NICE advice

Natural Cycles for monitoring fertility

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is the Natural Cycles app for monitoring fertility to prevent a pregnancy for people wishing to use a calendar fertility-awareness method of contraception. Other more reliable forms of contraception are available.
- The **innovative aspects** are that Natural Cycles is the first fertility-awareness app that comes with a basal thermometer and has been CE-marked as a medical device.
- The intended **place in therapy** is as a fertility-awareness contraception method. It would be used as a strategy to monitor ovulation, predict fertility, and may be used alongside abstinence or a barrier contraceptive method.
- The **main points from the evidence** summarised in this briefing are from 3 studies (2 retrospective analyses and 1 prospective observational study). These included 70,113 people using the app at home with typical follow-up of 6 to 9 months. They show that Natural Cycles can be used as a fertility-awareness contraception method. No evidence was identified on using the app to help plan a pregnancy.

- **Key uncertainties** around the evidence or technology are that Natural Cycles has not been directly compared with any other contraception.
- The **cost** of Natural Cycles is £49.99 for a 1-year subscription. Most other contraception is available at no charge to the user from standard NHS services.

The technology

Natural Cycles (Natural Cycles Nordic AB) is an app available for iOS and Android mobile devices. The user inputs daily basal body temperature measurements and menstruation data. A proprietary algorithm then uses this information to predict ovulation and fertility. The app will be able to provide a more accurate prediction for the user as they input more data. The user can choose to share their anonymised data with the company (for research purposes).

The results for each day are reported as either a 'green day', which means the user is unlikely to be fertile; or a 'red day', which means the user is likely to be fertile. This means they should either abstain from sex or use barrier contraceptives to avoid pregnancy. It is also possible to switch modes in the app, so the data can be used to tell the user when they are most likely to be able to conceive, if they are trying to get pregnant.

The app is unlikely to be suitable for people with highly irregular menstrual cycles. This is because predicting fertility is more difficult in these circumstances, resulting in an increased number of 'red days' (when the user must abstain from sex or use barrier contraceptives). The user must also take their basal temperature each morning as soon as they wake up, so a regular sleeping pattern improves the accuracy of this.

Innovations

Natural Cycles is the first app-based contraceptive with a CE mark that integrates basal thermometer body temperature readings. Natural Cycles differs from other non-hormonal contraception methods (such as fertility awareness planning on a calendar) because it is easier to use and training is not needed.

Current care pathway

There is a wide range of contraception methods available to people in the UK. These

include barrier methods (condoms, caps and diaphragms), hormonal methods (combined pill, progesterone-only pill, contraceptive injections and patches), and other devices (implants, intrauterine devices and systems, and vaginal rings). Natural family planning (fertility awareness) can also be used as a method of contraception, but the effectiveness of this method depends on appropriate education and adherence. Only barrier contraceptives can protect against sexually transmitted diseases.

NICE's guideline on long-acting reversible contraception has been identified as relevant to this care pathway.

Population, setting and intended user

Natural Cycles may be used alongside barrier contraceptives or instead of other fertility-awareness methods. It works best with a regular menstrual cycle and sleeping pattern.

Natural Cycles is most likely to be used by people who prefer to use a non-hormonal method, and when other methods of contraception are unsuitable or contraindicated.

The app will be used at home and includes instructions on its correct use. It is expected that minimal input from clinicians will be needed.

Costs

Technology costs

Natural Cycles costs £49.99 for a 1-year subscription. This includes the basal thermometer.

Costs of standard care

Most types of contraception are available free of charge as part of standard NHS services. Some people may choose to pay for some methods because of convenience of access or for other reasons. The cost of the oral contraceptive pill is between £11 and £18 per year to the NHS.

Resource consequences

Natural Cycles does not need a prescription or consultation. The company states that it is currently being used by about 250,000 people in the UK.

If more people use the Natural Cycles app as a method of contraception there may be a decrease in the number of appointments for contraception advice. However, if Natural Cycles is not as effective at preventing pregnancy as the methods users used before Natural Cycles, there may be an increase in resources needed for a termination of pregnancy or delivery of an unplanned pregnancy.

Regulatory information

Natural Cycles is a CE-marked class IIb medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Natural Cycles may not be suitable for people with a learning disability. It is intended for use by women and trans people who ovulate. Sex and gender are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with NICE's interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Five studies are summarised in this briefing. These include data from 70,113 people (it is

likely that there was substantial overlap between the people in the studies).

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The 5 studies comprise observational data from people using the app who gave consent for their data to be shared for research purposes when downloading the app. The studies collected real-world data from people using the app. These people had no additional instructions or information from the investigators. There are no studies comparing Natural Cycles with other contraceptives and none that examine the effectiveness and accessibility of using the app to help plan a pregnancy. The life table analyses show Natural Cycles has a typical-use pregnancy rate of around 7%. This compares favourably with rates for calendar fertility-awareness methods (24%) or condom use (8%). NICE has endorsed an FPA resource comparing different contraceptive methods. Failure rate measures for different contraceptive methods are known to vary by country, age of person using the method, previous pregnancies, and type of previous contraceptive use. Grenfell et al. 2020 reports qualitative data of people in the UK about their experiences using a fertility-awareness app. This has not been summarised in the briefing because it does not report the efficacy of the app to prevent or help pregnancy.

Bull et al. (2019)

Study size, design and location

Prospective observational study using data from 16,331 people using the app (using app in pregnancy prevention mode) in Sweden.

Intervention and comparator

Natural Cycles.

Key outcomes

On average, users entered data for 8 months. A 1-year typical use pearl index (PI) of 6.1 plus or minus 0.2 and a 13-cycle failure rate of 6.3% plus or minus 0.6%. People who had

not recently used hormonal methods of contraception (n=9,381) had a PI of 5.1 plus or minus 0.3 and a 13-cycle failure rate of 5.2% plus or minus 0.7%. People who had recently used hormonal methods of contraception (n=6,950) had a PI of 7.5 plus or minus 0.4 and a 13-cycle failure rate of 8.1% plus or minus 1.0%. People that used condoms as a primary form of contraception before using Natural Cycles (n=2,411) had a PI of 3.5 plus or minus 0.5 and a 13-cycle failure rate of 3.6% plus or minus 1.0%. People that used the contraceptive pill before using Natural Cycles (n=4,023) had a PI of 8.1 plus or minus 0.6 and a 13-cycle failure rate of 8.7% plus or minus 1.3%.

Strengths and limitations

The study used data from all people who were paying to use the Natural Cycles app between 1 September 2016 and 30 October 2017 (and who had agreed to share data for research purposes). The study results are based on people engaging with the app; of the 16,331 people who met the inclusion criteria, 5,683 contributed at least 9 months. The cohort design was based on self-reported contraceptive use. The investigators made some assumptions about the pregnancy status if people stopped using the app. For example, people were assumed to be pregnant if they stopped during the late luteal phase or if they reported a high basal temperature. The study was funded by the company.

Kleinschmidt et al. (2019)

Study size, design and location

Data analysis of 26,626 cycles from a cohort of 42,579 people (using the app in pregnancy prevention mode) to compare the accuracy of identifying the fertility window using different methods of fertility awareness in Sweden.

Intervention and comparator

Intervention: Natural Cycles.

Comparators: rhythm method; standard days method.

Key outcomes

The analysis compares the fraction of accurately and inaccurately predicted non-fertile days (described as green day [GD] and wrong green days [WGD], respectively) between

Natural Cycles, rhythm method and standard day methods of fertility awareness. Natural Cycles' algorithms allocated 59% (95% confidence interval [CI] 58 to 59) GDs in cycle 12 and an average of 0.08% (95% CI 0.07 to 0.09) WDG. The rhythm method resulted in 46% (95% CI 45 to 46) GDs and 0.18% (95% CI 0.16 to 0.20) WGD over 12 cycles (excluding cycles 1 to 6), compared with Natural Cycles over 12 cycles (excluding cycles 1 to 6) 58% (95% CI 58 to 59) GDs and 0.07% (95% CI 0.07 to 0.08) WGDs. The standard day method over 12 cycles was 58% (95% CI 58 to 58) GD and 0.93% (95% CI 0.89 to 0.97) WGDs compared with Natural Cycles 56% (95% CI 56 to 56) GDs and 0.07 (95% CI 0.06 to 0.08) WGDs.

Strengths and limitations

The study used data from people paying to use the app collected prospectively between 1 September 2017 and 1 March 2019. The Natural Cycles app used was version 3.0. Basal body temperature measurements, menstruation dates and urinary luteinising hormone test results were recorded by the users directly into the app. People that had variable cycles, or cycles with fewer than 20 days did not take part in the study. This shows that the findings may not be generalisable to the wider population. The assumed 'true' ovulation day is based on retrospective placement according to the Natural Cycles algorithm and is associated with a small margin of error. The data were limited because of the lack of consecutive cycles with complete data entry, which reduced the number of cycles analysed in the study. The study was funded by the company.

Scherwitzl et al. (2017)

Study size, design and location

Prospective observational study using data from 22,785 people using the app (in pregnancy prevention mode) in Sweden.

Intervention and comparator

Natural Cycles.

Key outcomes

On average, users entered data into the app for 9.8 cycles. App data were used to calculate perfect and typical PIs. Typical-use PI: 6.8 (95% CI 6.4 to 7.2) and 13-cycle

typical-use failure rate of 8.3% (95% CI 7.8 to 8.9). Perfect use PI: 1.0 (95% CI 0.5 to 1.5) and a typical-use failure rate of 8.3% (95% CI 7.8 to 8.9) over 13 cycles. Discontinuation over 12 months was 54%. Perfect use was defined as a cycle with no unprotected sex during a 'red day'.

Strengths and limitations

The study used data from all people paying to use the app between August 2014 and August 2017 (and who had agreed to share data for research purposes). Calculation of perfect use required that people record in the app when they had sex. It was optional for users to enter these data. The investigators relied on users to report pregnancies and give information by email. The investigators made some assumptions about pregnancy status if the person stopped using the app. For example, people were assumed to be pregnant if they stopped during the late luteal phase or if they reported a high basal temperature. The study was company funded.

Scherwitzl et al. (2016)

Study size, design and location

Retrospective analysis using data from 4,054 people (using the app in pregnancy prevention mode) in Sweden.

Intervention and comparator

Natural Cycles.

Key outcomes

On average, people entered data into the app for 6.3 cycles. A total of 143 unplanned pregnancies happened during the study, giving a PI of 7.0 for typical use and a life table analysis gave a pregnancy rate of 7.5% per year (95% CI 5.9 to 9.1%). Ten of these pregnancies may have been because of the app incorrectly reporting a 'safe day' during the fertile window, giving a pregnancy rate of 0.5%.

Strengths and limitations

The study contains additional qualitative survey data, which were optional for users to

input. It is unlikely that the data were collected across the whole group. Assumptions about pregnancy status were made in the absence of confirmation. The study was funded by the company.

Scherwitzl et al. (2015)

Study size, design and location

Retrospective study using data from 317 app users in Sweden.

Intervention and comparator

Natural Cycles.

Key outcomes

App users entered basal body temperature, ovulation test results and menstruation data. The mean delay between the first positive ovulation test to the temperature-based estimation of the ovulation day was 1.9 days. The length of the luteal phase varied on average by 1.25 days per person. Only 0.05% of non-fertile days were falsely attributed and found to be within the fertile window.

Strengths and limitations

This study was company funded.

Sustainability

The company submitted no sustainability claims.

Recent and ongoing studies

The company has stated that 2 manuscripts are being prepared, reporting a UK-specific analysis of observational data and a real-world effectiveness study on contraception using Natural Cycles in 2 countries.

Expert comments

Comments on this technology were invited from clinical and academic specialists working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 4 experts were familiar with or had used this technology before.

Level of innovation

Three experts agreed that Natural Cycles was novel compared with services currently offered by the NHS, such as fertility-awareness counselling. One expert stated that it was a minor variation to existing fertility-awareness methods. There are several fertility awareness apps that are similar to Natural Cycles, but none are CE-marked or available on the NHS.

Potential patient impact

The experts stated that the potential benefits of Natural Cycles include:

- people not having to access a health service for fertility advice
- that it is non-hormonal and has no side effects
- that it supports users to develop an increased awareness of natural body rhythm, and
- that it is easy to use and private.

The experts also noted that Natural Cycles provides another contraceptive option and that this may be preferred by people who are unable to, or do not wish to, use other methods of contraception. One expert noted that Natural Cycles may benefit people who are already using fertility-awareness methods in terms of its usability. Three experts noted that Natural Cycles can also be used by people who want to get pregnant.

One expert noted that Natural Cycles might be more suitable to monitor the menstrual cycle rather than as a contraceptive in some users. This is because there are a number of factors that can affect basal body temperature, such as medications, stress, alcohol, and disturbed or irregular sleep.

Potential system impact

All experts stated that Natural Cycles would be used as well as current service provision in the NHS. Two experts noted that there could be reduced health service visits for people trying to conceive and fewer referrals to assisted reproduction clinics if the app is proven to help conception. Two experts agreed that Natural Cycles is likely to be cheaper than a contraception or fertility counselling session. One felt that there could be an increase in the rate of termination of pregnancy, whereas another thought there could be a decrease. One expert noted that there could be reduced costs for unwanted pregnancies for people who currently use fertility awareness methods. One expert noted that the annual cost of Natural Cycles was less than the annual cost of an oral contraceptive prescription. Three experts advised that using Natural Cycles would not need any change in service provision. One highlighted the need for training for GPs providing advice on contraception and fertility.

General comments

Three of the experts highlighted the need for further evidence before Natural Cycles can be adopted in the NHS.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Rebecca French, associate professor in sexual and reproductive health research, London School of Hygiene and Tropical Medicine. Dr French received financial compensation from the company for advice and research services.
- Dr Kulsum Jaffer, consultant in reproductive and sexual health, University Hospitals Birmingham NHS Foundation Trust. Did not declare any interests.
- Dr Hedda Joyce, GP. Dr Joyce has received a consultancy fee from the company.
- Professor Jill Shawe, director of the Institute of Health and Community and professor in women's health, University of Plymouth. Professor Shawe has received consultancy and travel fees from the company.

Development of this briefing

This briefing was developed by NICE. NICE's interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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