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Research Article

Pregnancy rates and outcomes in women with cystic fibrosis in the UK: comparisons with the general population before and after the introduction of disease-modifying treatment, 2003–17

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Objective To compare pregnancy rates and outcomes for women with cystic fibrosis in the UK with those of the general population and assess the effect of the introduction of disease-modifying treatment.

Design A population-based longitudinal study, 2003–17.

Setting United Kingdom.

Population Women aged 15–44 years in the UK cystic fibrosis (CF) Registry compared with women in England and Wales.

Methods We calculated pregnancy and live-birth rates for the CF population and the general population of England and Wales. For women with CF we compared pregnancy rates before and after ivacaftor was introduced in 2013. We further used CF registry data to assess pregnancy outcomes for mothers with CF, and to assess the relationship between maternal pre-pregnancy lung function and nutritional status and child gestational age.

Main outcome measures Pregnancy and live-birth rates and child gestational age.

Results Of 3831 women with CF, 661 reported 818 pregnancies. Compared with the general population, the pregnancy rate was 3.3 times lower in the CF population (23.5 versus 77.7 per 1000 woman-years); the live-birth rate was 3.5 times lower (17.4 versus 61.4 per 1000 woman-years) with 70% of pregnancies in CF women resulting in live births; termination of pregnancy rates were also lower (9% versus 22%). Pregnancy rates increased post-ivacaftor for eligible women with CF, from 29.7 to 45.7 per 1000 woman-years. There was no association between pre-pregnancy lung function/nutrition status and gestational age.

Conclusions Pregnancy rates in women with CF are about one-third of the rates in the general population with favourable outcomes, and increased for eligible women post-ivacaftor.

Keywords cystic fibrosis transmembrane conductance regulator modulator, cystic fibrosis, ivacaftor epidemiology, pregnancy.

Tweetable abstract Pregnancy rates in women with CF are about a third of the rate in England and Wales with 70% live births. Ivacaftor increases the rate.

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Abbreviations

%FEV1, percent predicted forced expiratory volume in 1 second; BMI, body mass index; CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator; IVF, in vitro fertilisation; LB, live birth; ONS, Office for National Statistics; UK, United Kingdom; wwCF, women with cystic fibrosis.

Introduction

Cystic fibrosis (CF) is the most common autosomal recessive disorder in Caucasians. It is a progressive multisystem disease caused by a reduction or loss of the cystic fibrosis transmembrane conductance regulator (CFTR) protein

function. Over 2000 mutations of CFTR have been discovered and the most common mutation in CF is deletion of phenylalanine 508 (F508del).[1]

Considerable advances in care, diagnosis, neonatal screening and treatments have improved survival over recent decades (Box 1). As of 2019, over half of babies born, and individuals aged 30 years and above, can expect to survive into at least their fifth decade compared with less than 10 years in the 1960s (Box 1).[2,3] One of the notable advancements in the care of CF is the availability of CFTR modulators such as ivacaftor. Ivacaftor targets the underlying cause of CF through increased chloride transport of the CFTR protein with significant improvement in lung function in people with CF since its launch in the USA in 2012.[4]

As people with CF are living longer, healthier lives, more women are considering having families of their own.[5]

Box 1 Key developments in CF care relevant to pregnancy

The first successful delivery of a baby in a woman with CF was first reported in 1960 at a time when median survival for CF was <5 years. Although several pregnancies were reported in subsequent years, pregnancy for women with CF was generally discouraged until the 1980s, an era when the CF protein and the CF transmembrane receptor (CFTR) gene were discovered (Figure A). Mutations in the gene lead to abnormal ion transport and a resulting build-up of thick, dehydrated, pH-imbalanced mucus, which adversely impacts the function of the respiratory, gastrointestinal and reproductive tracts.

Pregnancy guidelines for women with CF were published in the UK in 2008 with recommendations for multidisciplinary care and a contraindication for women with lung function below a percent predicted force expiratory volume of 50%, with pancreatic insufficiency and CF-related diabetes as the main risk factors for preterm delivery and caesarean section. Despite improvements in treatments such as DNase for thinning mucus secretions allowing ease of airway clearance and antimicrobials, the majority of people with CF will eventually develop respiratory failure and many are considered for lung transplantation.

However, a new class of treatments, CFTR modulator therapies, which include Ivacaftor (UK, 2013), combination therapies of Symkevi (tezacaftor/ivacaftor, available in UK, 2018) and Orkambi (lumacaftor/ivacaftor available in UK, 2018) and triple therapy – Kaftrio (elexacaftor/tezacaftor/ivacaftor, available in UK, 2020) have ushered in a new era of care for people with CF with over 90% of the people with CF eligible for modulator therapies in the UK. These therapies target the CFTR mutations, increasing the flow of ions across the CFTR protein, which helps to alleviate the symptoms of CF, with notable improvements in mucus clearance, lung function and weight gain.

With the substantial gains in health experienced by people with CF over the last 20 years and anticipated future therapies, obstetricians are increasingly likely to become part of the multidisciplinary teams of women with CF who become pregnant.

Figure A. Timeline of key milestones in treatment and care of people with CF and life expectancy.

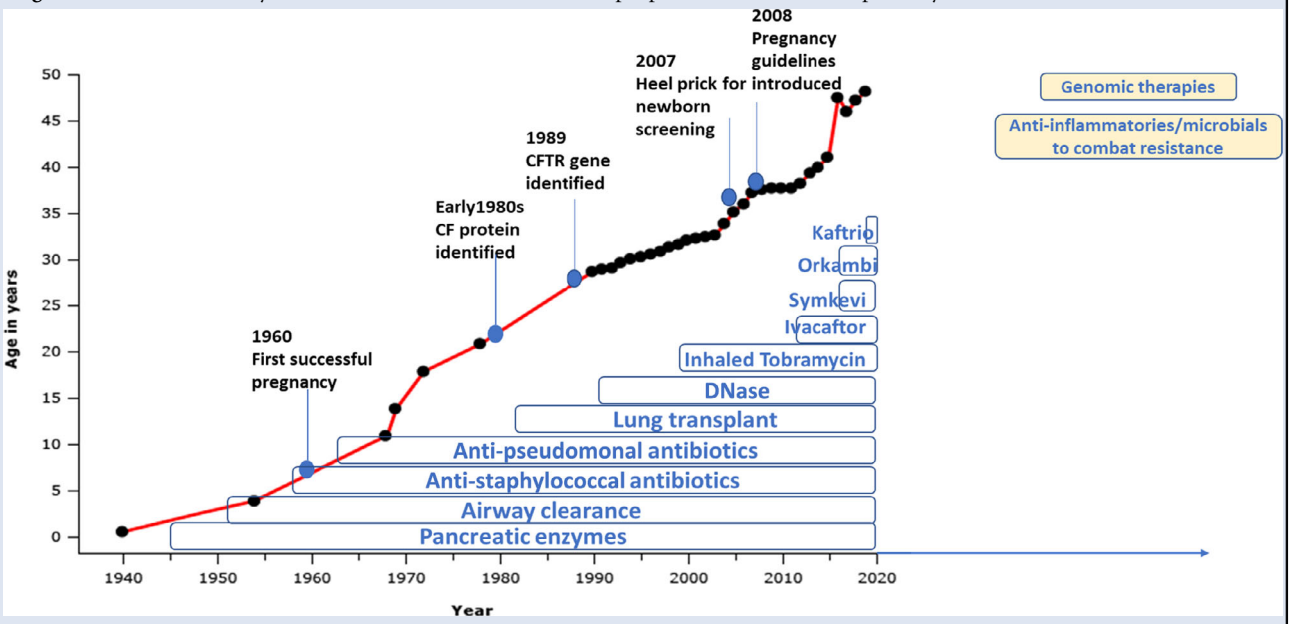

Figure A illustrates the improvements in care, availability of treatments and increasing life expectancy. Future therapies and changes are highlighted in yellow. (Data points from Survival of CF patients – UpToDate https://www.uptodate.com/contents/image?imageKey=PULM%2F61930&topicKey=PEDS%2F110933&source=outline_link and timelines adapted from the UK Cystic Fibrosis Trust https://www.cysticfibrosis.org.uk/get-involved/fundraising/join-our-fundraising-campaigns/cf-week/research-what-the-cf).

Recent studies from Australia, Europe and the USA have reported successful pregnancy outcomes in women with CF (wwCF) with reduction in maternal morbidity and mortality; but with limited information on pregnancy outcomes for wwCF compared with the general population.[6-11] Patel et al. and Girault et al. both found that pregnancies occurred at younger ages in the CF population compared with the general population in France (Patel et al., 26.5 versus 27.6 years, $P = 0.006$; Girault et al., 28.7 versus 32.1 years, $P = 0.003$).[12,13] Patel et al. used nationwide records and reported an increased risk of preterm labour (adjusted odds ratio 2.2; 95% CI 1.9–2.6)[13]; whereas Girault et al. demonstrated similar levels of uncomplicated deliveries, gestational age and birthweight among the CF and non-CF populations, although their findings were limited by a small sample size of only 33 wwCF from a single centre.[12] In the UK, recently available evidence on pregnancy in wwCF from the Obstetric Surveillance System data did not capture all wwCF and their pre-pregnancy clinical characteristics such as body mass index (BMI), lung function or genotype.[9] These factors determine preconception health status and may be linked to pregnancy outcomes.[14] Further, there is a paucity of large population-based studies on pregnancy in the era of CFTR modulators, with only one study published to date.[11]

The objective of this study was to determine current pregnancy rates and outcomes in the whole CF population and compare these with the UK general population, and explore the potential impact of the availability of ivacaftor on pregnancy rates and outcomes based on analysis of data from a sub-population of eligible women who have had access to ivacaftor since 2013.[15] This will provide useful information for clinicians counselling or managing women with CF who are currently pregnant or would like to start a family.

Methods

Study design, setting and participants

We conducted a retrospective longitudinal observational study of pregnancy rates and outcomes among wwCF of childbearing age (15–44 years inclusive) in the UK CF Registry between 2003 and 2017. We describe the baseline characteristics of women of childbearing age (15–44 years inclusive) in the UK CF registry who became pregnant. Then two comparisons were made. First, rates and outcomes in the wwCF were compared with those in the general population of England and Wales. Second, for the wwCF only, we compared pregnancy rates and outcomes before and after the availability of ivacaftor for eligible wwCF with all wwCF.

Data sources and baseline characteristics

The UK CF Registry records data from each patient's comprehensive annual review with a specialist clinician for evaluation of clinical status, pulmonary function, microbiology of respiratory tract secretions and use of major CF-related therapies.[16] Records date back to the 1990s and are estimated to capture approximately 99% of the current CF population with approximately 80% from England.[16] Baseline characteristics of interest were ethnicity, genotype, age at the end of year the woman became pregnant, employment status, CF-related diabetes, pancreatic insufficiency, BMI and percent predicted forced expiratory volume in 1 second (%FEV1) based on the Global Lung Initiative reference equations at annual review visit in the 3 years pre-pregnancy.[17] We used %FEV1 measures across 3 years because of the large visit-to-visit variation in the measurement of FEV1, meaning that mean values over multiple time-points give a better estimate of underlying true lung function.[18]

Conceptions and legal abortions for England and Wales are published annually by the Office of National Statistics (ONS).[19] Data on early pregnancy loss (miscarriages) are not included in conception publications. Live birth data are available from the ONS Vital Statistics and birth characteristics publications.[20]

Outcome measures

The main outcomes of interest were pregnancy rates and outcomes. We adopted the ONS definition of conceptions for pregnancies – 'pregnancy of a woman that leads either to a maternity or an abortion', where abortion refers to legal abortion according to the 1967 abortion act.[19] The UK CF Registry codes pregnancy as a binary event (yes/no) during annual review with possible outcomes recorded in the case of a 'yes' response: live birth, stillbirth, therapeutic abortion (abortion), spontaneous abortion (miscarriage), undelivered and unknown. For full questions related to pregnancy captured in the UK CF Registry at annual review, see Appendix S1: Methods, Supplementary File. Women who were pregnant in two consecutive years with outcome 'undelivered' in the former year were counted as a pregnancy case in the former year, but not the latter.

Other pregnancy-related outcomes captured in the registry include gestational age (recorded as weeks of completed pregnancy), congenital anomalies, use of in vitro fertilisation (IVF) and CF status of child, all recorded as categorical variables with possible options of Yes, No or Unknown. We were also interested in the number of women who were pregnant with a mean %FEV1 below 50% in the 3 years pre-pregnancy as this is a contraindication for pregnancy.[21]

Further, we assessed the pregnancy rates and outcomes among wwCF with at least one G551D mutation (the group first eligible for disease modulator therapy) to explore the effects of modulator therapy on pregnancy rates. The information on genotype was recorded for each

mutation and ivacaftor was recorded as a binary variable with possible options of Yes or No.

Statistical analyses

The analyses progressed in four stages. First, we described the characteristics of the population of women of childbearing age (15–44 years inclusive) in the registry who became pregnant.

Second, we compared pregnancy and live-birth rates between 2003 and 2017 among women of childbearing age (15–44 years inclusive) for both populations (wwCF and the general population of women in England & Wales) calculating 3 yearly averages to account for year-on-year variation. In the data for England and Wales, pregnancies resulting in a miscarriage are excluded from the numerator; for better comparison, we excluded miscarriages from the numerator for wwCF in determining the pregnancy and live-birth rates. Pregnancy rates were calculated as the total number of pregnancies for the specified time period divided by the total number of woman-years for the same time period whereas live-birth rates were calculated as the total number of live births divided by the total number of woman-years for the specified time period and presented as a rate per 1000 woman-years (rate calculations, Appendix S1: Methods, Supplementary File). Both pregnancy and live-birth rates were broken down into the childbearing age groups to determine the age-specific rates – the number of pregnancies or live births per 1000 woman-years for a specific age group. For abortion, miscarriages and stillbirths we considered the proportion of pregnancies resulting in these outcomes and made the comparison between both populations where possible.

Third, for wwCF only we compared the pregnancy rate and outcomes for all wwCF with women who had a G551D mutation (those initially eligible for ivacaftor) in the period before (2008–12) and the period after (2013–17) ivacaftor becoming available.

Fourth, for wwCF only, we assessed the association between aspects of maternal health – mean 3-year pre-pregnancy maternal BMI and %FEV1 – and gestational age of infant using a linear regression model.

Baseline data were summarised as mean and standard deviations (SD) or median and interquartile range (IQR) for continuous variables, and percentages for categorical variables. All analyses were performed using STATA V14 (StataCorp, College Station, TX, USA) and R V 3.16 (R Foundation for Statistical Computing, Vienna, Austria). All rates were reported with 95% CI using the Byar's method.[22]

Results

Population characteristics

A total of 3831 women were followed up during the study period, of whom 661 became pregnant, with a total of 818 pregnancies. A flow chart of selection of the study population from the UK CF Registry is provided in Figure S1. Pregnant women with CF were predominantly of white ethnicity (97%), diagnosed in childhood, had two copies for F508del mutation (43.7%), were in employment or education (45%) with pre-pregnancy mean BMI 22.1 kg/m^2 (SD 3.5) and %FEV1 69.5% (SD 20.1) (Table 1). One-fifth reported CF-related diabetes (21%) and the majority had pancreatic insufficiency (81%). Of women who became pregnant, 14% had a %FEV1 below 50%.

Pregnancies in women with CF and rates compared with the general population

A total of 818 pregnancies were reported in the UK CF Registry between 2003 and 2017; 59% of wwCF who became pregnant reported only one pregnancy but some had up to five (Table 2). Records on IVF in the CF population were available in 2016 and 2017 only, of which 34 women with IVF had 25 pregnancies and six women were recorded twice with no information on the number of IVF

Table 1. Baseline clinical and demographic characteristics of the CF study population

Baseline characteristics	Mean	SD	Range
Age at diagnosis	6.4	9.66	0–43.6
Lung function	69.5	20.1	15.6–130.2
BMI (kg/m^2)	22.2	3.5	14.1–39.4
Baseline characteristics	***n***		**%**
Genotype			
F508del_Homozygous	289		43.7
F508del_Heterozygous*	240		36.3
G551D**	51		7.7
Other/Unknown	81		12.3
Ethnicity			
White	643		1
Non-white	18		0.03
Employment status			
Full-time	148		22.4
Part-time	110		16.6
Home maker	150		22.7
Student	42		6.4
Disabled	16		2.4
Unemployed	123		18.6
Not known	72		10.9
Pre-pregnancy comorbidities			
CF-related diabetes	138		21
Pancreatic insufficiency	533		81

These are women captured in the UK CF Registry aged 15–44 years who have had a pregnancy between 2003 and 2017 (n = 661).
*Excluding women with at least one G551D mutation.
**Women with at least one G551D mutation.

Table 2. Pregnancy-related outcomes of all wwCF (15–44 years) who become pregnant and those with at least one G551D mutation from the UK CF Registry, 2003–17

Pregnancies in wwCF	wwCF, 2003–17, *n* = 818* (*n*, %)	G551D mutation, 2008–12, *n* = 19 (*n*, %)	G551D mutation, 2013–17, *n* = 35 (*n*, %)
Total number of pregnancies			
1	481 (58.8)	<5	23 (65.7)
2	271 (33.1)	11 (57.9)	8 (22.9)
3	52 (6.4)	<5	<5
4	<15	<5	<5
5	<5	<5	<5
Maternal age (years), median (IQR)	26 (23–31)	27 (23–29)	29 (23–34)
Outcome			
Live births	539 (69.7)	12 (63.2)	26 (74.3)
Stillbirths	<5	0	0
Miscarriages	90 (11.6)	<10	<5
Abortion	74 (9.6)	<5	<5
Undelivered**	67 (8.2)	0	<5
Unknown	<40	0	0
IVF	34	<5	<5
Maternal age (years), median (IQR)	31 (27–34)		
Pregnancies	25	—	—
Live birth	15 (60)	—	—
Miscarriages	<5	—	—
Stillbirth	<5	—	—
Undelivered	5 (20)	—	—

*661 women had 818 pregnancies.
**Outcomes are not complete for 2017, of the 67 recorded as undelivered, 28 were recorded in 2017; numbers below 5 are not displayed to reduce the risk of deductive disclosure; — Numbers not displayed not applicable.

cycles per woman. Median age at pregnancy was higher among women with IVF in comparison with all wwCF who became pregnant (median 31, IQR 27–34 versus median 27, IQR 23–31) (Table 2).

Pregnancy rates over the study period in wwCF and in the general population were relatively stable (Figure 1). Overall, compared with the general population the pregnancy rate was 3.3 times lower in women with CF (23.5 versus 77.7 per 1000 woman-years). The pregnancy rate was highest at 30–34 years for wwCF compared with 25–29 years for the general population (Figure 2). The lowest pregnancy rate was among the youngest and oldest for wwCF and those aged 40–44 years for the general population (Figure 2, Table S2). Conceptions for women aged 15–19 years are on the decline in the general population but have remained fairly stable at a low rate in wwCF (Figure 2).

Pregnancy outcomes in women with CF and live-birth rates compared to the general population

Pregnancy outcome was available for 773 pregnancies for wwCF, of which 70% had a live birth, 11.6% had a miscarriage, 9.6% had an abortion and the remaining were undelivered (8%) or stillbirths (<1%) (Table 2). Of the pregnancies that were undelivered, 42% were recorded in 2017, the last year of the study. Those with IVF had a live-birth rate of 60% (Table 2). The median age of wwCF with a live birth was 27 years (IQR 23–31 years) and similar to the median age of pregnancy.

The overall live-birth rate in wwCF was 3.5 times lower than the rate for the general population (17.4 versus 61.4 per 1000 woman-years). The age specific live-birth rates followed a similar trend of higher rates in the general population across all age groups except for those aged 40–44 years, where the rates were similar (Figure S2).

The percentage of pregnancies resulting in abortion for women in the general population was double that of wwCF (wwCF 9.6% versus general population 21.6%). Miscarriage rate was 11.6% in wwCF, but the estimate for the general population is 10–20%.[23]

Pregnancy rates and outcomes in women with CF eligible for ivacaftor with a G551D mutation

Forty-three women had at least one G551D mutation and were eligible for ivacaftor between 2013 and 2017, representing 6.2% of all wwCF of childbearing age between 2013 and 2017. Of these women, 86% had a recording of ivacaftor for at least 1 year over the 5-year period. The median number of years of ivacaftor prescription was 4 (IQR 2–5 years).

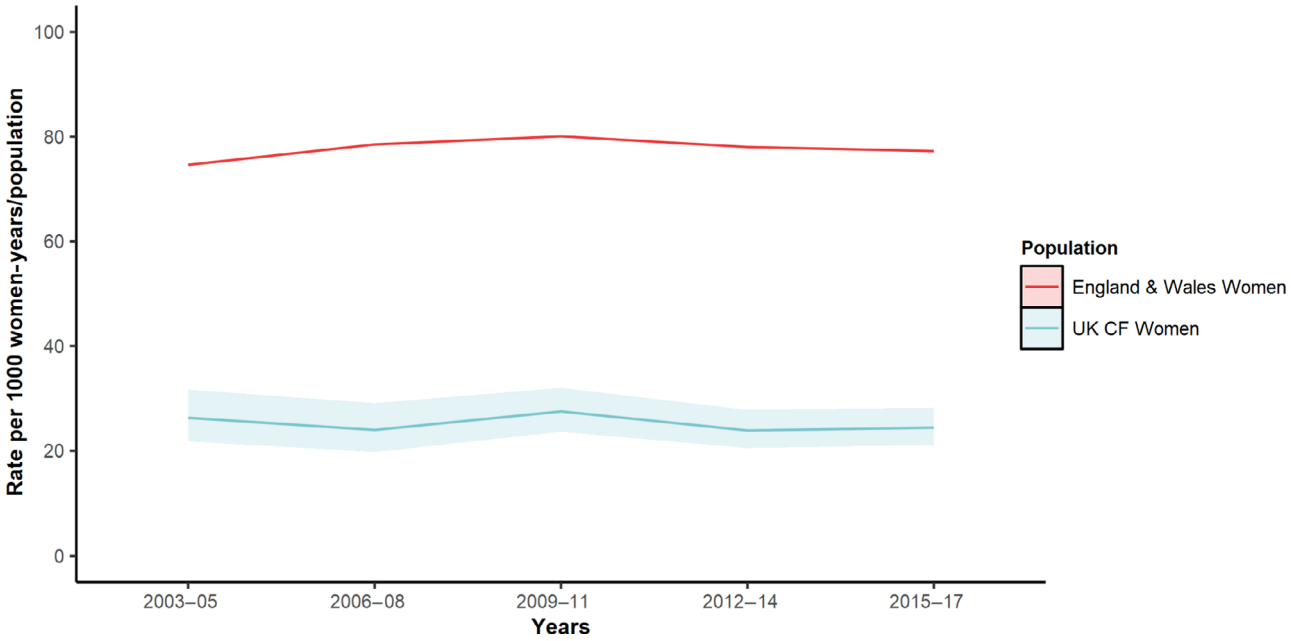

Figure 1. Pregnancy rates in women with CF (15–44 years) in comparison with women in England and Wales, 2003–17.

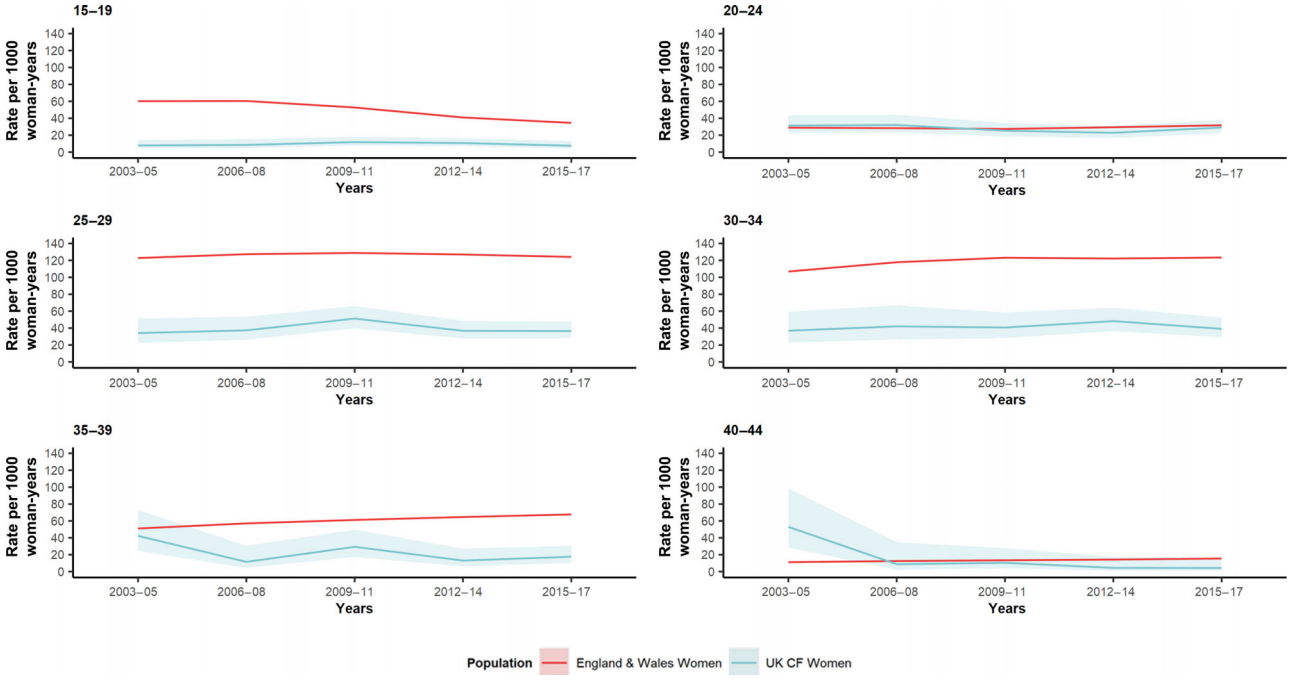

Figure 2. Three-yearly age-specific pregnancy rate per 1000 woman-years/population of women with CF and women in England and Wales, 2003–17.

Sixty-eight pregnancies were recorded for 51 wwCF with at least one G551D mutation between 2003 and 2017 with half of pregnancies recorded in the 5 years since ivacaftor became available in 2013. There was a 1.5-fold increase in pregnancy rates between the 2008–12 and 2013–17 periods from 29.7 per 1000 woman-years (95% CI 19.0–46.7) to

45.7 per 1000 woman-years (95% CI 32.4–62.8) (Table 2). Where information was available, outcomes were favourable with more pregnancies resulting in a live birth in the post-ivacaftor period (74% versus 60%) (Table 2).

Association of pre-pregnancy lung function and nutrition status with child gestational age for wwCF

Gestational age was available for 186 babies (35%) born to wwCF with a median of 37 completed weeks (IQR 35–38 completed weeks). There was no correlation between pre-conception %FEV1 and gestational age (R = 0.066, 95% CI −0.16 to 0.28) or preconception BMI and gestational age (R = −0.083, 95% CI −3.0 to 0.14) (Figure S3).

Discussion

Main findings

In this large comparative study of pregnancy in women with CF in the UK, we found that wwCF were approximately 3.3 times less likely to become pregnant than women from the general population (23.5 versus 77.7 per 1000 woman-years). Pregnancy rates were highest for women aged 25–29 and 30–34 years for both wwCF and the general population and lowest for those aged 15–19 and 40–44 years. Live births mirrored pregnancy rates with a 3.5-fold difference in the live-birth rate (17.4 versus 61.4 per 1000 woman-years). The proportion of pregnancies resulting in abortion was lower in wwCF (9% versus 22% in the general population). Following the introduction of ivacaftor for eligible women with CF who carry the G551D mutation, the pregnancy rate increased by one and a half-fold.

Strength and limitations

Our study has several notable strengths. First, we were able to follow up about 99% of wwCF of childbearing age using the UK CF Register with baseline characteristics and pre-pregnancy clinical status, hence providing the most up-to-date pregnancy estimates using population-level data across all CF centres in the UK. Further, this is the first study of pregnancies in the UK of wwCF following the availability of the first approved CFTR modulator. As more people with CF become eligible for modulator therapy, prognosis is expected to improve with more wwCF and their partners likely to consider having children. The comparison with the general population allows people with CF and their partners to understand pregnancy-related outcomes for wwCF in relation to women of similar age in the general population. This information can be used to facilitate person-centred discussions about the outcomes of pregnancy in wwCF between clinicians and patients.

There are limitations in the data available on pregnancy-related outcomes in the UK CF Registry. It was not possible to ascertain exact pregnancy dates, maternal outcomes (e.g. delivery method) and neonatal outcomes (e.g. birthweight) with limited reporting of gestational age. As such, we were unable to compare delivery method, birthweight or gestational age of neonates born to wwCF with neonates born to women in the general population. Moreover, pregnancy outcomes for 2017 were incomplete for wwCF, hence outcomes for this period are underestimated. Further, data on conceptions were only available for England and Wales, whereas the CF Registry covers the UK. However, this is unlikely to have had a major impact on our results as Scotland and Northern Ireland represent <15% of the UK population, and the overall pattern of pregnancy rates in wwCF was similar to that in women in England & Wales.

For assessing the impact of modulator therapy on pregnancy rates, we used the initial eligibility criteria for ivacaftor and have therefore not captured all women who may have had the opportunity to receive ivacaftor. Following the first approval of ivacaftor for people with at least one mutation for G551D in 2013 in the UK, there has been a progressive increase in those eligible for ivacaftor and other modulator therapies are now available and approved for use in the UK (Orkambi, Symkevi, 2019 and Kaftrio, 2020) with up to 90% of the CF population eligible for modulator therapy.[24,25] This raises the need for continued research and improved data completion of the UK CF Registry data on pregnancy-related outcomes in this new era of care for people living with CF.

Interpretation

The overall pregnancy rate in wwCF reported in our study was twice the rate reported in the Italian CF population (23.5 versus 10.6 per 1000 woman-years) but similar to that in the USA (25.5 per 1000 woman-years). In contrast, there was a four-fold difference in the pregnancy rate in US wwCF and that of the US general population due to a higher overall pregnancy rate in the US population. During our study period there was one and a half-fold increase in pregnancy rates in the years 2013–17 for wwCF with at least one G551D mutation following the introduction of ivacaftor. This is in line with the study in the USA by Heltshe et.al who found an increase in pregnancy rates for women with at least one G551D mutation during the post-approval period (2012–14) for ivacaftor.[11]

Over our study period, the live-birth rate for younger wwCF was relatively stable in comparison with the rate in the general population, which has declined from 2009–11 onwards. This decrease in the general population coincided with an increase in the proportion of pregnancies leading to abortion.[19,26] Although, we were unable to assess age-specific abortion rates over time in the CF population, the overall percentage of pregnancies resulting in abortions was half that of the general population, (9.6% versus 21.6%), with miscarriages (11.6%) at a similar level to the general population.[23]

Similar to other studies, pregnant wwCF in this study had good nutritional status (mean BMI 22.1 kg/m^2) and respiratory function (mean %FEV1 69%) with most reporting first pregnancies.[12,13,27,28] This is not surprising as most women will consider getting pregnant before their lung function begins to decline and will work at achieving good nutritional status in agreement with their clinical care teams before pregnancy. Guidelines published in 2008 suggest that a %FEV1 below 50% is a contraindication for pregnancy, with CF-related diabetes and pancreatic insufficiency as potential risk factors for preterm delivery and caesarean section.[21] In our study, 14% of women had mean %FEV1 below 50%, over 20% with CF-related diabetes and over 80% had pancreatic insufficiency. Although we did not assess the impact of these factors on pregnancy outcomes, recent evidence now shows that pregnancy may not negatively impact maternal health with favourable respiratory function and nutritional status in women with %FEV1 as low as 40%, but pancreatic insufficiency remains a risk for small-for-gestational-age infants[7,14,29]

Gestational age was only available for a subset of wwCF. We did not find any correlation between pre-pregnancy BMI or %FEV1 and gestational age as reported by others.[6,9,28] This may be due to the definition of these baseline characteristics, and the sample sizes considered in previous studies. For instance, in the study by Ashcroft and colleagues in the UK, they included 56 women and used the %FEV1 and BMI at pregnancy booking (˜13 weeks) for baseline recording whereas we used the mean in the 3 years pre-pregnancy; an Australian study only included 20 women.[6,9]

Conclusion

This observational study represents the largest multicentre study of pregnancy rates in wwCF of childbearing age in comparison with women in the general population in the pre- and post-approval periods of ivacaftor in the UK. Pregnancy rates were over three times lower in wwCF than the general population with about 70% resulting in a live birth. The availability of ivacaftor for 6.2% of wwCF of childbearing age increased the pregnancy rate in this group. Extrapolating this result to the much larger adult CF population now eligible for modulator therapy (90%), we can expect improved health outcomes and survival in CF and an increase in pregnant wwCF in Obstetric departments. It is important that obstetricians are aware of the current and expected future trends of pregnancy and CF to help wwCF, their partners and clinical teams in the decision process on whether to start a family.

Disclosure of interests

OBE is funded by the Welsh Government Research for Patient and Public Benefit, during the conduct of the study. JD reports grants from Welsh Government Research for Patient and Public Benefit, during the conduct of the study and personal fees from Chiesi, Vertex, Trudell, Insmed and Merke, outside the submitted work. SBC reports speaker honoraria from Chiesi, is a member of the advisory board for Chiesi, Profile Pharma and Vertex, is Chair of the UK Registry Steering Committee and UK CF Trust and received payment to institution from Pharmaxis outside the submitted work. All other authors have no conflicts of interest to disclose. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

DKS, DT-R and JD conceived the original idea for this study. DKS, OBS and DT-R designed the study. OBS, DKS and DT-R developed the analysis plan. OBS extracted the data and prepared the data sets. OBS analysed the data and conducted the literature searches. SBC and JD helped identify previous work and gave the clinical interpretation. OBS, DKS and DT-R wrote the first draft of the paper. All authors were involved in interpreting the findings and revising drafts and agreeing the final version.

Details of ethics approval

The UK CF Registry has NHS research ethics approval: (Huntingdon Research Ethics Committee 07/Q0104/2) for the collection of data into the registry. The CF Trust Registry Research Committee approved the use of anonymised data in this study, under the terms of the NHS ethics approval. Patients were not involved in the development of this research. Core outcome sets were not used. This study was funded by a Welsh Government Research for Patient and Public Benefit grant.

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Data availability statement

The data that support the findings of this study are available from the UK CF Registry upon request for research purposes only. Restrictions apply to the availability of these data, which were used under license for this study.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Supplementary file. Supplementary information. ■

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