



## ARTICLE

## Do fertility tracking applications offer women useful information about their fertile window?



## BIOGRAPHY

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## KEY MESSAGE

Available mobile fertility tracking applications are heterogenous in their underlying methods of predicting fertile days, the price to obtain full app functionality and in content and design. Inaccurate and unreliable calendar applications remain the most commonly available fertility applications.

## ABSTRACT

**Research question:** To characterize mobile fertility tracking applications (apps) to determine the use of such apps for women trying to conceive by identifying the fertile window.

**Design:** An exploratory cross-sectional audit study was conducted of fertility tracking applications. Ninety out of a possible total 200 apps were included for full review. The main outcome measures were the underlying app method for predicting ovulation, the fertile window, or both, price to download and use the app, disclaimers and cautions, information and features provided and tracked, and app marketing strategies.

**Results:** All the apps except one monitored the women's menstrual cycle dates. Most apps only tracked menstrual cycle dates ( $n = 49$  [54.4%]). The remainder tracked at least one fertility-based awareness method (basal body temperature, cervical mucus, LH) ( $n = 41$  [45.6%]). Twenty-five apps measured dates, basal body temperature, LH and cervical mucus (27.8%). Seventy-six per cent of apps were free to download with free apps having more desirable features, tracking more measures and having more and better quality educational insights than paid apps. Seventy per cent of apps were classified as feminine apps, 41% of which were pink in colour.

**Conclusions:** Mobile fertility tracking apps are heterogenous in their underlying methods of predicting fertile days, the price to obtain full app functionality, and in content and design. Unreliable calendar apps remain the most commonly available fertility apps on the market. The unregulated nature of fertility apps is a concern that could be addressed by app regulating bodies. The possible benefit of using fertility apps to reduce time to pregnancy needs to be evaluated.

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Declaration: Joyce Harper has been commissioned to analyse data from the fertility app *Natural Cycles* and is founder of the web-based forum [www.globalwomenconnected.com](http://www.globalwomenconnected.com). Dr Ali and Gürtin have no competing interests. This study was funded by University College London.

## KEYWORDS

Apps  
Conception  
Fertile window  
Fertility  
Menstrual cycle

## INTRODUCTION

Rising smartphone ownership and usage (*Office for National Statistics, 2019*) and the exponential growth seen in the software application or 'app' market (*Boogerd et al., 2015*) have precipitated a new era of digital self-tracking behaviours. Diet, exercise, sleep, blood sugars and even measures of happiness are being tracked by millions of people worldwide (*IMS Institute for Healthcare Informatics, 2015; Lupton et al., 2017*). Mobile fertility tracking apps (FTA) have emerged alongside this trend under the category of mobile health (mHealth) apps. The FTA are predominantly used by women to track their menstrual cycle, but as they tell women the day they ovulate, they are often marketed to women who wish to achieve or avoid pregnancy (*Ford et al., 2020*).

Ideally, FTA need to accurately identify the 6-day fertile window given that cycle phase lengths vary considerably between individuals (*Bull et al. 2019*). The fertile window is when conception can occur and is defined as the day of ovulation and the preceding 5 days based on spermatozoa and oocyte viability within the female reproductive system (*Wilcox et al., 1995*). Women who want to avoid pregnancy should avoid sexual intercourse within the fertile window, and couples wanting to conceive can time sexual intercourse during the window to maximize their chances of conception (*Dunson et al., 1999; Gnoth et al., 2003; Manders et al., 2015*).

Unfortunately, the most used method of fertility tracking is the calendar method, which typically identifies ovulation as occurring 14 days before the start of next menstruation (*Fehring et al., 2013*). Variation of cycle characteristics, including the day of ovulation, exists even in women with regular cycles (*Creinin et al., 2004; Fehring et al., 2006; Johnson et al., 2018; Bull et al., 2019*). Therefore, looking at menstrual cycle dates cannot be used to identify the fertility window accurately. *Bull et al. (2019)* found that the average day of ovulation was day 16.9, and this varied significantly with cycle length and age. Three accurate fertility-awareness-based methods (FABM) are available: measurement of daily oral basal body temperature (BBT) to identify a rise of 0.2–0.4°C at ovulation (*Marshall et al.,*

*1968*), identification of changes in cervical fluid consistency, which are described as characteristically 'egg-white' like closest to ovulation (*Fehring et al., 2002; Alliende et al., 2005; Scarpa et al., 2006*) and measurement of urinary LH levels, which rise 24–36 h before ovulation, thus identifying the 'peak' fertile day (*Direito et al., 2013*). Less evidence-based FABM are available, such as cervical position and sensation (*Owen, 2013*).

Each FABM has its own strengths and limitations, which are often different for each individual (*Owen, 2013*). The FTA use one or a combination of these fertility indicator methods to predict ovulation and thus the fertile window.

Previous studies exploring the content of FTA mostly focus on their utility for use as contraception as opposed to conception (*Freundl et al., 1998; Berglund Scherwitzl et al., 2015; 2016; 2017; Duane et al., 2016; Simmons et al., 2017; Bull et al., 2019b; Earle et al., 2020*). Small observational studies provide an insight into what apps are available and their features and functionality; however, minimal data collection points and large exclusion criteria means that little is still known about the apps and the FTA market (*Setton et al., 2016; Moglia et al., 2016; Freis et al., 2018; Fowler et al., 2020*). Moreover, the difference in the rate of scientific paper publication versus the swift rate of app publication or update means that previous studies are already outdated. Therefore, the present study aims to characterize FTA available on Apple's iOS app store and review their utility for use for conception. This study is particularly targeted to women who use these apps, healthcare professionals, researchers and regulatory bodies as it aims to provide an overview of currently available FTA and what information they provide to, and collect from, users, and whether these apps are useful and should be recommended for couples trying to conceive.

## MATERIALS AND METHODS

An exploratory cross-sectional audit study was conducted to review all available FTA on Apple's mobile iOS app store (*App Store, 2019*), which has the largest mobile app market share in the UK (*Artyom, 2019*). Android's GooglePlay platform (*Google Play, 2019*) was also used to check whether

apps were available in both platforms and to extract information about app downloads to give an indication of app popularity. A pilot study of 10 apps that were present on both platforms were screened for differences in the app store information and user interface to ensure that apps were not drastically different to their iOS counterparts. All apps were similar in content and user interface across both platforms, thereby allowing for meaningful discussions regarding app popularity using GooglePlay's app downloads as a parameter.

The search term 'fertility tracker' was inputted into the search feature of the iOS app store after independent pilot searches using all possible permutations of the terms 'fertility', 'ovulation', 'menstrual', 'menstruation' and 'period', combined with either one of 'tracker', 'calculator', 'calendar' and 'predictor'. The top 10 apps were noted and were searched for within the term 'fertility tracker', the combination providing the most search results (200 apps total), which encompassed all resulting apps and thus was selected as the search term for this study. The first 10 apps available via iOS app store searches reflect the most relevant results to the search term (*Patel, 2019*).

A total of 200 apps were eligible for inclusion as limited by the search results possible on the iOS app store database. Inclusion criteria consisted of apps that attempted to predict ovulation, the fertile window, or both, apps that could be used for conception (whether stated or inferred from app use), apps available in English language and those usable without requiring a connected device. Apps that were faulty, had not been updated for at least 3 years as well as those with an unknown date of last update were excluded from the study.

The FTA meeting inclusion criteria were reviewed in three phases of data collection. All apps eligible for inclusion were identified by the first search (February 2019). App presence on GooglePlay and number of downloads were also recorded at this stage. The second phase (March to May 2019) included the selection of each app in turn and inputting relevant information as per the codebook (Supplementary Table 1) using the app's app store description page, website and on app use. Purchases were made where

required for app download or to obtain a fully functioning version of the app. Data collection points were informed by research evaluating websites, apps, or both, as well as previous studies reviewing FTA (Eysenbach and Wyatt, 2002; Lee and Raghu, 2014; Duane et al., 2016; Moglia et al., 2016; Setton et al., 2016; Freis et al., 2018). The final phase of data collection took place over a 2-week period in June 2019 when all inputted data were re-checked and updated where appropriate.

Each FTA was described in terms of the underlying method used to predict ovulation, the fertile window, or both, the cost required to download the app and additional purchases leading to a fully functioning version of the app. The underlying app method was determined using the app store description page, website, the app itself or as a last resort, by emailing the app developers. App ratings were analysed only on apps with more than 100 reviews at the time of data collection. ‘Feminine’ apps were defined by a predominantly pink colour scheme or feminine figures and images within the app such as flowers, hearts or female characters, also known as ‘pinkification’ (Gambier-Ross et al., 2018).

Descriptive statistics were used to analyse the resulting data with further stratification by app prediction method and price where appropriate. Review by an ethical review board was not required for this study as no risks to human participants were perceived.

## RESULTS

### What fertility apps exist?

A total of 106 out of 200 apps met the inclusion criteria. Ninety-four apps were excluded initially, of which 44 apps were not relevant to fertility and seven did not attempt to predict the fertile window (FIGURE 1). A further 16 apps were excluded because the underlying app method could not be determined. Ninety apps were, therefore, included for full app review and analysis (Supplementary Table 2). Nine groups of underlying prediction methods were identified (TABLE 1). All the apps except one monitored the women’s menstrual cycle dates. Most apps only tracked menstrual cycle dates ( $n = 49$  [54.4%]) of which 12 apps (28.6%) measured other fertility indicators such as BBT but did not include them in their predictions for

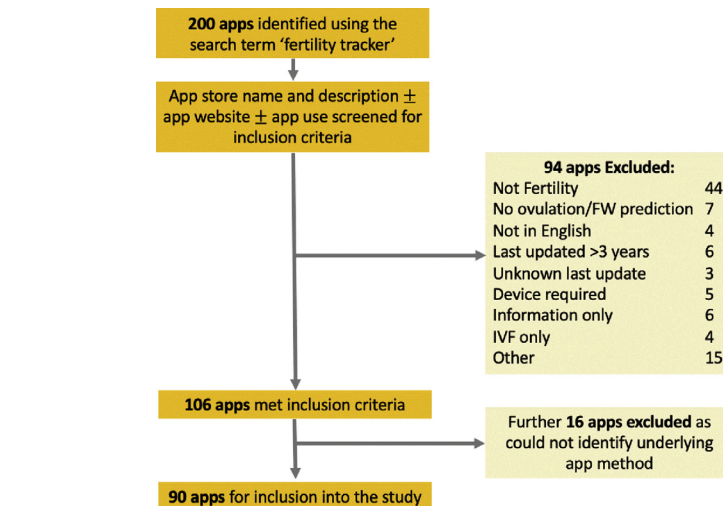


FIGURE 1 Method of application selection. App, application.

ovulation, the fertile window, or both. The remainder tracked at least one fertility-based awareness method (BBT, cervical mucus, LH) ( $n = 41$  [45.6%]). Twenty-five apps measured dates, BBT, LH and cervical mucus (27.8% overall [ $n = 25$ ]). Overall, a total of 16 apps (17.8%) allowed users to track fertility indicators, which were not included in ovulation and fertile window predictions.

Sixty-eight apps (76%) were free to download and 22 apps (24%) required purchase, ranging from £0.99 to £9.99 (FIGURE 2A). Of the 68 apps that were free to download, 31 apps (46%) were completely free requiring no additional charge for full app access. Overall, 38 (42%) apps had in-app purchases, including 37 of the 68 free to download apps (54%) and one of the 22 apps requiring purchase to download (5%). The in-app purchases ranged in price from £1.99 to £363.48 annually (FIGURE 2B). No association was found between app price and app method.

Most apps (78%) could be found in the ‘Health and Fitness’ category of the iOS app store. Eleven of these 70 apps (16%) were placed in the Top 200 for this category with *Flo* placing highest at fifth. Other categories included medical (17%), lifestyle (4%) and entertainment (1%). Fifty-one apps (57%) provided their users with a caution or disclaimer, of which five apps (10%) advised against the use of their app for contraception purposes, 18 apps (35%) cautioned users on the accuracy of the app’s predictions and only nine apps (18%) stated that their app was not a medical device, and thus

should not be used for medical purposes. *Natural Cycles* was the only app to explicitly state in all available locations, i.e. app store name, app store description page, app website and the app itself, its intended use as contraception.

Only 50% of apps ( $n = 45$ ) were regularly updated by app developers (FIGURE 3). The most frequently updated apps were *BetterME*, *MIA FEM*, *Flo* and *Clue*. *BetterME* and *MIA FEM* were released in 2019, whereas *Flo* and *Clue* were released in 2015 and 2013, respectively, yet are still able to maintain close to weekly updates. These two apps were also two of 30 apps that were also available on GooglePlay and were downloaded over 10 million times each on GooglePlay alone (FIGURE 4). They were only surpassed by *Period Tracker Period Calendar*, which had over 100 million downloads.

Only 29 apps (32%) had over 100 app reviews and were, therefore, included for further analysis of app ratings. All these apps had a rating of at least four out of five (FIGURE 5). The two apps with over 10,000 reviews were *Clue* and *Flo* with 36,546 and 66,799 reviews, respectively. Both apps had an average rating of 4.7. The top-rated app was *MIA FEM* with a rating of 5, although with only 138 reviews. Calendar apps (45%) were rated similarly to apps with calendar, BBT, cervical mucus and LH functionality (40%).

### What additional features are provided by the apps?

The range of features tracked or provided by the apps in this study are presented

**TABLE 1 APPLICATION METHOD FOR PREDICTING OVULATION, THE FERTILE WINDOW, OR BOTH**

App method	Total apps n (%)	Number of apps that tracked other fertility indicator measures but did not use them in their predictions		
		Total apps, n (%) <sup>a</sup>	Types of other measures tracked	n
Calendar	49 (54.4)	14 (28.6)	BBT + CM + LH	8
			BBT + CM	4
			BBT	2
Calendar + BBT + CM + LH	25 (27.8)	0 (0)	NA	n/a
Calendar + BBT + CM	7 (7.8)	0 (0)	NA	n/a
Calendar + BBT + LH	1 (1.1)	0 (0)	NA	n/a
Calendar + BBT	2 (2.2)	1 (50.0)	LH + CM	1
Calendar + CM	3 (3.3)	1 (33.3)	LH	1
Calendar + CM + LH	1 (1.1)	0 (0)	NA	n/a
Calendar + LH	1 (1.1)	0 (0)	NA	n/a
CM	1 (1.1)	0 (0)	NA	n/a
Total	90	16 (17.8)		

App, application; BBT, basal body temperature; NA, not appropriate.

<sup>a</sup> As a percentage of number of apps for that application method, e.g. 14 apps or 29% of the 49 calendar applications.

in **TABLE 2**. All features were regarded as 'desirable' except for advertisements as reported by *Gambier-Ross et al. (2018)*. Free apps provided or tracked more features than those requiring purchase to download. Only free apps, however, contained advertisements, of which 62% allowed removal of these with an additional in-app purchase. Specific women's health-related issues were tracked by very few apps (**TABLE 3**).

Of the 32 apps (36%) that link to other apps and devices, 88% linked to Apple Health, 16% to FitBits and 12% to Apple or Google Calendar only. Thirty-eight apps (42%) allowed users to share their tracked information with others, i.e. their doctor, partner or anyone else. Only 27 apps (30%) had a community feature in which users could engage with other users via the app. Twenty-four apps (27%) had a public forum, with one app (*GP Apps*) requiring an additional purchase to access this feature. Private messaging was available on 11 apps, of which five required an additional purchase (*Glow, Eve, Ovia, MIA FEM* and *Maya*). These five apps also required additional purchase to access healthcare professionals or health coaches via the app. Two apps allowed access to this feature for free (*Moody Month* and *billingsMentor*). Only four apps (4%) had all three features (*Ovia* [only to its US users], *Ela Fertility and Ovulation Tracker*, *Glow* and *Kindara*).

Forty-four apps (49%) provided users with educational insights, of which six were paid (27% of all paid apps), 38 were free (56% of all free apps) and two apps required an additional purchase for access (*BetterME* and *Glow*). The quality ratings are shown in **FIGURE 6**. *Clue* and *SmileReader* scored highest for quality of educational insights provided, with *Ovia* and *Ovulation Calculator Fertile Tracker* scoring three points. All six paid apps scored 1 for quality of educational insights provided.

#### How do the apps market themselves?

Eighty-one apps (90%) targeted females only, seven apps (8%) targeted both genders and two apps (2%) targeted males only (*Female Calculator for Men* and *Period Tracker for Men*) (**FIGURE 7**). Apps targeting both genders were set for female users as default. They also asked users, however, if they wanted to use the male version of their app instead. All apps targeting males allowed input of their partner's menstrual data or allowed linking their profile with their partner's profile.

Most apps (63%) were targeted towards users aged 12 years and over (**FIGURE 8**). Only seven apps (8%) were targeted at users aged 17 years and over (*Natural Cycles, Eve, Ovulation Calculator & Fertility, Hormone Horoscope Lite* and *Pro, Maya* and *Easy@Home*). Twenty-five apps, however, targeted users aged 4 years and over or 9 years and over. Only

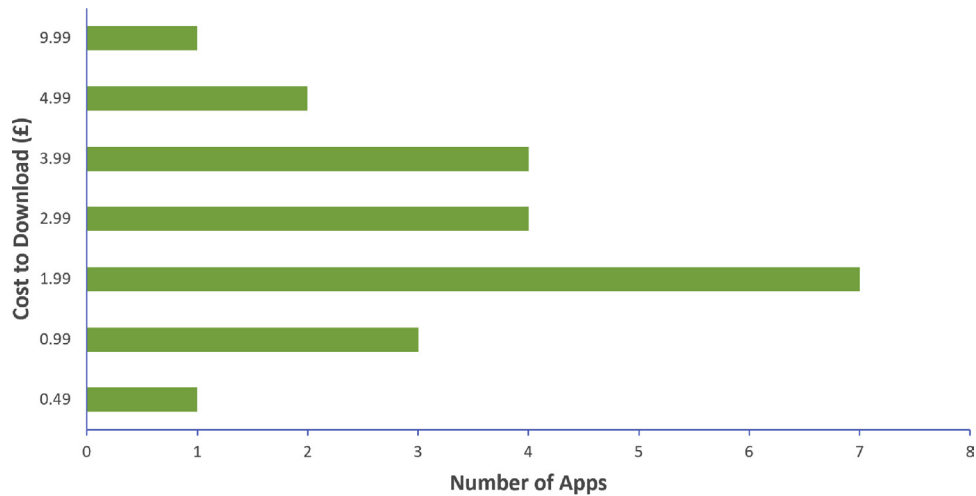
one app (*Magic Girl Teen*) specifically stated its audience within its name, description and on app use. This app was tailored to girls from menarche into their adolescent years (target age group  $\geq 9$  years); however, it was the only app to also have a parental control feature.

Sixty-three apps (70%) were classified as 'feminine' apps, of which 26 apps had a predominantly pink colour scheme. Six of these apps had both male and female versions, of which three changed their colours and themes for male users (*Glow, Femometer* and *Easy Period-Lite*). The other three apps did not change their look according to user gender (*Ela Fertility and Ovulation, Cycles* and *Ovulation Calculator App*).

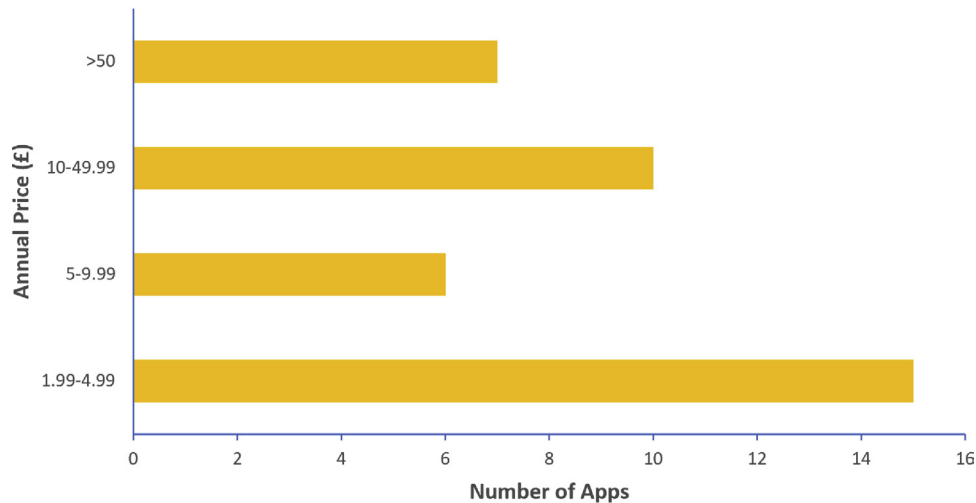
One particular app included in this study related the female menstrual cycle to phases of the moon (*Goddess Moon Dial*). This app clearly markets itself towards users who believe these cycles are related; however, the underlying method of the app is a calendar app that calculates its predictions from cycle length and dates of menstruation.

## DISCUSSION

The principal aim of the exploratory cross-sectional study was to characterize all available FTA on the iOS app store to determine if they offer women accurate and useful information regarding their fertile window. Ninety



(a)



(b)

**FIGURE 2** Cost to download applications and in-application purchases: (2A) the price distribution of applications that required purchase; and (2B) the spread of price of applications that had in-application purchases.

apps were reviewed and varied vastly in their underlying method of predicting fertile days, price to users to enable full functionality, information collected and provided to users, and their positioning and market strategy within the FTA market.

It is impossible to predict the day a woman ovulates by simply looking at her menstrual cycle dates (*Creinin et al., 2004; Fehring et al., 2006; Scarpa et al., 2006; Manders et al., 2015; Johnson et al., 2018; Bull et al., 2019*). It is alarming that calendar apps were found to be the most commonly available FTA, accounting for 54.4% of apps in the present study (**TABLE 1**). These apps

are giving women inaccurate information about their fertile window. Those trying to conceive using these apps may waste precious time if a couple have intercourse at the wrong time, and for those trying to avoid pregnancy they may conceive as they are avoiding intercourse on the wrong days. *Freis et al. (2018)* scored calendar FTA as 0/30 in their app evaluation and rating scale. In the present study, 28.6% of the calendar apps reviewed were found to track other fertility indicator measures, such as BBT, cervical mucus or LH; however, they do not incorporate such measures into their prediction algorithms. Again, this gives women inaccurate information about their fertile window. It is, therefore,

extremely important that users are made aware that the time, effort and cost they spend measuring such fertility indicator measures may be wasted, and that the apps may not actually be refining their fertility predictions based upon these indicators. To our knowledge, this is the first study to quantify such a phenomenon.

Despite this, 45.6% of FTA use evidence-based fertility indicator measures (*Manhart et al., 2013*) in their predictions (**TABLE 1**), although the specific method variation and the algorithm used is extremely difficult or impossible to determine, and thus will have variable efficacies when only considering

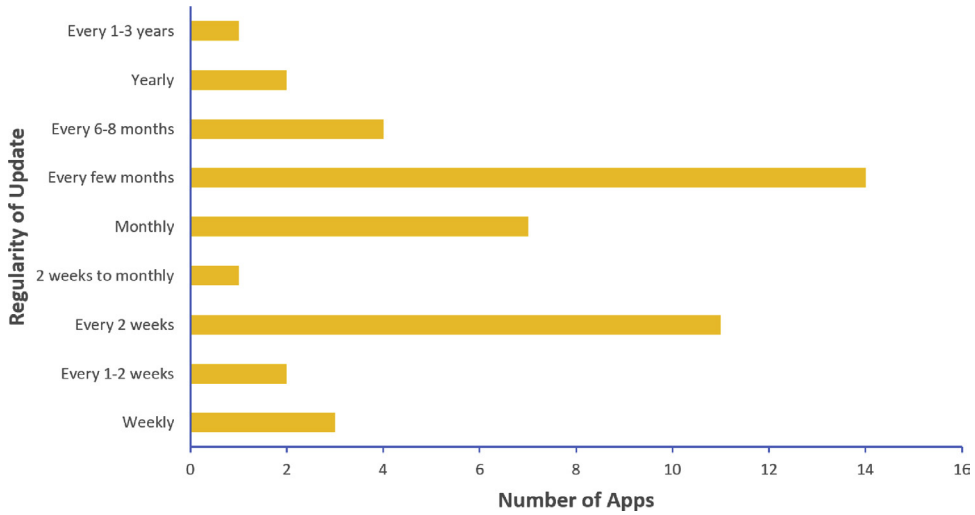


FIGURE 3 Regularity of application update. Includes applications with at least two updates occurring at regular intervals only.

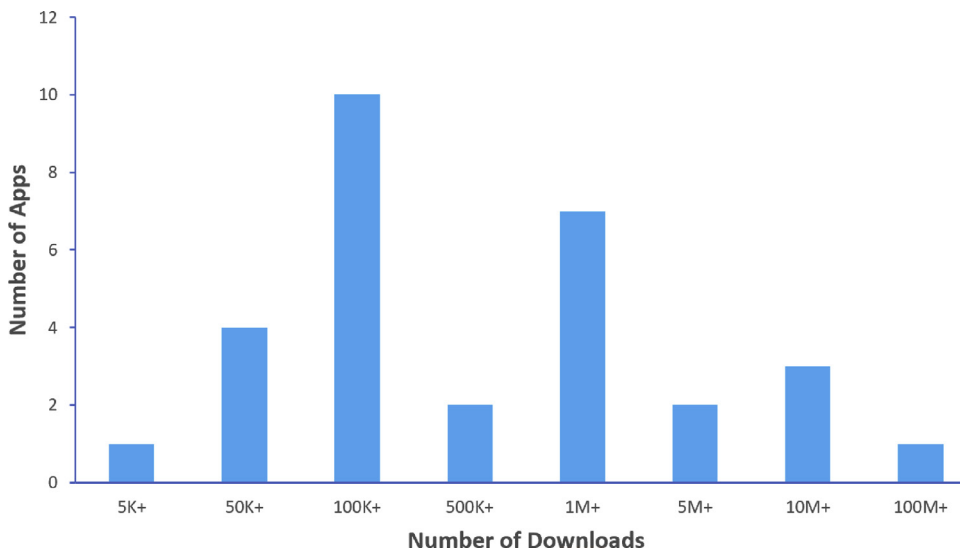


FIGURE 4 Number of application downloads in Google Play Store. K, thousand, M, million.

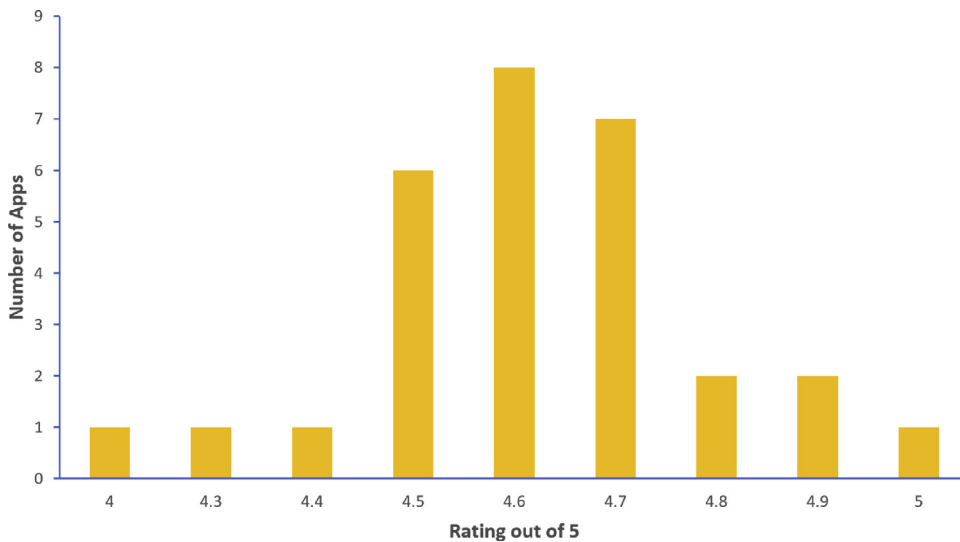


FIGURE 5 Application store rating for the 29 applications with over 100 reviews.

**TABLE 2 THE NUMBER OF APPLICATIONS TRACKING ADDITIONAL FEATURES**

Additional features	Free apps, n (%) (n = 68)	Paid apps, n (%) (n = 22)	Total, n (%) (n = 90)
Bleeding type	47 (69)	12 (55)	59 (66)
Intercourse	49 (72)	14 (64)	63 (70)
Symptoms	46 (68)	12 (55)	58 (64)
Mood	42 (62)	11 (50)	53 (59)
Sleep	20 (29)	3 (14)	23 (26)
Weight	28 (41)	7 (32)	35 (39)
Pregnancy tests	24 (35)	7 (32)	31 (34)
Journal	47 (69)	15 (68)	62 (69)
Pregnancy mode	25 (37)	6 (27)	31 (34)
Pill reminders	25 (37)	4 (18)	29 (32)
Fertility treatment	6 (9)	0 (0)	6 (7)
Customizable theme	24 (35)	8 (36)	32 (36)
Push notifications	61 (90)	10 (45)	71 (79)
Privacy	23 (34)	12 (55)	35 (39)
Link to other apps	28 (41)	4 (18)	32 (36)
Share information	27 (40)	11 (50)	38 (42)
Advertisements	22 (32)	0 (0)	22 (24)
Community	22 (32)	5 (23)	27 (30)
Educational insight	38 (56)	6 (27)	44 (48)

APP, applications.

**TABLE 3 THE NUMBER OF APPLICATIONS TRACKING SPECIFIC WOMEN'S HEALTH-RELATED ISSUES**

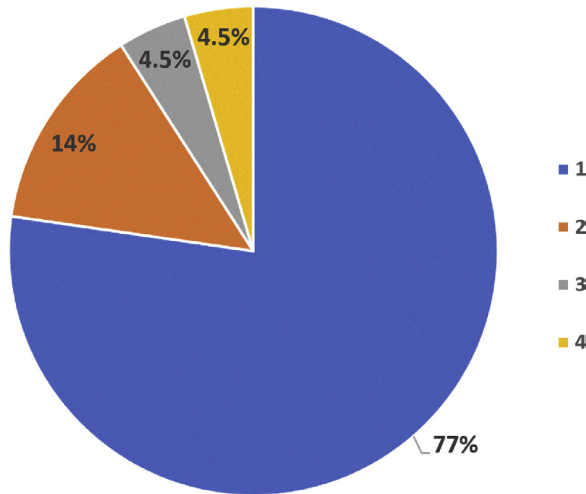
Tracked features	Apps, n (%) (n = 90)
Preconception: folic acid	1 (1)
Pregnancy: morning sickness, miscarriage	2 (2)
Menopause: hot flashes, vaginal dryness, other symptoms	3 (3)
Breast: examination, mammogram	5 (6)
Pelvic: examination, cervical smear	2 (2)
Menstruation: blood collection method	1 (1)
Infections: thrush, sexually transmitted infections	2 (2)

perfect use. For this reason, the broad categorization of nine app methods classified by the present study needs further characterization and evaluation. Moreover, the fact that no FABM are 100% accurate (*Manhart et al., 2013*) makes the fact that only 20% of apps in the present study cautioned users about the app's potential method inaccuracies is concerning. In addition, *Fowler et al. (2020)* found that the availability of a terms of service, privacy policy, or both, that typically contain such cautions or disclaimers were either lacking or difficult to find within fertility tracking apps.

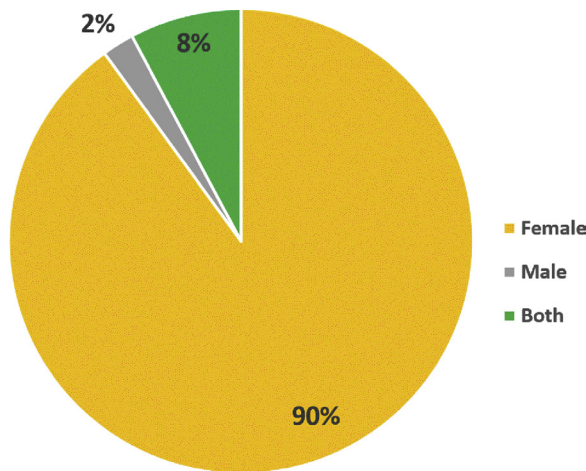
Only 10% of apps mentioned their app was not to be used as a medical

device. The European *Medical Device Directive (1993)* identifies 'software' as 'medical devices', only *Natural Cycles* is registered with the Medicine and Healthcare Products Regulatory Agency (MHRA) in England (*Anonymous, 2012; Buijink et al., 2012; Cummings et al., 2013; McCartney, 2013*). The MHRA defines a 'medical device' as one that can potentially harm its users, including those that interpret data to perform a calculation. It is therefore unusual that FTA, which routinely predict ovulation, the fertile window, or both, using data collected from users, i.e. cycle and period dates, FABM, or both), are not currently regarded as 'medical devices' necessitating regulation.

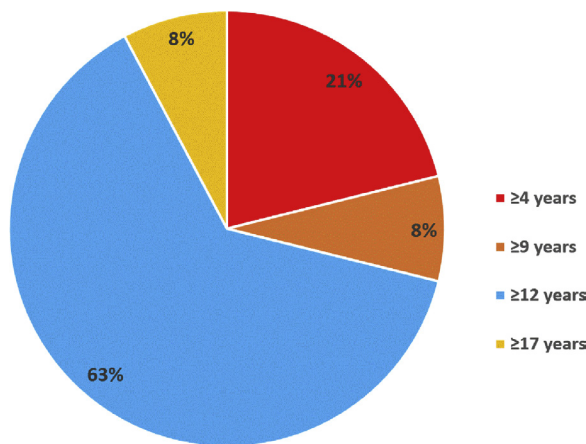
Surprisingly, free apps consistently track and provide more desirable features than paid apps (*TABLE 2*), which have been suggested previously to be better quality (*Lee and Raghu, 2014*). Apps tracking women's health-related issues specifically are small in number, suggesting there is scope and opportunity for developers to conduct health promotion practices to positively influence public health. An ideal fertility app will provide its users who are trying to conceive with information about preconception care, such as being a healthy weight, regular exercise, folic acid reminders and smoking cessation (*Stephenson et al., 2018*). The app would also ideally discuss female fertility decline (*Harper et al., 2017*) and provide its users with advice or recommend them to their clinician if users had not conceived within a year of trying (*Lupton, 2015; Harper et al., 2017*). This provides exciting opportunities for healthcare providers and public health bodies to engage with FTA development to encourage and engage such positive health behaviours. Further opportunities exist for healthcare professionals to counsel users within these apps. *Starling et al. (2018)* recommend community interactive features, particularly access to healthcare professional personal advice within FTA to ensure users are well-supported in their fertility goals.



**FIGURE 6** The quality rating of educational insights. Scores 1 to 4 from lowest to highest: 1, no references; 2, no peer-reviewed references; 3, some peer-reviewed references; 4, all peer-reviewed references.



**FIGURE 7** Application gender target.



**FIGURE 8** Application age target.

The present study provides new insights into the FTA market and potential user experience. The main strength of this study is its simplicity. A broad overview of the current state of fertility apps that can be used by couples wanting to conceive has not been previously described. Questions such as ‘what FTA exist’, ‘what information do they ask for’, ‘what information do they provide’ and ‘how do they market themselves’, have not been previously answered. This study makes huge strides to understand this market and has identified opportunities to grasp and concerns to address for users, developers, healthcare providers and policy makers alike. The study is, however, limited by its lack of specific detail, although the authors hope that this study can be used by future researchers to explore these highlighted areas in more detail. Furthermore, the FTA reviewed may have been updated after the end of data collection and certainly by publication and, therefore, the findings presented may be inaccurate.

In conclusion, the currently available mobile fertility tracking apps are heterogenous in their underlying methods of predicting fertile days, the price to obtain full app functionality, and in content and design. Inaccurate and unreliable calendar apps remain the most commonly available apps on the market but give women inaccurate information about their fertile window. Such apps must stop telling women about their day of ovulation. Only apps that measure at least one FABM should be marketed as FTA. The unregulated nature of fertility apps is a major concern that needs to be addressed by app regulating bodies. A great opportunity exists for healthcare professionals to become involved with app development and improvement, as well as opportunities for direct-to-user public health engagement and fertility education through these apps. Future work to characterize the number, quality and type of educational insights to evaluate the underlying app prediction methods and to assess the presence of unsubstantiated claims are all important next steps to improving research and knowledge within this field.

**SUPPLEMENTARY MATERIALS**

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.rbmo.2020.09.005](https://doi.org/10.1016/j.rbmo.2020.09.005).



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