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SYSTEMATIC REVIEW

The potential of mobile health applications to improve couples' fertility: a systematic review and meta-analysis of randomized controlled trials

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Abstract

The purpose of this systematic review was to examine the safety and effectiveness of mobile health applications in couples with infertility. Nineteen databases were searched from their inception to August 2022. Only randomized controlled trials (RCTs) in which mobile health was used as an intervention in infertile couples were included. A quantitative analysis of RCTs was employed using RevMan software. Study selection, data extraction and validation were performed by two independent reviewers according to the guidelines. The Cochrane criteria for risk-of-bias were used to evaluate the methodological quality of the trials. Eight RCTs met the inclusion criteria. Among the eight RCTs, two RCTs were from the Netherlands and the remaining six RCTs were from China. Meta-analysis showed that mobile health interventions in infertile couples in China were found to be superior to usual care in terms of clinical pregnancy rate (p = 0.001), psychological status (SAS (Self-Rating Anxiety Scale): $p < 0.001$; SDS (Self-Rating Depression Scale) $p < 0.001$;), infertility knowledge levels ($p < 0.001$), quality of life ($p < 0.001$), and serum levels of 5-hydroxytryptamine ($p < 0.001$). The effects on intervention groups using mobile health interventions in the Netherlands were not superior to the control groups that used usual care in terms of improving dietary factors ($p > 0.05$). In general, the positive effect of mobile health on improving clinical pregnancy rate, psychological status, infertility knowledge levels, quality of life and satisfaction with information was better than that of usual care. Mobile health interventions could be a viable supplement to the usual care for infertile couples. However, more high-quality RCTs need to be included in the future to provide additional evidence of the positive effects of mobile health in infertile couples.

Keywords

Mobile health; Infertility; Systematic review

1. Introduction

Infertility was defined as the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse, which affected 48.5 million couples in the world [1, 2]. About half of these couples decided to turn to assisted reproductive technologies, including *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) [3]. Currently, assisted reproductive technologies have been applied more than 1 million times a year in the United States and Europe [4–7]. De Neubourg *et al.* [8] found that in developed countries, the live birth rate after three completed IVF cycles is about 50%. However, the IVF/ICSI treatment cycle is extremely long. Most women need hormone injections to activate their ovaries to produce enough oocytes. Additionally, they need to take medicines to increase the chances of survival of the embryo inside the uterus. Thus, most infertile women have to experience side effects of drugs and psychological pressure during IVF/ICSI, which makes adherence to all IVF/ICSI low [9, 10]. Gameiro *et al.* [11] reported that one in every three couples discontinued IVF due to the side effects of the drugs and psychological distress. Fertility physicians must therefore solve the lifestyle factors relating to infertility, reduce IVF-related burdens and improve the probability of successful IVF.

A guideline of the European Society of Human Reproduction and Embryology stated that the fertility physician should meet the emotional and cognitive needs of infertile couples, and ultimately improve pregnancy outcomes through changes in nutritional status and lifestyle [12]. As a modifiable factor, lifestyle changes, *e.g.*, fruit and vegetable intake, smoking cessation and stopping drinking have been shown to have a significant positive correlation with pregnancy rate [13, 14]. However, so far, only a small group of infertile couples may receive pre-conceptional counseling from a fertility physician [13]. Most fertility clinics have not provided lifestyle improvement programs for couples receiving IVF. This may also explain why one-third of IVF couples still seek complementary and alternative medicine for improving their lifestyle outside their fertility clinics [15]. Furthermore, for those infertile patients with low socioeconomic status in remote areas, local medical resources are relatively scarce, making them unable to get help and treatment from an infertility doctor nearby. The time burden of going to fertility clinics is the second major source of pressure for fertility couples [16]. Furthermore, travel expenses to the fertility clinic account for one-third of the indirect economic cost of infertile couples. At the same time, the cost of infertility treatment in many developing countries, such as China, has not yet been included in the national medical insurance system. Thus, the financial burden of receiving infertility treatment is still large, which also leads to less support for infertile couples to obtain fertility-related health information.

During the COVID-19 (Corona Virus Disease2019) pandemic, to reduce the risk of infection, the American Society of Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology suggested postponing the treatment and diagnosis of infertility and suspending the treatment of assisted reproductive technology. However, delay in infertility treatment can cause negative emotions and psychological distress in infertile couples [17]. At the same time, delay in infertility treatment also increases the age of couples, which has been proven to have a negative impact on pregnancy outcomes [18]. Based on this, it is necessary to find a solution for infertile couples to reduce the waiting time for the diagnosis and treatment of the fertility physician while coping with the COVID pandemic.

Lundsberg *et al.* [19] reported that more than 40% of women in the United States stated that the Internet is the main source of health education information on infertility. In 2020, the ASRM also recommended that fertility physicians can use mobile health to provide remote reproductive counseling, to perform remote assessment and to provide health education for infertile couples during the COVID-19 pandemic [20]. In 2019, only 11% of infertile couples received mobile health services. However, during the COVID-19 pandemic, this number increased to 50% [21]. The World Health Organization has defined mobile health as the use of mobile wireless devices for medical and public health practice [22]. Mobile health and electronic health both fall under the broader umbrella of digital health interventions and have the potential to become high-quality, cost-effective tools to improve health outcomes [23]. Electronic health refers to healthcare services and information provided with the support of information and communication technology (ICT)—such as computers, mobile phones and satellite communications [24]. Mobile health is actually a sub-segment of electronic health, which refers to mobile and wireless applications, including text messaging, mobile health applications, wearable devices, remote sensing, and the use of social media such as WeChat, Facebook and Twitter, for the delivery of health-related services [25]. Thus, compared to electronic health, mobile health is more concerned with smartphones. Owing to the popularity of low-cost smartphones and global mobile communication networks, tens of millions of people who cannot access fixed line phones or computer networks can use smartphone devices as a tool for daily communication and data transmission. Mobile health can be used as an access point to obtain patients' data or as a remote tool to provide information for healthcare providers, which makes mobile health more personal when compared to electronic health [26].

Mobile health can realize functions of "storage and transmissions", "real-time telemedicine" and "patient remote health monitoring supported by wearable devices" in the medical field. The "store and forward" function of mobile health can help fertility physicians to obtain medical information from infertile couples and provide virtual infertility consultations online. The "real-time telemedicine" function can simulate the traditional patient/doctor interaction on-site, including the collection of medical history and physical examination by the fertility physician, by building a virtual visit space and by video conference and online communication. The function of "patient remote health monitoring supported by wearable devices" can help fertility physicians obtain objective examination data from infertile couples in real time. In general, mobile health interventions have a positive impact on users and can help patients adhere to treatment [27, 28]. Mobile health applications, one of the mobile health technologies, can be well-integrated into self-care programs, psychological education, online peer support, psychological cognitive behavior therapy and other interventions to promote the change to healthy behaviors by improving patient self-efficacy [29] and ultimately, patients' clinical outcomes [30, 31].

A mobile health application can increase the sense of security and control of patients over the treatment process [32], and provide users with more effective digital services to meet personalized needs. Mobile health improves patient satisfaction and is cost-effective. For example, the virtual medical environment provided by mobile health reduces the travel time and economic costs for infertile couples, and can prevent lost wages by reducing the number of days off [33]. Previous research suggested that mobile health had a positive effect on improving nutritional deficiency, lifestyle and medication adherence in infertile couples [34, 35]. The development of mobile devices makes health education information related to infertility interactive and innovative; video media especially improve the understanding of infertile couples in relation to health education. However, the ability of infertile couples to accept this new online information needs to be further evaluated, including how they use online health education and whether this information meets their individual demands [36].

According to Parry [37], infertile couples usually seek IVF at the age of 18 to 50 years. Recent research showed that more than 98% of Americans aged 18–50 years owned and used the Internet [38]. 70% of Canadians aged 18–50 years reported having smartphones, and the Internet usage and smartphone ownership rate of Canadians aged 18–50 years continued to grow [39]. Thus, mobile health can complement the treatment of traditional infertility clinics and forms of health education. Mobile health can also provide medical services for infertile couples who traditionally find it difficult to obtain the diagnosis and treatment of a fertility physician, such as men, immigrants, ethnic minorities and patients with stigma of infertility [40]. In view of the potential of mobile health applications to reduce stress, to improve the ability of patients to make behavioral changes, and to provide user-friendly information to a wide range of people, these may become a new solution to solve the needs of psychological education and psychosocial support for couples with infertility.

Previously, Overdijkink *et al.* [41] performed a systematic review and found that lifestyle programs based on mobile health technology could improve the level of knowledge of pregnant women, change the living habits of spouses, promote health behaviors in spouses, and improve pregnancy rates. However, Overdijkink *et al.* [41] only included pregnant women, and so the effect of smart health on couples with subfertility is still unclear. Furthermore, Overdijkink *et al.* [41] only explored the effect of smart health interventions on pregnant women in high-income countries, and so the effect of smart health on low-income pregnant women in developing countries is still unknown. These known gaps have not been resolved and so this systematic review was aimed at exploring the effectiveness and safety of mobile health for infertile couples, in both developed and developing countries.

2. Materials and methods

This systematic review was performed following the principle of Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [42] (**Supplementary File A**). This protocol has been registered with the Open Science Framework. The registration number is osf.io/kvhpe.

2.1 Data sources and search strategy

The following databases were searched from their inception until August 2022, without language restrictions: PubMed, Embase, Sino-Med, CiNii, KoreaMed, *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (LILACS), Africa Health Research Institute (https://www.ucl.ac.uk/infection-immunity/research/africa-health-research-institute), the Cochrane Central Register, the Cochrane Reproductive and Sexual Health Group Trials Register, and the IEEE Xplore Digital Library.

The key search terms included: "cellphone", "smartphone", "mobile phone", "personal digital assistant", "mobile health", "telemedicine", "text messaging", "texting", "smart health", "computers", "telemonitor", "web", "website", "ipod", "ipad", "internet", "subfertility", "infertility", "randomized controlled trial" and "controlled clinical trial". Search strategies are listed in **Supplementary File B** (Medline *via* PubMed).

2.2 Criteria for study selection

2.2.1 Types of studies

This systematic review included randomized control trials (RCTs) that assess the effectiveness and safety of mobile health applications for infertile couples. However, *in vitro* experiments, retrospective studies and survey studies were excluded.

2.2.2 Type of participants

Infertility was defined as the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse [1, 2]. Couples who met the infertility definition were included in this systematic review. However, infertile couples who suffered from other serious complications were excluded.

2.2.3 Types of interventions and comparators

All types of mobile health-delivered education programs, *i.e.*, Smartphone, including apps, text messaging, personal digital assistant, social media on mobile devices, such as Facebook, Twitter, Instagram, WeChat and QQ, among others, and telemedicine, were included. Comparators included usual care, which contained health education through verbal discussion, paper-based educational materials on infertility, and self-management and self-monitoring of infertility. If the mobile health intervention were included in usual care, it would be excluded.

2.2.4 Types of outcome measures

2.2.4.1 Primary outcome

Clinical pregnancy rate.

2.2.4.2 Secondary outcomes

① Psychological status: A self-rated anxiety scale (SAS) was used to examine the degree of anxiety. There were 20 items on the scale, including 15 positive scores and 5 negative scores, with 4-level scores [43]. A self-rated depression scale (SDS) was used to assess the degree of depression. There were 20 items on the scale, including 10 positive scores and 10 negative scores, with 4-level scores [44]. A higher score in these scales indicated higher anxiety and depression levels.

② Knowledge level: The infertility knowledge scale was used to assess the perceived level of knowledge of the patient about infertility. This scale included 7 dimensions and each dimension was scored on 1 to 5 grades, and the total score of this scale ranged from 7 to 35. A higher score on this scale indicated a higher level of knowledge about infertility [45].

③ Quality of life (QoL): The Ferti QoL scale was used to assess the QoL of patients with infertility. This scale had 36 items, with a total score of 0-100. The higher the score of this scale, the higher the QoL of infertile patients [46].

④ Evaluation of dietary and lifestyle modification: The number of people consuming vegetables >200 g/d, fruits >2 pieces/d, quitting smoking, and quitting drinking alcohol.

⑤ Satisfaction with information: Numeric scale rating (NSR) scores were applied to examine the outcome, ranging from 0 to 10. A higher NSR score indicated higher satisfaction with the information [47].

⑥ Serum biomarkers: Serum levels of 5-hydroxytryptamine (5-HT), serum levels of folate, and serum levels of luteinizing hormone.

2.3 Screening procedures of eligible studies

Two review authors (YL and WJS) independently assessed abstracts and titles of studies identified by the literature search. Duplicates were omitted using EndNote software (X7 version, Clarivate Analytics, Philadelphia, PA, USA). Relevant studies were selected against the predefined inclusion criteria. If necessary, reviewers would examine full-text reports to identify eligible studies. EndNote software was also used to manage records. Any disagreement was confirmed by the third reviewer (WXL).

2.4 Data extraction

Data extraction was performed with a pre-piloted, standardized form by two independent reviewers (YL and WJS). For each trial, the specific extracted information included study characteristics, intervention details and controls, including content details and main outcomes. Any disagreement was confirmed by the third reviewer (WXL).

2.5 Assessment of risk of bias in included studies

Two authors (YL and WJS) independently assessed the risk of bias using the Cochrane Handbook criteria. The following risk of bias domains were assessed: sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessment (detection bias); incomplete outcome data (attrition bias); selective outcome reporting (reporting bias); and other bias. The final decisions were made by a third reviewer (WXL) if inconsistent results appeared.

2.6 Assessment of heterogeneity and data synthesis

The I^2 statistic was used to assess the heterogeneity of the included studies, as the criterion, $I^2 < 50\%$, indicates low heterogeneity, while $I^2 > 50\%$ indicates high heterogeneity [48]. The meta-analysis of intervention and outcome measure methods was conducted by RevMan software [49]. If the statistical heterogeneity were low ($I^2 < 50\%$), the fixed-effect model would be used to combine the data, while if the statistical heterogeneity were high ($I^2 > 50\%$), the random-effect model would be used. However, if the heterogeneity level were significant, a descriptive analysis would be performed.

2.7 Sensitivity analysis

Sensitivity analyses were conducted to explore the robustness of the meta-analysis results by varying the analytic data or methods.

2.8 Publication bias

We would use the funnel plot to visually assess publication bias if the number of included trials is more than 10 [50].

3. Results

3.1 Search results

When databases and registers were initially searched, 320 relevant trials were obtained. After removing duplicated published trials and ineligible trials, a total of 250 trials were screened and reviewed further. After further screening of the titles and abstracts of 250 trials, 220 trials were excluded. A full text search and review of the remaining 30 trials was conducted and it was found that 5 trials were research protocols, 5 trials did not perform a RCT research design, and the outcomes of 12 trials did not conform to the inclusion criteria of this study. After deleting these 22 trials, 8 trials were finally included for the subsequent systematic review (Fig. 1).

3.2 Description of the included trials

Among the eight RCTs, two RCTs [45, 51] were from the Netherlands and the remaining six RCTs [52–57] were from China. The Dutch medical system is based on general practitioners (GPs) who provide community-based integrated medical health services for patients [58]. As the first trigger point for patients to use community health services, a GP plays the role of "gatekeeper" and also plays the key role of "medical healthcare coordinator". The GP has a close cooperation with various primary healthcare providers including physiotherapists, pharmacists, psychologists, dentists, nurses and midwives [58]. At present, nearly 90% of GPs in the Dutch primary medical community have provided mobile health for their patients [59]. What is different from the Netherlands is that Chinese medical resources are excessively concentrated in level III class A hospitals (the highest level medical institutions in China), and patients often directly choose level III class A hospitals for receiving medical healthcare, which leads to a relative shortage of medical resources at the community hospitals [60]. In recent years, China has vigorously promoted the "hierarchical medical system". On the one hand, through the establishment of the "medical treatment combination", the Chinese government has increased financial investment in primary medical care and improved the service capacity of primary medical care. On the other hand, through the reform of the medical insurance payment system, the Chinese government has guided the development of "family physician contract services" in the community. However, despite the considerable efforts made by the Chinese National Health Commission, the proportion of Chinese patients receiving the first visit from the GP is only 23.1% [60].

The development of mobile health in China is also slower than that in the Netherlands. Until 2018, the Chinese National Health Commission issued several policy documents to promote the development of mobile health. Unlike the Netherlands, where most mobile health practitioners are GPs, the implementers and managers of mobile health tend to focus on the specialists in the level III class A hospitals [61]. Owing to the different medical backgrounds between China and the Netherlands, it is necessary for subgroup analysis to be performed according to different countries, so as to reduce clinical heterogeneity. All RCTs have been published in the last 3 years. 50% of the RCTs were followed up for 8 weeks, while 37.5% of the RCTs were followed for 24 weeks or more. All RCTs [45, 51–57] compared the effects of mobile health combined with usual care and usual care alone in infertile couples. The forms of mobile health in the intervention group included the mobile platform, the mobile health Smarter Pregnancy program, the Patient Journey App, and video communication in combination with electronic health. Details of the included RCTs are summarized in Table 1.

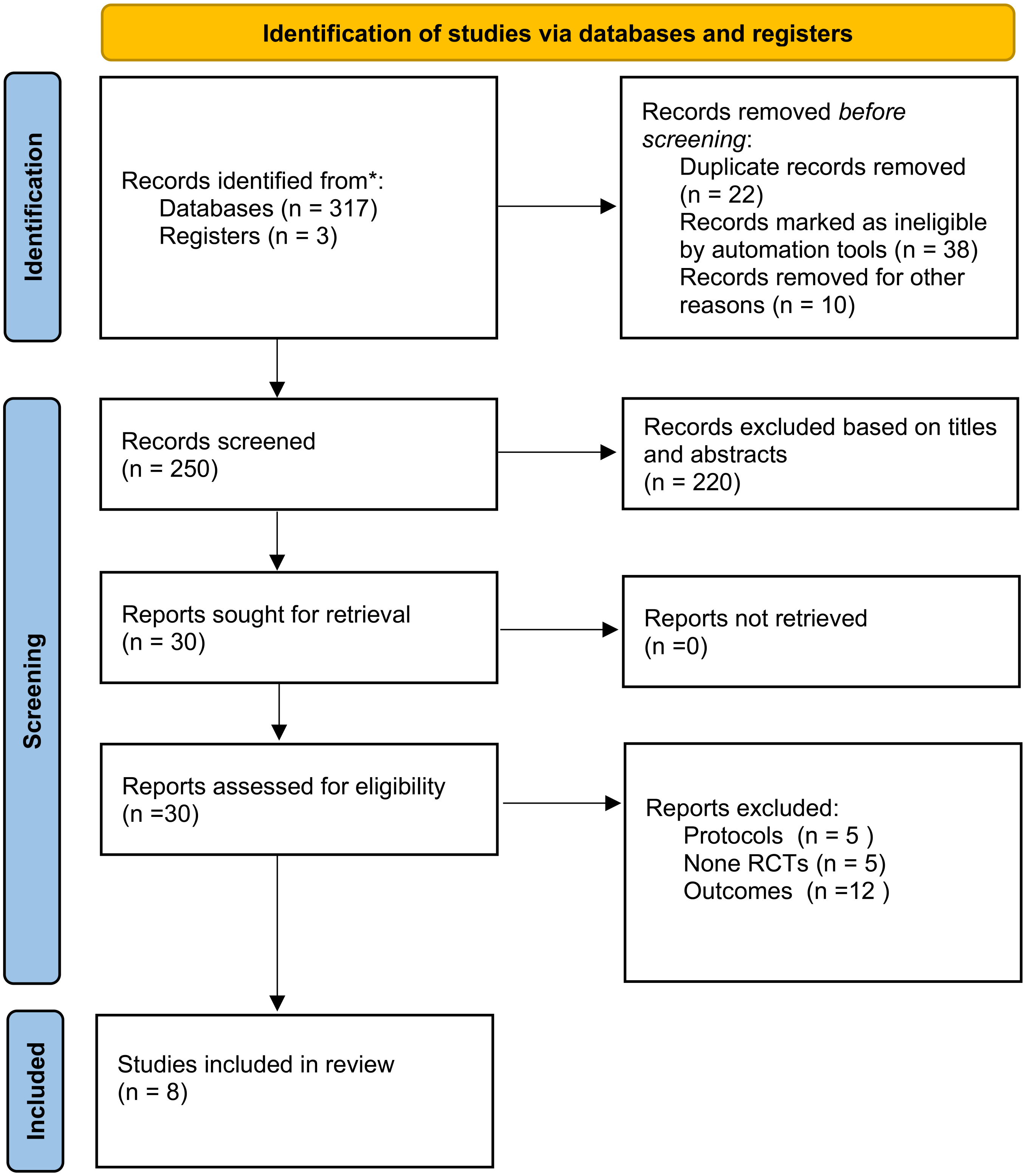

FIGURE 1. Flowchart of the trial selection process. RCTs, randomized controlled trials.

TABLE 1. Main characteristics of included studies.

Study (Author, year and country)	Sample size/study design	Follow-up	Intervention group	Control group	Main outcomes	Intergroup Differences
Pan [53] 2021 China	165 RCT	8 weeks	(A) Mobile platform (WeChat Public platform and QQ platform): Daily use, therapists receive patient consultation, and provide informatized health education, emotional platform for ART, peer education WeChat group, and E-health based lifestyle modification (n = 80). Plus (B)	(B) Usual care (n = 85)	1. Psychological status: SAS, SDS. 2. Pregnancy outcome: Clinical Pregnancy.	SAS: MD, 8.79 (7.48, 10.10), $p < 0.001$ SDS: MD, 6.13 (5.31, 6.95), $p < 0.001$ RR, 1.40 (1.04, 1.89), $p = 0.023$
Oostingh [51] 2020 Netherlands	222 RCT	36 weeks	(A) mHealth Smarter Pregnancy program: short online questionnaire recording nutritional and lifestyle behaviors; tailored coaching based on sex, pregnancy status, and behaviors; a maximum of three e-mails or text messages per week that contained tips, recommendations, feedback on progress, and additional questions addressing pregnancy status (n = 106). Plus (B)	(B) Usual care (n = 116)	Dietary and lifestyle modification assessment: the number of people reaching 1. Vegetables, >200 g/d 2. Fruits, >2 pieces per day 3. Quit smoking rate 4. Quit Alcohol drinking rate	RR, 1.41 (0.96, 2.08), NS RR, 1.59 (1.22, 2.08), $p < 0.001$ RR, 1.17 (1.04, 1.31), $p = 0.007$ RR, 1.09 (0.74, 1.61), NS
Timmers [45] 2021 Netherlands	48 RCT	4 weeks	(A) The Patient Journey App (Interactive Studios): The information was disseminated over different phases of the IVF process: introduction, welcome to the fertility center, what is IVF, medication usage, IVF intake consultation, medication reminders, treatment schedule (hormone injections, side effects, and echography), oocyte retrieval, embryo transfer, and a pregnancy test (n = 28). Plus (B)	(B) Usual care (n = 20)	1. Level of knowledge. 2. Satisfaction with information.	MD, 4.24 (2.61, 5.87), $p < 0.001$ MD, 1.57 (0.93, 2.21), $p < 0.001$
Wang [55] 2021 China	80 RCT	8 weeks	(A) Video communication in combination with eHealth: The remote health team provide weekly calls and weekly video communication (n = 40). Plus (B)	(B) Usual care (n = 40)	1. Level of knowledge 2. Pregnancy outcome: clinical pregnancy.	MD, 5.51 (4.19, 6.11), $p < 0.001$ RR, 1.00 (0.65, 1.55), $p = 1.00$

TABLE 1. Continued.

Study (Author, year and country)	Sample size/study design	Follow-up	Intervention group	Control group	Main outcomes	Intergroup Differences
Pang [54] 2020 China	88 RCT	8 weeks	(A) Mobile platform (WeChat Public platform and WeChat group): Daily use, infertility physicians and infertility nurses are responsible for explaining and answering questions about ART to patients in the WeChat group (n = 44). Plus (B)	(B) Usual care (n = 44)	1. Psychological status: SAS, SDS. 2. Pregnancy outcome: clinical pregnancy.	SAS: MD, 7.62 (6.22, 9.02), $p < 0.001$ SDS: MD, 6.96 (5.46, 8.46), $p < 0.001$ RR, 1.48 (1.03, 2.12), $p = 0.036$
Mao [52] 2020 China	120 RCT	8 weeks	(A) Mobile platform (WeChat Public platform and WeChat group): Daily use, WeChat Public platform: infertility related knowledge, peer support, Group psychological intervention *via* WeChat group. (n = 60) Plus (B)	(B) Usual care (n = 60)	Psychological status: SAS, SDS.	SAS: MD, 8.09 (6.94, 9.24), $p < 0.001$ SDS: MD, 6.29 (5.02, 7.56), $p < 0.001$
Xia [56] 2020 China	80 RCT	24 weeks	(A) Mobile platform (WeChat Public platform and WeChat group): Daily use, health education on infertility related knowledge was carried out in WeChat communication groups by delivering relevant videos and pictures (n = 40). Plus (B)	(B) Usual care (n = 40)	1. Psychological status: SAS, SDS. 2. Ferti QoL. 3. Pregnancy outcome: clinical pregnancy. 4. Serum neurotransmitter (5-HT)	SAS: MD, 8.09 (6.94, 9.24), $p < 0.001$ SDS: MD, 6.29 (5.02, 7.56), $p < 0.001$ MD, 6.50 (5.94, 7.06), $p < 0.001$ RR, 1.41 (1.02, 1.95), $p = 0.029$ MD, 6.82 (6.27, 7.37), $p < 0.001$
Yao [57] 2019 China	101 RCT	24 weeks	(A) Mobile platform (WeChat Public platform and WeChat group): Daily use, good pregnancy WeChat Public platform: Remind infertility couples to actively pay attention to the content delivered by the WeChat public platform every day with the help of WeChat group; Set keyword reply in WeChat Public platform (n = 50). Plus (B)	(B) Usual care (n = 51)	Ferti QoL.	MD, 6.40 (3.66, 9.14), $p < 0.001$

Note: ART: Assisted Reproductive Technology; IVF: In Vitro Fertilization; NS: Not significant; QoL: Quality of Life; SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; RCT: randomized controlled trials; MD: Mean Difference; RR: Relative Risk.

3.3 Methodological quality

Except for one trial [55], the included trials adopted randomization methods. Only four RCTs [45, 51, 56, 57] carried out concealment of allocation by sealed envelopes. Due to the nature of mobile health interventions, it is not possible to blind participants and performers. However, only three RCTs [45, 51, 57] reported blinding of the assessor and withdrawal of the participants. The selective reporting results were reported in all eight RCTs (Figs. 2,3).

3.4 The effects of mobile health on infertile couples in China

3.4.1 Clinical pregnancy rate

There were 4 RCTs [53–56] that used the clinical pregnancy rate as the outcome to explore the effect of mobile health on infertile couples. Three of the trials [53, 54, 56] indicated positive effects on the clinical pregnancy rate between groups, while the remaining one [55] did not. The meta-analysis suggested that, compared to usual care, mobile health interventions plus usual care had a favorable effect on the clinical pregnancy rate (RR = 1.34, 95% CI (1.12, 1.59), p = 0.001), with low heterogeneity ($Chi^2 = 2.16$, $p = 0.54$, $I^2 = 0\%$) (Fig. 4).

3.4.2 Psychological status

There were three RCTs [52–54] in which SAS and SDS were used as measurements of the effects of mobile health on infertile couples. The meta-analysis suggested that, compared to usual care, mobile health interventions plus usual care had a favorable effect on alleviating the psychological burden of infertile couples (SAS: MD = 8.18, 95% CI (7.45, 8.92), $p < 0.001$, with low heterogeneity: $Chi^2 = 1.47$, $p = 0.48$, $I^2 = 0\%$; SDS: MD = 6.31, 95% CI (5.69, 6.94), $p < 0.001$, with low heterogeneity: $Chi^2 = 0.90$, $p = 0.64$, $I^2 = 0\%$).

3.4.3 Knowledge level

Only one RCT [55] used the infertility knowledge scale as an outcome to test the effect of mobile health on the level of knowledge of Chinese infertile couples. The result suggested that, compared to usual care, mobile health interventions plus usual care had statistically significant favorable effects on improving the level of knowledge of infertile couples (MD = 55.51, 95% CI (4.19, 66.11), $p < 0.001$) (Table 1).

3.4.4 Quality of life

There were two RCTs [56, 57] using Ferti QoL to measure the QoL of infertile couples. The result of the meta-analysis showed that, compared to usual care, mobile health plus usual care had favorable statistically significant effects in improving the QoL of infertile couples (MD = 6.50, 95% CI (5.95, 7.04), $p < 0.001$) (Fig. 5).

3.4.5 Serum 5-HT

Only one RCT [56] used 5-HT as an outcome to test the effect of mobile health on Chinese infertile couples. The result suggested that, compared to usual care, mobile health interventions plus usual care had statistically significant favorable effects in improving the serum levels of 5-HT in infertile couples (MD = 6.82, 95% CI (6.27, 7.37), $p < 0.001$) (Table 1).

3.5 The effects of mobile health on infertile couples in the Netherlands

One trial [51] from the Netherlands used the number of people consuming vegetables >200 g/d, fruits >2 pieces/d, stopping smoking and quitting alcohol consumption as a measurement to explore the dietary and lifestyle modification of infertile couples. Mobile health plus usual care interventions on the number of people eating vegetables >200 g/d, and fruits >2 pieces/d indicated no statistically significant effect compared to usual care (the number of people eating vegetables >200 g/d: RR = 1.41, 95% CI (0.96, 2.08), $p > 0.05$; quit alcohol drinking rate: RR = 1.09, 95% CI (0.74, 1.61), $p > 0.05$). However, the mobile health plus usual care intervention in the other outcomes of dietary and lifestyle modification indicated a statistically significant effect when compared to usual care (the number of people consuming fruits >2 pieces/d : RR = 1.59, 95% CI (1.22, 2.08), $p < 0.001$; quit smoking rate: RR = 1.17, 95% CI (1.04, 1.31), $p = 0.007$) (Table 1).

Another trial from the Netherlands [45] used NRS as a measure to test the effect of mobile health on satisfaction with information in infertile couples. Compared to usual care, mobile health plus usual care had positive effects on improving the satisfaction of infertile couples with information (MD = 1.57, 95% CI (0.93, 2.21), $p < 0.001$) (Table 1).

Only one trial [45] from the Netherlands used the infertility knowledge scale as an outcome to test the effect of mobile health on the level of knowledge of infertile couples. The result suggested that, compared to usual care, mobile health interventions plus usual care had statistically significant favorable effects on improving the level of knowledge of infertile couples (MD = 4.24, 95% CI (2.61, 5.87), $p < 0.001$) (Table 1).

4. Discussion

4.1 Principle of findings

In this systematic review, of eight identified RCTs, two RCTs [45, 51] were from the Netherlands and the remaining six RCTs [52–57] were from China, covering 904 participants involved in a comparison of mobile health interventions with usual care for infertility. In summary, for Chinese infertile couples, mobile health interventions were found to be superior to usual care in terms of clinical pregnancy rate, psychological status, levels of knowledge of infertility and QoL. For Dutch infertile couples, the intervention groups using mobile health interventions were not superior to the control groups that used usual care in terms of decreasing the number of people consuming vegetables >200 g/d, and fruits >2 pieces/d. However, mobile health interventions were found to be superior to usual care in terms of levels of knowledge of infertility, and satisfaction with information.

4.2 Comparisons with previous work

The results of this study are similar to those of Overdijkink *et al.* [41]. Overdijkink *et al.* [41] explored the feasibility, acceptability and effectiveness of the mobile health

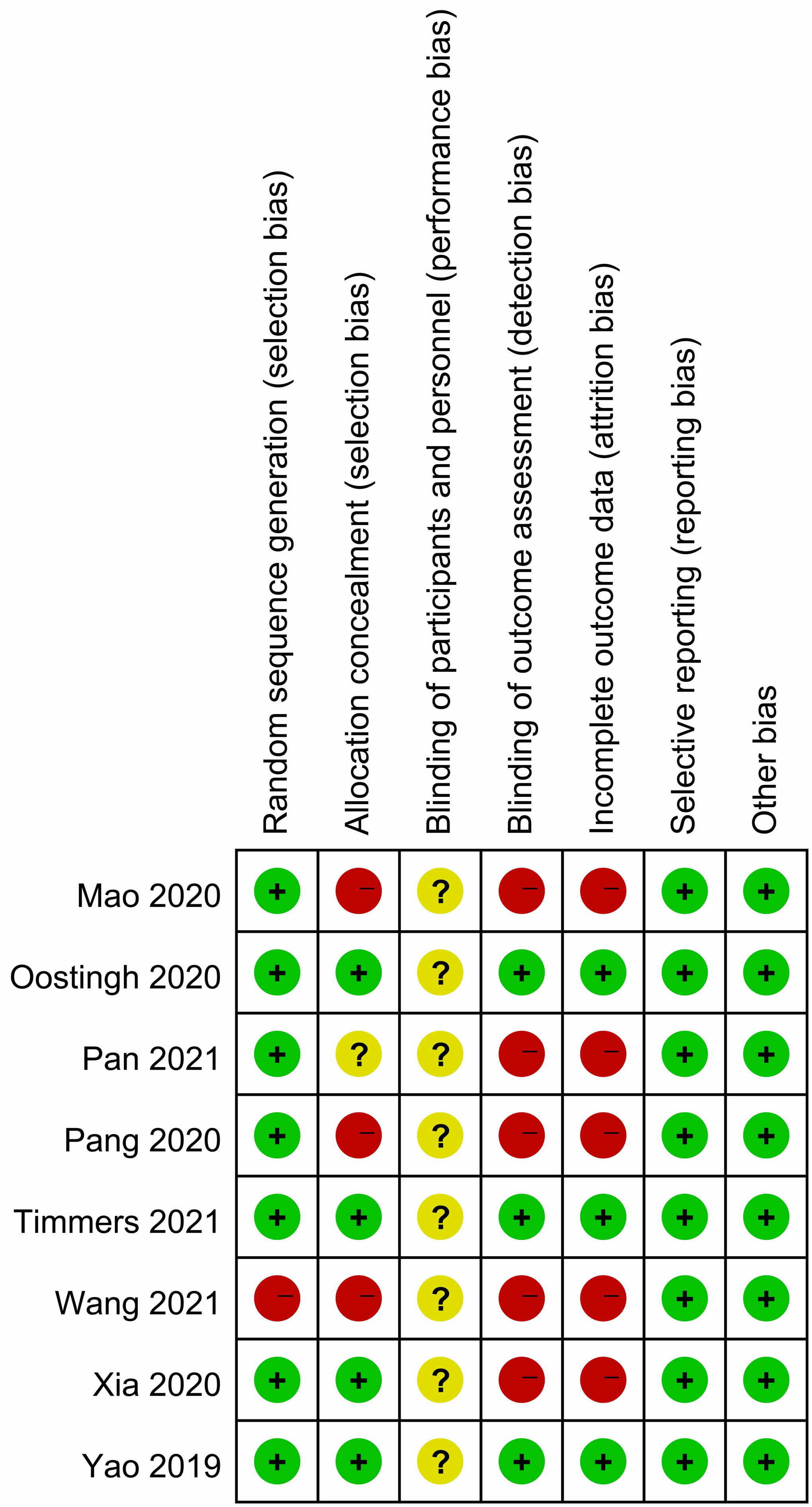

FIGURE 2. **Risk of bias summary: review authors' judgments about each risk of bias item for each included study.**

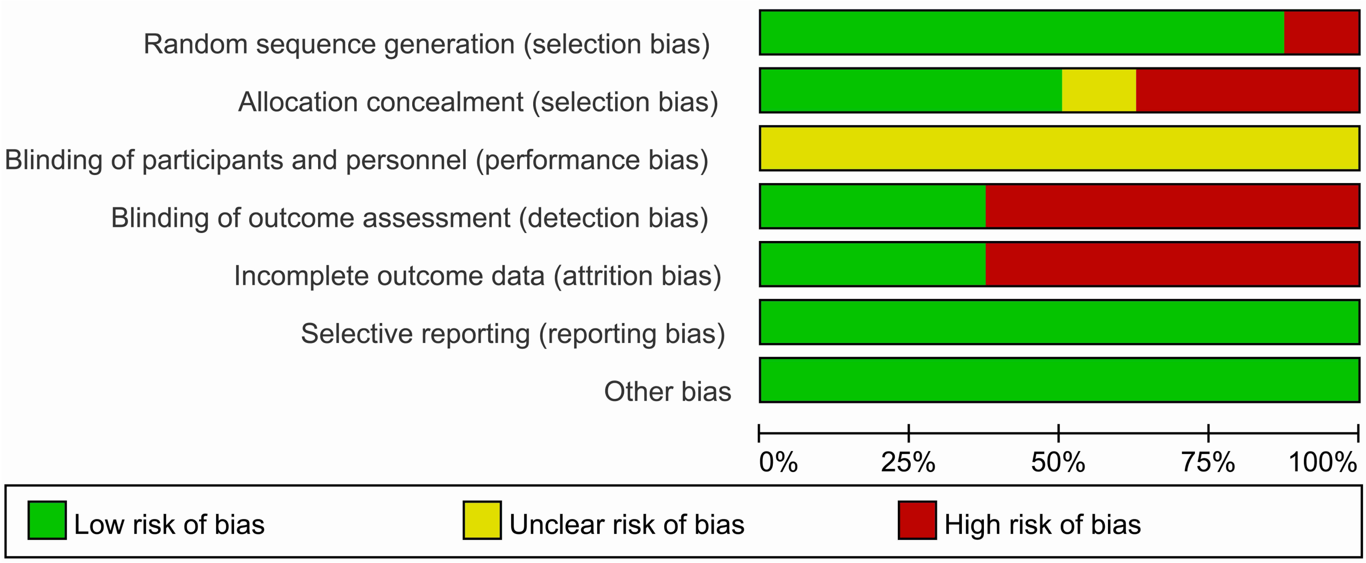

FIGURE 3. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

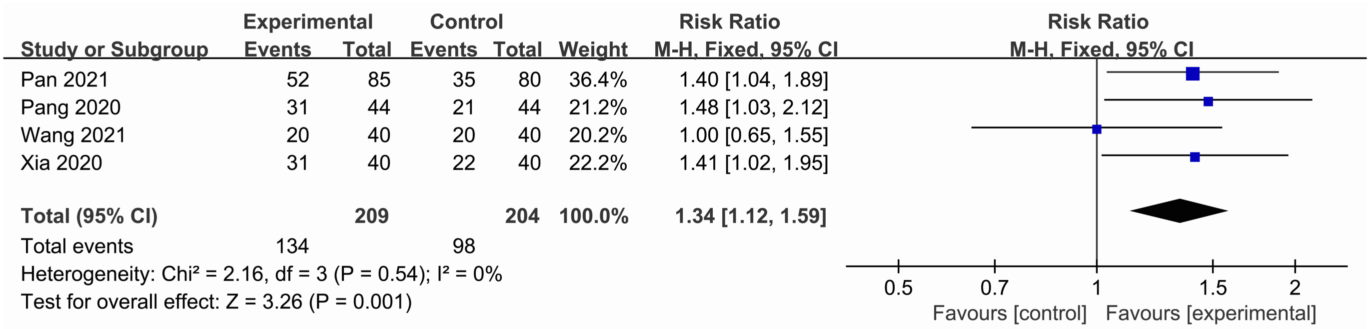

FIGURE 4. Mobile health Plus usual care *vs.* usual care on clinical pregnancy rate. Note: CI: Confidence Interval.

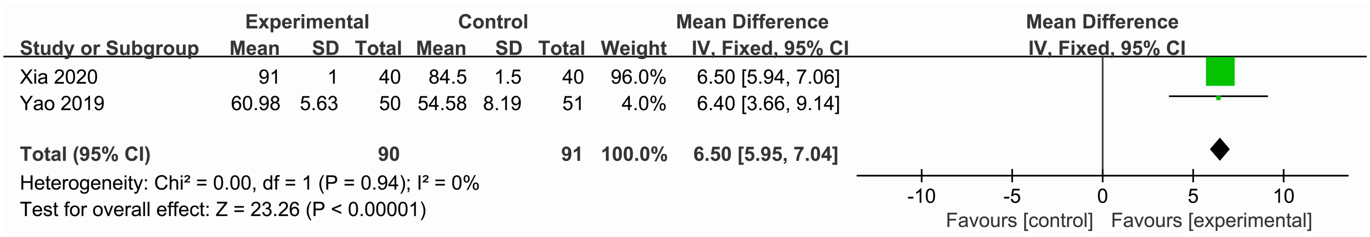

FIGURE 5. Mobile health Plus usual care *vs.* usual care on QoL. Note: SD: Standard Deviation, CI: Confidence Interval.

coaching-driven Smarter Pregnancy Program applied to pregnant women in high-income countries through a systematic review. The results showed that the mobile health coaching-driven Smarter Pregnancy Program could effectively improve the clinical pregnancy rate, increase awareness of pregnancy on pre-conception care, reduce the weight of pregnant women, help pregnant women's spouses to quit smoking, and ultimately improve the healthy behavior of both spouses. However, the systematic review by Overdijkink *et al.* [41] only included pregnant women, and so the effect of smart health on couples with subfertility is still unclear. Furthermore, the systematic review of Overdijkink *et al.* [41] only explored the effect of smart health intervention on pregnant women in high-income countries, and so the effect of smart health on low-income pregnant women in developing countries is still unknown. Compared to Overdijkink's research [41], in this systematic review, except for two RCTs [45, 51] from a high-income country, *i.e.*, the countries (Netherlands), the remaining six RCTs [52–57] are from a developing country, *i.e.*, China, and can complement Overdijkink's research [41].

4.3 Quality of included trials

In this systematic review, the evidence quality of two Dutch researchers' RCTs [45, 51] is high. It is not possible to blind the performers due to the nature of mobile health interventions. Thus, althoughfor the score for performance bias is "unclear", the other items are evaluated as "low risk". However, the quality of evidence in six Chinese researchers' RCTs [52–57] is low. For the allocation concealment, the group assignment was adequately concealed in none of the included studies, which can overestimate the results [62]. Moreover, none of the included trials mentioned blinding assessors. Only 16.67% of the included studies reported an incomplete outcome, which could result in attrition bias [63].

4.4 Mechanism of intervention of mobile health in infertile couples

Assuming that mobile health is beneficial for infertile couples, the intervention mechanism of mobile health in infertile couples is of interest.

(1) Telemedicine monitoring.

With the development of 5G technology, infertile couples and fertility physicians can appear in virtual fertility clinics at the same time. Through telemedicine monitoring, fertility physicians can complete the diagnosis and treatment of fertility couples in a virtual environment. Through wearable devices, some vital sign data, *e.g.*, heart rate, blood pressure and blood oxygen saturation, from infertile couples can be transmitted to the doctor's terminal in real time. Hormone levels in urine and saliva can be tested at home using commercially available home kits [58]. Home-based ovulation testing with luteinizing hormone kits is also an immediate need. The above monitoring results can be recorded in real time using a smart wristband and the data can be transmitted to fertility physicians. In the future, the development of family pelvic ultrasound technology can further help fertility physicians to evaluate the embryo from a remote location. Various telemedicine methods can be further improved with the development of technology.

(2) Promote male infertility patients to actively receive treatment.

In their systematic review, Oostingh *et al.* [51], from the Netherlands assessed the effect of mobile health on the dietary and lifestyle modification of infertile patients. The results showed that compared to the control group, a mobile health intervention could potentially encourage male infertility patients to correct risk factors for infertility, *e.g.*, male infertility patients have less alcohol, effectively improve the fertility knowledge of male patients, and ultimately improve pregnancy outcomes. To explore this issue, compared to women, men with infertility tend to have lower health literacy, and are not active in seeking fertility-related health information and using healthcare services. Male infertility patients are also more likely to have unhealthy eating habits and to become addicted to smoking [64]. Thus, both the ASRM and the National Institute of Health and Care Excellence suggest that male and female infertile patients need to receive an evaluation and health education in relation to infertility [65]. Mutual encouragement and mutual supervision between husband and wife can better promote a change in health behavior and improve compliance with participating in health behavior change programs [14]. However, Culley *et al.* [66] found that reproductive medicine clinical research often lacks the participation of male infertility patients, and male infertility patients are unwilling to accept infertility self-management programs with female infertility patients. Mahalik *et al.* [67] found that male infertility patients believe that seeking a fertility physician's help is a sign of their own weakness, and accepting the male masculinity. Hanna [68] and Grace [69] also found that feelings of worthlessness and the stigma attached to male inferiority caused by infertility can prevent men from seeking information related to infertility directly from fertility physicians. The online resources of mobile health have the advantages of confidentiality and accessibility, which solve the privacy problems of male infertility patients and increase the enthusiasm of male infertility patients to improve their own reproductive health.

(3) Alleviate psychological stress from couples with infertility.

There were three RCTs [52–54] from China which explored the effects of mobile health on the psychological stress of infertile couples. The meta-analysis suggested that, compared to usual care, mobile health interventions plus usual care had a favorable effect on alleviating the psychological burden of infertile couples. A recent cross-sectional online survey in the United States found that infertility is the most common stressor among the general population, almost equivalent to the fear of the COVID-19 pandemic itself [70]. In fact, the IVF treatment cycle is extremely long, which brings psychological pressure on couples with infertility. Most importantly, infertile couples tend to have more negative emotions due to poor IVF treatment results [18]. The study by Gameiro *et al.* [71] showed that electronic healthcare can help fertility physicians understand the family composition of patients through a variety of environments, and provide information support through timely delivery of notifications from remote apps to reduce anxiety and depression in fertility couples. In addition, the family can be a safer and more comfortable place for infertile couples than receiving consultation from fertility physicians in fertility clinics. Online consultation reduces the time for fertility couples to return to fertility clinics frequently, thus greatly alleviating psychological pressure on fertility couples [72, 73].

4.5 Economic aspects

Cost-benefit evidence is the most important reference basis for political decision-makers in promoting and applying large-scale home-based mobile health to infertile couples. In the early stage, Oostingh *et al.* [74] performed a cost-effectiveness analysis on the mobile health coaching-driven Smarter Pregnancy Program. The results showed that compared to usual care, the mobile health coaching-driven Smarter Pregnancy Program could save an average of €340 after two cycles of IVF per family. However, this research is limited to two IVF cycles, and the effect of the mobile health coaching-driven Smarter Pregnancy Program on cost-effectiveness that exceeds two IVF cycles is still unclear. To explore this issue, Reeder *et al.* found that [75] the use of cost-effectiveness in clinical research is closely related to the technical level of mobile health. In pilot study research, more attention is often paid to the feasibility of mobile health; in RCTs, the problems that need to be solved are often more complex. Only when mobile health technology is mature, researchers pay more attention to the economic benefits of mobile health. However, in this systematic review, economic aspects have not been taken into account in the mobile health studies of both Dutch researchers and Chinese researchers. In the future, when exploring effectiveness of mobile health applications in couples with infertility, economic aspects should be considered as an important outcome measurement.

4.6 Implications of clinical practice and further considerations

Firstly, when developing a mobile health application, the engineering teams in both China and the Netherlands are required to constantly correct technical obstacles as in the process of using the mobile health application, the inability to resolve technical barriers on time may affect the trust of users in the product, thus interrupting the use of the mobile health application [76]. Secondly, there are currently some fertility-related apps that can provide healthcare information and support for couples receiving IVF. However, Farag *et al.* [77] found that of the 2179 apps reviewed, only 7 apps were considered useful for infertile couples. In addition, due to the lack of certification as a professional fertility physician, the app score in the Apple iTunes and Google Play stores does not fully reflect the professionalism of the app. However, the score of apps in the application market will affect the selection of app by infertile couples in both China and the Netherlands. Thus, in the future, professional fertility physicians are required to participate in the development of infertility-related apps [78]. Thirdly, the privacy of infertility may be leaked on the network. Fertility physicians in both China and the Netherlands need to work with engineers to enhance the security of data transmission through blockchain technology. Fourthly , mobile health lacks uniform charging rules in the process of using it in China and the Netherlands. In China, there is no independent charging item for mobile health services. Thus, mobile health still needs to match the Chinese corresponding independent medical insurance financial system in the clinical practice process to run smoothly. Different from China, the Netherlands has established a complete mobile health services medical insurance system in both Dutch public health insurance and commercial supplementary medical insurance [79]. However, the mobile health service in the Netherlands still has the following shortcomings. First, the awareness of Dutch patients regarding mobile health is not high, *i.e.*, only 20%. Second, under the condition that the medical insurance compensation of mobile health services in the Netherlands is paid according to the number of people served and the items, the income of GPs may decrease accordingly. The introduction of mobile health services may lead to a mismatch of benefits, and so some Dutch GPs lack enthusiasm for providing mobile health services to their patients [80]. In this regard, medical insurance payers and policy makers need to work together to solve the corresponding interest mismatch problem through negotiation. Last but not least, although mobile health can facilitate the convenience of consulting infertile couples, there is also a shortage of fertility physicians' resources. Obstetricians and gynecologists, and advanced practice nurses may be able to achieve the corresponding qualification through embryology training. Due to the difference in the medical background between China and the Netherlands, the Netherlands, which focuses on community healthcare, can cope with the shortage of fertility physicians in the future by training advanced practice nurses, while China is more prone to select obstetricians and gynecologists who complete embryology training to supply the shortage of fertility physicians. In the future, infertile couples do not need to see fertility physicians in person every time they visit. After the first offline appointment with fertility physicians, infertile couples may meet with a fertility physician online regularly at key points. After infertile couples meet fertility physicians for the first time and receive an examination, the corresponding results will be synchronized to the electronic records of fertility physicians through the cloud platform, and the infertile couples will start 3 clomiphene city/intranet injection cycles and then move on to IVF. However, the obstacles to home detection technology (home pelvic ultrasound detection, hormone testing) still restrict the implementation of home-based mobile health intervention in infertile couples. Additionally, whether virtual access can largely replace face-to-face access with fertility physicians still needs more supporting evidence.

4.7 Limitations

This systematic review may have several limitations. Firstly, only eight RCTs were included in this system review. A systematic review of the Cochrane system by Oostingh *et al.* [81] showed that there were still only a few RCTs of mobile health interventions in infertile couples, and more RCTs should be included in the future. In addition, in this systematic review, although the evidence quality of two Dutch researchers' RCTs is high, the quality of evidence in six Chinese researchers' RCTs is low. Selection bias, detection bias and attrition bias are very common in Chinese researchers' RCTs, which appeared to result in the positive results found. Secondly, previous research indicated that the number of people who logged into the mobile health application would drop rapidly after using the mobile health application for 8 weeks [82]. In the intervention time of mobile health can be limited to 8 weeks to improve the utilization rate of infertile couples and to reduce the dropout rate. Thirdly, the results of our systematic review found that the short-term mobile health application intervention could improve the level of infertility knowledge of infertile couples, but it is unclear whether the mobile health application intervention can improve infertility knowledge levels of infertile couples in the long-term, which requires more longitudinal studies to prove. Fourthly, the mobile health application intervention has requirements for the knowledge and cultural level of infertile couples. Thus, it is difficult for infertile couples with a low educational level to seek online consultations with a fertility physician over the Internet. Lastly, IVF and ICSI times, and serum folate levels were not included in the outcomes.

5. Conclusions

Overall, the positive effect of mobile health on improving clinical pregnancy rate, psychological status, infertility knowledge levels, QoL and satisfaction with information was better than that of usual care. Mobile health interventions could be a viable supplement to the usual care for infertile couples. However, more high-quality RCTs need to be included in the future to prove the positive effects of mobile health on infertile couples further.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article (and supplementary material).

AUTHOR CONTRIBUTIONS

YL and WJS—designed the research study. YL, WJS, XLW and XWJ—performed the research. XWJ—analyzed the data. YL and WJS—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.jomh.org/files/article/1641249371115667456/attachment/Supplementary%20material.zip.

REFERENCES

[1] Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, *et al*. The international glossary on infertility and fertility care, 2017. Human Reproduction. 2017; 32: 1786–1801.
[2] Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Medicine. 2012; 9: e1001356.
[3] Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Human Reproduction. 2007; 22: 1506–1512.
[4] Wang J, Sauer MV. *In vitro* fertilization (IVF): a review of 3 decades of clinical innovation and technological advancement. Therapeutics and Clinical Risk Management. 2006; 2: 355–364.
[5] De Geyter C, Calhaz-Jorge C, Kupka MS, Wyns C, Mocanu E, Motrenko T, *et al.* ART in Europe, 2015: results generated from European registries by ESHRE. Human Reproduction Open. 2020; 2020: hoz038.
[6] Kissin DM, Boulet SL, Jamieson DJ. Fertility treatments in the United States: improving access and outcomes. Obstetrics & Gynecology. 2016; 128: 387–390.
[7] Wyns C, Bergh C, Calhaz-Jorge C, De Geyter C, Kupka MS, Motrenko T, *et al.* ART in Europe, 2016: results generated from European registries by ESHRE. Human Reproduction Open. 2020; 2020: hoaa032.
[8] De Neubourg D, Bogaerts K, Blockeel C, Coetsier T, Delvigne A, Devreker F, *et al*. How do cumulative live birth rates and cumulative multiple live birth rates over complete courses of assisted reproductive technology treatment per woman compare among registries? Human Reproduction. 2016; 31: 93–99.
[9] Barrière P, Avril C, Benmahmoud-Zoubir A, Bénard N, Dejager S. Patient perceptions and understanding of treatment instructions for ovarian stimulation during infertility treatment. Reproductive Biomedicine & Society Online. 2019; 9: 37–47.
[10] Mourad SM, Hermens RPMG, Cox-Witbraad T, Grol RPTM, Nelen WLDM, Kremer JAM. Information provision in fertility care: a call for improvement. Human Reproduction. 2009; 24: 1420–1426.
[11] Gameiro S, Boivin J, Domar A. Optimal *in vitro* fertilization in 2020 should reduce treatment burden and enhance care delivery for patients and staff. Fertility and Sterility. 2013; 100: 302–309.
[12] Gameiro S, Boivin J, Dancet E, de Klerk C, Emery M, Lewis-Jones C, *et al.* ESHRE guideline: routine psychosocial care in infertility and medically assisted reproduction-a guide for fertility staff. Human Reproduction. 2015; 30: 2476–2485.
[13] Van Dijk MR, Huijgen NA, Willemsen SP, Laven JS, Steegers EA, Steegers-Theunissen RP. Impact of an mHealth platform for pregnancy on nutrition and lifestyle of the reproductive population: a survey. JMIR mHealth and uHealth. 2016; 4: e53.
[14] van Dijk MR, Koster MPH, Willemsen SP, Huijgen NA, Laven JSE, Steegers-Theunissen RPM. Healthy preconception nutrition and lifestyle using personalized mobile health coaching is associated with enhanced pregnancy chance. Reproductive BioMedicine Online. 2017; 35: 453–460.
[15] Smith JF, Eisenberg ML, Millstein SG, Nachtigall RD, Shindel AW, Wing H, *et al*. The use of complementary and alternative fertility treatment in couples seeking fertility care: data from a prospective cohort in the United States. Fertility and Sterility. 2010; 93: 2169–2174.
[16] Wu AK, Elliott P, Katz PP, Smith JF. Time costs of fertility care: the hidden hardship of building a family. Fertility and Sterility. 2013; 99: 2025–2030.
[17] Lawson AK, McQueen DB, Swanson AC, Confino R, Feinberg EC, Pavone ME. Psychological distress and postponed fertility care during the COVID-19 pandemic. Journal of Assisted Reproduction and Genetics. 2021; 38: 333–341.
[18] Luk BH, Loke AY. The Impact of Infertility on the Psychological well-being, Marital relationships, sexual relationships, and quality of life of couples: a systematic review. Journal of Sex & Marital Therapy. 2015; 41: 610–625.
[19] Lundsberg LS, Pal L, Gariepy AM, Xu X, Chu MC, Illuzzi JL. Knowledge, attitudes, and practices regarding conception and fertility: a population-based survey among reproductive-age United States women. Fertility and Sterility. 2014; 101: 767–774.e2.
[20] American Society for Reproductive Medicine. Patient management and clinical recommendations during the coronavirus (COVID-19) pandemic (as of March 17, 2020). Obstetrical & Gynecological Survey. 2020; 75: 356–357.
[21] Adelman DS, Fant C, Summer G. COVID-19 and telehealth: applying telehealth and telemedicine in a pandemic. The Nurse Practitioner. 2021; 46: 34–43.
[22] World Health Organization. Global diffusion of mHealth: making universal health coverage achievable. 3th edn. WHO Document Peoduction Services: Geneva. 2016.
[23] Moss RJ, Süle A, Kohl S. EHealth and mHealth. European Journal of Hospital Pharmacy. 2019; 26: 57–58.
[24] DeLuca JM, Enmark R. E-health: the changing model of healthcare. Frontiers of Health Services Management. 2000; 17: 3–15.
[25] Mechael PN. The case for mhealth in developing countries. Innovations: Technology, Governance, Globalization. 2009; 4: 103–118.
[26] Grady A, Yoong S, Sutherland R, Lee H, Nathan N, Wolfenden L.

Improving the public health impact of eHealth and mHealth interventions. Australian and New Zealand Journal of Public Health. 2018; 42: 118–119.
[27] Free C, Phillips G, Watson L, Galli L, Felix L, Edwards P, *et al.* The effectiveness of mobile-health technologies to improve health care service delivery processes: a systematic review and meta-analysis. PLoS Medicine. 2013; 10: e1001363.
[28] Hamine S, Gerth-Guyette E, Faulx D, Green BB, Ginsburg AS. Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. Journal of Medical Internet Research. 2015; 17: e52
[29] Payne HE, Lister C, West JH, Bernhardt JM. Behavioral functionality of mobile apps in health interventions: a systematic review of the literature. JMIR mHealth and uHealth. 2015; 3: e20.
[30] Berrouiguet S, Baca-García E, Brandt S, Walter M, Courtet P. Fundamentals for future mobile-health (mHealth): a systematic review of mobile phone and web-based text messaging in mental health. Journal of Medical Internet Research. 2016; 18: e135.
[31] Donker T, Petrie K, Proudfoot J, Clarke J, Birch MR, Christensen H. Smartphones for smarter delivery of mental health programs: a systematic review. Journal of Medical Internet Research. 2013; 15: e247.
[32] Martin T. Assessing mHealth: Opportunities and barriers to patient engagement. Journal of Health Care for the Poor and Underserved. 2012; 23: 935–941.
[33] Andino J, Zhu A, Chopra Z, Daignault-Newton S, Ellimoottil C, Dupree JM. Video visits are practical for the follow-up and management of established male infertility patients. Urology. 2021; 154: 158–163.
[34] Steegers-Theunissen RPM, Steegers EAP. Embryonic health: new insights, mHealth and personalised patient care. Reproduction, Fertility and Development. 2015; 27: 712–715.
[35] Barker D, Barker M, Fleming T, Lampl M. Developmental biology: support mothers to secure future public health. Nature. 2013; 504: 209–211.
[36] Lazard AJ, Watkins I, Mackert MS, Xie B, Stephens KK, Shalev H. Design simplicity influences patient portal use: the role of aesthetic evaluations for technology acceptance. Journal of the American Medical Informatics Association. 2016; 23: e157–e161.
[37] Parry JP, Chen SH, Ku L, Anderson K, Keller SL, Omurtag K, *et al*. Is telehealth a valuable resource in reproductive endocrinology and infertility? Fertility and Sterility. 2022; 117: 690–695.
[38] Duggan M. Mobile technology fact sheet. Pew Research Institute. 2014.
[39] Montgomery R. Smartphone Video Storytelling. 1st edn. Routledge: New York. 2018.
[40] Boedt T, Dancet E, Lie Fong S, Peeraer K, De Neubourg D, Pelckmans S, *et al*. Effectiveness of a mobile preconception lifestyle programme in couples undergoing *in vitro* fertilisation (IVF): the protocol for the PreLiFe randomised controlled trial (PreLiFe-RCT). BMJ Open. 2019; 9: e029665.
[41] Overdijkink SB, Velu AV, Rosman AN, van Beukering MD, Kok M, Steegers-Theunissen RP. The usability and effectiveness of mobile health technology-based lifestyle and medical intervention apps supporting health care during pregnancy: systematic review. JMIR mHealth and uHealth. 2018; 6: e109.
[42] 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.
[43] Zung WW. A rating instrument for anxiety disorders. Psychosomatics. 1971; 12: 371–379.
[44] ZUNG WW. A self-rating depression scale. Archives of General Psychiatry. 1965; 12: 63–70.
[45] Timmers T, Keijsers M, Kremer JAM, Janssen L, Smeenk J. Supporting women undergoing IVF treatment with timely patient information through an app: randomized controlled trial. JMIR mHealth and uHealth. 2021; 9: e28104.
[46] Mousavi SA, Masoumi SZ, Keramat A, Pooralajal J, Shobeiri F. Assessment of questionnaires measuring quality of life in infertile couples: a systematic review. Journal of Reproduction & Infertility. 2013; 14: 110–119.
[47] Peltonen LM, Junttila K, Salanterä S. Front-line physicians' satisfaction with information systems in hospitals. Studies in Health Technology and Informatics. 2018; 247: 865–869.
[48] Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in Medicine. 2002; 21: 1539–1558.
[49] Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, *et al.* Updated guidance for trusted systematic reviews: a new edition of the cochrane handbook for systematic reviews of interventions. Cochrane Database of Systematic Reviews. 2019; 10: ED000142.
[50] Stuck AE, Rubenstein LZ, Wieland D, Vandenbroucke JP, Irwig L, Macaskill P, *et al*. Bias in meta-analysis detected by a simple, graphical. BMJ Clinical Research. 1998; 316: 469.
[51] Oostingh EC, Koster MPH, van Dijk MR, Willemsen SP, Broekmans FJM, Hoek A, *et al*. First effective mHealth nutrition and lifestyle coaching program for subfertile couples undergoing *in vitro* fertilization treatment: a single-blinded multicenter randomized controlled trial. Fertility and Sterility. 2020; 114: 945–954.
[52] Mao J. The effect of eHealth-based information support on family function, anxiety and depression of infertility patients. China Health Care Nutrition. 2020; 30: 70–71.
[53] Pan RH, Yuan XM, Gu WJ, Liu RH, Cao HX, Huang LT, *et al*. Evaluation of the effect of nursing mode based on mobile platform on assisted reproductive technology for infertility patients. Nursing Practice and Research. 2021; 18: 2789–2792.
[54] Pang XY, Ma ZT, Zhang W, Tang D, Zhang Y. The effect of information support intervention on infertility patients treated with assisted reproductive technology. Journal of Guang Dong Medical College. 2020; 38: 721–724. (In Chinese)
[55] Wang LS. Application of telemedicine on assisted reproductive technology for infertility patients. Journal of Modern Medicine & Health. 2021; 37: 624–626.
[56] Xia XF, Ma ZF, Hu YM, Zhao CC, Tan X, Li ZJ, *et al*. The role of health guidance based on WeChat platform in the treatment of infertility by *in vitro* fertilization/intracytoplasmic sperm microinjection. Chinese Journal of Family Planning & Gynecotokology. 2020; 12: 52–56.
[57] Yao N. The impact of continues nursing based on WeChat platform on the psychological status and quality of life of infertility patients [Doctoral dissertation]. Shaanxi University of Chinese Medicine. 2019.
[58] Watson R. Netherlands tops European healthcare index. BMJ. 2016; 352: i538.
[59] Peeters JM, Krijgsman JW, Brabers AE, Jong JD, Friele RD. Use and uptake of ehealth in general practice: a cross-sectional survey and focus group study among health care users and general practitioners. JMIR Medical Informatics. 2016; 4: e11.
[60] Yip W, Fu H, Chen AT, Zhai T, Jian W, Xu R, *et al*. 10 years of health-care reform in China: progress and gaps in universal health coverage. the Lancet. 2019; 394: 1192–1204.
[61] Zheng X, Rodríguez-Monroy C. The development of intelligent health-care in China. Telemedicine Journal and E-Health. 2015; 21: 443–448.
[62] Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA. 1995; 273: 408–412.
[63] Tierney JF, Stewart LA. Investigating patient exclusion bias in meta-analysis. International Journal of Epidemiology. 2005; 34: 79–87.
[64] Baker P. Who self-cares wins: an updated perspective on men and self-care. Trends in Urology & Men's Health. 2019; 10: 19–22.
[65] Schlegel PN, Sigman M, Collura B, De Jonge CJ, Eisenberg ML, Lamb DJ, *et al*. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part II. Fertility and Sterility. 2021; 115: 62–69.
[66] Culley L, Hudson N, Lohan M. Where are all the men? The marginalization of men in social scientific research on infertility. Reproductive BioMedicine Online. 2013; 27: 225–235.
[67] Mahalik JR, Backus Dagirmanjian FR. Working men's constructions of visiting the doctor. American Journal of Men's Health. 2018; 12: 1582–1592.
[68] Hanna E, Gough B. The social construction of male infertility: a qualitative questionnaire study of men with a male factor infertility diagnosis. Sociology of Health & Illness. 2020; 42: 465–480.
[69] Grace B, Shawe J, Johnson S, Stephenson J. You did not turn up… I did not realise I was invited…: understanding male attitudes towards engagement in fertility and reproductive health discussions. Human Reproduction Open. 2019; 2019: hoz014.
[70] Vaughan DA, Shah JS, Penzias AS, Domar AD, Toth TL. Infertility

remains a top stressor despite the COVID-19 pandemic. Reproductive BioMedicine Online. 2020; 41: 425–427.
[71] Gameiro S, Canavarro MC, Boivin J. Patient centred care in infertility health care: direct and indirect associations with wellbeing during treatment. Patient Education and Counseling. 2013; 93: 646–654.
[72] Logan S, Anazodo A. The psychological importance of fertility preservation counseling and support for cancer patients. Acta Obstet Gynecol Scand. 2019; 98: 583–597.
[73] Patel P, Kohn TP, Cohen J, Shiff B, Kohn J, Ramasamy R. Evaluation of reported fertility preservation counseling before chemotherapy using the quality oncology practice initiative survey. JAMA Network Open. 2020; 3: e2010806.
[74] Oostingh EC, Ophuis RH, Koster MP, Polinder S, Lingsma HF, Laven JS*, et al.* Mobile health coaching on nutrition and lifestyle behaviors for subfertile couples using the smarter pregnancy program: model-based cost-effectiveness analysis. JMIR mHealth and uHealth. 2019; 7: e13935.
[75] Reeder B, Meyer E, Lazar A, Chaudhuri S, Thompson HJ, Demiris G. Framing the evidence for health smart homes and home-based consumer health technologies as a public health intervention for independent aging: a systematic review. International Journal of Medical Informatics. 2013; 82: 565–579.
[76] Linardon J, Fuller-Tyszkiewicz M. Attrition and adherence in smartphone-delivered interventions for mental health problems: a systematic and meta-analytic review. Journal of Consulting and Clinical Psychology. 2020; 88: 1–13.
[77] Farag S, Chyjek K, Chen KT. Identification of iPhone and iPad applications for obstetrics and gynecology providers. Obstetrics & Gynecology. 2014; 124: 941–945.
[78] Shaia KL, Farag S, Chyjek K, Knopman J, Chen KT. An evaluation of mobile applications for reproductive endocrinology and infertility providers. Telemedicine Journal and E-Health. 2017; 23: 254–258.
[79] Huygens MWJ, Vermeulen J, Swinkels ICS, Friele RD, van Schayck OCP, de Witte LP. Expectations and needs of patients with a chronic disease toward self-management and eHealth for self-management purposes. BMC Health Services Research. 2016; 16: 232.
[80] Swinkels ICS, Huygens MWJ, Schoenmakers TM, Oude Nijeweme-D'Hollosy W, van Velsen L, Vermeulen J*, et al.* Lessons learned from a living lab on the broad adoption of eHealth in primary health care. Journal of Medical Internet Research. 2018; 20: e83.
[81] Oostingh EC, Hall J, Koster MPH, Grace B, Jauniaux E, Steegers-Theunissen RPM. The impact of maternal lifestyle factors on periconception outcomes: a systematic review of observational studies. Reprod Biomed Online. 2019; 38: 77–94.
[82] Kruglova K, O'Connell SBL, Dawadi S, Gelgoot EN, Miner SA, Robins S*, et al.* An mHealth app to support fertility patients navigating the world of infertility (infotility): development and usability study. JMIR Formative Research. 2021; 5: e28136.

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