

Proactive Fertility Digital Platform Shows Potential To Reduce Adverse Maternal Health Risks

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Submitted to: Journal of Medical Internet Research
on: August 26, 2025

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Abstract

Background: Approximately one in three pregnancies in the United States (US) is complicated by one or more adverse pregnancy outcomes, ranging from gestational diabetes to preterm birth. [1] This high prevalence contributes to the high rates of maternal and infant mortality in the US. The US maternal mortality rate is several times higher than that of other developed countries. [2] Intervention during the pre-pregnancy period may help reduce not only the incidence of maternal health risks, but also the associated costs for payers: every \$1 invested in pre-pregnancy care may save up to \$5 on infant and maternal health costs. [3]

Objective: The digital health company, Doveras Fertility, has built a pre-pregnancy digital health platform for individuals and couples seeking to optimize their fertility potential in order to conceive. Targeting users prior to initiation of pregnancy, the platform is also able to screen, identify, and personalize recommendations to reduce risk of adverse maternal health outcomes with lifestyle interventions. We investigated the potential for the digital tool to identify individuals high-risk for adverse pregnancy outcomes prior to pregnancy.

Methods: This paper reports on 400 people who sought Doveras' services in a one month period between May and June, 2024 by completing a digital eligibility assessment. In this paper, self-reported data was analyzed for six healthy pre-pregnancy lifestyle factors known to influence maternal health risk and each participant was given a composite score between 0-6 to represent the number of these healthy behaviors reported. The six healthy pre-pregnancy lifestyle factors include a body mass index [BMI] 18.5 to 24.9 kg/m², not currently smoking, 150 min/wk or more of moderate-to-vigorous physical activity, healthy eating, no daily alcohol intake, and use of a prenatal multivitamin. [1]

Results: The majority (61%) of participants received a composite score of 3 factors or fewer and less than 5% scored 6 out of 6. These results suggest that nearly all survey participants have potential risk factors for adverse maternal outcomes and therefore the potential to adopt at least one improvement in their lifestyle behavior, which may give the opportunity to reduce their risk of adverse outcomes.

Conclusions: By reaching this population with accessible and affordable fertility interventions during the preconception period, the digital health platform not only aims to improve fertility, but might also help to reduce maternal health adverse outcomes and associated costs.

(JMIR Preprints 26/08/2025:83023)

DOI: <https://doi.org/10.2196/preprints.83023>

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Original Manuscript

Proactive Fertility Digital Platform Shows Potential To Reduce Adverse Maternal Health Risks

Abstract / Overview

Approximately one in three pregnancies in the United States (US) is complicated by one or more adverse pregnancy outcomes, ranging from gestational diabetes to preterm birth. [1] This high prevalence contributes to the high rates of maternal and infant mortality in the US. The US maternal mortality rate is several times higher than that of other developed countries. [2] Intervention during the pre-pregnancy period may help reduce not only the incidence of maternal health risks, but also the associated costs for payers: every \$1 invested in pre-pregnancy care may save up to \$5 on infant and maternal health costs. [3] The digital health company, Doveras Fertility, has built a pre-pregnancy digital health platform for individuals and couples seeking to optimize their fertility potential in order to conceive. Targeting users prior to initiation of pregnancy, the platform is also able to screen, identify, and personalize recommendations to reduce risk of adverse maternal health outcomes with lifestyle interventions. We investigated the potential for the digital tool to identify individuals high-risk for adverse pregnancy outcomes prior to pregnancy. This paper reports on 400 people who sought Doveras' services in a one month period between May and June, 2024 by completing a digital eligibility assessment. In this paper, self-reported data was analyzed for six healthy pre-pregnancy lifestyle factors known to influence maternal health risk and each participant was given a composite score between 0-6 to represent the number of these healthy behaviors reported. The six healthy pre-pregnancy lifestyle factors include a body mass index [BMI] 18.5 to 24.9 kg/m², not currently smoking, 150 min/wk or more of moderate-to-vigorous physical activity, healthy eating, no daily alcohol intake, and use of a prenatal multivitamin. [1] The majority (61%) of participants received a composite score of 3 factors or fewer and less than 5% scored 6 out of 6. These results suggest that nearly all survey participants have potential risk factors for adverse maternal outcomes and therefore the potential to adopt at least one improvement in their lifestyle behavior, which may give the opportunity to reduce their risk of adverse outcomes. By reaching this population with accessible and affordable fertility interventions during the preconception period, the digital health platform not only aims to improve fertility, but might also help to reduce maternal health adverse outcomes and associated costs.

Introduction

The United States has witnessed a critically worsening maternal mortality rate — one that is several times higher than that of other industrialized and high-income countries and adversely affects the overall quality of health care in the US. [2] The real-world experience for the American woman is that she is more than twice as likely to die from complications related to pregnancy or childbirth than a woman in another developed nation. [2] There are multiple approaches that may reverse the worsening maternal mortality rate in the US and improve maternal health outcomes overall. [4]

One such approach is effective lifestyle intervention during the pre-pregnancy, or preconception, period. Nurses' Health Study II, for example, a large longitudinal cohort study run by Harvard Medical School, Brigham and Women's Hospital, and Harvard T.H. Chan School of Public Health, showed that women with the highest adherence to a "pre-pregnancy healthy lifestyle" had a substantially lower risk of adverse pregnancy outcomes and suggested that these lifestyle factors could be targeted as an effective intervention for the prevention of adverse pregnancy outcomes." [1] The benefits of a pre-pregnancy healthy lifestyle extend beyond the mother to the infants, as well. A study from the Pregnancy Environment and Lifestyle cohort found that healthy diet, healthy weight, and low-levels of stress during the preconception period were associated with reduced risk of preterm birth [5] and a meta-analysis of 17 clinical trials found that micronutrient supplementation during the preconception period reduced the risk of having an infant with low birth weight. [6] However, more intervention studies are needed to effectively demonstrate that lifestyle interventions during this critical preconception period can significantly reduce both maternal and infant health risks.

Given the high-quality evidence for the importance of lifestyle factors in the preconception window for maternal health outcomes, numerous public health bodies encourage women trying to conceive to engage in preconception counseling. According to the American College of Obstetricians and Gynecology, “the goal of pre-pregnancy care is to reduce the risk of adverse health effects by optimizing health and addressing modifiable risk factors.” [7]

Since nearly 90% of women do not receive pre-pregnancy care, it likely that the opportunity for preconception intervention to reduce adverse maternal health risks is not being well captured by the current health system. [8,9] More effective and wide-spread intervention might be possible through a digital health solution. By capturing those at the high-engagement point of trying to conceive, interventions might be able to target people in the important preconception window to assess a user’s potential risks and deliver personalized intervention in an accessible and affordable way.

Methods

Doveras has designed and developed preconception lifestyle and behavioral intervention programs, delivered through its innovative digital health platform, for individuals and couples to improve various endpoints along the reproductive health journey. These personalized interventions are based on relevant data from existing clinical studies on preconception lifestyle factors and their impacts on various reproductive health endpoints. The Doveras platform (1) facilitates the assessment of baseline lifestyle risk factors, (2) identifies modifiable behavior opportunities and potential adverse fertility and maternal health risks to mitigate, and (3) delivers personalized programming to help users sustain simple behavior changes that target their unique risk to improve their overall reproductive health outcomes.

The present study evaluated the anonymized data of the first 400 verified participants who sought services from the Doveras digital health platform during a one month period (mid May to mid June 2024). These participants were directed to the Doveras website through their engagement with social media advertisements to naturally improve fertility with personalized, data-driven lifestyle interventions. Enrollment criteria was completion of a digital eligibility assessment, the “Fertility Quiz”, encompassing self-reported personal demographics and various lifestyle and behavioral characteristics. The included participants self-reported as female who reported attempting to conceive via sexual intercourse with a male partner; those who reported they were using or planning to use assisted reproduction technologies to conceive were excluded for the purposes of this study. The study met the criteria for Human Subject Research Exemption as determined by Salus IRB (IRB: 24072).

For the purposes of this study, self-reported behavioral and demographic data from these participants was analyzed using the maternal health risk framework developed through the Nurses’ Health Study II’s definition of a participant’s Healthy Pre-Pregnancy Lifestyle Factor score. [1] This framework observed 15,509 women and 27,135 pregnancies and identified six healthy Pre-Pregnancy Lifestyle Factors associated with a lower risk of adverse maternal health outcomes. These factors included:

1. Healthy body mass index [BMI] 18.5–24.9
2. Not currently smoking
3. 150 min/wk or more of moderate-to-vigorous physical activity
4. Healthy eating
5. Less than 15 grams/day alcohol daily
6. Use of a prenatal multivitamin

Participants answered questions on these and other topics as part of a single time-point survey, the “Fertility Quiz.” Following the method from the Nurses’ Health Study II, self-reported behaviors of the present study cohort was analyzed according to each of these six variables. These six variables were coded as binary (0 or 1) and summed for each participant to compute their total healthy pre-pregnancy lifestyle score. Regarding diet, participants who reported “I would say I mostly eat healthy” received a score of “1”, while those who answered “I have some healthy habits” or “I would say my diet needs a lot of help to be considered healthy” received a score of “0”. For the smoking variable, participants who reported that they were a “social smoker” received a “1” as not regular smokers. For the alcohol variable, those who reported “no” to the question of whether they drink daily received a “1” and those who responded “yes — 1 drink daily” or “yes — 2+ drinks daily” received a score of “0.” Participants also self-reported data on how long they have been trying to conceive a pregnancy and if they or a family member has been diagnosed with diabetes or pre-diabetes.

A one-way ANOVA was used to test for differences in mean values of continuous variables across the six groups of healthy lifestyle scores, while a chi-square test (or a Fisher's test for low cell count values) was used to assess the association between categorical variables and these six groups.

Results

The analysis included 400 female-identifying participants, with a mean age of 32.9 years ($SD \pm 6.3$). 53% of participants identified as non-Hispanic White.

Assessment of Healthy Pre-Pregnancy Lifestyle Factors

Among survey participants, the median number of the six healthy pre-pregnancy lifestyle factors was 3.0, with 61% scoring a 3 or below and 86% scoring a 4 or below (Figure 1).

Figure 1: Proportion of Healthy Pre-Pregnancy Lifestyle Score of Total Survey Participants

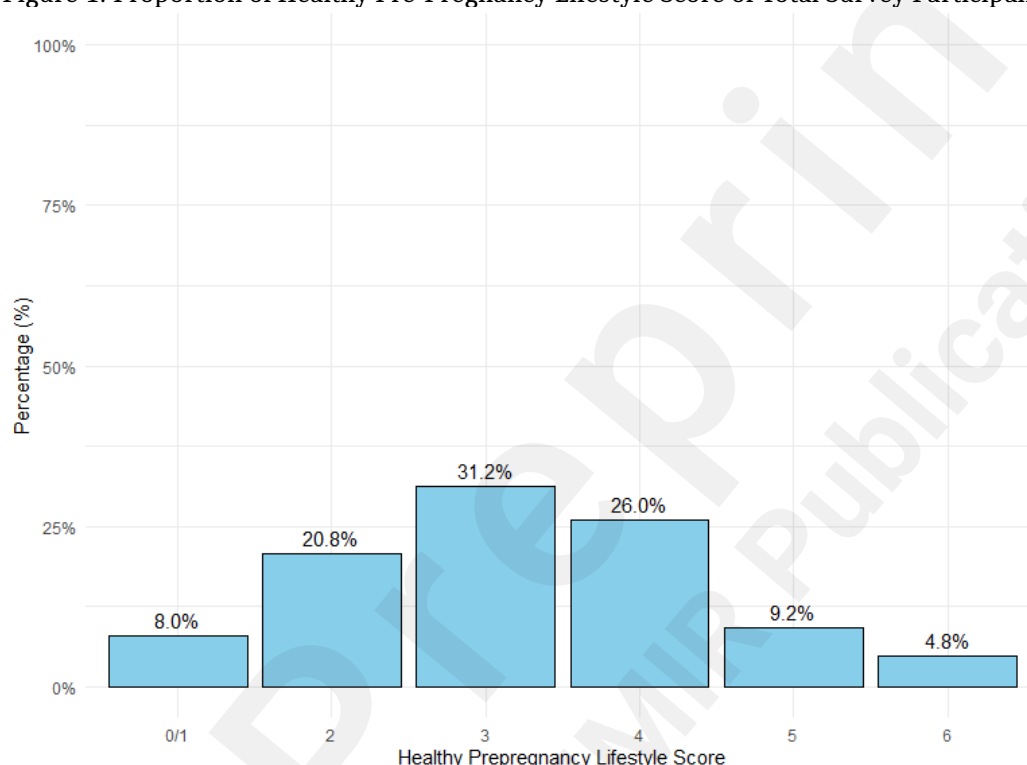


Table 1: Presence of Healthy Pre-Pregnancy Lifestyle Factors in Doveras Cohort (2024), Nurses'Health Study II (2005) and from Nationally Representative Samples of Women Aged 18 to 44 Years (National Health and Nutrition Examination Survey, 2017-2018)

Healthy lifestyle factors	Doveras, 2024	Nurses II, 2005	NHANES, 2017-2018
Body mass index, 18.5-24.9 kg/m ²	18.0%	52.1%	32.2%
Current non-smoker	83.8%	94.3%	81.4%
Moderate to vigorous exercise, ≥ 150 min/week	50.5%	33.9%	54.3%
Healthy diet	21.3%	38.6%	40.0%
Alcohol intake, 0-15g/day	92.0%	93.5%	92.9%
Multivitamin use	55.3%	48.4%	19.4%

The average participant had a median BMI of 31.9 (25th percentile: 26.6, 75th percentile: 37.9), with 82% of participants outside of a BMI range defined as healthy (18.5–24.9). There were significant differences in the mean BMI of participants across the different healthy pre-pregnancy lifestyle scores, (F -value:17.6, $p < 0.001$), and demonstrated that participants with lower healthy pre-pregnancy lifestyle scores had higher average BMI levels. Compared to the Nurses' Health II study and nationally representative samples from NHANES [1], the Doveras Cohort had a greater proportion of respondents with unhealthy BMI and unhealthy diets (Table 1). However the

Doveras Cohort's smoking, physical activity and alcohol intake were similar to the general population.

5% of participants received the highest healthy pre-pregnancy lifestyle score of 6. Within this group, the majority of participants were White or Caucasian (79%).

Unsurprisingly, regarding behavioral characteristics, it was generally observed that participants with lower healthy pre-pregnancy lifestyle scores had lower proportions of healthy behavior. For example, among participants who said they rarely or never exercised (n=63), 85% had a healthy pre-pregnancy lifestyle score of 3 or lower. As for diet, 25% (n=100) of participants felt their diet "needs a lot of work to be considered healthy." In a similar pattern, 84% of people who scored 2 or lower (n=118) believe they could use help with their diet. Furthermore, 44% of all participants did not report taking a prenatal vitamin.

However, there were certain healthy behaviors that the majority of the respondents reported. For example, 92% (n=368) of participants did not report daily alcohol use and 77% (n=307) did not report currently smoking. Although, among those who did report drinking one or more drinks daily, 55% had a healthy pre-pregnancy lifestyle score of 0 or 1 suggesting that individuals who drink daily are more likely to lack other healthy lifestyle behaviors as well.

Associated Health History The survey also assessed self-reported past medical and fertility history (Table 2). 15.3% (n=61) of participants reported they have been diagnosed with prediabetes or diabetes and 25% (n=98) reported a close family member had been diagnosed with diabetes. Among participants who report having diabetes or pre-diabetes, only 1 (1.6%) had a healthy pre-pregnancy lifestyle score of 5 or 6, suggesting individuals with these health conditions are at higher risk for adverse maternal health outcomes and would benefit from improvements in healthy behaviors.

Regarding fertility, 46% (n=182) of people report that they have been trying to conceive for 1 or more years. Among those who reported giving birth prior to the program (n=230), 56% (n=10) of individuals with a pre-pregnancy healthy lifestyle score of 0 or 1 (n=18) took >1 year to conceive. In contrast, 15% (n=2) of those with a score of 6 (n=13) took the same amount of time to conceive.

Table 2: Participant Characteristics by Healthy Pre-Pregnancy Lifestyle Score

	Total*	Healthy Pre-Pregnancy Lifestyle Score						p-value
		0 or 1	2	3	4	5	6	
Women	400	32	83	125	104	37	19	
Demographic Characteristics								
Race/Ethnicity	397							0.01
American Indian or Alaskan Native		0	2	3	0	0	0	
Asian		0	3 (3.5)	5 (4)	5 (5)	2 (5.4)	1 (5.3)	
Black or African American		11 (34)	31 (36)	23 (18)	23 (23)	2 (5.4)	0 (0)	
Hispanic or Latino		2 (6.3)	11 (13)	17 (13)	14 (14)	7 (19)	1 (5.3)	
Mixed Race		1 (3.1)	6 (7.0)	4 (3.2)	5 (5.0)	1 (2.7)	1 (5.3)	
Prefer not to say		3 (9.4)	2 (2.3)	5 (4.0)	1 (1.0)	1 (2.7)	0	
Race not listed		0	0	2 (1.6)	2 (2)	1 (2.7)	1 (5)	
White or Caucasian		12 (38)	31 (36)	67 (53)	50 (50)	23 (62)	15 (79)	
Age	400	32.4±6.4	33.3±6.5	32.3±6.3	33.1±6.3	32.6±5.6	34.6±5.7	0.55
Healthy Pre-Pregnancy Lifestyle Factors								
BMI	397	34.8±7.5	35.9±8.1	34.4±8.4	30.9±7.3	27.5±7.8	21.3±1.5	<.001
Smoking	397							<.001
Yes		18 (56.3)	20 (23)	6 (4.8)	2 (2)	0	0	
Social smoker		7 (22)	5 (5.8)	4 (3.2)	0	0	0	
Former		1 (3.1)	7 (8.1)	4 (3.2)	13 (13)	2 (5.4)	1 (5.3)	
No		3 (9.4)	54 (63)	112 (89)	85 (85)	35 (95)	18 (95)	
Physical Activity	397							<.001
I rarely or never work out		15 (24)	18 (29)	22 (35)	7 (11)	1 (1.6)	0	
~.5 hours/week		5 (16)	19 (22)	8 (6.3)	7 (7)	0	0	
~1.5 hours/week		3 (9.4)	8 (9.3)	9 (7.1)	5 (5.0)	2 (5.4)	0	
~2 hours/week		3 (9.4)	18 (21)	14 (11)	5 (5.0)	0	0	
~2.5 hours/week		0	2 (2.3)	5 (4.0)	9 (9.0)	4 (11)	3 (16)	
3+ hours/week		0	12 (14)	56 (44)	66 (66)	29 (78)	16 (84)	
Alcohol use	397							0.63
No		22 (69)	76 (88)	120 (95)	95 (95)	36 (97)	19 (100)	
Yes – 1 drink daily		5 (16)	7 (8.1)	5 (4.0)	5 (5.0)	1 (2.7)	0	
Yes – 2+ drinks daily		2 (6.3)	3 (3.5)	1 (0.8)	0	0	0	
Diet	397							<.001
I would say I mostly eat healthy		0	3 (3.5)	9 (7.1)	25 (25)	29 (79)	19 (100)	
I have some healthy habits		15 (47)	49 (57)	83 (66)	58 (58)	7 (19)	0	
My diet needs a lot of work to be considered healthy		14 (44)	34 (40)	34 (27)	17 (17)	1 (2.7)	0	
Prenatal Vitamin	397							<.001
No		28 (88)	71 (83)	60 (48)	14 (14)	3 (8.1)	0	
Yes		1 (3.1)	15 (17)	66 (52)	86 (86)	34 (92)	19 (100)	
Reproductive and Clinical History								
Clinical definition of infertility	182	17 (53)	39 (47)	65 (52)	45 (43)	13 (35)	3 (15.8)	0.04
Previous birth	230	7 (22)	36 (43)	59 (47)	51 (49)	11 (30)	3 (16)	0.01
Hormone imbalance	268	20 (63)	57 (69)	78 (62)	69 (66)	28 (76)	16 (84)	0.37
Diabetes or pre-diabetes	61	9 (28)	12 (15)	17 (14)	22 (21)	1 (2.7)	0	0.01
Endometriosis	42	6 (19)	7 (8.4)	12 (9.6)	13 (13)	2 (5.4)	2 (11)	0.51

*Total survey respondents who answered the survey question completely

Discussion

The population of people seeking Doveras' services present, before joining the platform, with considerably lower Healthy Pre-Pregnancy Lifestyle Factor scores than those reported in the Nurses' Health Study. Since the Doveras preconception platform is marketed for its fertility benefits, this research may have oversampled people who are having trouble conceiving, which could contribute to why this cohort represents a particularly at-risk group of people for adverse pregnancy outcomes. The Doveras cohort is also demographically diverse, roughly matching the general population. The unique lifestyle and demographic baseline of this cohort points to a few avenues of significance and areas for future research, discussed below.

The Risk Reduction Potential of The Population Seeking Services from Doveras

These results suggest that the majority of people seeking preconception services during this period from Doveras have the potential to adopt additional healthy behaviors that may contribute to reducing their risk of adverse maternal health outcomes via the personalized lifestyle programming the digital health platform provides.

The lifestyle factor gaps exhibited in these participants during the preconception window have been shown to be related to various risks they might experience during pregnancy. For example, a prospective cohort of 2449 women as a part of the Pregnancy Environment and Lifestyle Study, found that modifiable lifestyle factors like healthy weight, high-quality diet, and low levels of stress were associated with a reduced risk of preterm birth by 42%, 32% and 40%, respectively. [1] Additionally, a meta-analysis looking at 17 trials encompassing 137,791 women found that taking multiple micronutrient supplements resulted in reduced risk of having a newborn infant with low birth weight. [5] The Nurses' Health Study II, which used the same six Healthy Pre-Pregnancy Lifestyle Factors as the present study, shows similar value in pre-pregnancy adherence to these lifestyle factors. This research showed that approximately one in three reported pregnancies ($n=9,702$, 35.8%) in the cohort was complicated by one or more adverse pregnancy outcomes. The researchers found that these six specific low-risk factors were inversely associated with risk of adverse pregnancy outcomes — including miscarriage, gestational hypertension, preeclampsia, gestational diabetes, preterm birth, and low birthweight — in a dose-dependent manner. Compared with women who had zero or one healthy pre-pregnancy lifestyle factor, those with six had a 37% lower risk of adverse pregnancy outcomes, driven primarily by lower risks of gestational diabetes, gestational hypertension, and low birth weight.

A digital health platform like Doveras, that identifies these risk factors and supports users to adopt personalized lifestyle changes to reduce their risk, may be a useful preventative tool. The Nurses' Health Study researchers concluded that if the observed relationships between the studied behaviors and adverse maternal health outcomes were causal, 19% of adverse pregnancy outcomes could have been prevented by the adoption of all six Healthy Pre-Pregnancy Lifestyle Factors.

Given that the Doveras cohort presents with considerably lower (i.e., less healthy) scores than the Nurses' cohort, the impact on the outcomes for this specific population might be even greater than previously reported.

Focus Areas for a Risk-Reduction Intervention for this Population

In addition to better understanding this population's risk as a whole, this analysis also elevates which parts of a lifestyle intervention may have the greatest impact on specific healthy behaviors and their known impacts on risk reduction. Specifically, the Doveras population over-indexed on the lack of these specific healthy factors: BMI, healthy diet, physical activity, and taking a prenatal, in that order. 82% of the Doveras participants reported a high BMI (≥ 25 kg/m²), which may put them at higher risk specifically of gestational hypertension, preeclampsia, gestational diabetes, and miscarriage, according to data from the Nurses Health Study II. [1] 44% of the study participants reported not currently taking a prenatal vitamin, which is associated with an increased risk for miscarriage and having an infant with low birth weight. [1]

The Nurses Health Study II also reported that the pre-pregnancy healthy lifestyle factors screened for, except avoiding harmful alcohol consumption and regular physical activity, were independently associated with lower risk of adverse pregnancy outcomes after mutual adjustment for each other. Healthy BMI, high-quality diet, and multivitamin supplementation showed the strongest inverse associations with adverse pregnancy outcomes.

The nutrition and metabolic health based programming of the Doveras digital health platform is particularly relevant to and will likely have the greatest impact for the population seeking its services.

The Potential of a Digital Preconception Health Platform to Deliver Intervention

A critical factor will be whether a digital intervention can facilitate sustained behavior change, and if so, whether such an intervention can decrease adverse pregnancy outcomes. Previous studies have suggested that lifestyle interventions deployed electronically during the preconception period can be effective [10-12]. Randomized controlled trials have reported that digital lifestyle interventions targeting weight loss, for example, had the same results as in-person or phone interventions, suggesting all methods of intervention are comparable in terms of effectiveness. [10,11] In the reproduction space, S. Smith *et al.* have shown that nudging behavior change during pre-pregnancy digital interventions to encourage pregnancy preparation is feasible. [12] These studies show strong promise for a digital platform like Doveras to deliver behavior change interventions electronically to target

identified risk factors. Future studies should validate the platform's usability and behavior change capabilities.

Potential Limitations and Validation of Self-Reported Measures

Both the self-selection of the program and the self-reported nature of the survey present inherent limitations. For example, the Doveras cohort may not be fully representative of all individuals trying to conceive, as participants who opt into this product might be more likely to be experiencing fertility challenges or have a higher motivation to improve their lifestyle behaviors. Furthermore, as with all self-reported data, the potential for recall error is another potential concern. In order to validate our measures, we compared diet and BMI values of participants who both completed this survey and who went on to purchase the full product and complete the more extensive assessment. For diet, we found that among a subset of participants who completed both the survey and the full Doveras product assessment, 86% showed consistency between their self-reported 'healthy eating' rating and their extensive "Dietary Approaches to Stop Hypertension" score. For BMI, after cleaning for outliers, we compared reported height and weight values between both surveys. While the product assessment occurred at a different time, the highest percentage difference was 3.3%, suggesting the reported BMI values are reasonably accurate, despite the survey respondents's high median BMI. While these validations were based on small samples, they provide a measure of reliability of the self-reported measures. Since this study was cross-sectional, we can only comment on associations and cannot yet determine if the online intervention can change maternal health outcomes. We hope to address this in future studies. Our study population is reflective of the general population of the United States, at least from a demographic standpoint. This cannot be said about most prior studies in reproductive medicine, suggesting a substantial benefit of an online platform for patient interaction.

Conclusions

To date, the Doveras platform has largely been marketed to and used by people interested in conception with a focus on fertility optimization, but given its unique intervention point during the pre-pregnancy window, it could be expanded to include all couples looking to optimize pregnancy and birth outcomes.

Our study shows the potential of such a digital health platform to identify pre-conception risk factors and to deliver personalized lifestyle interventions during the preconception window with the intention of proactively preventing adverse pregnancy outcomes. At least 86% of people seeking the fertility services from the Doveras digital health platform exhibit more than 2 known lifestyle risk factors that can impact their chances of a healthy pregnancy and birth. The platform therefore may have substantial opportunity to intervene in an affordable and accessible way and lower adverse maternal health risks of this population — including miscarriage, gestational diabetes, and gestational hypertension.

Author Disclosure Statement

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: N.L. is the founder and CEO of Doveras Fertility Inc. J.C., A.J.G, P.S., and E.M. are advisors for Doveras Fertility Inc.

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Supplementary Files

Figures

Proportion of healthy pre-pregnancy lifestyle score of total survey participants.

