BACKGROUND: Women with multiple pregnancies are at risk for maternal complications such as preterm birth. Hazardous working conditions, such as physically demanding work and long and irregular working hours, might increase the risk of preterm birth.

OBJECTIVE: This study primarily aimed to determine whether certain working conditions up to 20 weeks of pregnancy increase the risk of preterm birth in multiple pregnancies. The secondary objective was to evaluate whether the working conditions of Dutch women with multiple pregnancy have been adjusted to the guidelines of the Netherlands Society of Occupational Medicine.

STUDY DESIGN: We performed a prospective cohort study alongside the ProTWIN trial, a multicenter randomized controlled trial that assessed whether cervical pessaries could effectively prevent preterm birth. Women with paid work of >28 hours per week completed questionnaires concerning general health and working conditions between 16 and 20 weeks of pregnancy. Univariable and multivariable logistic regression analyses were performed to identify work-related factors associated with preterm birth (32–36 weeks’ gestation) and very preterm birth (<32 weeks’ gestation). We analyzed a subgroup of participants who worked for more than half of the week (>28 hours). We calculated the proportion of women who reported work-related factors not in accordance with guidelines.

RESULTS: We studied 383 women, of whom 168 (44%) had been randomized to pessary, 142 (37%) to care as usual, and 73 (19%) did not participate in the randomized part of the study. After adjusting for confounding variables, working >28 hours was associated with very preterm birth (n=33; 78%) (adjusted odds ratio, 3.0; 95% confidence interval, 1.1–8.1), and irregular working times were associated with preterm birth (n=26, 17%) (adjusted odds ratio, 2.0; 95% confidence interval, 1.0–4.1) and very preterm birth (n=10; 24%) (adjusted odds ratio, 2.7; 95% confidence interval, 1.0–7.3). Within a subgroup of 213 participants working >28 hours per week, multivariable analysis showed that irregular working times (n=16; 20%) (adjusted odds ratio, 3.5; 95% confidence interval, 1.2–10.1) and no/little freedom in performance of tasks (n=23; 28%) (adjusted odds ratio, 3.0; 95% confidence interval, 1.3–7.3) were associated with preterm birth. Irregular working times (n=9; 27%) (adjusted odds ratio, 3.4; 95% confidence interval, 1.0–11.1), requiring physical strength (n=9; 27%) (adjusted odds ratio, 5.3; 95% confidence interval, 1.6–17.8), high physical workload (n=7; 21%) (adjusted odds ratio, 3.9; 95% confidence interval, 1.1–13.9), and no/little freedom in performing tasks (n=10; 30%) (adjusted odds ratio, 3.2; 95% confidence interval, 1.1–9.6) were associated with very preterm birth. Before 20 weeks of pregnancy, 224 (58.5%) women with multiple pregnancy continued to work under circumstances that were not in accordance with the guidelines.

CONCLUSION: In our cohort study, nearly 60% of women with multiple pregnancy continued to work under circumstances not in accordance with the guidelines to avoid physical and job strain and long and irregular working hours. Irregular hours were associated with preterm and very preterm birth, and long hours were associated with preterm birth.

Key words: job strain, maternity protection legislation, occupational exposure, physical workload, shift work, working hours
The ProTWIN trial, a multicenter, open-label randomized controlled trial that assessed cervical pessaries as a preventive measure for PTB in women with multiple pregnancies, has been adjusted in accordance with the guidelines and whether working conditions in multiple pregnancy have been adjusted in accordance with the guidelines. The second aim was to identify whether certain working conditions up to 20 weeks’ gestation increase the risk of PTB in multiple pregnancies.

Materials and Methods
Study design
We performed a cohort study alongside the ProTWIN trial, a multicenter, open-label randomized controlled trial that assessed cervical pessaries as a preventive measure for PTB in women with a multiple pregnancy. The study protocol and trial report have been published elsewhere. Women with multiple pregnancy between 12 and 20 weeks of gestation eligible for the ProTWIN trial were asked to participate in this sub-study. Regardless of whether they decided to participate in the trial, women could participate in this sub-study. All participating women provided written informed consent. In addition to the approval of the ProTWIN trial, this additional cohort study on work-related factors in pregnancy was approved by the research ethics committee of Amsterdam University Medical Center, location AMC (MEC 09-107) and by the boards of each of the 40 participating hospitals. The trial was registered in the Dutch trial register (NTR1858).

Guidelines
We used the recommendations for multiple pregnancy from the Dutch guideline “Pregnancy, Postpartum Period and Work” (Figure 1). We defined work-related risk factors as >40 hours of work per week, irregular working times, ≥16 h/wk of standing and walking, physical strain, and problems with job strain. The exact definitions of these risk factors are listed in Table 1. We constructed a composite work risk variable, with which we compared “working in accordance with guidelines” (score 0 on risk factors) with “working in the presence of ≥1 risk factors” (score 1–5).

Data collection
We used a validated questionnaire on psychosocial job strain and physically demanding work, supplemented with questions on other working conditions, for example, (irregular) working times, chemical, biological, and physical factors, work adjustments, leisure time, and household characteristics.

Data on the gestational age at delivery and other outcomes related to delivery and maternal and perinatal morbidity were retrieved from patient files by local research nurses or midwives.

Procedure
From May 2010 until March 2012 every woman eligible for the ProTWIN study received a questionnaire (in Dutch language) at 16, 24, and 32 weeks’ gestation, handed out by the attending research nurse, midwife, or obstetrician. The first questionnaires had to be completed before 20 weeks’ gestation, the second before 28 weeks, and the third at 34 weeks’ gestation. Completed questionnaires were received, checked, and digitalized.

Participants
The study focused on women with a multiple pregnancy, at 12 to 20 weeks of gestation, eligible for the ProTWIN trial, and with paid employment or self-employed, defined as paid work for at least 8 hours per week during the woman’s first trimester.

Outcome measurements
The main outcome of this study was gestational age at delivery. The secondary outcome was the proportion of women with multiple pregnancy who are exposed to work-related risk factors, as defined in Table 1 (participant-reported and retrieved from the questionnaires [Supplemental Table 1]), that exceed the recommendations from the guideline “Pregnancy, Postpartum Period and Work” concerning multiple pregnancy, up to 20 weeks of gestation.

Statistical analysis
Baseline characteristics were presented as absolute numbers with percentages for categorical variables, and means with standard deviation (SD) or median with interquartile range (IQR) for continuous variables.

The analysis of the main outcome measure, PTB, was performed using logistic regression to estimate crude (OR) and adjusted odds ratios (aOR) with...
From: NVAB. Practice guideline — Pregnancy, postpartum period and work. Advice and guidance by the occupational physician. NVAB, the Netherlands Society of Occupational Medicine: recommendations multiple pregnancy and work.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.

95% confidence intervals (CIs). We compared women with PTB (32–36 weeks gestation) and very PTB (<32 weeks gestation) with women who delivered at term (≥37 weeks gestation). Demographic and pregnancy characteristics and working conditions at 16 to 20 weeks’ gestation were used as explanatory variables. ORs were adjusted for a set of predetermined risk factors known to be associated with risks for PTB (age, body mass index [BMI], level of education, parity) and factors with significant baseline differences between groups (parity, assisted conception, ethnicity). A subgroup analysis for the association between gestational age and working conditions in the group of participants working >28 hours per week was performed by stratification. We opted for a cutoff of >28 hours because this equals to working for more than half a week (>3.5 days per week) and can be considered as the point at which work-related factors become an important part of daily life.

A sum score of “physical workload” was calculated on the basis of 4 questions concerning physical work. Scale reliability (Cronbach) was 0.83. For analysis, these questions were dichotomized: “never sometimes” (score 0) vs “often always” (score 1), and then the sum score was calculated. The sum score of physical workload was dichotomized into: “high” (score 3–4) vs “low-moderate” (≤2).

TABLE 1

| Work-related factors that exceed the limit values of guidelines for multiple pregnancy (<20 weeks) |
|-------------------------------------------------------------------------------------------------|
| 1. Working times >40 h/wk |
| 2. Irregular working times (working in the evening and/or at night) |
| 3. Standing + walking ≥16 h/wk |
| 4. Physical strain* |
| 5. Problems with pressure: often/always |

* Sum score from 6 questions: bending, squatting, reaching high, requiring physical strength, physically demanding, uncomfortable or strenuous postures.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
results over imputation sets was done using Rubin’s rules.⁶¹

Analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp, Armonk, NY). P values < .05 were considered statistically significant.

**Results**

Between May 2010 and March 2012, 996 women met the cohort’s inclusion criteria, of whom 813 had been recruited in the ProTWIN trial. Because questionnaires on workload were introduced later during the trial, 324 participants had a history of PTB. Almost one-third (32%) of the participants (31%) worked in the healthcare sector, and 62% worked in a company with > 50 employees. A total of 672 women (68%) who received a questionnaire, 449 (67%) returned a completed one. Of these 449 women, 61 women (16%) did not have paid employment, and 5 women (1%) worked <8 h/wk and were excluded, whereas 383 (85%) had paid employment status and were suitable for our analysis (Figure 2). The analysis population of this study consisted of these 383 women, of whom 189 (49%) delivered at term (≥37 weeks’ gestation), 152 (40%) delivered between 32 and 36 weeks, and 42 (11%) delivered at <32 weeks.

Baseline characteristics are outlined in Table 2, Supplementary Tables 2 and 3. Mean maternal age at inclusion was 32 (SD, 4.1) years and the mean BMI was 25 (IQR, 21.3–26.3). Most women were White (n = 358; 93%) and had completed a higher professional education or university (n = 260; 68%). Of the included women, 223 (58%) were nulliparous and 160 (42%) multiparous, of whom 9 (6%) had a history of PTB. Almost one-third (31%) of the participants worked in the healthcare sector, and 62% worked in a company with > 50 employees. A total of 168 (44%) women had been randomized to pessary use and 142 (37%) to the control group, and 73 (19%) women did not participate in the randomized part of the study.

**Associations between working conditions and gestational age**

Results of univariable analysis with demographic and pregnancy characteristics are listed in Table 3. PTB occurred more frequently among participants with ethnic origin “other than Caucasian” (OR, 3.5; 95% CI, 1.1–11.4) and nulliparity (OR, 1.8; 95% CI, 1.2–2.9). Nulliparity (OR, 4.8; 95% CI, 2.0–11.2) and assisted conception (OR, 2.1; 95% CI, 1.1–4.2) were associated with very PTB.

Table 4 and Supplemental Table 4 show the results of univariable analyses with working conditions and PTB within the total population. Working >28 hours at 16 to 20 weeks of gestation (OR, 3.3; 95% CI, 1.5–7.2) and performing irregular working times (OR, 2.5; 95% CI, 1.1–5.7) were associated with very PTB.

In the subgroup of participants working >28 hours per week, irregular working times (OR, 2.8; 95% CI, 1.1–6.9) and no/little freedom in performance of tasks (OR, 2.4; 95% CI, 1.1–5.1) were associated with PTB (Table 7; Supplemental Table 5). Furthermore, the following work-related factors were associated with very PTB: irregular working times (OR, 4.2; 95% CI, 1.5–12.0), requiring physical strength (OR, 4.2; 95% CI, 1.5–12.1), high physical workload (sum score of 4 questions concerning physical work) (OR, 4.0; 95% CI, 1.2–13.0), and no/little freedom in performance of tasks (OR, 2.6; 95% CI, 1.02–6.7) (Table 5; Supplemental Table 5).

Results of the multivariate analysis between working conditions and PTB are shown in Tables 6 and 7. In the analyses within the total study population, working >28 hours was associated with very PTB (aOR, 3.02; 95% CI, 1.1–8.1), and irregular working times were associated with PTB (aOR, 2.0; 95% CI, 1.01–4.1) and very PTB (aOR, 2.7; 95% CI, 1.0–7.3) (Table 6).

In the subgroup analyses with participants working >28 hours per week, irregular working times (aOR, 3.5; 95% CI, 1.2–10.1) and no/little freedom in performance of tasks (aOR, 3.0; 95% CI, 1.3–7.3) were associated with PTB (Table 7). Within this subgroup, irregular working times (aOR, 3.4; 95% CI, 1.02–11.1), requiring physical strength (aOR, 5.3; 95% CI, 1.6–17.8), high physical workload (aOR, 3.9; 95% CI,
1.1–13.9), and no/little freedom in performing tasks (aOR, 3.2; 95% CI, 1.1–9.6) were associated with very PTB.

### Adherence to guidelines

From 16 to 20 weeks of pregnancy, 224 (58.5%) women with multiple pregnancy continued to work under circumstances that were not in accordance with the guidelines (Table 8). An overview of risk factors contributing to exceeding the limits of guidelines and legislation on work during pregnancy is shown in Table 3. Physical strain (sum score of 6 questions concerning physical work) (166; 43%) and prolonged standing and walking (119; 31%) were the risk factors most frequently exceeded before 20 weeks of pregnancy.

### Comment

**Principal findings**

In this study, we found that before 20 weeks of pregnancy, working >28 hours and irregular working times were associated with very PTB (<32 weeks of gestation), and irregular working times were associated with PTB (32–36 weeks of gestation). In the subgroup of participants working >28 hours per week, irregular working times and no/little freedom in performing tasks were associated with PTB (32–36 weeks of gestation) and very PTB. Requiring physical strength and high physical workload were associated with very PTB.

Before 20 weeks of pregnancy, nearly 60% of women with multiple pregnancy continued to work under circumstances not in accordance with the guidelines of the Netherlands Society of Occupational Medicine (NVAB). Physical strain (43%) and prolonged standing and walking (31%) were the most frequently exceeded risk factors.

### Results in the context of what is known

Our study found a proportion of nearly 60% of women with multiple pregnancy who continued to work under circumstances not in accordance with the guidelines, which is higher than that found in groups of women with low-risk pregnancies (40% before 20 weeks’ gestation). There are only a few

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**TABLE 2**

Baseline characteristics of the study population

| N = 383 | After imputation |
|---------|-----------------|
| **Demographics and general health** | | |
|Maternal age\(^b\) (y) (Mean, SD) (IQR) | 32 (4.1) (30–35) |
| – ≤ 35 | 298 (77.8%) |
| – > 35 | 83 (21.7%) |
|BMI (Mean, SD) (IQR) | 25 (5) (21–26) |
| – < 18.5 | 10 (3%) |
| – 18.5–25.0 | 247 (65%) |
| – > 25.0–30.0 | 71 (18%) |
| – > 30.0 | 55 (14%) |
|Ethnic origin: | | |
| – White European | 358 (93%) |
| – Non-White European | 25 (7%) |
|Highest educational level | | |
| – Primary or secondary school or Lower professional education | 123 (32%) |
| – Higher professional education or University | 260 (68%) |
|Smoking during pregnancy | 21 (6%) |
|Physical activity (sports) during pregnancy | 118 (31%) |
|**Pregnancy characteristics** | | |
|Nulliparous | 223 (58%) |
|Multiparous | 160 (42%) |
|Multiparous, previous preterm birth | 9 (6% [from 160]) |
|Cervical length (20 wk) ≤ 25 mm | 19 (5%) |
|Conception\(^c\) | | |
| – Spontaneous conception – no (%) | 231 (60%) |
| – Assisted conception | 135 (35%) |
|Triplets | 11 (3%) |
|Monochorionic | 82 (21%) |
|Pessary\(^d\) | 168 (44%) |
|Gestation (wk) | | |
| – < 32 | 43 (11%) |
| – 32 to <37 | 152 (40%) |
| – ≥ 37 | 189 (49%) |
|Work: general aspects | | |
| – Health care | 118 (31%) |
| – Financial and business services | 70 (18%) |
| – Education, child care, and welfare | 67 (17%) |
| – Government | 46 (12%) |
| – Retail and hospitality industry | 37 (10%) |

\(^a\) Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.

\(^b\) Age in years.

\(^c\) Spontaneous conception.

\(^d\) Pessary.
guidelines (accessible and in English) on multiple pregnancy with recommendations on working conditions, mostly limited to general advice.23–25 It is unknown whether they are followed.

There are no previous studies into the impact of working conditions on PTB in multiple pregnancies because these pregnancies are usually excluded because of their high risk of PTB. Two recent meta-analyses showed that long working hours, rotating shifts, and high physical workload were associated with PTB in singleton pregnancies.26–27 The difference between singleton and multiple pregnancies, which have higher risk of complications, may explain why the ORs are somewhat higher in our study.

Strengths and limitations

In this study, we prospectively and accurately identified various work-related risk factors of women with multiple pregnancies at different periods of pregnancy.

This study examined the impact of working conditions in multiple pregnancies and provided direct evidence for the recommendations of the NVAB guideline. These have been formulated in accordance with (weighting the strength of) scientific evidence on the increased risk of PTB, growth restriction, and pre-eclampsia in multiple pregnancies.

To prevent bias, we only included pregnant women with paid work because employment during pregnancy is associated with a reduction in the risk of PTB.26 Compared with the baseline characteristics of a recent randomized controlled trial (n=13,520) in a low-risk pregnancy population in the Netherlands, BMI and age were comparable, but the highly educated, White, nulliparous, and nonsmoking women were overrepresented in our study.27 The sectors in which the participants worked are a reflection of the national Dutch figures.28 In our study, nulliparas were overrepresented. As in our study, they have been found to have a higher risk of PTB than multiparous women without a history of PTB.29 Probably because of the low number of multiparas with previous PTB (6%), their risk of PTB was not increased in our study. Therefore, we only adjusted for the variable of parity.

The number of participants who gave birth between 32 and 36 weeks’ gestation was lower than the average in the Netherlands (40% vs 45%), whereas the number of those who gave birth before 32 weeks’ gestation was slightly higher (11% vs 10%).12 The rate of mono-chorionic pregnancies, which have a higher risk of PTB compared with dichorionic pregnancies, was comparable to the mean incidence (21% vs 20%).29 To minimize the impact of demographic and pregnancy-related factors on the outcome of PTB, we adjusted for the risk factors that significantly increased the risk of PTB (parity, ethnicity, and assisted conception).

Presentation of the results took place approximately 10 years after data collection. Because medical and occupational health policies for women with multiple pregnancies have not changed during this period, we do not expect this to affect the primary and secondary outcomes of our study.

The association between the composite work-related variable (working according to guideline, as measured using various separate working conditions) and gestational age did not clearly reveal the value of independent components for this score, and therefore we chose not to present these results.

Missing values of demographic and pregnancy characteristics could have caused bias of the results, despite imputation. Data were mainly missing from women eligible for participating in the ProTWIN trial who refused randomization and did allow their pregnancy outcomes to be recorded.

Implications for research and practice

Adverse pregnancy outcomes, such as PTB, have an enormous impact on well-being of parents and children.12 No guideline identified an effective strategy for women with multiple pregnancies to prevent PTB.31 This study confirms that avoiding physical

### TABLE 2

Baseline characteristics of the study population (continued)

| N=383 | After imputation |
|-------|------------------|
| Industry/transport | 25 (6%) |
| Culture, recreation | 14 (4%) |
| Other or unknown | 6 (2%) |
| Number of employees in the company >50 | 239 (62%) |
| Travel distance commuting, km (mean, SD) (IQR) | 33 (±37) (6–48) |
| Travel time commuting, min/h (mean, SD) (IQR) | 58 (+-40) (0-240) |
| Household conditions | |
| Care for children (living at home): Yes | 162 (42%) |
| 1 child | 2 children |
| • 0—4 y | 143 (37%) |
| 11 (3%) |
| • >5 y | 50 (13%) |
| 19 (5%) |
| No half-day eq. childcare (mean, SD) (min-max) (n=152) | 5 (+2) (1–10) |
| Housekeeping largely done by participant herself | 87 (23%) |

BMI, body mass index; IQR, interquartile range; SD, standard deviation.

a All variables shown as number (percentage); b Missing: 2 (0.5%); c Missing: 17 (5%); d Not participating in randomized part of the study: 73 (19%).

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
### TABLE 3
Univariable associations with demographic and pregnancy characteristics in women with preterm birth and very preterm birth compared with women with delivery at term (total study population)

| Participants at 16–20 weeks' pregnancy | N (%): Total | ≥37 wk | 32–36 wk | <32 wk | OR (95% CI) | OR (95% CI) |
|--------------------------------------|-------------|--------|--------|-------|------------|------------|
| Total study population               | 383 (100%) |        |        |       |            |            |
| Age >35 vs ≤35                       | 83 (21.8%) | 23.4   | 20.3   | 19.6  | 0.83       | 0.49–1.41  |
| BMI groups                           |            |        |        |       |            |            |
| 18.5–25 (ref)                        | 247 (65%)  | 61.4   | 69.8   | 59.5  |            |            |
| BMI <18.5 vs 18.5–25                 | 10 (3%)    | 3.1    | 2.6    | 1.4   | 0.72       | 0.14–3.63  |
| BMI >25–30 vs 18.5–25                | 71 (18%)   | 18.4   | 16.3   | 26.3  | 0.78       | 0.43–1.43  |
| BMI >30 vs 18.5–25                   | 55 (14%)   | 17.2   | 11.1   | 13.5  | 0.57       | 0.28–1.15  |
| Education, low-middle vs high        | 123 (32%)  | 30.3   | 35.4   | 27.5  | 1.25       | 0.77–2.04  |
| Ethnic origin, other vs White European | 25 (7%) | 3.3    | 10.3   | 7.5   | 3.50       | 1.07–11.44 |
| Parity, 0 vs >0 (ref)                | 223 (58%)  | 48.7   | 63.3   | 81.9  | 1.83       | 1.16–2.86  |
| Previous PTB, yes vs no              | 9 (2%)     | 2.4    | 2.2    | 2.8   | 1.34       | 0.29–6.11  |
| Twin monochorionic vs dichorionic     | 82 (21%)   | 17.8   | 26.2   | 24.3  | 1.64       | 0.94–2.87  |
| Cervical length ≤25 mm vs >25 mm      | 19 (5%)    | 3.6    | 6.6    | 5.6   | 2.04       | 0.44–9.38  |
| Smoking                              | 21 (6%)    | 5.7    | 5.2    | 6.6   | 0.85       | 0.25–2.92  |
| Assisted conception                   | 135 (37%)  | 34.4   | 35.8   | 52.5  | 1.07       | 0.67–1.69  |

BMI, body mass index; CI, confidence interval; OR, odds ratio; PTB, preterm birth; ref, reference.

*Association is statistically significant.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.

### TABLE 4
Univariable associations with working conditions in women with preterm birth and very preterm birth compared with women with delivery at term: total study population

| Participants at 16–20 weeks' pregnancy | Total | ≥37 wk | 32–36 wk | <32 wk | OR (95% CI) | OR (95% CI) |
|--------------------------------------|-------|--------|--------|-------|------------|------------|
| Total study population               | 383   |        |        |       |            |            |
| Working >28 h/wk vs ≤28 (ref)         | 56    | 52     | 54     | 78    | 1.06       | 0.69–1.63  |
| Irregular working times: yes vs no    | 15    | 11     | 17     | 24    | 1.65       | 0.89–3.08  |
| Standing/walking ≥15 h/wk             | 31    | 28     | 35     | 36    | 1.21       | 0.94–1.54  |
| High physical workload               | 12    | 9      | 14     | 19    | 1.66       | 0.84–3.30  |
| Job strain                           |       |        |        |       |            |            |
| Problems with pressure               | 13    | 11     | 13     | 19    | 1.14       | 0.59–2.20  |
| Freedom in performing tasks          | 29    | 25     | 34     | 29    | 1.56       | 0.97–2.52  |
| Influence on pace                    | 47    | 44     | 50     | 52    | 1.32       | 0.86–2.04  |

CI, confidence interval; OR, odds ratio; ref, reference.

*Association is statistically significant.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
and job strain and long and irregular working hours throughout pregnancy may be able to prevent (very) PTB. Because there are hardly any evidence-based guidelines for working women with other medically complicated pregnancies, it is worth considering applying these recommendations to them as well.

Experiences observed during the COVID-19 pandemic seem to support these recommendations. During periods of strict restrictive measures to prevent the transmission of SARS-CoV-2, the number of PTBs fell in several countries. In Australia, this reduction was higher in women with a previous PTB, who may have benefited from restrictive measures such as cessation of working. Further research is needed in working women with multiple pregnancy and other medically complicated pregnancies, with lower educational level and ethnicity other than White. In addition to PTB, also focusing on adverse outcomes such as growth restriction and pre-eclampsia may help support the cost-effectiveness of work adjustment early in pregnancy for working pregnant women with high-risk pregnancies.

### TABLE 5

| Participants at 16–20 weeks’ pregnancy | Total | ≥37 wk | 32–36 wk | <32 wk | 32–36 wk vs ≥37 wk | <32 wk vs ≥37 wk |
|---------------------------------------|-------|--------|----------|--------|-------------------|------------------|
| Subgroup working ≥28 h/wk             | 213   | 99 (46%) | 81 (38%) | 33 (16%) |                  |                  |
| Irregular working times: yes vs no    |       |        |          |        | 2.78a  1.12–6.88a | 4.22a  1.47–12.10a |
| Standing/walking ≥15 h/wk              | 34    | 29     | 29       | 34     | 1.56   0.83–2.96   | 1.38   0.60–3.18   |
| Requiring physical strengthb          | 14    | 8      | 16       | 27     | 2.16   0.85–5.50   | 4.22a  1.47–12.10a |
| High physical workloadc                | 10    | 6      | 11       | 21     | 1.87   0.64–5.49   | 4.02a  1.24–13.00a |
| Job strain                            |       |        |          |        |                   |                  |
| Problems with pressureb                | 15    | 15     | 21       | 16     | 0.97   0.42–2.20   | 1.49   0.55–4.05   |
| Freedom in performing tasksd          | 22    | 14     | 28       | 30     | 2.37a  1.10–5.11a  | 2.63a  1.02–6.74a |
| Influence on pacee                    | 45    | 39     | 49       | 54     | 1.54   0.84–2.82   | 1.90   0.86–4.23   |

CI, confidence interval; OR, odds ratio; ref, reference.

a Association is statistically significant; b Often-always vs never-sometimes (ref); c Sum score of physical workload, high vs low–moderate: sum of 4 variables: lifting, physically very demanding, requiring physical strength, strenuous postures; d Never-sometimes vs often-always (ref).

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.

### TABLE 6

| Participants at 16–20 weeks’ pregnancy | 32–36 wk vs ≥37 wk | <32 wk vs ≥37 wk |
|---------------------------------------|-------------------|------------------|
| Total study population, n=383         |                   |                  |
| Working ≥28 h/wk vs ≤28 (ref)          | 0.95              | 0.57–1.58        |
| Irregular working times                | 2.03b             | 1.01–4.07b       |
| Physical work                          |                   |                  |
| Requiring physical strengthb           | 1.56              | 0.82–3.03        |
| High physical workloadc                | 1.67              | 0.77–3.6         |

aOR, adjusted odds ratio; CI, confidence interval; ref, reference.

a Adjusted for parity, assisted conception, ethnicity, age, body mass index, age, education; b Association is statistically significant; c Often-always vs never-sometimes (ref); d Sum score of physical workload, high vs low–moderate: sum of 4 variables: lifting, physically very demanding, requiring physical strength, strenuous postures.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
Conclusion
In multiple pregnancies before 20 weeks’ gestation, long (>28 h/wk) and irregular working hours were associated with very PTB (<32 weeks of gestation), and irregular working hours were associated with PTB (32–36 weeks of gestation). In the group of participants working >28 hours per week, irregular working hours and little or no freedom in performance of tasks were associated with PTB and very PTB, and working with high physical strain was associated with very PTB. Before 20 weeks of gestation, nearly 60% of women with multiple pregnancy continued to work under circumstances not in accordance with the guidelines of the NVAB. Adjustment of working conditions according to the recommendations of the NVAB guideline on multiple pregnancies (to avoid physical and job strain and long and irregular working hours throughout pregnancy) may be able to prevent (very) PTB.

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Table 7
Multivariable associations with working conditions in women with preterm birth and very preterm birth compared with women with delivery at term: subgroup of participants working >28 h/wk

| Participants at 16–20 weeks’ pregnancy | 32–36 wk vs ≥37 wk | <32 wk vs ≥37 wk |
|---------------------------------------|--------------------|-----------------|
| Subgroup working >28 h/wk n=213       | aOR(95% CI)        | aOR(95% CI)     |
| Irregular working times               | 3.5c (1.23–10.05c) | 3.36c (1.02–11.06c) |
| Physical work                         |                     |                 |
| Requiring physical strength           | 1.99 (0.66–6.0)     | 5.31c (1.59–17.78c) |
| High physical workload                | 1.94 (0.6–6.23)     | 3.87c (1.08–13.94c) |
| Job strain                            | 3.02 (1.25–7.25c)   | 3.21 (1.08–9.56c) |

aOR adjusted odds ratio; BMI, body mass index; CI, confidence interval; ref, reference.

Table 8
Number and specification of work-related risk factors that exceeded the limit values of guidelines

| Work-related risk factors that exceeded the limit values of guidelines (N=383) |
|-----------------------------------|-----------------|----------------|
| Number of risk factors            | Specification of risk factors | 16–20 weeks’ pregnancy |
| None                              | >40 h/wk         | 16 (4%)         |
| ≥1                                | Irregular working times | 57 (15%)        |
| 1                                 | ≥16 h standing/walking/wk | 119 (31%)       |
| 2                                 | Physical strain   | 166 (43%)       |
| 3                                 | Problems with job strain often/always | 48 (13%) |
| 4                                 | 5 (1%)            |                 |

a Shown as number (percentage); b Sum score of 6 questions on: bending, squatting, reaching high, requiring physical strength, physically demanding, uncomfortable, or strenuous postures.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
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Authors are willing to share data on reasonable request.

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**SUPPLEMENTAL TABLE 1**

Questions used for information about risk factors (Table 1)

1. How many hours per week do you currently work on average? _____ hours a week
2. Do you work in irregular shifts?
   - No
   - Yes
   How many of your working hours do you on average spend on these shifts a week?
     - _____ % in day shifts
     - ______ % in evening shifts (until 23:00)
     - _______ % in night shifts
3. During your work, how many hours a day do you have to:
   - Walk? ____ %
   - Stand? ____%
   - Sit? ____%

For the next couple of questions, please indicate every time how often certain things occur at the moment.

You can choose between the following answers: never, sometimes, often, always.

| Question                                                                 | Never | Sometimes | Often | Always |
|-------------------------------------------------------------------------|-------|-----------|-------|--------|
| 4. Do you have to bend over during work?                                |       |           |       |        |
| 5. Do you have to squat during work?                                    |       |           |       |        |
| 6. Do you have to reach high during work?                               |       |           |       |        |
| 7. Do you think your work is requiring physical strength?               |       |           |       |        |
| 8. Do you think your work is very physically demanding                  |       |           |       |        |
| 9. Do you work in an uncomfortable or strenuous position?              |       |           |       |        |
| 10. Do you have problems with the pressure of work?                     |       |           |       |        |

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
### Work status and working conditions by gestational time

| Work status and working conditions | 16–20 weeks’ pregnancy (N=383) | 24–28 weeks’ pregnancy (N=333) | 32–36 weeks’ pregnancy (N=216) |
|-----------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Current work status**           |                                 |                                 |                                 |
| Usual working hours               | 284 (74%)                       | 141 (42%)                       | 32 (15%)                        |
| Less than usual because of illness| 99 (26%)                        | 109 (33%)                       | 29 (13%)                        |
| No work because of illness        | 0                               | 75 (23%)                        | 114 (53%)                       |
| Pregnancy leave                   | 0                               | 8 (2%)                          | 41 (19%)                        |
| At work                           | n=383 (100%)                    | n=250 (75%)                     | n=61 (28%)                      |
| **Working hours**                 |                                 |                                 |                                 |
| H/wk                              | 29 (±9) (8–70)                  | 24 (±10) (4–50)                 | 23 (±11) (4–42)                 |
| Irregular working times (yes)     | 58 (15%)                        | 11 (4%)                         | 1 (2%)                          |
| H/wk per shift                    |                                 |                                 |                                 |
| • Day shifts                       | 18 (±9) (0–42)                  | 21 (±8) (6–34)                  | n=1, 10 h/wk                    |
| • Evening shifts                  | 10 (±7) (0–30) (n=57)           | 5 (±2) (2–9) (n=11)             |                                 |
| • Night shifts                    | 2 (±4) (0–18) (n=14)            | n=1, 6 h/wk                     |                                 |
| **Physical work**                 |                                 |                                 |                                 |
| Work posture (hours/week)         | NA                              | NA                              | NA                              |
| • Walking                         | 7 (±6) (0–30)                   |                                 |                                 |
| • Standing                        | 5 (±6) (0–40)                   |                                 |                                 |
| • Sitting                         | 18 (±12) (0–70)                 |                                 |                                 |
| **Physical work (often/always)**  |                                 |                                 |                                 |
| Lifting/carrying                  | 68 (18%)                        | 14 (6%)                         | 1 (2%)                          |
| Bending                           | 122 (32%)                       | 39 (15%)                        | 3 (5%)                          |
| Reaching high                     | 29 (8%)                         | 13 (5%)                         | 2 (3%)                          |
| Repetitive motion                 | 142 (37%)                       | 79 (33%)                        | 15 (25%)                        |
| Physically demanding              | 82 (21%)                        | 35 (14%)                        | 8 (14%)                         |
| Requiring physical strength       | 68 (18%)                        | 20 (8%)                         | 4 (7%)                          |
| Uncomfortable or strenuous postures| 50 (13%)                      | 20 (8%)                         | 4 (7%)                          |
| On a strenuous machine or assembly line | 3 (1%)                      | 1 (0%)                          | 0                               |
| **Job strain (often/always)**     |                                 |                                 |                                 |
| Problems with work pace           | 9 (2%)                          | 12 (5%)                         | 4 (7%)                          |
| Problems with the pressure        | 48 (13%)                        | 25 (10%)                        | 8 (13%)                         |
| Like to take things a little easier| 77 (21%)                       | 51 (22%)                        | 10 (16%)                        |
| Freedom in performance of tasks   | 273 (71%)                       | 201 (80%)                       | 52 (86%)                        |
| Influence on the pace             | 202 (53%)                       | 164 (66%)                       | 46 (77%)                        |
| Planning own work                 | 237 (62%)                       | 183 (73%)                       | 52 (86%)                        |
| Support from manager              | 260 (68%)                       | 182 (73%)                       | 46 (76%)                        |
| Support of colleagues             | 309 (81%)                       | 214 (86%)                       | 51 (44%)                        |
| Varied work                       | 289 (75%)                       | 192 (77%)                       | 49 (80%)                        |
| freedom planning working times    | 143 (37%)                       | 143 (57%)                       | 43 (71%)                        |
| Physical factors (yes)            | NA                              | NA                              | NA                              |

*Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.* (continued)
## SUPPLEMENTAL TABLE 2
Work status and working conditions by gestational time

| Work status and working conditions | 16—20 weeks' pregnancy N=383 | 24—28 weeks' pregnancy N=333 | 32—36 weeks' pregnancy N=216 |
|-----------------------------------|-----------------------------|-----------------------------|-----------------------------|
| Heat                              | 24 (6%)                     |                             |                             |
| Cold                              | 19 (5%)                     |                             |                             |
| Noise                             | 46 (13%)                    |                             |                             |
| Biological agents                 | 147 (38%)                   | NA^c                        | NA^c                        |
| Small and/or sick children        | 77 (20%)                    |                             |                             |
| Sick adults                       | 73 (19%)                    |                             |                             |
| Blood or other bodily fluids      | 59 (15%)                    |                             |                             |
| Animals, raw meat, waste (-water)| 25 (8%)                     |                             |                             |
| Stool                             | 64 (17%)                    |                             |                             |
| Nature (forests, gardens)         | 5 (1%)                      |                             |                             |
| Chemical agents (yes) (more options) | 78 (20%)              | NA^c                        | NA^c                        |
| Cleaning supplies                 | 49 (13%)                    |                             |                             |
| Solvents (paint, lacquer, glue, detergents) | 16 (4%)                     |                             |                             |
| Anesthetic gases                  | 5 (1%)                      |                             |                             |
| Cancer inhibitory medication      | 10 (3%)                     |                             |                             |
| Pesticides                        | 3 (1%)                      |                             |                             |
| Heavy metals/metallic compounds   | 5 (15%)                     |                             |                             |
| Other “medication”                | 6 (2%)                      |                             |                             |
| Hair dye/nail polish remover      | 4 (1%)                      |                             |                             |

NA, not applicable.

^a All variables shown as number (percentage); ^b (mean, standard deviation) (min-max); ^c Not in questionnaire.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
### SUPPLEMENTAL TABLE 3
**Work advice and adjustments\(^a\)**

| At work | 16–20 weeks’ pregnancy n=383 | 24–28 weeks’ pregnancy n=333 | 32–36 weeks’ pregnancy n=216 |
|---------|------------------------------|------------------------------|------------------------------|
| Work adjustment because of current pregnancy | 143 (37%) | 169 (68%) | 52 (85%) |
| • Less physically demanding work | 55 (15%) | 59 (24%) | 10 (16%) |
| • Other working hours | 41 (11%) | 41 (16.5%) | 13 (21%) |
| • Less hours a day | 90 (24%) | 120 (48%) | 34 (56%) |
| • Plan work yourself | 44 (12%) | 57 (23%) | 20 (33%) |
| • Other (less work, slower work pace) | 83 (22%) | 105 (42%) | 19 (31%) |
| Advice to adjust work from: | | | |
| • Own initiative | 43 (16%) | 95 (38%) | 38 (62%) |
| • Obstetrician | NA\(^b\) | 104 (42%) | 24 (40%) |
| • Occupational physician | 2 (1%) | 53 (21%) | 10 (16%) |
| • Manager | 25 (9%) | 45 (18%) | 14 (23%) |
| • Other (partner, colleague, obstetrician) (\(\approx\)first questionnaire) | 9 (2%) | 23 (9%) | 6 (10%) |

NA, not applicable.
\(^a\) All variables shown as number (percentage); \(^b\) Not in questionnaire.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
### Univariable associations with working conditions in women with preterm birth and very preterm birth compared with women with delivery at term (total study population)

| Participants at 16–20 weeks' pregnancy | Total | ≥37 wk | 32–36 wk | <32 wk | 32–36 wk vs ≥37 wk | <32 wk s ≥37 wk |
|----------------------------------------|-------|--------|----------|--------|--------------------|----------------|
| Total study population                 | 383   | 189 (49%) | 152 (40%) | 42 (11%) |                     |                |
| Working hours >28 h/wk vs ≤28 (ref)    | 56    | 52     | 54       | 78     | 1.06               | 0.69–1.63 .80  |
| Irregular working times: yes vs no     | 15    | 11     | 17       | 24     | 1.65               | 0.89–3.08 .11  |
| Physical work                          |       |        |          |        |                    |                |
| Standing/walking ≥15 h/wk              | 31    | 286    | 35       | 36     | 1.21               | 0.94–1.54 .15  |
| a. Lifting                             | 18    | 16     | 19       | 22     | 1.21               | 0.68–2.13 .52  |
| b. Physically very demanding           | 21    | 20     | 22       | 26     | 1.15               | 0.68–1.95 .61  |
| c. Requiring physical strength         | 18    | 15     | 21       | 26     | 1.54               | 0.88–2.73 .13  |
| d. Strenuous postures                  | 13    | 11     | 14       | 19     | 1.28               | 0.67–2.45 .46  |
| Sum score a–d, high vs low–moderate    | 12    | 9      | 14       | 19     | 1.66               | 0.84–3.30 .17  |
| Job strain                             |       |        |          |        |                    |                |
| Problems with pressure                 | 13    | 11     | 13       | 19     | 1.14               | 0.59–2.20 .71  |
| Freedom in performing tasks            | 29    | 25     | 34       | 29     | 1.56               | 0.97–2.52 .07  |
| Influence on pace                      | 47    | 44     | 50       | 52     | 1.32               | 0.86–2.04 .21  |

CI, confidence interval; OR, odds ratio; ref, reference.

a Sum score of physical workload, high vs low—moderate: sum of 4 variables: lifting, b physically very demanding, b requiring physical strength, b strenuous postures.

b Association is statistically significant.

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.
## SUPPLEMENTAL TABLE 5
### Univariable associations with working conditions in women with preterm birth and very preterm birth compared with women with delivery at term (subgroup of participants working >28 h/wk)

| Participants at 16–20 weeks’ pregnancy | Subgroup working >28 h/wk | Total | >37 wk | 32–36 wk | <32 wk | 32–36 wk vs >37 wk | <32 wk vs >37 wk |
|---------------------------------------|---------------------------|-------|--------|----------|--------|---------------------|-----------------|
|                                       |                           |       | %      | %        | %      | OR (95% CI)         | P value         |
| Irregular working times: yes vs no    |                           |       |        |          |        |                     |                 |
|                                       |                           | 16    | 8      | 20       | 27     | 2.78 1.12–6.88      | .028<sup>a</sup> |
| Physical work                         |                           |       |        |          |        |                     |                 |
| Standing/walking ≥15 h/wk             |                           | 34    | 29     | 39       | 34     | 1.57 0.83–2.96      | .169            |
| a. Lifting<sup>b</sup>                |                           | 17    | 15     | 17       | 21     | 1.11 0.49–2.53      | .801            |
| b. Physically very demanding<sup>b</sup> |                         | 16    | 13     | 16       | 27     | 1.25 0.55–2.88      | .596            |
| c. Requiring physical strength<sup>b</sup> |                         | 14    | 8      | 16       | 27     | 2.16 0.85–5.50      | .108            |
| d. Strenuous postures<sup>b</sup>     |                           | 12    | 10     | 11       | 22     | 1.11 0.43–2.87      | .837            |
| Sum score a–d, high vs low—moderate  |                           | 10    | 6      | 11       | 21     | 1.87 0.64–5.49      | .254            |
| Job strain                            |                           |       |        |          |        |                     |                 |
| Problems with pressure<sup>b</sup>   |                           | 15    | 15     | 21       | 16     | 0.97 0.42–2.20      | .932            |
| Freedom in performing tasks<sup>c</sup> |                         | 22    | 14     | 28       | 30     | 2.37 1.10–5.11      | .028<sup>a</sup> |
| Influence on pace<sup>c</sup>        |                           | 45    | 39     | 49       | 54     | 1.54 0.85–2.82      | .159            |

CI, confidence interval; OR, odds ratio; ref, reference.

<sup>a</sup>Sum score of physical workload, high vs low—moderate: sum of 4 variables: lifting,<sup>b</sup> physically very demanding,<sup>b</sup> requiring physical strength,<sup>b</sup> strenuous postures.<sup>b</sup>

<sup>a</sup> Association is statistically significant; <sup>b</sup> Often-always vs never-sometimes (ref); <sup>c</sup> Never-sometimes vs often-always (ref)

Van Beukering. Working conditions in women with multiple pregnancy, impact on preterm birth and adherence to guidelines. Am J Obstet Gynecol 2022.