


### RESEARCH ARTICLE

## Iron supplementation during the first trimester of pregnancy after a national change of recommendation: a Danish cross-sectional study

Line B. Løvschal<sup>1</sup>, Stinne Høgh<sup>1,2</sup>, Thomas Bergholt<sup>1,3,4</sup>, Kate Maslin<sup>5</sup>, Jill Shawe<sup>5,6</sup>, Hanne K. Hegaard<sup>1,2,3</sup> and Mie G. de Wolff<sup>1,2,7\*</sup> 

<sup>1</sup>Department of Obstetrics, The Juliane Marie Centre, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark

<sup>2</sup>Research Unit Women's and Children's Health, The Juliane Marie Centre, Copenhagen University Hospital Rigshospitalet, Section 7821, Blegdamsvej 9, DK-2100 Copenhagen, Denmark

<sup>3</sup>Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3B, København N, 2200 Copenhagen, Denmark

<sup>4</sup>Department of Obstetrics and Gynaecology, Herlev-Gentofte Hospital, Borgmester Ib Juuls Vej 1, 14, 2730 Herlev, Denmark

<sup>5</sup>School of Nursing and Midwifery, University of Plymouth, Devon PL4 8AA, UK

<sup>6</sup>Royal Cornwall Hospitals NHS Trust Clinical School, Truro Cornwall TR1 3HD, UK

<sup>7</sup>Department of Gynaecology and Obstetrics, Copenhagen University Hospital, Hvidovre. Kettegaards Alle 30, 2650 Hvidovre, Denmark

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### Abstract

In 2013, the Danish Health Authorities recommended a change in prophylactic iron supplementation to 40–50 mg/d from gestational week 10. Hence, the aims of the present study were (1) to estimate the prevalence of women who follow the Danish recommendation on iron supplementation during the last 3 weeks of the first trimester of pregnancy and (2) to identify potential sociodemographic, reproductive and health-related pre-pregnancy predictors for iron supplementation during the first trimester. We conducted a cross-sectional study with data from the hospital-based Copenhagen Pregnancy Cohort. Characteristics were analysed by descriptive statistics and multivariable logistic regression analysis was performed to examine the associations between predictors and iron supplementation during the last 3 weeks of the first trimester. The study population consisted of 23 533 pregnant women attending antenatal care at Copenhagen University Hospital - Rigshospitalet from October 2013 to May 2019. The prevalence of iron supplementation according to recommendations was 49.1%. The pre-pregnancy factors of  $\geq 40$  years of age, the educational level below a higher degree and a vegetarian or vegan diet were identified as predictors for iron supplementation during the first trimester of pregnancy. Approximately half of the women were supplemented with the recommended dose of iron during the first trimester of pregnancy. We identified pre-pregnancy predictors associated with iron supplementation. Interventions that target women of reproductive age are needed. An enhanced focus on iron supplementation during pregnancy should be incorporated in pre-pregnancy and interpregnancy counselling.

**Key words:** Health behaviour: Iron deficiency anaemia: Iron supplementation: Preconception: Pregnancy

**Abbreviations:** aOR: adjusted odds ratio; BMI: body mass index; ID: iron deficiency; IDA: iron deficiency anaemia; OR: odds ratio

\* **Corresponding author:** Mie G. de Wolff, email: [mie.gaarskjaer.de.wolff@regionh.dk](mailto:mie.gaarskjaer.de.wolff@regionh.dk)



## Introduction

Iron is a micronutrient of significant importance as it is a vital component in the production of blood formation as well as being the oxygen-binding element of haemoglobin<sup>(1–3)</sup>. In pregnancy, the physiological requirement for iron doubles during the second and third trimesters due to the increasing maternal blood volume, the development of the placenta, foetal growth and the expected blood loss during delivery<sup>(4,5)</sup>. Hence, the maternal plasma volume increases by 40–50 % during pregnancy<sup>(6)</sup>. However, this process develops incommensurately with the erythrocyte mass, which only increases by 25 %<sup>(6)</sup>. Therefore, women with low iron stores at conception or women who do not meet the nutritional iron requirement during pregnancy are at increased risk of developing iron deficiency (ID) (serum ferritin <15 µ/l) or iron deficiency anaemia (IDA) (haemoglobin concentrations of <110 g/l and serum ferritin of <15 µ/l)<sup>(1,7)</sup>.

Globally, the prevalence of maternal anaemia varies vastly, mainly due to differences in nutritional status in low- and high-income countries<sup>(8)</sup>. According to the World Health Organization (WHO), the global prevalence of maternal anaemia during pregnancy is nearly 42 %, of which half is presumed to be caused by ID<sup>(8)</sup>. It is estimated that a body iron store of ≥500 mg in early pregnancy is required to complete a normal singleton pregnancy without iron supplementation<sup>(9)</sup>. Nevertheless, a predominance of European women of reproductive age is estimated to have a body iron reserve of only 200–300 mg<sup>(9)</sup>, below the required to complete a pregnancy without ID or IDA. In Europe, the average recommended daily dietary iron intake for women of reproductive age is 15 mg/d<sup>(10)</sup>. However, a review of forty-nine studies from twenty-nine European countries showed that 61–97 % of women of reproductive age had dietary iron intake below this recommendation. In Denmark, the dietary iron intake was only 9.7 mg/d<sup>(10)</sup>. Furthermore, a review based on eleven European studies showed that the prevalence of ID and IDA was 28–85 and 21–35 % at 32 and 39 weeks of gestation, respectively, among pregnant women who did not take iron supplements<sup>(7)</sup>.

The WHO<sup>(11)</sup> has established a global prophylactic iron recommendation of 30–60 mg/d throughout pregnancy depending on the individual IDA prevalence in low- and high-income populations<sup>(11)</sup>. As a result, recommendations are inconsistent around the world. Countries such as the UK and Australia only recommend iron supplementation for women who show symptoms of ID or IDA<sup>(12,13)</sup>. A Danish RCT found that 40 mg/d is enough to prevent ID or IDA in 90 and 95 %, respectively, of all pregnancies in Denmark<sup>(14)</sup>. Thus in 2013, the Danish Health Authorities changed their recommendation on prophylactic iron supplementation from 50–70 mg/d from week 20 of pregnancy to 40–50 mg/d from week 10, for the remaining duration of pregnancy (or week 18 at the latest if pregnancy nausea or vomiting preclude iron supplementation)<sup>(15)</sup>.

To our knowledge, no Danish study has examined iron supplementation during the first trimester since the revised national recommendation was implemented. However,

previous studies have identified maternal age, education, employment status, parity, degree of pregnancy planning, use of other food supplements and body mass index (BMI) as influencing factors on the intake of iron supplementation during pregnancy<sup>(16–19)</sup>. Therefore, it is important to highlight such predictors and evaluate whether pregnant women follow the national recommendation when changed to strengthen pre-conception and pregnancy counselling. Hence, the present study's aims were (1) to estimate the prevalence of women who follow the Danish recommendation on iron supplementation during the last 3 weeks of the first trimester of pregnancy and (2) to identify potential sociodemographic, reproductive and health-related pre-pregnancy predictors for iron supplementation during the last 3 weeks of the first trimester.

## Methods

### Design and study population

We conducted a cross-sectional study using data from the Copenhagen Pregnancy Cohort. The cohort consisted of pregnant women followed at the Department of Obstetrics at Copenhagen University Hospital Rigshospitalet, Denmark. The hospital serves pregnant women living in the capital without known health-related risk factors and is a tertiary referral facility for the country's eastern region. In 2018, there were 5381 deliveries, equivalent to about 11 % of all deliveries nationally<sup>(20)</sup>.

The Danish national prenatal screening programme offers all pregnant women a first-trimester scan. The cohort was implemented on 16 September 2012. An email with a data link to a web-based clinical questionnaire consisting of twenty-five items with additional related sub-questions was automatically sent digitally to all women who had booked an appointment for a first-trimester scan at the Obstetric Department. In Denmark, >90 % of all pregnant women attend the first-trimester ultrasound scan<sup>(21)</sup>. After that, responses were transferred to their medical records for use during their antenatal care. Subsequently, responses were also stored in a clinical database for use in scientific studies if approved by the National Health Authorities. On average, women from the Copenhagen Cohort responded to the clinical questionnaire at gestational week 10.2 (SD 2.1)<sup>(22)</sup>. The questionnaire was accessible in Danish and English and contained sociodemographic characteristics, reproductive and obstetric history, health status and health behaviour, including dietary behaviour. The data provided were subsequently transferred to the participant's medical records.

From 16 September 2012 to 24 May 2019, a total of 33 465 women received the questionnaire. In the present study, we only used data from 1 October 2013 when the revised recommendation on iron supplementation during pregnancy was implemented. From 1 October 2013 to 24 May 2019, a total of 28 017 women received the questionnaire. Women who had a miscarriage (*n* 1116), moved to another borough (*n* 27), or were transferred to another birth facility (*n* 151), were excluded from the study leaving an eligible study population of 26 723. Out of these, 24 203 responded to the clinical

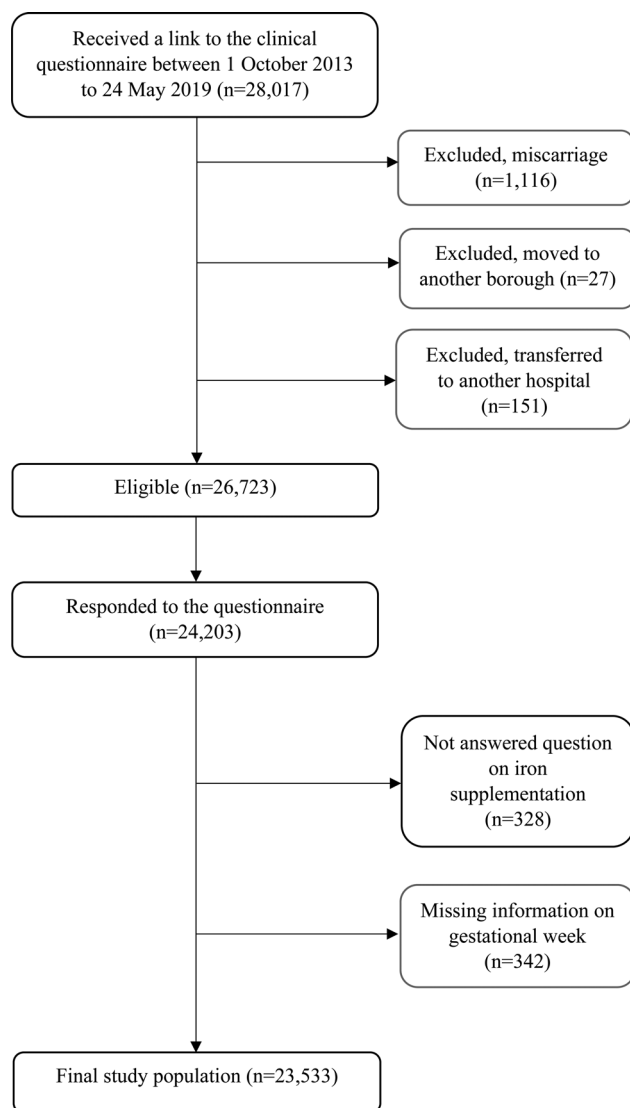


Fig. 1. Flowchart of the study population.

questionnaire, resulting in a response rate of 90.6%. Of the completed questionnaires, 328 women had not answered the question on iron supplementation, and a further 342 had missing information on the gestational week, so these were also excluded. This resulted in a final study population of 23 533 pregnant women (Fig. 1).

### Study variables

In the category of food supplements, the specific question of interest on prophylactic iron supplementation was phrased as ‘Do you currently take a daily iron supplement of at least 40–50 mg?’ The question could be answered as yes or no. For the present study, we defined women who answered yes as ‘users of iron’ and women who answered no as ‘non-users’.

Additionally, the following variables on maternal characteristics were extracted from the questionnaire. Sociodemographic characteristics included maternal age (<25, 25–29, 30–34, 35–39 and ≥40 years), highest obtained educational level (compulsory education, technical degree, short degree (1–2 years),

intermediate degree (3–4 years) or higher degree), employment status (employed, unemployed, student or other) and cohabiting with a partner/spouse (no/yes). Danish language skills were evaluated with the ability to read and understand Danish (no/yes).

Reproductive history included parity (nulliparous or multiparous), degree of pregnancy planning, evaluated by using the Swedish Pregnancy Planning Scale<sup>(23)</sup> (high degree of pregnancy planning, neither planned nor unplanned, low degree of pregnancy planning), method of conception [spontaneous or assisted reproductive technology (ART)] and previous miscarriages (no/yes).

Information on health status included chronic conditions (no/yes). The women could tick ‘yes’ for the following conditions at the time of pregnancy: high blood pressure, lung disease, diabetes type 1 or 2, metabolic disorder, arthritis, epilepsy, mental illness, heart disease, migraine or other diseases, or ‘no, I did not suffer from any diseases’. They were not asked about prior conditions with IDA. Health behaviour factors before pregnancy included pre-pregnancy BMI [calculated from weight and height and grouped according to the WHO recommendations<sup>(24)</sup> as underweight (BMI: <18.5 kg/m<sup>2</sup>), average weight (BMI: 18.5–24.9 kg/m<sup>2</sup>), overweight (BMI: 25–29.99 kg/m<sup>2</sup>) and obese (BMI: ≥30 kg/m<sup>2</sup>)], smoking status before pregnancy (no/yes) and exercise before pregnancy defined as ≥3.5 h/week (no/yes) corresponding to the Danish Health Authority’s recommendation<sup>(25)</sup>. Finally, the questionnaire also yielded information on dietary behaviour during pregnancy (ordinary varied, ordinary not varied and vegetarian or vegan) and the dietary supplement folic acid intake, including pregnancy multivitamins containing folic acid (no/yes) at the time of conception.

### Statistical analysis

We calculated the prevalence in number (*n*) and percentage (%) of iron supplementation for users and non-users and analysed the characteristics of the study population through descriptive statistics. We used generalised estimating equations to account for women with more than one pregnancy in the cohort. To examine the association between potential predictors and the intake of prophylactic iron supplementation during the first trimester, univariate and multivariable logistic regression analyses were performed and presented as crude odds ratio (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI). The sociodemographic variables maternal age and education, reproductive history, parity and health behaviour variable BMI have previously been determined as predictors for iron supplementation in comparable studies<sup>(16–18)</sup>. These were therefore included in the multivariable logistic regression analysis as potential pre-pregnancy predictors. In addition, we hypothesised that the health behaviour variables folic acid supplementation at the time of conception, dietary behaviour during pregnancy, exercise before pregnancy and smoking before pregnancy could be potential pre-pregnancy health behaviour predictors for iron supplementation as they have previously been determined as predictors for iron intake during pregnancy<sup>(16,19)</sup>. The variable dietary



behaviour comprised diet during pregnancy in the clinical questionnaire. However, previous studies have estimated that a predominance of pregnant women does not change their dietary behaviour regarding enhancing food intake that contributes to important nutrients essential for the development of a normal pregnancy<sup>(26,27)</sup>. This variable was therefore also hypothesised as a potential pre-pregnancy health behaviour predictor and included in the analysis. We checked for interaction effects between co-variables in the regression model and found no evidence to support this. Also, the assumptions for the multivariable logistic regression model were checked before performing analysis, and no evidence for a violation of the assumptions was found.

A two-sided  $P < 0.05$  was considered statistically significant. Statistical analyses were conducted in SPSS (IBM Statistics SPSS version 25).

## Results

### *Iron supplementation during the first trimester of pregnancy*

In the present study, the prevalence of iron supplementation of 40–50 mg/d was 49.1 % (95 % CI 48.5, 49.8) ( $n$  11 559) during the last 3 weeks of the first trimester.

### *Maternal characteristics of the study population*

The overall maternal characteristics of the study population ( $n$  23 533) in relation to iron supplementation are presented in Table 1. The majority of the study population was between 30 and 34 years of age (39.9 %) with a mean age of 32 years (SD 4.4), had a higher degree (53.5 %), were employed (72.9 %), living with a partner (91.8 %), and were able to read and understand Danish (94.5 %). A predominance was nulliparous (62.7 %) and had conceived spontaneously (86.8 %), had a high degree of pregnancy planning (74.4 %) and had no previous miscarriages (73.4 %). Mostly, the women had a normal BMI (18.5–24.9 kg/m<sup>2</sup>) (73.2 %) and were non-smokers before current pregnancy (87.6 %), as well as exercised  $\geq 3.5$  h/week (57.8 %) before their pregnancy. Generally, the women reported to have an ordinary, varied diet (78.9 %) and had taken folic acid supplementation at the time of conception (55 %). A considerable part of the population reported having a chronic condition (22.4 %) (Table 1).

### *Predictors for iron supplementation during the first trimester of pregnancy*

Results from the multivariable logistic regression analyses are shown in Table 2. Data from 23 533 women were included in the analyses, of which 5469 women contributed to the study with two to four pregnancies. The following predictors were identified in the multivariable logistic regression analysis. In the sociodemographic category, women who were  $\geq 40$  years of age had 17 % higher odds (aOR: 1.17; 95 % CI: 1.02, 1.35) of being users of iron supplementation during the first trimester compared with women who were 30–34 years of age. Regarding the highest obtained educational level, women with a compulsory education had 17 % higher

**Table 1.** Characteristics of the study population,  $n$  23 533

|  | <i>n</i> (%)  |
|--|---------------|
| Iron supplementation during early pregnancy        | 23 533 (100)  |
| Users of iron                                      | 11 559 (49.1) |
| Non-users  | 11 974 (50.9) |
| Missing  | 0             |
| Maternal age (years)                               |               |
| <25  | 994 (4.2)     |
| 25–29  | 7372 (31.3)   |
| 30–34  | 9377 (39.9)   |
| 35–39  | 4666 (19.8)   |
| $\geq 40$  | 1054 (4.5)    |
| Missing  | 70 (0.3)      |
| Mean (sd) (years)                                  | 32 (4.4)      |
| Highest obtained educational level                 |               |
| Higher degree                                      | 12 585 (53.5) |
| Intermediate degree (3–4 years)                    | 6851 (29.1)   |
| Short degree (1–2 years)                           | 1389 (5.9)    |
| Technical degree                                   | 738 (3.1)     |
| Compulsory education                               | 1428 (6.1)    |
| Missing  | 542 (2.3)     |
| Employment status                                  |               |
| Employed   | 17 159 (72.9) |
| Unemployed   | 1261 (5.4)    |
| Student  | 3225 (13.7)   |
| Other, i.e. maternity leave/retired                | 1454 (6.2)    |
| Missing  | 434 (1.8)     |
| Cohabitation                                       |               |
| No   | 1816 (7.7)    |
| Yes  | 21 593 (91.8) |
| Missing  | 124 (0.5)     |
| Read and understand the Danish language            |               |
| No   | 1068 (4.5)    |
| Yes  | 22 239 (94.5) |
| Missing  | 226 (1.0)     |
| Parity   |               |
| Nulliparous  | 14 754 (62.7) |
| Multiparous  | 8779 (37.3)   |
| Missing  | 0             |
| Degree of pregnancy planning                       |               |
| High degree of pregnancy planning                  | 17 492 (74.4) |
| Neither planned nor unplanned                      | 3867 (16.4)   |
| Low degree of pregnancy planning                   | 1890 (8.0)    |
| Missing  | 284 (1.2)     |
| Method of conception                               |               |
| Spontaneous  | 20 432 (86.8) |
| Assisted reproduction technology (ART)             | 2809 (12.0)   |
| Missing  | 292 (1.2)     |
| Previous miscarriage                               |               |
| No   | 17 274 (73.4) |
| Yes  | 6259 (26.6)   |
| Missing  | 0             |
| Chronic condition                                  |               |
| No   | 18 263 (77.6) |
| Yes  | 5270 (22.4)   |
| Missing  | 0             |
| Pre-pregnancy body mass index (kg/m <sup>2</sup> ) |               |
| Underweight (<18.5)                                | 1066 (4.5)    |
| Normal (18.5–24.9)                                 | 17 232 (73.2) |
| Overweight (25–29.9)                               | 2998 (12.8)   |
| Obese ( $\geq 30$ )                                | 1042 (4.4)    |
| Missing  | 1195 (5.1)    |
| Smoking before pregnancy                           |               |
| No   | 20 614 (87.6) |
| Yes  | 2740 (11.6)   |
| Missing  | 179 (0.8)     |
| Exercise before pregnancy <sup>a</sup>             |               |
| No   | 9937 (42.2)   |
| Yes  | 13 596 (57.8) |
| Missing  | 0             |

*Continued*

**Table 1.** Continued

|  | <i>n</i> (%)  |
|--|---------------|
| Folic acid supplementation at the time of conception |               |
| No   | 10 435 (44.3) |
| Yes  | 12 936 (55.0) |
| Missing  | 162 (0.7)     |
| Dietary behaviour during pregnancy                   |               |
| Ordinary, varied                                     | 18 572 (78.9) |
| Ordinary, not varied                                 | 2257 (9.6)    |
| Vegetarian or vegan                                  | 1475 (6.3)    |
| Missing  | 1229 (5.2)    |

<sup>a</sup>  $\geq 3.5$  h/week corresponding to the Danish Health Authority's recommendation.

odds (aOR: 1.17; 95 % CI: 1.02, 1.33) of being users, women who had a technical degree had 19 % higher odds (aOR: 1.19; 95 % CI: 1.01, 1.40) and women who had a short degree (1–2 years) had 22 % higher odds (aOR: 1.22; 95 % CI: 1.08, 1.38) of being users, and women who had an intermediate degree (3–4 years) had 10 % higher odds (aOR: 1.10; 95 % CI: 1.03, 1.17) of being users of iron supplementation during the first trimester than women with a higher degree. Finally, the analysis showed that women who had reported to be vegetarians or vegans had 18 % higher odds (aOR: 1.18; 95 % CI: 1.05, 1.31) of being iron users compared with women with an ordinary, varied diet.

**Table 2.** Univariate and multivariable associations between sociodemographic, reproductive history, pre-pregnancy health behaviour predictors and iron supplementation during the first trimester, *n* 23 533

| Iron supplementation during early pregnancy          | Users of iron<br><i>n</i> (%) | Non-users<br><i>n</i> (%) | Crude<br>OR | Adjusted OR <sup>a</sup><br>95 % (CI) |
|--|-------------------------------|---------------------------|-------------|---------------------------------------|
| <b>Sociodemographic</b>                              |                               |                           |             |                                       |
| Maternal age (years)                                 |                               |                           |             |                                       |
| <25  | 484 (4.2)                     | 510 (4.3)                 | 0.99        | 0.89 (0.76–1.05)                      |
| 25–29  | 3558 (30.8)                   | 3814 (31.9)               | 0.97        | 0.94 (0.88–1.01)                      |
| 30–34  | 4593 (39.8)                   | 4784 (39.9)               | Ref.        | Ref.                                  |
| 35–39  | 2337 (20.2)                   | 2329 (19.4)               | 1.05        | 1.05 (0.97–1.13)                      |
| $\geq 40$  | 548 (4.7)                     | 506 (4.2)                 | 1.13        | 1.17 (1.02–1.35)                      |
| Missing: 70  | 39 (0.3)                      | 31 (0.3)                  |             |                                       |
| Highest obtained educational level                   |                               |                           |             |                                       |
| Higher degree  | 6040 (52.2)                   | 6545 (54.7)               | Ref.        | Ref.                                  |
| Intermediate degree (3–4 years)                      | 3421 (29.6)                   | 3430 (28.6)               | 1.08        | 1.10 (1.03–1.17)                      |
| Short degree (1–2 years)                             | 724 (6.3)                     | 665 (5.5)                 | 1.18        | 1.22 (1.08–1.38)                      |
| Technical degree                                     | 380 (3.3)                     | 358 (3.0)                 | 1.14        | 1.19 (1.01–1.40)                      |
| Compulsory education                                 | 714 (6.2)                     | 714 (6.0)                 | 1.08        | 1.17 (1.02–1.33)                      |
| Missing: 542   | 280 (2.4)                     | 262 (2.2)                 |             |                                       |
| <b>Reproductive history</b>                          |                               |                           |             |                                       |
| Parity   |                               |                           |             |                                       |
| Nulliparous  | 7320 (63.3)                   | 7434 (62.1)               | Ref.        | Ref.                                  |
| Multiparous  | 4239 (36.7)                   | 4540 (37.9)               | 0.95        | 0.94 (0.88–1.00)                      |
| Missing: 0   | 0                             | 0                         |             |                                       |
| <b>Pre-pregnancy health behaviour factors</b>        |                               |                           |             |                                       |
| Pre-pregnancy Body Mass Index (kg/m <sup>2</sup> )   |                               |                           |             |                                       |
| Underweight (<18.5)                                  | 520 (4.5)                     | 546 (4.5)                 | 0.98        | 0.97 (0.85–1.11)                      |
| Normal (18.5–24.9)                                   | 8506 (73.6)                   | 8726 (72.9)               | Ref.        | Ref.                                  |
| Overweight (25–29.9)                                 | 1442 (12.5)                   | 1556 (13.0)               | 0.95        | 0.96 (0.89–1.04)                      |
| Obese ( $\geq 30$ )                                  | 491 (4.2)                     | 551 (4.6)                 | 0.91        | 0.90 (0.79–1.03)                      |
| Missing: 1195  | 600 (5.2)                     | 595 (5.0)                 |             |                                       |
| Exercise before pregnancy                            |                               |                           |             |                                       |
| No   | 4825 (41.7)                   | 5112 (42.7)               | 0.96        | 0.96 (0.91–1.02)                      |
| Yes  | 6734 (58.3)                   | 6862 (57.3)               | Ref.        | Ref.                                  |
| Missing: 0   | 0                             | 0                         |             |                                       |
| Smoking before pregnancy                             |                               |                           |             |                                       |
| No   | 10104 (87.4)                  | 10510 (87.8)              | Ref.        | Ref.                                  |
| Yes  | 1360 (11.8)                   | 1380 (11.5)               | 1.02        | 1.03 (0.94–1.12)                      |
| Missing: 179   | 95 (0.8)                      | 84 (0.7)                  |             |                                       |
| Folic acid supplementation at the time of conception |                               |                           |             |                                       |
| No   | 5086 (44.0)                   | 5349 (44.7)               | 0.97        | 0.97 (0.92–1.03)                      |
| Yes  | 6391 (55.3)                   | 6545 (54.6)               | Ref.        | Ref.                                  |
| Missing: 162   | 82 (0.7)                      | 80 (0.7)                  |             |                                       |
| Dietary behaviour                                    |                               |                           |             |                                       |
| Ordinary, varied                                     | 9102 (78.8)                   | 9470 (79.1)               | Ref.        | Ref.                                  |
| Ordinary, not varied                                 | 1067 (9.2)                    | 1190 (9.9)                | 0.94        | 0.93 (0.85–1.02)                      |
| Vegetarian or vegan                                  | 789 (6.8)                     | 686 (5.7)                 | 1.19        | 1.18 (1.05–1.31)                      |
| Missing: 1229  | 601 (5.2)                     | 628 (5.3)                 |             |                                       |

<sup>a</sup> In the adjusted model, all results are adjusted for age, highest obtained educational level, parity, pre-pregnancy body mass index, exercise before pregnancy, smoking before pregnancy, folic acid at the time of conception and dietary behaviour



## Discussion

In this large hospital-based cross-sectional study, the estimated prevalence of iron supplementation of 40–50 mg/d during the last 3 weeks of the first trimester was 49.1 %. The present study was the first to estimate the prevalence of iron supplementation after a change in the national recommendation for iron supplementation introduced in October 2013. Pre-pregnancy predictors for adherence to the national recommendation for iron supplementation were higher maternal age, an educational level below a higher degree and a vegetarian or vegan diet.

In the present study, this prevalence of 49.1 % for iron supplementation during the first trimester differed from a prior Danish study from 2007 ( $n$  50 902)<sup>(16)</sup>. This previous study showed that only 9.9 % of the women had an intake of iron supplementation of 50–70 mg/d, which corresponded to the previous Danish recommendations on iron supplementation during pregnancy<sup>(16)</sup>. However, the same study found that 77.2 % of the study population were users of iron supplementation at any time between early pregnancy and gestational week 30. However, the daily iron dose ranged between 1 and >101 mg<sup>(16)</sup>. A lack of uniformity may explain the wide range in iron doses at the time in iron brands marketed to pregnant women<sup>(16)</sup>. Several brands contained 100 mg, which may have resulted in the women not being aware that their iron supplement of choice exceeded the recommended iron dose of 50–70 mg/d. Therefore, it is difficult to compare the study results on iron supplementation during pregnancy.

Previous studies that have examined iron supplementation during pregnancy in Finland<sup>(18)</sup>, Germany<sup>(19)</sup> and Austria<sup>(28)</sup> found an overall prevalence between 65.2 and 68.3 % of iron supplementation during pregnancy<sup>(18,19,28)</sup>. In addition, a French study reported an increasing prevalence of iron supplementation from only 18.5 % in the first trimester to 63.9 % in the third trimester<sup>(17)</sup>. However, although the study results on prevalence are similar, a comparison should be made with caution as none of these countries recommend prophylactic iron supplementation during pregnancy. The lack of international consensus is apparent as the previous studies have examined any form and dose of iron supplementation during pregnancy<sup>(17–19,28)</sup>. This may signify that generalisation between global study populations regarding iron supplementation is not feasible. Therefore, individual study results should be interpreted in the context of the local, national recommendations.

We aimed to identify pre-pregnancy predictors for iron supplementation during the last 3 weeks of the first trimester. We found that advanced age was a predictor for iron supplementation as women  $\geq 40$  years of age had 17 % higher odds of being users of iron supplementation during the first trimester. This is in line with previous studies that found the same association between higher age and an increased likelihood of iron supplementation throughout pregnancy<sup>(16–18)</sup>.

Surprisingly, women with all levels of education below a higher degree had higher odds of being users of iron supplementation during the first trimester. This result contrasts with previous studies that found that pregnant women with the highest obtained educational level were more likely to be iron users<sup>(16,18)</sup>. We cannot preclude that our finding was

one of chance as none of the associations were strong, and there was not a pattern of a stronger adherence to the iron recommendation as the educational level decreased. Previous studies that have examined adherence to recommendations on exercise<sup>(29)</sup> and smoking<sup>(30)</sup> during pregnancy found that women with a higher educational level were more likely to adhere to national recommendations regarding exercise and smoking cessation during pregnancy<sup>(29,30)</sup>. Also, a previous Danish study examining health literacy in the general Danish population found that people with a higher educational level had a better ability to understand health information and therefore had a healthier lifestyle than people with a lower educational level<sup>(31)</sup>. Therefore, it is noteworthy that women with a higher degree in the present study had lower odds of being users of iron supplementation during the first trimester. However, as the CPC population on average responded to the clinical questionnaire at gestational week 10.2<sup>(22)</sup>, a possible explanation could be that the women with a higher degree may have been aware of the Danish Health Authorities recommendation to postpone iron supplementation until gestational week 18 if they suffered from pregnancy symptoms as nausea or vomiting<sup>(15)</sup>, compared with women with a lower educational level. Yet, the present results suggest that promoting iron supplementation in clinical practice should be targeted at all educational levels in pregnant women.

Finally, the present study showed that pregnant women who had a vegetarian or vegan diet had 18 % higher odds of being users of iron supplementation during the first trimester than women with an ordinary, varied diet. This is in line with a previous German study that found that pregnant women with a vegetarian diet were more likely to use iron supplementation during pregnancy<sup>(19)</sup>. However, only 6.3 % reported having a vegetarian or vegan diet in the present study, while 9.6 % reported having an ordinary, not varied diet. It is noteworthy that women with an ordinary, not varied diet were less likely to be users of iron supplementation during pregnancy, as it previously has been established that a majority of European women of reproductive age have a suboptimal dietary intake of iron<sup>(10)</sup> and that women with an unvaried diet are known to have an increased risk of developing ID or IDA<sup>(26)</sup>. Therefore, a heightened focus on dietary behaviour for this group of pregnant women during preconception and pregnancy counselling may be needed.

As the present study identified maternal age, education and dietary behaviour as pre-pregnancy predictors for iron supplementation during the last 3 weeks of the first trimester, results may indicate a general need for an increased focus on preconception care and pregnancy counselling regarding the importance of iron supplementation during pregnancy. Preconception counselling has especially gained an increased focus in recent years<sup>(32)</sup>. Poor nutritional status in the preconception period has been associated with adverse maternal and foetal outcomes and influences future maternal and child health<sup>(32–34)</sup>. As the majority of European women of reproductive age have iron levels below what is required to complete a normal pregnancy without developing ID or IDA<sup>(9)</sup>, preconception counselling targeting all women of reproductive age has the potential to heighten the knowledge of the importance of improved nutritional status before pregnancy and thereby also iron supplementation during pregnancy.



In the present study, three out of four women in the population reported having a high degree of pregnancy planning. Yet, the present study found that only 49.1 % of the population were users of iron supplementation during the first trimester despite the Danish recommendation for iron supplementation during pregnancy. This may reflect a need to strengthen health counselling before pregnancy, and preconception counselling for women actively planning for their first pregnancy could be a window of opportunity when they are more likely to seek information and are more open to changes in health behaviour<sup>(35)</sup>. Nevertheless, incorporating such counselling into current healthcare efforts in connection with women planning their first pregnancy and unplanned pregnancies has proven difficult<sup>(35)</sup>, and further research on the subject is needed. A heightened focus on interpregnancy counselling may be an important opportunity to reduce the risk of developing ID or IDA in future pregnancies as these women are already in contact with healthcare providers.

### Strengths and limitations

A notable strength of the study is the large sample size. In Denmark, all pregnant women are offered a first-trimester scan, and in 2017 approximately 92 % accepted this offer<sup>(36)</sup>. All pregnant women who booked an appointment for a first-trimester scan at the Department of Obstetrics were eligible to participate and were therefore invited to answer the clinical questionnaire. The study had a high response rate, which, combined with the large sample size, was representative of all pregnant women at the birth facility and reduced the risk of selection bias. However, a risk of selection bias is present as the study only included data from one birth facility. Compared with a previous Danish study on iron supplementation<sup>(16)</sup>, the clinical questionnaire was also available in English which meant that we were able to include more of the 4.5 % of the study population who did not master the Danish language, making the study population more representative and increasing external validity.

Nevertheless, as the clinical questionnaire was only available in these two languages, we may have been unaware of women unable to provide data due to linguistic challenges. Also, it may not be possible to refer to the results as representative of all pregnant women in Denmark. The study population predominantly consisted of urban women who were well educated and reported data indicating a generally healthy lifestyle. The risk of recall bias was minimised as the data was obtained during early pregnancy around the gestational age, where the Danish Health Authorities recommend that pregnant women commence iron supplementation<sup>(15)</sup>.

The study has further limitations which need to be addressed. The risk of reporting bias must be acknowledged as data from the clinical questionnaire were self-reported. A potential overestimation of the results must be recognised, as some women may have been aware of the national recommendation and thus untruthfully answered yes to the clinical question on iron supplementation. Moreover, the clinical questionnaire only yielded an arbitrary assessment of dietary intake of iron based on diet status, as a detailed analysis was not

included in the present study. Future studies could include more extensive and detailed questions on the subject, including questions on prior conditions with ID.

Furthermore, the question on iron supplementation was not validated, which increased the risk of information bias. Hence, the study results may not represent an adequate answer to why the overall prevalence of iron supplementation during the last 3 weeks of the first trimester was 49.1 %. In addition, as the study population only answered the clinical questionnaire once during early pregnancy, it was not possible to assess iron supplementation intake throughout pregnancy. We were, therefore, unable to assess whether the prevalence remained unchanged throughout the second and third trimesters. However, in previous studies<sup>(16,17)</sup>, an increase in prevalence has been observed, and we hypothesise that the same tendency could be seen in our study population.

### Implications

The present study identified pre-pregnancy predictors associated with the intake of iron supplementation during the last 3 weeks of the first trimester of pregnancy. Despite the recommendation of commencing iron supplementation from gestational week 10, under half of the study population were users of iron supplementation during the last 3 weeks of the first trimester. The study, therefore, elucidates the need for an increased focus on the importance of iron supplementation during pregnancy and pregnancy counselling. However, our findings also suggest that the potential risk of developing ID or IDA during pregnancy needs to be addressed before conception, and preconception counselling interventions targeted at all women of reproductive age are required. In addition, as prophylactic iron supplementation during pregnancy is still a subject of international disagreement<sup>(11–13)</sup>, further research to examine the effect on ID and IDA in pregnant women should be undertaken.

### Conclusion

Despite a high degree of pregnancy planning, the prevalence of self-reported iron supplementation during the last 3 weeks of the first trimester was approximately 50 % in the present Copenhagen Pregnancy Cohort. The present study found that the pre-pregnancy factors of advanced age, an educational level below a higher degree and having a vegetarian or vegan diet were predictors for the intake of iron supplementation during early pregnancy. Future studies examining the intake of iron supplementation throughout pregnancy are needed. Our findings indicate that the change of national recommendation on iron supplementation has not yet been fully taken aboard by pregnant women. Therefore, there is a need for an enhanced focus on the importance of iron supplementation during pregnancy to be incorporated in preconception care and pregnancy and interpregnancy counselling.

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There are no conflicts of interest.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Danish Data Protection Agency (Jr. No. RH\_2017-346, I-suite No. 06055). The Danish Patient Safety Authority has granted permission to disclosure patient information from medical records for the purpose of research use (File No. 3-3013-2754/1).

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