection location on (1) seminal parameters (semen volume, sperm concentration, total sperm count, sperm motility, total motile sperm count, progressive motile sperm, and normal sperm morphology); and (2) fertility outcomes (fertilization rates, usable blastocyst, pregnancy, miscarriage, and live birth rates).

Materials and Methods

Eligibility criteria, information sources, and search strategy

A systematic literature review was conducted following the Cochrane Handbook for Systematic Reviews of Interventions[17] and was reported according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE).[18] The review protocol was registered with International Prospective Register of Systematic Reviews (registration number CRD42021268246).

To identify potentially eligible studies, a systematic literature search was conducted by authors using the major electronic databases from their inception to September 2021, including MEDLINE via Ovid, EMBASE, Scopus, CINAHL, and the Cochrane Central Register of Controlled Trials Database (CENTRAL) (Supplemental Appendices). The reference lists of articles were checked, and authors of the trials were contacted to obtain additional data if necessary. ClinicalTrial.gov and the World Health Organization Internal Clinical Trials Registry Platform (http://www.who.int/ictrp) were searched for unpublished, planned, and ongoing trial reports. Open Grey (http://www.opengrey.eu) was used to search for grey literature.

The PICO-S elements of this review were Population—any man, Intervention—at-home semen collection, Comparison—in-clinic semen collection, and outcomes of interest were—location of semen collection, semen parameters (semen volume, sperm concentration, total sperm count, sperm motility, total motile sperm count, progressive motile sperm, and normal sperm morphology), fertility outcomes (fertilization rates, usable blastocyst rates, pregnancy rates, miscarriage rates, and live birth rates), and study design. We included randomized controlled trials (RCTs) and observational studies published as full-reports or conference abstracts regardless of the language of publication, publication status, year of publication, or sample size.

Study selection and data extraction

The titles and abstracts of the studies retrieved by electronic search were screened independently by 2 authors. Titles and abstracts that did not meet the inclusion criteria were excluded. Two authors retrieved and independently reviewed the full texts for potentially eligible studies and extracted relevant data. Any disagreements on relevance were resolved through consensus with a third person.

Risk of bias assessment

Two tools as follows were used to evaluate the risk of bias: (1) the revised Cochrane risk of bias tool for randomized trials (RoB 2)[19] for RCTs; and (2) the risk of bias in non-randomized studies of interventions (ROBINS-I).[20] For observational studies, 2 authors independently assessed the risk of bias. Any disagreements were resolved by consensus with a third reviewer.

Data synthesis

The data extracted from the review were pooled and analyzed using Review Manager software version 5.4.1(The Cochrane Collaboration, 2022).[21] Means with standard deviations (SD) or converted means and SDs in cases where studies provided data as medians, ranges, and interquartile ranges using a standard formula were used in the metaanalysis.[22] Outcomes were measured as mean difference with a 95% confidence interval (CI) or risk ratio with a *P* value

<.05 considered statistically significant. Heterogeneity of the studies was assessed using I^2, which defined values between 75% and 100%, and a chi-squared test, with a significance level of 0.10 being considered as heterogeneous.[23] When heterogeneity was high, a random effects model was used. Subgroup or sensitivity analyses were planned for a specific population or study type to assess the robustness of the results.

Quality of evidence

The certainty of the body of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. The GRADE approach covered the following 5 domains: (1) risk of bias in the included studies; (2) inconsistency between studies' (3) imprecision in the effect estimate; (4) indirectness of evidence; and (5) publication bias. The GRADE approach rates the overall certainty of evidence as high, moderate, low, or very low quality.[24]

Results

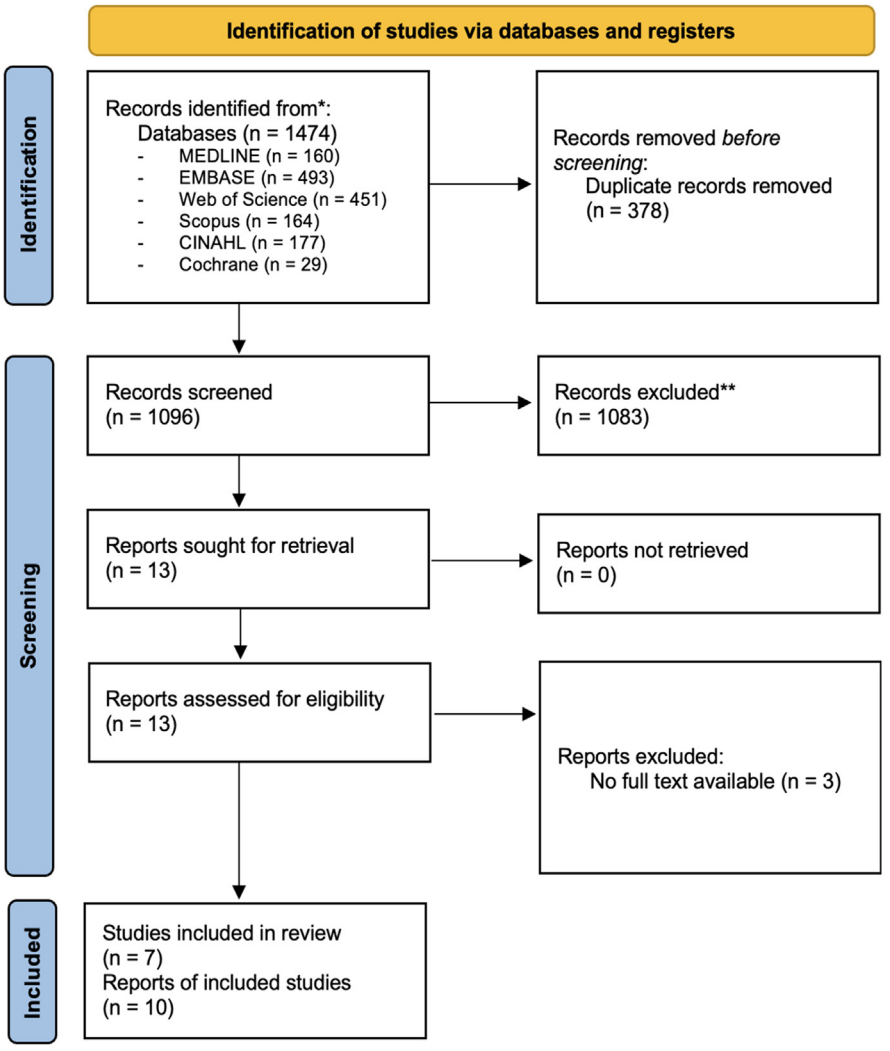
Study selection

Figure 1 presents the PRISMA flowchart for the study selection. A broad search yielded 1229 reports from electronic database searches and other sources. After removing duplicates, 903 reports remained for screening, and 892 that did not meet the inclusion criteria were excluded. After reviewing the full texts of 11 reports that potentially met the review inclusion criteria, 1 was excluded, because the full text was unavailable. Finally, 10 reports from 7 studies involving 3018 samples were included in the qualitative synthesis.

Characteristics of included studies

A total of 7 studies[13–16,25–27] conducted in the period ranging from 2004 to 2021 were included for this review. There were 6 observational studies,[14–16,25–27] most of which were retrospective, and 1 was an RCT.[13] Three studies reported only semen parameters,[13,14,25] 1 reported only fertility outcomes,[16] and 3 reported both semen parameters and fertility outcomes.[15,26,27] The detailed characteristics of the studies are presented in Table.

FIGURE 1
PRISMA 2020 flow diagram for systematic review and metaanalysis



(*Single asterisk*) Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
(*Double asterisks*) If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71.[31]

For more information, visit: http://www.prisma-statement.org/.

Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

Risk of bias in the included studies

Figures 2 and 3 present a summary of the risk of bias in each included study. The risk of bias for 6 studies[14–16,25–27] was assessed using the ROBINS-I tool, because they were observational studies. The risk of bias for the RCT[13] was assessed using the Cochrane RoB2 tool.

With respect to observational studies, the 4 included studies[15,16,26,27] were

TABLE
Characteristics of included studies

Study	Year	Country	Study design	Home (n)	Clinic (n)	Inclusion criteria	Exclusion criteria	Study outcomes
Elzanaty and Malm[25]	2008	Sweden	Cross-sectional study	106	273	Men undergoing infertile assessment	Azoospermia	Volume, concentration, total count, progressive motility, morphology
Gao et al[13]	2020	China	RCT	53	49	Men 18–55 y, infertility for at least 1 y	- Presence of dysuria, urinary urgency, and increased frequency of urination - erectile or ejaculatory dysfunction - inability to follow instructions because of impaired cognition	Volume, concentration, total count, progressive motility, morphology
Licht et al[14]	2008	United States	Prospective cohort study	232	215	Men undergoing work up for infertility and for IUI	Not mentioned	Volume, concentration, total count, motility, total motile count, morphology
Sacha et al[15]	2021	United States	Retrospective cohort study	125	119	Men undergoing for IVF/ICSI	Not mentioned	Volume, concentration, motility, total motile count, morphology, forward progression, fertilization rate, D5 usable blastocyst rate, pregnancy rate
Song et al[26]	2007	United States	Retrospective study	236	397	Men undergoing for IUI	Not mentioned	Total count, motility, total motile count, progressive motility, pregnancy rate
Stimpfel et al[27]	2021	Slovenia	Retrospective study	837	244	Men undergoing for IVF/ICSI	Not mentioned	Volume, concentration, total count, motility, morphology, fertilization rate, blastocyst rate, embryo utilization rate, pregnancy rate
Yavas and Selub[16]	2004	United States	Retrospective study	95	37	Men undergoing for IUI	Not mentioned	Pregnancy rate

ICSI, intracytoplasmic sperm injection; *IUI*, intrauterine insemination; *IVF*, in vitro fertilization; *RCT*, randomized controlled trials.

Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

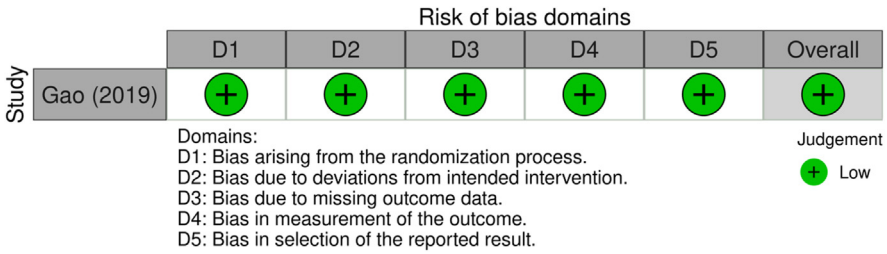
assessed to have a moderate risk of bias owing to confounding factors such as age, days of abstinence, sperm quality, and laboratory methods. The confounding factors were appropriately controlled so that they did not pose a severe residual effect. In 2 of the 6 included studies,[14,25] bias was deemed serious, because there was no mention of how confounders could be controlled.

Vis-à-vis domain selection bias, all studies were judged to have a moderate risk of bias, because they were observational. In studies in which participants could choose which group they preferred (ie, without randomization), the outcome could have been skewed.[14–16,25–27]

All studies were judged to have a low risk of bias vis-à-vis intervention classification, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported result domain.[14–16,25–27]

In the case of RCTs, only 1 study was evaluated using the Cochrane RoB2 tool. However, all domains of the risk of bias (eg, selection, performance, detection, attrition, and reporting) were judged to have a low risk of bias.

FIGURE 2
Risk of bias assessment of randomized controlled trials by risk of bias tool for randomized trials (RoB 2 tool)



Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

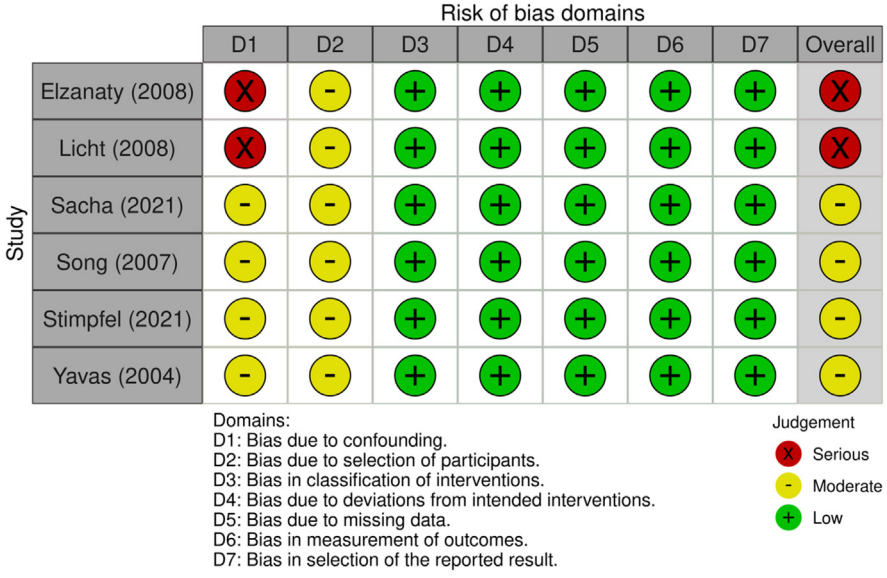
Synthesis of results

Primary outcome

Six studies (5 observational studies and 1 RCT) reported semen parameters.[13–15,25–27] Three studies compared overall at-home collected semen parameters with at-clinic collected parameters.[25–27] Only 1 study reported individual sample outcomes between the at-home and in-clinic parameters from the same participants,[14] whereas 2 studies[13,15] reported overall and individual semen parameters. All studies reported basic semen parameters, either as means with SDs or medians with interquartile ranges, depending on data distribution. After requesting for outcome data as mean±SD, only 1 study[25] was converted to means using the Wan formula.[22]

Six studies[13–15,25–27] including 3018 semen samples were included in the metaanalysis of semen parameters (semen volume, sperm concentration, total sperm count, sperm motility, total motile sperm count, progressive motile sperm, and normal sperm morphology). Comparisons between at-home and in-clinic semen collections are presented as a forest plot showing the mean difference (Figure 4).

FIGURE 3
Risk of bias assessment of observational studies by the risk of bias in nonrandomized studies of interventions (ROBINS-I) tool



Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

Semen volume

The semen volume did not differ significantly when it was collected at home or in the clinic. Subgroup analysis indicated no significant difference in semen volume between the 2 comparison groups when stratified by overall (mean difference [MD], 0.37; 95% CI, −0.10 to 0.85; 4 studies; 1806 samples)[13,15,25,27] and individual comparisons (MD, −0.08; 95% CI, −0.38 to 0.22; 3 studies; 628 samples)[13–15] (Figure 4, A).

Sperm concentration

There was no significant difference between sperm concentration parameters in the samples collected at home and in the clinic or between overall samples (MD, 5.46; 95% CI, −1.23 to 12.15; 5 studies; 2439 samples)[13,15,25–27] and individual samples (MD, 0.82; 95% CI, −7.09 to 8.73; 3 studies; 628 samples)[13–15] (Figure 4, B).

Total sperm count

Overall, semen collection at home did not reduce the total sperm count. In addition, the subgroup analysis indicated no significant benefit in collecting semen at home vis-à-vis increasing semen concentration overall (MD, 14.16; 95% CI, −2.88 to 31.20; 3 studies; 1562 samples)[13,25,27] or individual comparisons (MD, −7.34; 95% CI, −33.43 to 18.76; 2 studies; 544 samples)[13,14] (Figure 4, C).

Sperm motility

The evidence was "very uncertain" on sperm motility regarding the effect of collecting semen at home vs in clinic. Subgroup analysis indicated no significant benefit in semen collection at home vis-à-vis increasing sperm motility whether considering overall (MD, 0.76; 95% CI, −4.39 to 5.92; 3 studies; 1958 samples)[15,26,27] or individual comparisons (MD, −0.55; 95% CI, −3.67 to 2.58; 2 studies; 424 samples)[14,15] (Figure 4, D).

FIGURE 4
Estimates of semen parameters

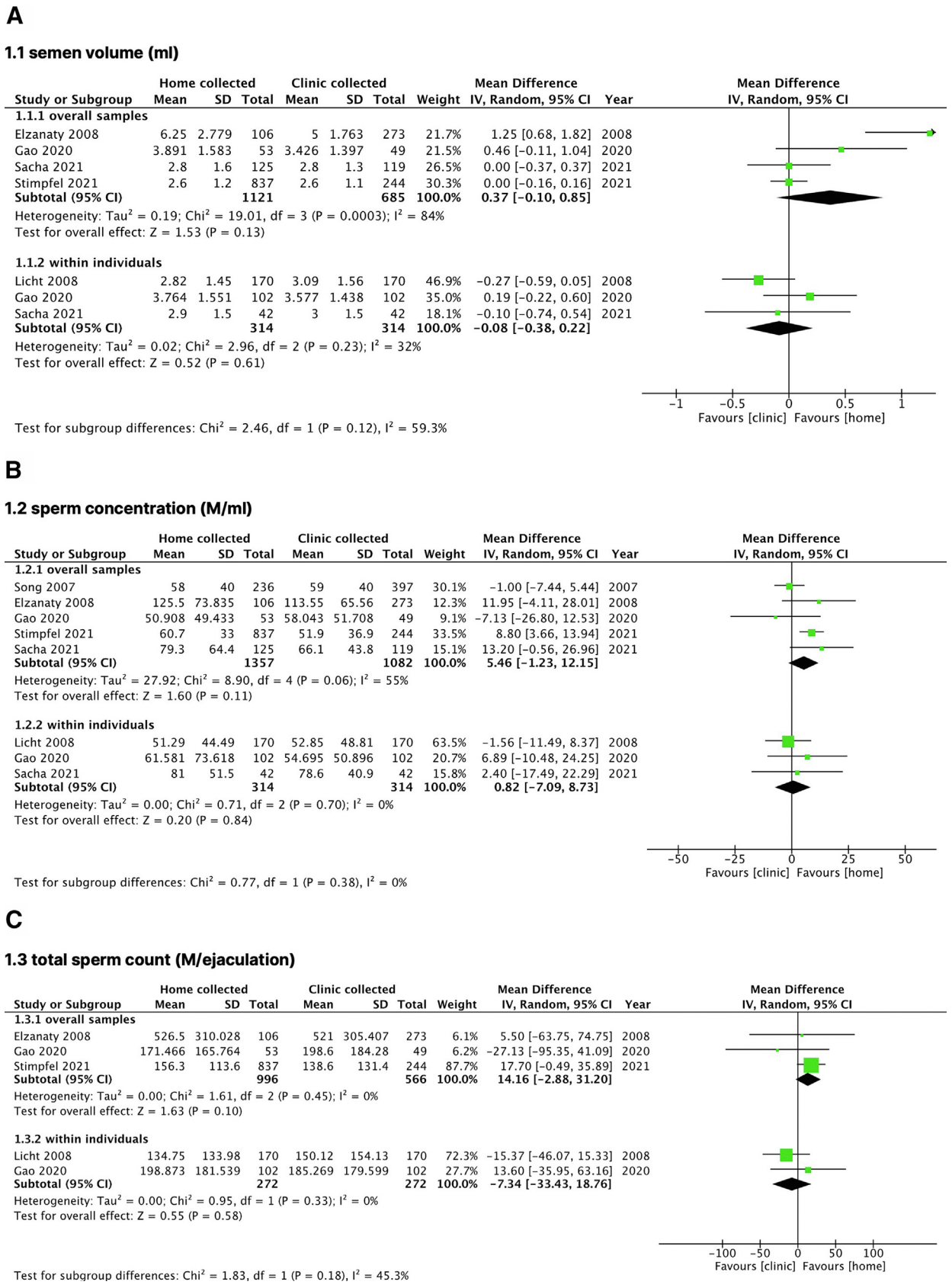
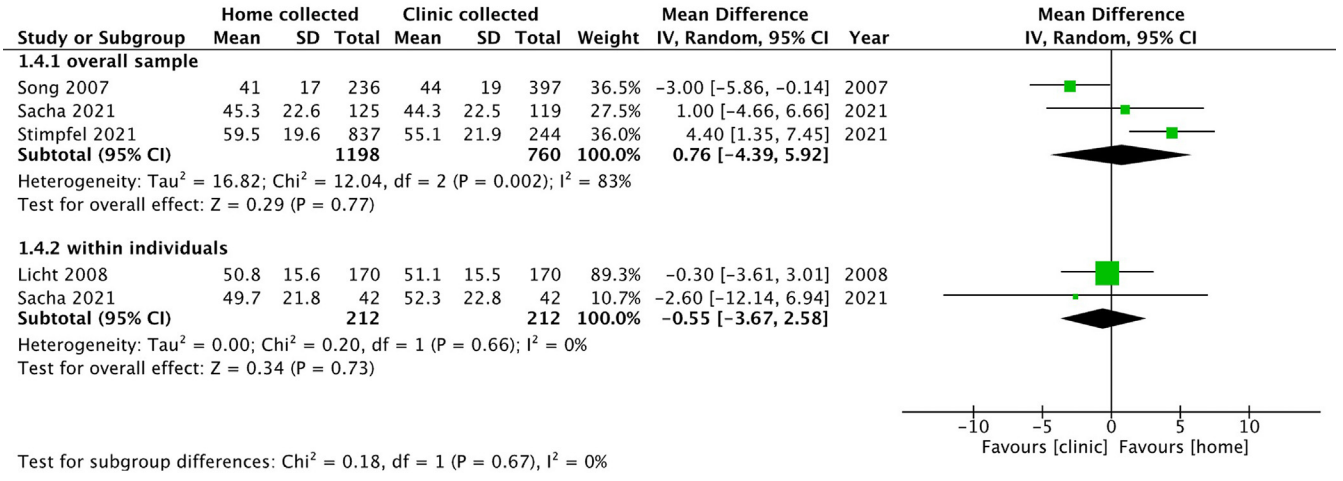


FIGURE 4
(Continued)

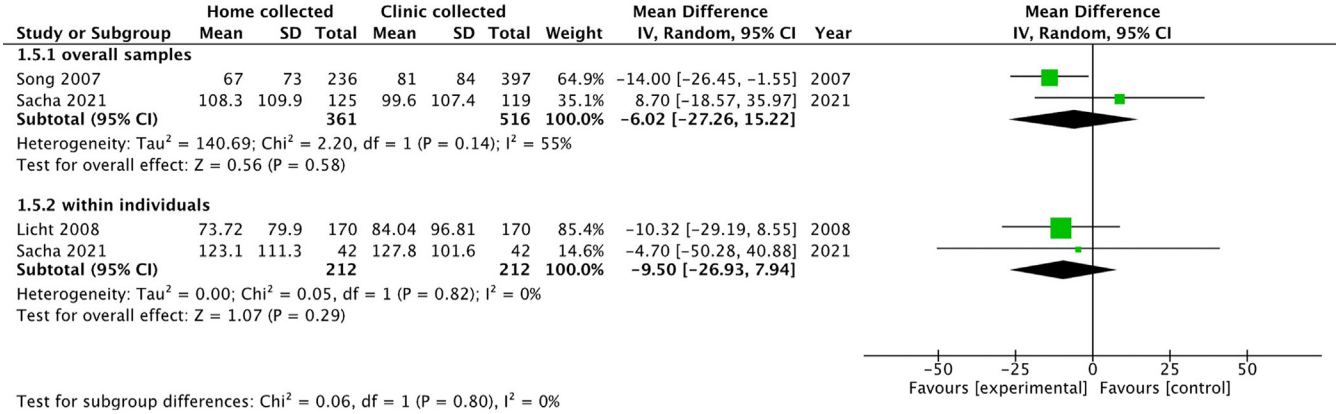
D

1.4 sperm motility (%)



E

1.5 total motile count (M)



Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

Total motile sperm count

In the respective overall subgroup and individual analyses, collecting semen at home vs in clinic did not seem to increase the total motile sperm count (MD, −6.02; 95% CI, −27.26 to 15.22; 2 studies; 877 samples)[15,26] and (MD, −9.5; 95% CI, −26.93 to 7.94; 2 studies; 414 samples)[14,15] (Figure 4, E).

Progressive motility

There was no significant difference in progressive motility between home- and clinic- collected semen groups regardless of the overall sample (MD, 1.17; 95% CI, −2.42 to 4.76; 3 studies; 1114 samples)[13,25,26] or individual samples (MD, 1.02; 95% CI, −2.94 to 4.99; 1 study; 204 samples)[13] (Figure 4, F).

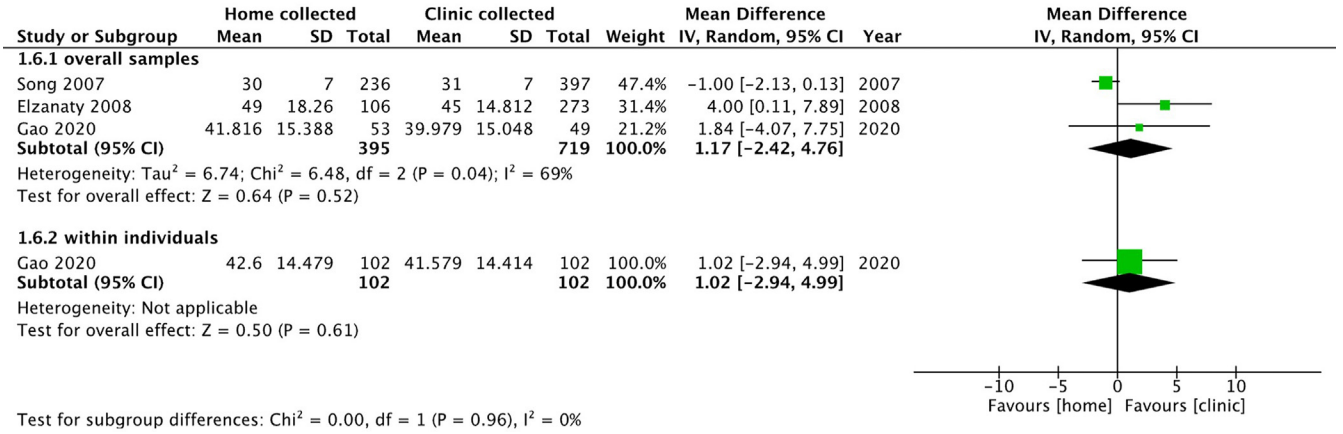
A, Comparison of semen volume; **B,** Comparison of sperm concentration; **C,** Comparison of total sperm count; **D,** Comparison of sperm motility; **E,** Comparison of total motile sperm count; **F,** Comparison of progressive sperm motility; **G,** Comparison of normal morphology.

CI, confidence interval; *IV*, weighted mean; *SD*, standard deviation.

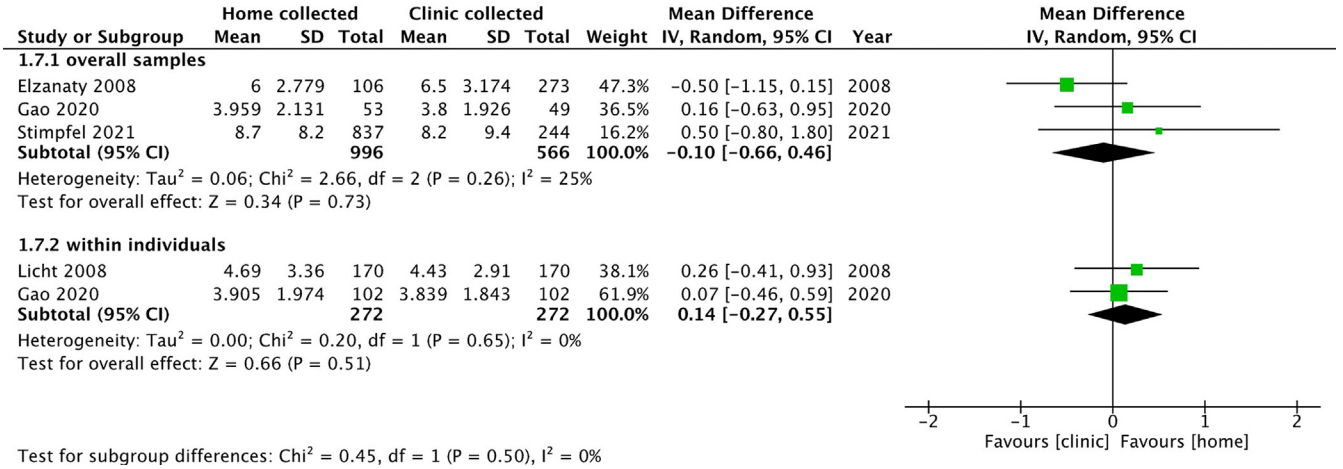
Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

FIGURE 4
(Continued)

F



G



Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

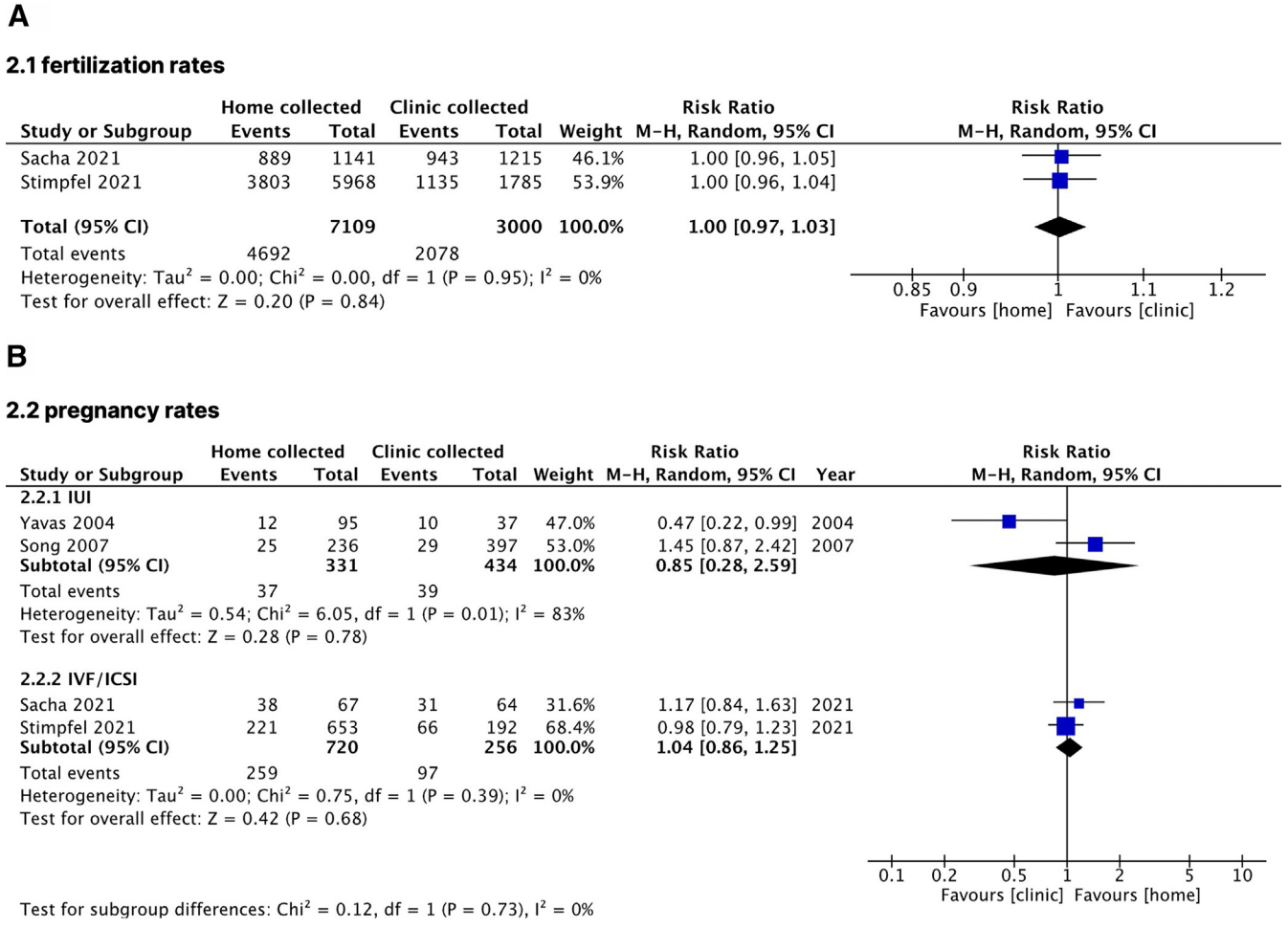
Normal morphology

Evidence suggests that collecting semen at home vs in the clinic does not change the normal sperm morphology. Subgroup analysis indicated no significant benefit to either location, whether it was overall samples (MD, −0.10; 95% CI, −0.66 to 0.46; 3 studies; 1562 samples)[13,25,27] or individual samples (MD, 0.14; 95% CI, −0.27 to 0.55; 2 studies; 544 samples)[13,14] (Figure 4, G).

Secondary outcome

The scope of fertility outcomes includes fertilization, usable blastocyst, pregnancy, miscarriage, and live birth rates. Two studies[15,27] were conducted with IVF or intracytoplasmic sperm injection (ICSI) populations and reported fertilization rates (defined as the number of 2 pronuclear stage embryos or number of metaphase II oocytes) with a total of 10,109 metaphase II oocytes and pregnancy rates (defined as the number of positive beta-human chorionic gonadotropin tests or embryo transfers) with a total of 976 transfers. The other 2 studies[16,26] were conducted among people who underwent IUI and reported only pregnancy rates (defined as an ultrasonographic finding of fetal cardiac activity/number of IUIs) with a total of 765 IUIs. Thus, a metaanalysis of pregnancy rates was conducted with these specific IVF/ICSI and IUI subgroups. Two studies[15,27] reported usable

FIGURE 5
Fertility outcomes between home and clinic semen collection



A, Comparison of fertilization rate; **B,** Comparison of pregnancy rate (intrauterine insemination/in vitro fertilization outcomes).

CI, confidence interval; *M-H,* Mantel-Haenszel.

Kerdtawee. Effect of semen collection location on parameters and outcomes. Am J Obstet Gynecol 2022.

blastocyst rates, but there were differences in the definitions and methods of outcome measurement. Sacha et al[15] defined the number of day 5 transferable and freezable quality blastocysts/number of 2 pronuclear stage embryos, but Stimpfel et al[27] defined it as the proportion of transferred or cryopreserved embryos (referred to as day 5/6 blastocysts) per number of embryos obtained. Consequently, we could not conduct a metaanalysis for this outcome, and there were no data on miscarriage and live birth rates in any of the included studies. Therefore, a metaanalysis could not be performed on these parameters either. Forest plots of the estimated fertility outcomes are shown in Figure 3.

Fertilization rates

Evidence suggests that collecting semen at home vs in clinic did not increase fertilization rates in the IVF cycle (risk ratio [RR], 1.00; 95% CI, 0.97−1.03; 2 studies; 6770 events) (Figure 5, B).[15,27]

Pregnancy rates

The evidence is very uncertain in relation to the effect of collecting semen at home on the pregnancy rate in the IUI and IVF/ICSI cycles (RR, 0.85; 95% CI, 0.28−2.59; 2 studies[16,26]; 76 events and RR, 1.04; 95% CI, 0.86−1.25; 2 studies[15,27]; 356 events, respectively) (Figure 5, A and B).

Quality of the studies

The quality of evidence for all semen parameters was very low owing to selection bias, lack of blinding, and imprecision of estimation in the included studies. We rated the quality of evidence for the fertility rate as very low because of a lack of information on participant selection and blinding in the included studies and small sample sizes. We rated the quality of evidence as very low for the pregnancy rate because of a lack of blinding, small sample size, and selection bias.

Comment

Principal findings

This present review is one of the earliest systematic reviews and metaanalyses to estimate the effect of location (home- vs clinic-collection) on semen parameters and fertility outcomes, including an estimated average from 3018 semen samples from participants between 20 and 58 years of age. We analyzed and reported the estimated outcomes in subgroup comparisons as overall and individualized samples but could not report the summarized outcome as total estimated, because the individual data were a subset of overall data in some studies.[13,15]

The results of the metaanalysis for each subgroup showed that the semen volume, sperm concentration, total sperm count, sperm motility, total motile sperm count, progressive motile sperm, and normal sperm morphology were not negatively affected by the location of semen collection. There are concerns that the transport time of taking semen collected at home to the laboratory may affect semen or sperm quality because of (1) increased exposure of spermatozoa to seminal plasma; or (2) changes in temperature during transport. However, no negative impact on at-home collected semen was found for any semen parameters, regardless of whether ICSI/IVF or IUI cycles were used. These results might be explained by the semi-controlled effect of some confounders such as length of abstinence (normally 2−7 days)[25] but can range between 1 and 30 days (median: 4 days). According to the WHO guidelines, most studies report transferring samples to the laboratory on time, but 3 studies[14,15,27] reported that the time to transport was between 1.5 and 2 hours with no negative impact on semen quality.

Other potential confounding effects on outcomes included baseline underlying medical conditions, endocrine system health, psychological status, medications or substances used, and methods used to collect semen. In addition, the techniques, instruments, and procedures used to analyze each semen parameter,[13−15,27] such as conventional manual procedures or computer-aided sperm analysis, could be confounders.

During this present COVID-19 pandemic, there were more confounding variables from COVID-19-related factors, such as history of viral infection, which may have effects on the male reproductive system from proposed hypotheses including viruses directly damaging the target cell, or inflammatory response by cytokines, or testicular damage from fever.[28] There was a report of low testosterone levels after recovery from COVID-19, especially in patients with a history of severe symptoms.[29] In addition, in a study by Gonzalez et al,[30] the status of COVID-19 mRNA vaccination may have an effect on the semen parameters, which showed a significant increase in the sperm parameters. However, small and larger samples are needed for effective conclusions. None of the included studies provided information about this potential confounder.

Only 2 included studies[15,27] reported the adjusted outcomes and added male age, whereas 1 study reported the number of days of abstinence and added female age, fertilization method, and the number of oocytes retrieved or embryos transferred for fertility outcomes. Other studies did not mention the potential confounding factors mentioned above, which might affect the certainty of the estimated outcome and might be a limitation of the review.

Sperm parameters and clinical outcomes can be proxied for infertility outcomes. The fertilization rate was comparable between the 2 groups with no heterogeneity in the 2 studies, and the pregnancy rates, even in the subgroups of those who underwent ICSI/IVF or IUI, were not significantly different between the at-home and in-clinic semen collections. Another point of concern is the effect of conventional IVF or ICSI on fertilization and pregnancy rates. Only 1 of the included studies, that is, the one by Stimpfel et al,[27] showed results regarding fertility outcomes (only pregnancy rate) in the IVF and ICSI subgroups. After we performed a metaanalysis, there was no difference in pregnancy rates between the 2 sites of semen collection when only conventional IVF cycles or ICSI cycles were included. These results may be owing to the nonsignificant differences in the semen parameters used in the ART procedure. For the estimated outcome of pregnancy rates in the IUI subgroup, there was high heterogeneity. Therefore, we explored this and assumed that the difference in outcome might be owing to differences in methodology and confounding factors such as baseline female factor, protocol, and the procedure used, which were not adjusted in some studies.

The reason these confounders were considered significant is that they may have contributed to the considerable heterogeneity in addition to the differences in design and methodology for each study. The overall quality of evidence was another factor determined by this metaanalysis. To this end, we used the GRADE system for cohort-type studies according to the study design itself. Considerable heterogeneity was found in semen volume and motility outcomes. Heterogeneity among studies often occurred within a subgroup of the overall sample, whereas within-person comparisons had no heterogeneity. This may be owing to differences in methodology and baseline characteristics, leading to interpersonal variation effects. The implications of the estimated outcomes from the current review should be generalized with caution because of the limitations of the review.

Strengths and limitations

This is one of the earliest systematic reviews and metaanalyses conducted with all currently available data and large samples comparing the effect of at-home vs in-clinic semen collection on semen parameters and clinical outcomes (ie, pregnancy rates). A systematic review was conducted following the Cochrane and MOOSE guidelines. In addition, subgroup analysis was used to reduce bias and the effects of heterogeneity among studies and to estimate robustness.

A limitation of this review is that most of the included studies were observational, with only 1 study being an RCT. A low-quality study design eroded the quality of evidence from the RCT, resulting in greater heterogeneity among

studies. Furthermore, most studies did not adjust for potential confounders, which may have affected the outcomes of the original studies. A lack of intermediate- and long-term clinical outcomes exists, for example, miscarriage and live birth rates. Therefore, more high-quality studies such as RCTs are needed to strengthen the evidence for future practice.

Comparison with existing literature

This review is one of the earliest systematic reviews and metaanalyses to estimate the outcome of location of semen collection and to inform whether it affects semen parameters and fertility outcomes. Thus, there are no existing reviews available for comparison with this review.

Conclusions and implications

Evidence indicates that collecting semen at home did not result in any significant difference in semen parameters, fertility rates, or pregnancy rates. Further studies should include more high-quality RCTs. The outcomes of this evidence-based metaanalysis support at-home semen collection as a qualitatively acceptable option, particularly during the COVID-19 pandemic, which may play a role in future routine ART services. ■

REFERENCES

1. World Health Organization. General's opening remarks at the media briefing on COVID-19. 2020. Available at: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19–11-march-2020. Accessed February 20, 2021.
2. Veiga A, Gianaroli L, Ory S, Horton M, Feinberg E, Penzias A. Assisted reproduction and COVID-19: a joint statement of ASRM, ESHRE and IFFS. Fertil Steril 2020;114:484–5.
3. American Society for Reproductive Medicine. Patient management and clinical recommendations during the coronavirus (COVID-19) pandemic 2020. 2022. Available at: https://www.asrm.org/news-and-publications/covid-19/statements/patient-management-and-clinical-recommendations-during-the-coronavirus-covid-19-pandemic/. Accessed May 30, 2021.
4. ESHRE COVID-19 Working Group. ESHRE guidance on recommencing ART treatments. 2020. Available at: https://www.eshre.eu/-/media/sitecore-files/Guidelines/COVID19/ESHRE-Guidance-on-Recommencing-ART-treatments_update-04052020.pdf?la=en&hash=A584F8A306C570BE7648C167CB190F994E21F05A. Accessed May 30, 2021.
5. Guo L, Zhao S, Li W, et al. Absence of SARS-CoV-2 in semen of a COVID-19 patient cohort. Andrology 2021;9:42–7.
6. Erbay G, Sanli A, Turel H, et al. Short-term effects of COVID-19 on semen parameters: a multicenter study of 69 cases. Andrology 2021;9:1060–5.
7. Holtmann N, Edimiris P, Andree M, et al. Assessment of SARS-CoV-2 in human semen-a cohort study. Fertil Steril 2020;114:233–8.
8. Ruan Y, Hu B, Liu Z, et al. No detection of SARS-CoV-2 from urine, expressed prostatic secretions, and semen in 74 recovered COVID-19 male patients: a perspective and urogenital evaluation. Andrology 2021;9:99–106.
9. World Health Organization. WHO laboratory manual for the examination and processing of human semen, 5th ed. Geneva, Switzerland: World Health Organization; 2010.
10. Aitken RJ, Baker MA, Sawyer D. Oxidative stress in the male germ line and its role in the aetiology of male infertility and genetic disease. Reprod Biomed Online 2003;7:65–70.
11. Appell RA, Evans PR. The effect of temperature on sperm motility and viability. Fertil Steril 1977;28:1329–32.
12. Griveau JF, Le Lannou D. Reactive oxygen species and human spermatozoa: physiology and pathology. Int J Androl 1997;20:61–9.
13. Gao J, Duan YG, Yi X, Yeung WSB, Ng EHY. A randomised trial comparing conventional semen parameters, sperm DNA fragmentation levels and satisfaction levels between semen collection at home and at the clinic. Andrologia 2020;52:e13628.
14. Licht RS, Handel L, Sigman M. Site of semen collection and its effect on semen analysis parameters. Fertil Steril 2008;89:395–7.
15. Sacha CR, Vagios S, Hammer K, Fitz V, Souter I, Bormann CL. The effect of semen collection location and time to processing on sperm parameters and early IVF/ICSI outcomes. J Assist Reprod Genet 2021;38:1449–57.
16. Yavas Y, Selub MR. Intrauterine insemination (IUI) pregnancy outcome is enhanced by shorter intervals from semen collection to sperm wash, from sperm wash to IUI time, and from semen collection to IUI time. Fertil Steril 2004;82:1638–47.
17. Higgins JPT, Thomas J, Chandler J, et al, eds. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Cochrane. 2021. Available from, www.training.cochrane.org/handbook. Accessed April 12, 2021.
18. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008–12.
19. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366. l4898.
20. Sterne JA, Hernán MA, Reeves BC, et al. Robins-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355. i4919.
21. Review Manager (RevMan) [Computer program]. Version 5.4. The Cochrane Collaboration; 2020.
22. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014;14:135.
23. Reeves BC, Deeks JJ, Higgins JPT, Shea B, Tugwell P, Wells GA. Chapter 24. Including non-randomized studies on intervention effects. In: Higgins JPT, Thomas J, Chandler J, et al, eds. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Cochrane. 2021. Available from, www.training.cochrane.org/handbook. Accessed May 31, 2021.
24. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64:401–6.
25. Elzanaty S, Malm J. Comparison of semen parameters in samples collected by masturbation at a clinic and at home. Fertil Steril 2008;89:1718–22.
26. Song GJ, Herko R, Lewis V. Location of semen collection and time interval from collection to use for intrauterine insemination. Fertil Steril 2007;88:1689–91.
27. Stimpfel M, Jancar N, Vrtacnik-Bokal E. Collecting semen samples at home for IVF/ICSI does not negatively affect the outcome of the fresh cycle. Reprod Biomed Online 2021;42:391–9.
28. Sheikhzadeh Hesari F, Hosseinzadeh SS. Asl Monadi Sardroud MA. Review of COVID-19 and male genital tract. Andrologia 2021;53:e13914.
29. Rastrelli G, Di Stasi V, Inglese F, et al. Low testosterone levels predict clinical adverse outcomes in SARS-CoV-2 pneumonia patients. Andrology 2021;9:88–98.
30. Gonzalez DC, Nassau DE, Khodamoradi K, et al. Sperm parameters before and after COVID-19 mRNA vaccination. JAMA 2021;326:273–4.
31. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.