## Feasibility and effectiveness of preconception check-ups at workplaces in Japan

3	Akiko Fujishima <sup>1</sup>	, Eri Maeda <sup>2</sup> ,	Koki Sato <sup>3</sup> ,	Hidekazu Saito <sup>4</sup>	, Chihiro Ozeki	<sup>5</sup> , Yukihiro '	Terada <sup>1</sup>
---	------------------------------	----------------------------	--------------------------	-----------------------------	-----------------	---------------------------	---------------------

5	<sup>1</sup> Department of Obstetrics and Gyr	naecology, Akita University	Graduate School of Medicine,	Akita, Japan
---	---	-----------------------------	------------------------------	--------------

<sup>6</sup> <sup>2</sup>Department of Public Health, Faculty of Medicine, Hokkaido University, Hokkaido, Japan

<sup>7</sup> <sup>3</sup>Specified Non-profit Corporation FORECIA, Akita, Japan

8 <sup>4</sup>Umegaoka Women's Clinic, Tokyo, Japan

<sup>9</sup> <sup>5</sup>Akita University School of Medicine, Department of Medicine, Akita, Japan

## 11 Correspondence

12 Akiko Fujishima, MD, Department of Obstetrics and Gynaecology, Akita University Graduate School of

13 Medicine, 1-1-1 Hondo, Akita 010-8543, Japan. Tel.: 018-834-1111; Fax: 018-884-6447; Email:

14 fujishimaa@med.akita-u.ac.jp; ORCID: 0000-0002-8609-484X

24	© The Author(s) 2024. Published by Oxford University Press. This is an Open Access article distributed
25	under the terms of the Creative Commons Attribution NonCommercial-NoDerivs licence
26	https://creativecommons.org/licenses/by-nc-nd/4.0/, which permits non-commercial reproduction and
27	distribution of the work, in any medium, provided the original work is not altered or transformed in any
28	way, and that the work is properly cited. For commercial re-use, please contact

29 journals.permissions@oup.com

#### 30 Abstract

31 **Objectives:** Despite the recent increase in infertility and perinatal complications, preconception care is 32 not commonly available in Japan. Working women are considered to have the greatest need for 33 preconception care, as they increasingly marry and have children later in life. This study aimed to assess 34 the feasibility and effectiveness of preconception check-ups in the workplace.

35 **Methods:** We provided 51 female employees aged 18–39 years with free preconception check-ups,

36 including additional blood tests and an online medical questionnaire, during mandatory health check-ups

37 at their workplace. A doctor provided online counselling based on the check-up results. We assessed

- 38 fertility knowledge using the Cardiff Fertility Knowledge Scale (CFKS-J) and childbearing desire pre-
- 39 and post-intervention.

40 **Results:** Preconception check-ups revealed various potential risk factors for future pregnancies, including 41 underweight (12%), obesity (20%), *Chlamydia trachomatis* IgG antibody positivity (22%), low Rubella 42 IgG antibody levels (47%), iron deficiency (12%), and 25-hydroxyvitamin D levels <30 ng/mL (98%). 43 Post-intervention, the participants reported high satisfaction with the check-ups and significantly 44 advanced their reproductive plans (P=0.008). Further, 95% of the participants indicated an intention to 45 seek medical attention or make lifestyle changes. The post-intervention CFKS-J score (mean  $\pm$  SD) was 46 higher than the pre-intervention score (71.7  $\pm$  19.3 versus 63.0  $\pm$  22.0, P=0.006).

47 **Conclusions:** We developed a preconception check-up package that can be integrated into workplace 48 health examinations, complemented by tailored counselling. This novel check-up package is a feasible 49 and effective approach for improving preconception health and fertility awareness.

50

52

53

54

55

56

57

51 **Keywords:** feasibility studies, preconception care, reproductive health service, women's health

#### 59 **Key Points**

#### 60 What is already known on this topic

- 61 With more women joining the labour force while pursuing reproductive goals, promoting their 62 health, including preventing infertility, is important for occupational health.
- 63 Preconception care can prevent infertility and perinatal complications, reduce health risks for future 64 generations, and promote longevity.
- 65 However, Japanese women are generally reluctant to visit clinics for gynaecological and 66 reproductive health concerns, which undermines their chances of learning about preconception care 67 and using it in their daily lives.
- 68

#### 69 What this study adds

- 70 To facilitate communication between reproductive-aged female workers and health professionals in 71Japan, we designed a free preconception check-up package for the workplace, integrating it with 72 workplace health examinations, complemented by tailored counselling.
- 73 This novel check-up package, supported by a local government, identified several pre-pregnancy 74 health risks, including being underweight or obesity, being significantly malnourished, and not 75 receiving sufficient gynaecological examinations. This check-up package warrants further attention 76 in occupational health settings.
- 77 Tailored preconception counselling based on blood tests and medical questionnaires improved the 78 fertility knowledge of the participants.
- 79 Participants reported high satisfaction with the package and significantly advanced their 80 reproductive plans after the preconception checkup.
- 81

- How this study might affect research, practice or policy
- Preconception check-ups for female employees during their annual workplace medical check-up removed barriers to preconception care such as cost, time constraints, and geographical access.
- 85 This model could be an effective approach for promoting preconception care, resulting in improved 86 health of female workers.
- 87

**ế**4

The global trend of postponing parenthood has led to an increase in the prevalence of infertility<sup>1</sup> and 89 90 various perinatal complications such as miscarriage, gestational diabetes, preeclampsia, labour dystocia, 91 and caesarean deliveries.<sup>2</sup> In Japan, the need for infertility treatment is increasing, with 1 in 4.4 couples undergoing infertility testing or treatment,<sup>3</sup> causing 23% of women undergoing infertility treatment to 92 93 leave the workforce.<sup>4</sup> Menstrual problems, such as irregular cycles, dysmenorrhoea, and heavy menstruation, not only lead to infertility but also cause an estimated annual productivity loss of 491.1 94 billion Japanese Yen (JPY; 3.3862 billion United States Dollars [USD]).<sup>5</sup> At the time of the study, 1 USD 95 = 145 JPY. Promoting women's health care and preventing infertility are extremely important in 96 97 occupational health.

98

99 Preconception care (PCC) could be an effective approach for addressing these increasing public health 100 issues.<sup>6</sup> PCC can prevent infertility and perinatal complications and reduce health risks in future 101 generations.<sup>7</sup> For example, a 10% decrease in pre-pregnancy body mass index (BMI) is associated with at 102 least a 10% risk reduction in preeclampsia and gestational diabetes.<sup>8</sup> Daily folic acid supplementation 103 before conception reduces the risk of neural tube defects by 70%.<sup>9</sup> Furthermore, considering a life-course 104 approach, PCC can prevent non-communicable diseases and promote healthy longevity,<sup>10</sup> regardless of 105 reproductive life plan.

106

In 2006, one recommendation by the Centers for Disease Control and Prevention (CDC) was to 'assure 107 108 that all women of childbearing age in the United States receive preconception care services (i.e., 109 evidence-based risk screening, health promotion, and interventions) that will enable them to enter pregnancy in optimal health.'11 Despite the increased number of health problems PCC can prevent, most 110 Japanese people remain unfamiliar with PCC;<sup>12</sup> moreover, fertility knowledge in the population is 111 112 low.<sup>13,14</sup> An international survey showed that the level of fertility knowledge in Japan was the lowest 113 among developed countries.<sup>13</sup> Japanese women are generally reluctant to visit clinics for gynaecological 114 and reproductive health concerns, as evidenced by the fact that 3.0% use oral contraceptives.<sup>15</sup> Only 10% of the women reported having a family doctor who could treat gynaecological conditions,<sup>16</sup> which 115

Downloaded from https://academic.oup.com/joh/advance-article/doi/10.1093/joccuh/uiae021/7659790 by guest on 30 April 2024

- 132
- 133

116

117

118

119

120

121

122

123

124

125

126

127

128

129

130

131

Methods 134

Participant recruitment and study procedure 135

occupational health measure in Japan.

136 The Occupational Safety and Health Act mandates annual health check-ups for regular employees in 137 Japan. Therefore, employees receive free health check-ups at their workplaces or contracted healthcare 138 facilities. Taking advantage of this statutory screening for employees, we developed a preconception check-up package that included additional blood tests for preconception health (e.g. serum folic acid), 139 140medical questionnaires, and individual online counselling by an obstetrician-gynaecologist (AF) based on 141 the test results (Figure 1). A non-profit organisation, acting as a 'hub' between the employee, employees, 142 and obstetrician-gynaecologist, was responsible for setting up and managing the preconception check-up 143 package. This arrangement reduced the burden on employers and employees while protecting participants' 144 privacy. Information regarding whether each employee applied for the program and details about test

undermined their chances of learning about PCC and using it in their daily lives. Additionally, universal

health insurance in Japan covers diseases and treatments but not preventive care, including PCC.

Presently, only a few clinics offer PCC as a private service and charge approximately 30,000–46,000

Previous studies have shown that tailored education and counselling by health professionals are

acceptable and effective for increasing fertility and PCC awareness.<sup>17</sup> To facilitate communication

between people of reproductive age and health professionals in Japan, we designed a free preconception

check-up package at workplaces by maximising the 'enabling factors' for health service use according to

Andersen's Behavioural Model.<sup>18</sup> Andersen's Behavioural Model is a sociological framework used to

predict and explain health service use. The model is designed to elucidate how an individual's use of

health services is influenced by factors such as their characteristics, health status, and the external

environment.<sup>18</sup> In this novel check-up package supported by a local government, we removed the barriers

of cost, time constraints, and geographical access to PCC and provided female employees with free

preconception check-ups and online counselling during mandatory workplace check-ups. This study

aimed to evaluate the feasibility and effectiveness of this novel check-up package to promote PCC as an

JPY (200–300 USD) per visit, making it unlikely for most people to become familiar with PCC.

results and counselling were kept confidential, with no disclosure to the company or its occupational

- 146 health professionals. To evaluate the feasibility and effectiveness of the preconception check-up package,
- 147 we conducted online surveys before and after the intervention.
- 148 We distributed a short brochure to employees at a welfare business and a hospital in Akita City. Only
- 149 interested employees participated in this study. The inclusion criteria were female employees aged 18–39
- 150 years who underwent workplace health check-ups. Pregnant women were excluded from the study. All
- study procedures were conducted from 1 November 2022 to 16 March 2023. This study was supported by
- 152 the Akita Prefecture's Technology Innovation Creation and Utilization Promotion Project [Industry-
- 153 Academia-Government Collaboration Booster Project]; there was no cost burden for companies or
- 154 individual participants.
- 155
- 156
- 157 **T1: Pre-intervention survey**
- 158 At T1, participants completed an online survey on sociodemographic characteristics, fertility knowledge,
- and childbearing desires.

160 Sociodemographic characteristics

We asked about age (in years), marital status (single, not married but partnered, or married), number of children (none, one, two, three, or more), working during night shifts (yes/no), working hours per week (<40 h or  $\geq$ 40 h), and university education (yes/no). Additionally, we asked about annual household income, which was categorised as <4 million JPY (<27,533 USD),  $\geq$ 4 million to <6 million JPY ( $\geq$ 27,533 to <41,300 USD),  $\geq$ 6 million to <8 million JPY ( $\geq$ 41,300 to <55,066 USD),  $\geq$ 8 million JPY ( $\geq$ 55,066 USD), or 'unknown'.

167 Fertility knowledge and childbearing desires

Participants completed the Japanese version of the Cardiff Fertility Knowledge Scale (CFKS-J).<sup>13,14</sup> To date, the CFKS, which has been translated into 12 languages and used in 18 countries, remains the only validated fertility knowledge scale. This scale consists of a 13-item questionnaire designed to investigate knowledge in three domains: indicators of reduced fertility, common misconceptions about fertility, and basic facts about infertility. All items were rated on a three-point scale of 'true', 'false', or 'do not know'; scores of zero and one point were assigned to an incorrect or 'do not know' answer and a correct answer, 174 respectively. Scores were reported as the percentage of the highest possible scores. The internal

175 consistency coefficient alpha among the participants was 0.80. Participants stated their desired number of

176 children/additional children and their plan to conceive ('I am currently trying to conceive', 'I will try to

177 conceive in a few months', 'I will try to conceive in one year', or 'I do not know yet'). For those with no

178 plan to conceive, we asked about the age at which they hoped to have their first or next child. For those

179 who planned to conceive within a year, we assumed the desired age to have the first/next child to be their

180 current age.

181 *Reasons for participating in this study* 

To understand the feasibility of this novel preconception check-up package, we asked participants the reason for participating in this study with options including 'because I want to know for the future', 'because I currently have problems with menstruation', 'because I currently have problems with infertility', and other reasons given in free-text comments. Additionally, we asked prerequisite conditions to receive preconception check-ups from the following options: 'additional blood sample at the annual check-up', 'without visiting medical institutions', 'without the company knowing', 'online counselling by an obstetrician/gynaecologist,' and other prerequisites provided by free-text comments.

189

#### 190 T2: Preconception check-ups

191 Mandatory workplace health check-ups

We obtained the following participants' information needed for PCC from the mandatory workplace 192 health check-ups: height, body weight, systolic and diastolic blood pressures, and blood tests, which 193 included haemoglobin (Hb; normal range,<sup>19</sup> 11.6–14.8 g/dL), HbA1c (4.6–6.2%), hepatic function tests 194 195 (i.e., aspartate aminotransferase [13–30 U/L], alanine transaminase [7–23 U/L], and gamma glutamyl 196 transferase [9-32 U/L]), and lipid profile (i.e., triglyceride [30-149 mg/dL], low-density lipoprotein cholesterol [60–139 mg/dL], and high-density lipoprotein cholesterol [40–96 mg/dL]). We evaluated the 197 198blood test results according to the Health Guidance Assessment Values established by the Ministry of 199Health, Labour and Welfare.

#### 200 Additional blood tests

We performed the following blood tests along with workplace examinations, according to recommendations<sup>20</sup> and previous studies, while considering cost and feasibility. The blood tests (normal

range) included tests for serum iron (40–188 µg/dL),<sup>19</sup> serum ferritin (<12 ng/mL),<sup>21</sup> serum zinc (≥80  $\mu$ g/dL),<sup>22</sup> serum folate ( $\geq$ 7.0 ng/mL),<sup>23</sup> and serum 25-hydroxyvitamin D (25(OH)D;  $\geq$  30 ng/mL) tests,<sup>24</sup> 204 205 thyroid function (i.e., thyroid stimulating hormone [0.35–4.9 µIU/mL], free triiodothyronine [1.71–3.71 206 pg/mL], and free thyroxine [0.70–1.48 ng/dL]), Chlamydia trachomatis (C. trachomatis) immunoglobulin 207 (Ig) antibodies (i.e., IgG and IgA; negative), syphilis (i.e., rapid plasma reagin [RPR] and treponema 208 pallidum haemagglutination [TPHA] tests; negative), and rubella IgG enzyme immunoassay 209 IU/mL).<sup>25</sup>

210 Medical questionnaires

203

211 For tailored preconception counselling, we asked participants about their lifestyle, medical history, and 212 reproductive history using an online medical questionnaire. Regarding lifestyle, participants reported their 213 and their partners' smoking status (yes, former, or never), alcohol consumption (<3 or  $\geq$ 3 times per week), 214 and current use of folic acid supplementation (yes/no).

We asked them about their history of chronic diseases (e.g. hyperthyroidism, hypothyroidism, diabetes, 215 and mental disorders), number of pregnancies and deliveries, and infertility experience (yes/no). For 216 217 menstruation, we assessed the regularity and length of the participants' menstrual cycle and the amount of 218 menstrual bleeding (light, moderate, or heavy). We assessed the severity of dysmenorrhoea using the 219 Dysmenorrhoea Score, the Use of Analgesics Score, and level of pain on a numerical rating scale (0-220 10).<sup>26</sup> The Dysmenorrhoea Score is based on the degree of work limitation during the last menstruation, 221 rated as none, mild (i.e. some loss of work or study efficiency), moderate (i.e. needing to rest in bed and/or loss of work), or severe (i.e.  $\geq 1$  day in bed). The Analgesics Score is rated based on the number of 222 223 days participants used analgesics during the last menstruation, with the following ratings: none, mild 224 (taking analgesics for 1 day), moderate (taking analgesics for 2 days), or severe (taking analgesics for 3 or 225 more days). Additionally, we checked whether they had undergone an annual or biennial cervical smear 226 test.

#### **Online** counselling

227

228

229 Counselling was conducted individually by an obstetrician-gynaecologist (AF). Sessions were primarily 230 conducted via Zoom (video calls). Alternatively, the session was conducted either via telephone or face to face. Following the guidelines of the CDC<sup>6</sup> and the Royal Australian and New Zealand College of 231

Downloaded from https://academic.oup.com/joh/advance-article/doi/10.1093/joccuh/uiae021/7659790 by guest on 30 April 2024

Obstetricians and Gynaecologists,<sup>20</sup> counselling was provided on the impact of the following factors on infertility, perinatal complications, and child health: age, body shape (BMI), blood pressure, anaemia, malnutrition (iron, vitamin D, zinc, and folate), and rubella IgG antibodies. It was not possible to make a diagnosis by examining the data used in this study; therefore, explanations were provided from a screening perspective.

We provided information on menstruation-related symptoms, problems (menorrhagia, dysmenorrhoea, and premenstrual syndrome), and management strategies; techniques for timing, if they planned to conceive; and appropriate contraception methods if they did not want to conceive based on their previous or current contraceptive methods (oral contraceptives, intrauterine devices or systems, condoms, rhythm method, withdrawal, emergency contraception, and none). After the counselling session, a document detailing the content of the counselling session was enclosed with the test results and sent to the participants' homes.

244

#### 245 **T3:** Post-intervention survey

We asked the participants to respond to the following items immediately after the counselling sessions: 246 247 CFKS-J, the number of children desired in the future, the desired age of the first/next child, and their plan to conceive. We asked about satisfaction with and recommendations for counselling on a 5-point Likert 248249 scale. Participants reported their feelings of security after counselling (feel relieved, feel neither, or feel 250 anxious), their intentions to change their behaviour after counselling (visit a gynaecologist, improvement in lifestyle, no future changes in behaviour, or free text comments), and changes in their reproductive life 251plan (finding a partner sooner, getting married sooner, getting pregnant sooner, having no effect, or free 252 253 text comments).

254

255

#### Statistical analyses

We described the distribution of the sociodemographic background, lifestyle, and medical and reproductive histories of the study participants. Additionally, we described the reasons for study participation and T3 feedback from the participants. We compared CFKS-J scores at T1 and T3 using paired t-tests to assess post-intervention changes in fertility knowledge and childbearing desire. Wilcoxon signed-rank tests and paired t-tests were used to compare changes in childbearing desires. All analyses

## 263 Results

- Overall, 51 women (26 from a welfare business and 25 from a hospital) participated in the study and completed the T1 survey and preconception check-up. The participation rate was 22% (26/117) in the former, but unknown in the latter because not all employees were informed about the study. Of the 51 participants, 44 received preconception counselling. Finally, 41 participants responded to the T3 survey (Supporting Information 1).
- 269

#### 270 Study population

Table 1 shows the sociodemographic characteristics of 51 participants. The median age was 29 years (interquartile range [IQR]: 26–32 years). Approximately half were in the middle-income group ( $\geq$  4 and < 8 million JPY), and 45% had university education. Approximately one-third of the participants were single and the rest were in a relationship. The largest proportion of respondents (65%) had no children.

275

The reasons for participating in the study were as follows: 78% wanted to know about the future, 18% participated because of current menstrual problems, 12% participated because of current infertility problems, and 6% had tried to conceive. Prerequisites for preconception check-ups included additional blood tests at annual check-ups (90%), without visiting medical institutions (39%), without the company's knowledge (24%), and online counselling by a gynaecologist (12%).

281

286

#### 282 Medical and reproductive histories and lifestyle

Table 2 shows the medical and reproductive histories and lifestyles of the study participants. While 12% of the participants were current smokers, >20% had partners who smoked. Less than 20% of the patients were taking folic acid supplements.

A total of 12 (24%) patients had a history of chronic diseases, including thyroid dysfunction and diabetes, and six (12%) had received infertility treatments. The most common method of contraception was condom use (86%), whereas only 12 (27%) used oral contraceptives.

Downloaded from https://academic.oup.com/joh/advance-article/doi/10.1093/joccuh/uiae021/7659790 by guest on 30 April 2024

293 294

290

291

292

#### 295 **Results from preconception check-ups**

Nearly 70% maintained a healthy weight, whereas about 10% were underweight (BMI <18.5 kg/m<sup>2</sup>) and 20% were overweight (BMI 25–29.9 kg/m<sup>2</sup>) or obese (BMI  $\ge$ 30 kg/m<sup>2</sup>) (Table 3). Although only a small proportion of the participants presented with abnormal lipid profiles or hepatic function; 16% of the participants had hypertension. Anaemia (haemoglobin <12 g/dL) and iron deficiency (ferritin < 12.0 ng/mL) were present in four (7.8%) and nine (17.6%) participants, respectively.<sup>21</sup>

A significant proportion of the participants had menstrual problems, with over 40% having irregular

cycles. Eleven (22%) participants had moderate to severe dysmenorrhoea, and 16 (31%) reported

moderate or severe analgesic use. The median (IOR) menstrual pain score on the numerical rating scale

was 4 (2–7). Less than half of the patients underwent annual or biennial cervical smears.

301

None of the patients tested positive for syphilis. One in five patients was suspected to have previous or current chlamydia infection. Approximately half of the patients had rubella IgG antibody levels below the level required to prevent congenital rubella syndrome. Only one participant had vitamin D sufficiency, and 42 (82%) had vitamin D deficiency (serum 25(OH)D <20 ng/mL).<sup>24</sup> Only half of the participants had serum folate >7.0 ng/mL, which is the level required before pregnancy to prevent neural tube defects in the foetus.<sup>23</sup>

- 308
- 309 Post-intervention (T3) survey

310 Figure 2 shows the T1-T3 changes in fertility knowledge and childbearing desires among the 41 311 participants in the T3 survey. The mean  $\pm$  SD score for the CFKS-J improved significantly from 312 63.0±22.0 to 71.7±19.3 percentage points (P=0.006, Figure 2a). However, no significant changes were 313 observed in the desired number of children/additional children (P=0.77, Figure 2b). Excluding those who 314did not want children and those who answered 'unknown', the desired age for the first/next child was 315 similar (31.3±3.6 at T1 and 31.1±3.7 at T3; P=0.30; paired t-test). However, the participants significantly 316 advanced their reproductive life plans; the number of participants trying to conceive doubled post-317 intervention (P=0.008, Figure 2c).

Table 4 shows the post-counselling feedback from 41 study participants. Participants' satisfaction was extremely high, and most wanted to recommend the preconception check-up to others. The majority of participants felt relieved rather than anxious after counselling. Moreover, preconception check-ups had an impact on future behaviour. More than 40% planned to attend an obstetrics and gynaecology clinic. Almost 80% planned to improve their lifestyle. More than half of them planned to speed up their reproductive life by finding a partner or moving their marriage or pregnancy plans forward.

325

#### 326 Discussion

327 We designed a preconception diagnostic package integrated with workplace health exams, complemented 328 by tailored counselling. Our findings suggest that this model is highly effective in enhancing fertility 329 awareness, motivating lifestyle changes, and expediting reproductive life planning. This approach will 330 help promote gender equality and women's active participation in the workforce and address infertility 331 issues, which are prevalent in the field of occupational health in Japan. We also identified several pre-332 pregnancy health risks, including relatively high proportions of underweight and obesity, significant 333 malnutrition (notably vitamin D and folic acid deficiencies), and low rates of gynaecological 334 examinations, that warrant further attention in occupational health settings. While this study's short-term 335 nature did not allow for the assessment of enhancements in preconception health or pregnancy outcomes, 336 future extended follow-ups will elucidate the benefits of such check-ups on participants' health.

337

Our preconception check-up package (Figure 1) satisfied the participants' needs. Apart from the advantage of integrating the checks into occupational health checks, many participants highlighted convenience and confidentiality as key incentives of the check-up package (Table 1). With more women in the workforce, promoting PCC in occupational settings is essential, although uncommon because of privacy concerns. Our approach, integrating a neutral mediator between employer, employee, and clinician, addressed these barriers. Aligning PCC with regular health checks makes it more accessible to employees. To our knowledge, this is the first PCC promotion study in an occupational context.

345

Tailored PCC counselling based on blood tests and medical questionnaires notably improved fertility knowledge, as indicated by an increase from 63.0±22.0 to 71.7±19.3 percentage points on the CFKS-J. While the increase was not substantial compared with when comprehensive information was provided,<sup>27</sup> our tailored approach neither induced anxiety nor reassured participants (Table 4), aligning with a previous tailored study<sup>17,28</sup> and contrasting with uniform ones.<sup>27</sup> Our data further suggest that imparting medical insights, like age-related fertility decline, can influence reproductive planning. While the desire for childbirth remained consistent, more women aimed for near-future conception (Figure 2c). A previous study indicated an advanced actual childbearing timing in the Japanese population.<sup>29</sup> Hence, long-term

354 follow-ups are essential to assess if reproductive plan changes reduce infertility or perinatal issues.

355

356 Preventing sexually transmitted infections and ensuring proper immunisation are vital for reducing 357 infertility and mother-to-child infections. This study revealed that about one in five women had a history 358 of C. trachomatis infection. C. trachomatis targets specific epithelial cells, causing cervicitis with often mild or no symptoms. However, some may develop pelvic inflammatory disease, leading to 359 complications such as ectopic pregnancy and infertility.<sup>30</sup> Chlamydia infections have increased since 2015, 360 especially among those in their 20s.<sup>31</sup> The Japanese survey, based on 1000 medical centres, could not 361 362 determine the total infection cases. This marks the first report of Chlamydia antibody prevalence in 363 Japan's general population.

364

372

Secondly, rubella antibody fitre and vaccination are essential. Rubella can cause congenital rubella syndrome in pregnant women, leading to hearing loss, cardiac issues, and visual disturbances. The World Health Organization advocates pre-pregnancy rubella vaccination to prevent congenital rubella syndrome and limit rubella spread.<sup>32</sup> Despite Akita City (study location) offering subsidised rubella tests and vaccinations, most participants were unaware of rubella infections during counselling. There is a clear knowledge gap in Japan regarding pregnancy-related infectious diseases, necessitating increased awareness.

This study found that many women experienced menstrual issues, such as irregular cycles, dysmenorrhoea, and hypermenorrhoea. Addressing this is pivotal for women's success and health and for countering declining birth rates. In our pre-intervention survey, 18% of respondents reported menstrual abnormalities, and most had not sought care from a gynaecologist. After the intervention, participants

became aware of their menstrual issues, with 42% indicating plans to visit the hospital. Since menstrual-

378 related productivity loss has a huge impact on society,<sup>5</sup> especially in settings where more women join the

- 379 labour force, visiting clinics and receiving appropriate treatments would not only improve preconception
- 380 health but also benefit employment.
- 381

In our study, 32% of the participants had an inappropriate weight: 12% were underweight and 20% were 382 obese. Being underweight can increase the risk of low birth weight (LBW) infants due to 383 undernutrition.<sup>8,33</sup> Obesity, which increases the likelihood of preeclampsia and premature birth, also 384 385 escalates the risk of LBW. Despite Japan's low infant mortality rate, its LBW rate surpasses that of other 386 regions in East Asia and the Pacific.<sup>34</sup> Initiatives like Health Japan 21 and Healthy Parents and Children 21 aim to address this by reducing LBW and underweight among the youth, and weight gain targets 387 during pregnancy have been revised.<sup>35,36</sup> However, the increase in LBW infants has not yet decreased. 388 During mandatory health check-ups, women outside the ideal weight range often receive generic advice, 389 excluding preconception health. Online counselling about the impact of weight on pregnancy may better 390 391 inform and influence women's behaviours.

392

In this study, the nutrient levels in the blood, which are not available in normal workplace health check-393 394 ups, increased the awareness of participants' potential health risks. Data on the serum concentrations of nutrients and trace elements in young Japanese non-pregnant women are scarce. The data from this study 395 396 are extremely useful for promoting preconception care suitable for Japanese women. Particularly, low 397 serum folate and vitamin D deficiencies were observed among women. Folate intake in Japan has been declining annually, with a small number of supplement recipients.<sup>37</sup> Folate is not only linked to the 398 prevention of foetal neural tube defects,<sup>25</sup> but, along with other nutrients, it is also associated with 399 pregnancy.<sup>38</sup> As folate intake in the Japanese population is declining and is particularly low among young 400401 people, folic acid supplementation should be promoted. Furthermore, serum 25(OH)D levels were below 402 the reference level in nearly all participants, suggesting the need for increased vitamin D intake. This may 403 be partly because this study was conducted in Akita Prefecture. Akita Prefecture is located at 39 °N and 404 has one of the shortest daylight hours in Japan. Winter (November to March), the season in which this 405 study was conducted, was particularly short, with less than 100 hours of sunlight per month. The average 406 temperature during the study period was approximately 0-10 °C, and the study area has snowfall. Factors 407 such as season, region, and ultraviolet radiation exposure play roles in these levels.<sup>39</sup> Vitamin D receptors are prevalent in the reproductive system, including the ovaries and endometrium.<sup>40</sup> Although the vitamin 408 409 D-fertility link is debated, sufficient levels are associated with higher clinical pregnancies and births. The 410 roles of vitamin D and folate were emphasised in counselling, and participants with deficiencies were advised on dietary considerations. Subsequent follow-up evaluations will be conducted to determine the 411 412 behavioural impact of these health assessments.

413

414 To expand our preconception check-up project and implement it in society, we must consider the costs, payer of these costs, and information management. This study was a high-cost project that provided 415 416 online counselling to all participants. To make it sustainable in the future, it will be necessary to reduce 417 the burden and cost for professionals who provide individual counselling. Selecting only women at high 418 risk who require individual counselling or developing automated digital communication, such as an AIbased chatbot, may reduce costs. Our approach, which includes a neutral mediator between the employer, 419 420 employee, and clinician, is feasible from an information management perspective. This study was funded 421 by the local government as a research project. However, in the future, employers could be another payer, 422 as in the case of cervical cancer screening as an optional test at a medical institution that conducts annual 423 health check-ups or mass influenza vaccinations at the workplace. For example, mass workplace influenza vaccination could reduce time costs and improve vaccine uptake<sup>41</sup>, thereby benefiting 424 employers, employees, and society<sup>42</sup>. Preconception check-ups supported by employers, together with the 425 426 government, can be a promising future model.

427

428

This study had several limitations. First, the generalisability of our findings may be limited by the small sample size and the self-selection bias of including only women who were interested in the project; a study with a larger number of participants is currently underway, which will provide a more detailed understanding of the health issues faced by working women. In addition, as a future direction, it would be crucial to include people who are not interested in PCC. Second, in evaluating the effects after the 434 intervention, we could only confirm the intention to change behaviour. In future research, we plan to 435 conduct follow-up surveys of the participants to assess their actual behavioural changes, such as dietary 436 habits, exercise routines, and medical consultations, in detail. Finally, this was a feasibility study, and we 437 could only perform one-armed pre-post comparisons. Larger studies with larger control groups are 438 warranted in the future.

439

#### 440 Conclusion

In this study, we provided preconception check-ups for female employees during their annual workplace medical check-ups. This novel check-up removed barriers to PCC, such as cost, time constraints, and geographical access. This study demonstrated that the preconception check-up model is feasible and effective for promoting PCC. We plan to evaluate the long-term effects of this model on participants' preconception and perinatal health, which will add to the importance of this novel project in the near future.

447

#### 448 Acknowledgements

We thank Prof. Jacky Boivin (Cardiff University), Dr. Osamu Hiraike (Department of Obstetrics and Gynecology, The University of Tokyo Hospital), Mr. Shiro Yamasaki (Special Advisor to the Cabinet, Japan), and Prof. Tadashi Kimura (Department of Obstetrics and Gynecology, Osaka University Graduate School of Medicine) for their expert advice. This study was supported by the Akita Prefecture Technology Innovation Creation and Utilisation Promotion Project–The Industry–Academic Government Collaboration Booster Project.

455

456

457

458

459

#### Author contributions

Author contributions: A.F., E.M. and K.S. conceived the ideas; K.S. and C.O. collected the data; E.M. analysed the data; H.S. and Y.T. provided comments and conceptual advice; and A.F. and E.M. led the writing.

460

#### 461 **Supplementary data**

462 Supplementary Information 1: Participant flowchart

Approval of the research protocol
This study was approved by the Ethics Board of the Akita University Graduate School of Medicine and
Faculty of Medicine (approval number: 2872).
Informed Consent
All procedures followed were in accordance with the ethical standards of the responsible committee on
human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its
latest amendments. Written informed consent was obtained from all patients for being included in the
study.
Animal Studies
N/A.
Conflict of Interest
Authors declare no Conflict of Interests for this article.
Study Funding
This study was supported by the Akita Prefecture Technology Innovation Creation and Utilisation
Promotion Project-The Industry-Academic Government Collaboration Booster Project.
Data availability
The data underlying this article will be shared on reasonable request to the corresponding author.
$(3^{\times})$
References
<ul> <li>American College of Obstetricians and Gynaecologists Committee on Gynaecologic Practice and</li> </ul>
Practice Committee. Female age-related fertility decline. Committee Opinion No. 589. Fertil Steril
2014;101:633-634.

464

465

466

467

468

469

470

471

472

473

474

475

476

477

478

479

480

481

482

483

484

485

486

487

488

489

490 2. Pregnancy at age 35 years or older: ACOG Obstetric Care Consensus No. 11. Obstet Gynecol

Downloaded from https://academic.oup.com/joh/advance-article/doi/10.1093/joccuh/uiae021/7659790 by guest on 30 April 2024

- 491 2022;140:348-366.
- 492 3. National Institute of Population and Social Security Research. The 16th Japanese National Fertility
- 493 Survey. https://www.ipss.go.jp/ps-doukou/j/doukou16/JNFS16gaiyo.pdf (in Japanese). Published
- 494 2022. Accessed August 22, 2023.
- 495 4. Minister of Health, Labour and welfare. Comprehensive research project on various issues related
- 496 to balancing infertility treatment and work. <u>https://www.mhlw.go.jp/file/04-Houdouhappyou-</u>
- 497 <u>11910000-Koyoukankyoukintoukyoku-Koyoukikaikintouka/0000197931.pdf</u>. Published 2017

498 Accessed October 23, 2023.

- Tanaka E, Momoeda M, Osuga Y, et al. Burden of menstrual symptoms in Japanese women:
  results from a survey-based study. J Med Econ 2013;16:1255-1266.
- 501 6. Centers for Disease Control and Prevention. Preconception health and health care is important for 502 all. https://www.cdc.gov/preconception/overview.html. Published 2023. Accessed August 11,
- 503 2023.

- 504 7. Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: nutrition and lifestyle in the
   505 preconception period and its importance for future health. Lancet 2018;391:1830-1841.
- 506 8. Schummers L, Hutcheon JA, Bodnar LM, Lieberman E, Himes KP. Risk of adverse pregnancy
- 507 outcomes by prepregnancy body mass index: a population-based study to inform prepregnancy
   508 weight loss counselling, Obstet Gynecol 2015;125:133-43.
- 509 9. De-Regil LM, Peña-Rosas JP, Fernández-Gaxiola AC, Rayco-Solon P. Effects and safety of
   510 periconceptional oral folate supplementation for preventing birth defects. Cochrane Database Syst
- 511 Rev 2015;2015:CD007950.
- 512 10. World Health Organization. Regional office for Europe. The life-course approach: from theory to
  513 practice: case stories from two small countries in Europe.
  - https://apps.who.int/iris/handle/10665/342210. Published 2018. Accessed September 20, 2023.
- 515 11. Johnson K, Posner SF, Biermann J, et al. CDC/ATSDR Preconception Care Work Group. Select
- panel on preconception care. Recommendations to improve preconception health and health
- 517 care—United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select
- 518 Panel on Preconception Care. MMWR Recomm Rep 2006;55;RR06:1-23.
- 519 12. Sato K, Yamazaki T, Maeda E, Yamada N. Differences in perceptions of the working environment

520		according to whether or not a person has experienced fertility treatment. The 80th Annual Meeting
521		of Japanese Society of Public Health. 2021;12. (in Japanese)
522	13.	Bunting L, Tsibulsky I, Boivin J. Fertility knowledge and beliefs about fertility treatment: findings
523		from the International Fertility Decision-making Study. Hum Reprod 2013;28:385-397.
524	14.	Maeda E, Sugimori H, Nakamura F, et al. A cross sectional study on fertility knowledge in Japan,
525		measured with the Japanese version of Cardiff Fertility Knowledge Scale (CFKS-J). Reprod
526		Health 2015;12:10.
527	15.	Yoshida H, Sakamoto H, Leslie A, Takahashi O, Tsuboi S, Kitamura K. Contraception in Japan:
528		current trends. Contraception 2016;93:475-477.
529	16.	Roche Diagnostics, Medical KK. Release: the Survey of Women's Primary Care Doctor.
530		https://www.rochediagnostics.jp/content/dam/rochexx/roche-diagnostics-
531		jp/documents/news/20210225.pdf (in Japanese). Published 2021. Accessed August 23, 2023.
532	17.	Skogsdal Y, Fadl H, Cao Y, Karlsson J, Tydén T. An intervention in contraceptive counseling
533		increased the knowledge about fertility and awareness of preconception health-a randomized
534		controlled trial. Ups J Med Sci 2019;124:203-212.
535	18.	Andersen RM. National health surveys and the behavioral model of health services use. Med Care
536		2008;46:647-653.
537	19.	Japanese Committee for Clinical Laboratory Standards, Common Reference Ranges Committee.
538		Common reference ranges for major Clinical Laboratory tests in Japan – commentary and user
539		guide. https://www.jccls.org/wp-content/uploads/2022/10/kijyunhani20221031.pdf. Published
540		2023. Accessed August 25, 2023.
541	20.	Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG).
542		Pre-pregnancy counselling. https://ranzcog.edu.au/wp-content/uploads/2022/05/Pre-pregnancy-
543		Counselling-C-Obs-3a-Board-approved_March-2022.pdf. Published 2021. Accessed August 21,
544		2023.
545	21.	The Japanese BioIron Society. Guidelines for the appropriate use of iron supplements in anemia
546		treatment. rev 3rd ed. 2022(12) (in Japanese)
547	22.	Hiroko K, Hiroshige I, Hiromitsu O, et al. Practice guideline for zinc deficiency. J Jpn Soc Clin
548		Nutr 2018;40:120-167. (in Japanese)

- 549 23. Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. Folate levels and neural tube defects.
- 550 Implications for prevention. JAMA 1995;274:1698-1702.
- 551 24. Okazaki R, Ozono K, Fukumoto S, et al. Assessment criteria for vitamin D
- 552 deficiency/insufficiency in Japan proposal by an expert panel supported by Research Program of
- 553 Intractable Diseases, Ministry of Health, Labour and Welfare, Japan, The Japanese Society for
- 554 Bone and Mineral Research and the Japan Endocrine Society [Opinion]. Endocr J 2017;64:1-6.
- 555 25. Mikamo H, Japanese Society for Infection Prevention and Control. Vaccine guidelines for
- healthcare professionals. Ver 3. http://www.kankyokansen.org/uploads/uploads/files/jsipc/vaccineguideline\_03-5.pdf (in Japanese). Published 2020. Accessed August 25, 2023.
- 558 26. Harada T, Momoeda M, Taketani Y, Hoshiai H, Terakawa N. Low-dose oral contraceptive pill for
- dysmenorrhea associated with endometriosis: a placebo-controlled, double-blind, randomized trial.
  Fertil Steril 2008;90:1583-1588.
- 561 27. Maeda E, Nakamura F, Kobayashi Y, et al. Effects of fertility education on knowledge, desires
  562 and anxiety among the reproductive-aged population: findings from a randomized controlled trial.
  563 Hum Reprod 2016;31:2051-2060.
- Petersen KB, Maltesen T, Forman JL, et al. The Fertility Assessment and Counseling Clinic does
  the concept work? A prospective 2-year follow-up study of 519 women. Acta Obstet Gynecol
  Scand 2017;96:313-325.
- Maeda E, Boivin J, Toyokawa S, Murata K, Saito H. Two-year follow-up of a randomized
  controlled trial: knowledge and reproductive outcome after online fertility education. Hum Reprod
  2018;33:2035-2042.
- 570 30. O'Connell CM, Ferone ME. *Chlamydia trachomatis* genital infections. Microb Cell 2016;3:390571 403.

573

- National Institute of Infectious Diseases. Japan. Trends in genital chlamydia infections, 2000-2020. https://www.niid.go.jp/niid/ja/chlamydia-std-m/chlamydia-std-idwrs/10630-chlamydia-21sep.html (in Japanese). Published 2021. Accessed August 23, 2023.
- 32. Best JM, Castillo-Solorzano C, Spika JS, et al. Reducing the global burden of congenital rubella
  syndrome: report of the World Health Organization Steering Committee On research related to
  measles and rubella vaccines and vaccination, June 2004. J Infect Dis 2005;192:1890-1897.

- 578 33. The World Bank Group. Mortality rate, infant (per 1,000 live births)
- 579 https://data.worldbank.org/indicator/SP.DYN.IMRT.IN. Published 2021. Accessed August 23,
- 580 2023.

- 581 34. Valero De Bernabé J, Soriano T, Albaladejo R, et al. Risk factors for low birth weight: a review.
- 582 Eur J Obstet Gynecol Reprod Biol 2004;116:3-15.
- 583 35. Komiyama Y, Minister of Health, Labour and Welfare. A basic direction for comprehensive
- 584 implementation of national Health Promotion. https://www.mhlw.go.jp/file/06-Seisakujouhou-
- 585 10900000-Kenkoukyoku/0000047330.pdf. Published 2012. Accessed August 23, 2023.
- 586 36. Minister of Health, Labour and Welfare. Healthy Parents and Children 21.
- 587 https://sukoyaka21.cfa.go.jp/. Published 2018. Accessed August 23, 2023.
- 588 37. Kikuchi D, Obara T, Usuzaki T, et al. Evaluating folic acid supplementation among Japanese
- 589 pregnant women with dietary intake of folic acid lower than 480 µg per day: results from TMM
- 590 BirThree Cohort Study. J Matern Fetal Neonatal Med 2022;35:964-969.
- Section 38. Cueto HT, Riis AH, Hatch EE, et al. Folic acid supplementation and fecundability: a Danish
  prospective cohort study. Eur J Clin Nutr 2016;70:66-71.
- 593 39. Macdonald HM, Mavroeidi A, Fraser WD, et al. Sunlight and dietary contributions to the seasonal
- vitamin D status of cohorts of healthy postmenopausal women living at northerly latitudes: a major
   cause for concern? Osteoporos Int 2011;22:2461-2472.
- Lerchbaum E, Obermayer-Pietsch B. Vitamin D and fertility: a systematic review. Eur J
  Endocrinol 2012;166:765-778.
- 598 41. Tsutsui Y, Benzion U, Shahrabani S, et al. A policy to promote influenza vaccination: a behavioral
  599 economic approach. Health Policy. 2010;97(2-3):238-49.
  - 42. Van Hooste WLC. Influenza vaccination at the workplace. Vaccine. 2022;40(16):2367-2368.

## 603 Tables

Table 1 Sociodemographic characteristics and T1 feedback of 51 participants

605

	N (%) c	N (%) or median (IQR)		
Sociodemographic characteristics				
Age	29	(26–32)		
Marital status				
Single	16	(31.4)		
Not married but partnered	12	(23.5)		
Married	23	(45.1)		
Number of children				
None	33	(64.7)		
One	8 1	(15.7)		
Two or more	10	(19.6)		
Night-shift	16	(31.4)		
Working hours per week	, ,			
<40 hours	16	(31.4)		
≥40 hours	35	(68.6)		
University education	23	(45.1)		
Annual household income				
<4 million JPY	9	(17.6)		
≥4 and <6 million JPY	13	(25.5)		
≥6 and <8 million JPY	12	(23.5)		
≥8 million JPY	8	(15.7)		
Unknown	9	(17.6)		
Cues for promotion of preconception care				
Reasons to participate in this study				
Because I want to know for the future	40	(78.4)		
Because I currently have problems with menstruation	9	(17.6)		
Because I currently have problems with infertility	6	(11.8)		
To start trying to conceive (free-text comments)	3	(5.9)		
Prerequisites for preconception check-ups		· ·		
Additional blood tests at the annual check-up	46	(90.2)		
Without visiting medical institutions	20	(39.2)		
Without the company knowing	12	(23.5)		
Online counselling by an obstetrician/gynaecologist	6	(11.8)		

Abbreviations: IQR, interquartile range; JPY, Japanese Yen

	N (%) or n	nedian (IQR)
lifestyles		
Smoking		
Current smokers	6	(11.8)
Partner's smoking, yes	12	(23.5)
Habitual drinker (≥3 times per week)	7	(14.0)
olic acid supplementation, yes	10	(19.6)
Iedical and reproductive history		$\sim$
Chronic disease, yes	12	(23.5)
Nulligravida	32	(62.7)
Nulliparity	33	(64.7)
Experience of infertility treatments	6	(11.8)
Contraception, ever used $^{\dagger}$		
Dral contraceptives	12	(27.3)
US/IUD	0	(0.0)
Condom	38	(86.4)
Rhythm methods	11	(25.0)
Withdrawal	20	(45.5)
Emergency contraception	4	(9.1)
lenstruation	Y	
Age of menarche (median, IQR)	12	(11–13)
Regularity		
Regular cycles	30	(58.8)
Cycle length (days)	29.5	(28–30)
rregular cycles	21	(41.2)
mount of menstrual bleeding		
Light	1	(2.0)
Aodest	45	(88.2)
Ieavy	5	(9.8)
ysmenorrhea score <sup>‡</sup>		
None	16	(31.4)
Aild	24	(47.1)
Aoderate	7	(13.7)
Severe	4	(7.8)
nalgesics score <sup>‡</sup>		
Ione	22	(43.1)
Aild	13	(25.5)
Moderate	12	(23.5)
Severe	4	(7.8)
Pain on Numerical Rating Scale (0–10)	4	(2–7)
Annual or biennial cervical smear tests (yes)	22	(43.1)

608 Table 2 Medical and reproductive histories and lifestyle of 51 participants

 $\ddagger$ The Dysmenorrhea and Analgesics scores are grouped according to a previous study.<sup>26</sup> 610

611 Abbreviations: IQR, Interquartile range; IUS/IUD, Intrauterine system/Intrauterine device.

	IN (%) 0.	r median (IQR)
Body mass index (kg/m <sup>2</sup> ) <sup>§</sup>		
Underweight (BMI<18.5)	6	12.0%
Normal (BMI 18.5–24.9)	34	68.0%
Overweight (BMI 25–29.9)	5	10.0%
Obese (BMI≥30)	5	10.0%
Blood pressure <sup>®</sup>		
Normal	33	64.7%
Elevated	10	19.6%
Hypertension stage 1	5	9.8%
Hypertension stage 2	3	5.9%
Blood tests		~
Haemoglobin (g/dL, median, IQR)	13.4	(12.6-14.0)
<12.0 g/dL (N, %) <sup>†</sup>	4	7.8%
Serum iron	102	(71–123)
<40 µg/dL (N, %)	3	5.9%
Ferritin (ng/mL, median, IQR)	30.9	(15.4–53.3)
<12.0 ng/mL (N, %)	9	17.6%
HbA1c (%, median, IQR)	5.0	(4.9–5.3)
$\geq 5.6\% (N, \%)^{\dagger}$	3	5.9%
Triglyceride (mg/dL)	68	(53–90)
$\geq 150 \text{ mg/dL} (N, \%)^{\dagger}$	3	5.9%
LDL cholesterol (mg/dL)	3 105	
		(95–122)
$\geq$ 120 mg/dL (N, %) <sup>†</sup>	14	27.5%
HDL cholesterol (mg/dL)	71	(57–84)
$\leq$ 39 mg/dL (N, %) <sup>†</sup>	0	0.0%
AST (IU/L)	17	(16–20)
$\geq$ 31 IU/L (N, %) <sup>†</sup>	2	3.9%
ALT (IU/L)	13	(11–18)
≥31IU/L (N, %) <sup>†</sup>	4	7.8%
GGT (IU/L)	15	(12–19)
$\geq$ 51 IU/L (N, %) <sup>†</sup>	1	2.0%
Serologic tests for syphilis: TPHA-positive or RPR-positive	0	0.0%
Chlamydia trachomatis IgA antibodies-positive	5	9.8%
Chlamydia trachomatis IgG antibodies-positive	11	21.6%
Rubella IgG antibodies <8.0 IU/mL (EIA)	24	47.1%
25-hydroxyvitamin D (ng/mL)	12.4	(9.2–17.5)
<20 ng/mL	42	82.4%
20.0–29.9 ng/mL	8	15.7%
≥30.0 ng/mL	1	2.0%
Serum zinc (µg/dL)	94	(86–99)
<60 μg/dL	0	0.0%
≥60 to <80 μg/dL	9	17.6%
≥80 μg/dL	42	82.4%
Serum folate (ng/mL)	7.2	(6.1–10.6)
<4.0 ng/mL	2	3.9%
$\geq 4.0 \text{ to } < 7.0 \text{ ng/mL}$	21	41.2%
$\geq$ 7.0 ng/mL	28	54.9%
Thyroid Stimulating Hormone (μIU/mL)	1.47	(1-1.81)
<0.35 µIU/mL	1	2.0%
$\geq 4.94 \ \mu \text{IU/mL}$	0	0.0%

612 Table 3 Results from mandatory and additional health check-up data of 51 study participants

613 §There was one missing data.

<sup>614</sup> ¶Blood pressure was classified into three categories (normal blood pressure: systolic blood pressure [sBP]

615 < 120 mmHg and diastolic reading [dBP] < 80 mmHg). Elevated blood pressure: sBP 120–129 mmHg

- and dBP < 80 mmHg. Stage 1 hypertension: sBP 130–139 mmHg or dBP 80–89 mmHg. Stage 2 hypertension: sBP  $\ge$  140 mmHg or dBP  $\ge$  90 mmHg)
- 618 Abbreviations: IQR, Interquartile range; BMI, body mass index; HbA1c, Haemoglobin A1c; LDL, Low

619 Density Lipoprotein; HDL, High Density Lipoprotein; AST, aspartate aminotransferase; ALT, alanine

transaminase; GGT, gamma glutamyl transferase; TPHA, treponema pallidum haemagglutination; RPR,
 rapid plasma reagin; EIA, enzyme-immunoassay.

- 622 <sup>†</sup>Cut-off values are based on the health guidance judgment values of the standard health check-up and
- 623 health guidance programme established by the Ministry of Health, Labour and Welfare.

#### Table 4 Results on counselling satisfaction and behaviour change (n=41)

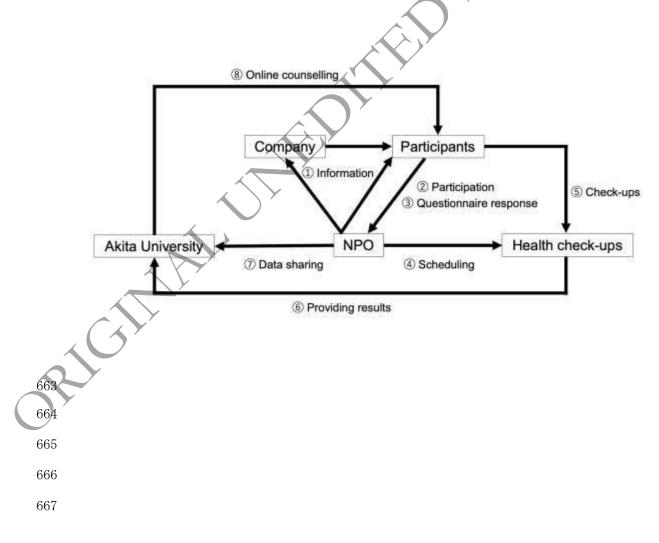
		Ν	(%)
	Are you satisfied with the counselling?		
	Strongly agree	30	(73.2)
	Strongly agree	11	(26.8)
	Neither agree nor disagree	0	(0.0)
	Disagree a little	0	(0.0)
	Strongly disagree	0	(0.0)
	Would you like to recommend the preconception check-up to others?		
	Strongly agree	27	(65.9)
	Agree a little	12	(29.3)
	Neither agree nor disagree	2	(4.9)
	Disagree a little	$\overset{2}{0}$	(0.0)
	Strongly disagree	0	(0.0)
	A sense of security after counselling		(0.0)
	Relieved	35	(85.4)
	Neither	30	(83.4) (9.8)
	Anxious	2	(9.8) (4.9)
			(4.9)
	Intention to change health behaviour after counselling See an obstetrician/gynaecologist	17	(115)
	Improve your lifestyle	32	(41.5)
	No change in future actions	52 2	(78.0)
	Free text comments	Z	(4.9)
	Take a folic acid supplement	2	(4,0)
		2	(4.9)
	Get rubella vaccine	1	(2.4)
	Changes in the reproductive life plan	4	(0, 0)
	Finding a partner sooner	4	(9.8)
	Getting married sooner	5	(12.2)
	Getting pregnant sooner	13 19	(31.7)
649	Having no effect	19	(46.3)
649 650			
690			
CE 1			
651			
	$\langle \mathbf{X} \rangle$		
	$\checkmark$		
	<u> </u>		
	× Y		
Á			
	CH-		

652 Figure legends

# Figure 1: Collaborative framework of the preconception check-up package managed by a nonprofit organisation

The figure depicts the flow of the preconception check-ups. 1) Non-profit organisation (NPO) provides information to the company and its employees; 2) those wishing to participate apply directly to the NPO and 3) complete a questionnaire; 4) the NPO coordinates the schedule with the medical examination provider; 5) participants undergo preconception check-ups at the same time as the staff medical examination; 6) the results of the medical examination are sent directly to Akita University; 7) the NPO shares the data of the examinees, including the questionnaire contents, with Akita University; and 8)

- 661 Akita University conducts online counselling based on the medical examination and questionnaire results.
- 662 Abbreviation: NPO, Non-profit organisation.



- **Figure 2: T1-T3 changes in fertility knowledge and childbearing desires (n = 41)**
- 669 (a) Comparison of the Japanese version of the Cardiff Fertility Knowledge Scale (CFKS-J) scores pre-
- 670 and post-intervention
- 671 Pre- and post-intervention mean (95% confidence interval) scores on the CFKS-J are shown. The
- 672 preconception check-up package intervention significantly improved the score from 63.0 (56.1–70.0) to
- 673 71.7 (65.6–77.8) percentage points (P = 0.006, paired t-tests).
- 674 (b) Desired number of additional children
- 675 Pre- and post-intervention distributions are shown and compared using the Wilcoxon signed rank test.
- 676 (c) Plan to try conceiving
- 677 Pre- and post-intervention distributions are shown and compared using the Wilcoxon signed rank test.
- 678 Those who desired  $\geq 1$  child were included (n = 32).

