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# Pregnant women at increased risk of adverse perinatal outcomes: A combination of less healthy behaviors and adverse psychosocial and socio-economic circumstances



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#### ABSTRACT

Smoking during pregnancy is associated with a multitude of health behaviors and with the psychosocial and socio-economic circumstances of pregnant women. Limited research has so far been conducted on the clustering of these characteristics and on their effect on pregnancy outcomes. This study aimed to identify different groups of pregnant women based on their behavioral, psychosocial and socio-economic characteristics and their pregnancy outcomes.

In total, 2455 women who were 12 weeks pregnant completed a questionnaire on smoking behavior, health behaviors and psychosocial and socio-economic characteristics. Neonatal and maternal outcomes were extracted from the Dutch perinatal registration. Subgroups were identified with latent class analysis and adverse pregnancy outcomes were compared between subgroups with logistic regression.

Women were classified into four latent classes. Two classes represented the healthy higher-educated pregnant women who did not smoke: one group of multigravida women and one of primigravida women, also characterized by less pregnancy-specific knowledge and more pregnancy-related stress. The remaining women were grouped into two less healthy groups. One group frequently quit smoking, reported less healthy eating, less physical activity and comparable stress levels as the healthy higher-educated groups. The last group contained the most smokers, had the highest scores on psychosocial and pregnancy-related stress and the most adverse socio-economic circumstances. This group had an increased risk of adverse maternal outcomes, in particular developing diabetes during pregnancy.

A comprehensive and integrated approach is needed to improve outcomes in pregnancies with a combination of adverse health, psychosocial, and socio-economic conditions.

#### 1. Introduction

Smoking during pregnancy can lead to adverse pregnancy outcomes (Aagaard-Tillery et al., 2008). Although smoking rates during pregnancy are declining, about 6% of pregnant women in the Netherlands still smoke (Lanting et al., 2012). Socio-economic status – including level of education, ethnicity, income and employment – is frequently found to be a predictor of smoking during pregnancy (Lanting et al., 2009; Riaz et al., 2018; Passey et al., 2014).

Although smoking in the general population often co-occurs with

other health behaviors, such as intake of alcohol, fruits and vegetables, there is limited data on whether and how smoking clusters with other health behaviors during pregnancy (Meader et al., 2016). Lanting et al. (2009) studied the co-occurrence of smoking with alcohol use and with breastfeeding after pregnancy and concluded that smoking might be a proxy for other health risks. A review reported that use of folic acid and abstention from alcohol were predictors of smoking cessation during pregnancy (Riaz et al., 2018). These studies, however, did not investigate other health behaviors as potential predictors, such as eating habits and physical activity.

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There is also evidence that women's psychosocial state is associated with smoking during pregnancy (Passey et al., 2014; Powers et al., 2013). Studies highlight the importance of stress and anxiety for smoking and smoking cessation during pregnancy (Riaz et al., 2018; Lobel et al., 2008). Smoking during pregnancy is also described as a potential buffer against psychosocial stress (Hauck et al., 2013) and as a coping mechanism to deal with psychosocial stress (Hauck et al., 2013; Jesse et al., 2006; Guardino and Schetter, 2014). In addition to health behaviors and psychosocial characteristics, smoking has been found to be associated with lower social support (Powers et al., 2013) and decreased pregnancy-specific knowledge and behavior (e.g. folic acid use) (Smedberg et al., 2014; Riaz et al., 2018).

In short, smoking behavior during pregnancy relates to a multitude of factors, which suggest a co-occurrence or interaction of these factors in pregnant women. Studies have found that looking at risk factors in combination was important for predicting adverse birth outcomes (Pei et al., 2017) and that a combination of healthy lifestyles was predictive for a lower risk of low birth weight and adverse maternal outcomes (Badon et al., 2017; Petherick et al., 2017). However, limited research has been conducted to examine the combination of smoking with a physical and psychosocial risk factors for adverse pregnancy outcomes. The main purpose of this study was therefore to explore whether different groups of pregnant women could be identified based on smoking behavior, other health behaviors, and psychosocial and socio-economic characteristics. We applied a latent class analysis (LCA) to identify subgroups. To judge the health impact of membership of these subgroups, we compared the prevalence of adverse neonatal and maternal outcomes between subgroups.

Distinguishing these subgroups of women and their perinatal outcomes might inform professionals providing care to pregnant women about at-risk groups in their population. The co-occurrence of specific health, psychosocial, and socio-economic conditions in certain groups could for example highlight the need for preventive practices that simultaneously address these conditions. These preventive practices would need to operate through multiple mechanisms and not be focused on just a single conditions (Singer et al., 2017).

# 2. Materials and methods

Data of a larger study were used (van Zwicht et al., 2016), specifically the baseline measurements of the participating pregnant women and their perinatal registrations.

# 2.1. Sample and sampling technique

Participants were recruited at midwifery practices (n=13) and hospitals (n=2) in the Netherlands. Midwives and obstetricians approached all low- and medium-risk pregnant women to participate (van Zwicht et al., 2016). All women under 24 weeks of gestational age at their first prenatal consultation who were able to communicate in Dutch (with assistance) were asked to participate in the study between mid-November 2013 and the first of May 2016. The care provider verbally informed the women at their first prenatal consultation (generally around 8–12 weeks gestational age) and asked them for informed consent. Participation included permission to collect women's routine pregnancy outcomes registered in the National Dutch Perinatal Data Registry (Perined). For participants under the age of 18, informed consent of their parents or caregivers was obtained.

Pregnant women were excluded if they had high-risk pregnancies (e.g. expecting twins, having severe chronic conditions, needing specialized antenatal care), did not provide written informed consent or had insufficient Dutch language skills.

# 2.2. Materials

At the intake, a questionnaire on health behavior, psychosocial and

socio-economic characteristics was provided to the pregnant women. The neonatal and maternal outcomes were extracted from the National Perined database, which contains validated routine care information concerning pregnancy, delivery, hospital (re)admissions and pregnancy outcomes (Perined, n.d.).

#### 2.3. Measurements

The following items were included in the analysis:

*Smoking behavior.* Women were categorized as non-smoker during pregnancy, quit smoking when aware of being pregnant, or current smoker.

Other health behaviors. For eating behaviors, we included the consumption of alcohol, vegetables, fruit, breakfast and snacks in the last seven days. For breakfast, vegetables, and fruits, the answers were categorized as 1 when consuming them 7 days a week and as 2 when consuming them < 7 days a week. Snacks were categorized into 1 for 3 days a week or less or 2 for > 3 days a week (following the norm of the Dutch Food Authority). Alcohol use in the last week was dichotomized into 1 (no alcohol) and 2 (one or more glasses). Folic acid use was categorized into (1) using or (2) not using folic acid prior to pregnancy.

Women were asked how many days in the last week they had been moderately to highly physically active for at least 30 min. Answers were categorized as 1 when active 5 days or more or 2 when active < 5 days a week.

Lifestyle and pregnancy-specific knowledge was measured using the nutrition test of the Nutrition Center in the Netherlands combined with the Prenatal and Postnatal Care Knowledge test by Ickovics and colleagues (Ickovics et al., 2007), resulting in an 18-statement list with the answers 1 or 2 being incorrect answers, 3 do not know and 4 or 5 being correct answers. An example statement about lifestyle-specific knowledge is: "When you are pregnant, you have to eat twice as much (eat for two)." An example of pregnancy-specific knowledge is: "A sudden increase in blood pressure could be a sign of pre-eclampsia." A mean sumscore was calculated, ranging from 1 to 5 with a higher score indicating more knowledge. The average score for lifestyle-specific knowledge was 4.59 and for pregnancy-specific knowledge 4.22: indicating relatively high knowledge scores. First women were categorized in below/equal or above this average score, but as we explicitly wanted to distinguish women with lower knowledge scores we also added a category reflecting women with low scores. Women were categorized into three groups: 1 lower levels of knowledge (< 4), 2 moderate levels (4 to 4.22/ 4 to 4.59) or 3 high levels (above the

Pregnancy-related and psychosocial stress. Pregnancy-related stress was measured by the 9-item Revised Pregnancy Distress Questionnaire, with answers ranging from 1 (not at all) to 3 (very) (Yali and Lobel, 1999) (Lobel et al., 2008). For instance, "Are you worried or anxious, at this moment of pregnancy, about whether your baby will be born prematurely?" A mean sumscore was calculated, ranging from 1 to 3 with a higher score indicating more stress (Cronbach's  $\alpha$  0.64). Average stress score was 1.35. Comparable to the knowledge scales we categorized women based on the average score and additionally included a category with women that have frequent stress: scores between 1.00 and 1.35 indicated limited stress, scores between 1.35 and 2.00 indicated some stress and scores equal or over 2.00 indicated frequent stress.

Psychosocial stress was covered by four items of the Cambridge Worry Scale, referring to concerns regarding housing, money, work or relationships with answers from 1 (not at all) to 3 (very) (Green et al., 2003). Cronbach's  $\alpha$  of 0.45 was low. Instead of calculating a mean sumscore, women were therefore categorized as having no concerns on any of these topics (category 1), some concerns (category 2) or frequent concerns (category 3).

Coping was measured by the 9-item Revised Prenatal Coping

Inventory, asking about the use of coping strategies in the last month. The inventory uses a 5-point scale ranging from 0 (never) to 4 (very often) (Hamilton and Lobel, 2008). For the current study, two items were selected that reflected negative coping styles. One question was about using food, alcohol, or drugs to feel better and the other about abreacting on others to feel better. Answers were categorized as 1 (never), 2 (sometimes) or 3 (often or very often)."

Social support was measured by the validated Prenatal Psychosocial Profile, a 12-item questionnaire using a 4-point Likert scale ranging from 1 (rarely or never) to 4 (very often) (Curry et al., 1998). An example question is: "Do people ever comfort you?" A mean sumscore was calculated, ranging from 1 to 4 with a higher score indicating a higher level of social support (Cronbach's  $\alpha$  0.91). The average score was 2.92. Comparable to the knowledge and pregnancy-related stress measures we categorized women based on the average score and added a category with women that had lower levels of support. Women were categorized as having a higher than average level of social support when scoring above average, a moderate level when scoring between 2.00 and 2.92 and a lower level when scoring below 2.00.

#### 2.4. Demographic and socio-economic characteristics

Ethnicity was based on the country of origin of the biological parents of the pregnant women. Women were coded as originating from the Netherlands when both parents were born in the Netherlands. They were coded as being born in another high-income country (based on the classification of the World Bank) or as originating from a low- to middle-income country when at least one of their parents was born in one of such countries. Level of education was determined by the highest level of education completed in that household (based on the level of education of the woman and her partner) and classified according to the International Standard Classification of Education: 1) low level: no education, primary education only or lower secondary education; 2) average level: higher secondary education or post-secondary non-tertiary education, or 3) high level: recognized tertiary education (Statistics UIf, 2012). Age was categorized into four groups: 22 or younger, 23 to 28 years old, 29 to 35 years old, or 36 or older. Parity was categorized into primigravida or multigravida. Employment was categorized into three categories: both prospective parents had paid work, one prospective parent had paid work, or neither prospective parent had paid work. Marital status was categorized as having a partner or not having a partner.

# 2.4.1. Neonatal and maternal health outcomes

Adverse neonatal outcomes are perinatal mortality and perinatal morbidity. Perinatal mortality is defined as deaths per 1000 births – including stillbirths and live births – from a gestational age (GA) above 22 weeks to seven days postpartum. Neonatal morbidity comprised: low birth weight ( $< 2500 \, \mathrm{g}$ ), small for gestational age (birth weight below 10th percentile), preterm birth ( $< 37 \, \mathrm{weeks}$  of GA), Apgar score below 7 after 5 min, admission to a neonatal intensive-care unit immediately after birth, and congenital birth defects/abnormalities. Adverse maternal outcomes included hypertension/eclampsia/HELLP, diabetes, placental abruption and postpartum hemorrhage ( $\geq 1000 \, \mathrm{ml}$ ). These neonatal and maternal outcomes were categorized as 0 (no adverse outcome) or 1 (one or more adverse outcomes).

# 2.5. Statistical analysis

First,  $\chi 2$  analyses and univariate regression analyses were conducted to examine the association between smoking behavior, the other health behaviors and the psychosocial and socio-economic characteristics.

LCA were conducted using RStudio (poLCA). The central idea of LCA is that a heterogeneous group of individuals can be classified into to several homogeneous subgroups based on their similarity in multiple

indicator variables. Based on these indicators the group of individuals is divided into mutually exclusive and exhaustive latent classes (Lanza, 2012). In current study, the indicator variables that were used to identify the latent classes were smoking behavior, eating behavior, physical activity, lifestyle- and pregnancy-specific knowledge, pregnancy-related stress and general stress, coping behaviors, social support, demographic and socio-economic characteristics. The competing models were compared for fit using the consistent Akaike Information Criterion (cAIC) and Bayesian Information Criterion (BIC), where lower values indicate a better fit of the model to the data (Nylund et al., 2007: Tein et al., 2013). Entropy is a measure that summarizes how clearly the latent classes can be distinguished (Ramaswamy et al., 1993). Entropy had values ranging from 0 to 1, with higher values indicating clearer distinctions between the latent classes. The models were then evaluated and compared according to the interpretability of the obtained solutions.

All women were categorized into one of the identified latent classes based on their predicted class memberships. These memberships were then linked to the neonatal and maternal outcomes of the women. Using logistic regression analyses, with neonatal and maternal outcomes as dependent variables and the latent classes as independent variables, we assessed the effects of class membership on adverse outcomes.

## 2.6. Results

Of the 2608 women that completed the questionnaire, 153 participants were excluded because of missing values; 2455 pregnant women were included in the analysis. 3.8% of these women continued smoking during pregnancy, 10.2% abstained after finding out they were pregnant and 86.0% of the women never smoked during pregnancy. Compared to women who quit smoking or continued smoking during pregnancy, women who had never smoked during their pregnancy often had higher levels of education, were older, had less stress, used abreaction on others less often as a coping mechanism, scored higher on pregnancy-related literacy, ate vegetables more often and took folic acid prior to pregnancy. Compared to women who quit smoking or did not smoke at all during their pregnancies, women who continued smoking more often had no partner, were unemployed, drank alcohol in the last week or used food, cigarettes or alcohol as coping mechanism. They less often reported high levels of social support, scored lower on knowledge and ate breakfast and fruit less often. There were no significant differences in adverse neonatal and maternal outcomes (see Table 1).

The next step was to identify the number of classes using LCA. a four-class model fits the data best according to the BIC and cAIC (see Appendix 1): thees indicators for goodness of fit decreased in the first four models

In the four-class model (Fig. 1), two of the classes resembled each other when looking at smoking, alcohol use, eating behavior, ethnicity, age and socio-economic characteristics. Their members did not smoke during pregnancy, had relatively healthy eating and exercise habits, had limited psychosocial stress, were or Dutch origin and had higher levels of education. They differed, however, on parity, pregnancy-related knowledge and stress. One class consisted of women that were pregnant with their first child, while the women in the other class were pregnant with a subsequent child. The primigravida class had less often used folic acid prior to pregnancy, had less knowledge regarding pregnancy and had more pregnancy-related stress than the multigravida class. These women could be defined as the healthy, highereducated primigravida women (28% of the women based on estimated class membership), and the healthy higher-educated multigravida women (40% of the women). The two other classes contained the less healthy pregnant women. One class included a high percentage of women with an average level of education, women who had quit smoking during pregnancy and women who reported more unhealthy eating and exercise behavior than the other classes: 22% of women

Table 1 Health behaviors and psychosocial and socio-economic characteristics sorted by smoking behavior.

		Total	Non-smoker $n = 2112$ , %n	Quit when pregnant, $n = 250$ , %n	Current smoker, $n = 93$ , %n
Parity	Primigravida	47.9	47.1	52.0	54.8
Level of education	Low	8.0	6.0	15.2	34.4
	Average	35.3	32.8	47.6	58.1
	High	56.6	61.0	37.2	7.5
Age	< 23 years	3.1	2.5	6.0	8.6
	23–28	33.6	32.1	42.0	46.2
	29-35	53.4	54.8	47.6	35.5
	> 35 years	9.9	10.7	4.2	9.7
Ethnicity	Dutch	85.5	85.4	86.0	88.2
	Low/middle-income country	7.8	8.1	6.4	4.3
	Other high-income country	6.6	6.4	7.6	7.5
Partner	With partner	98.5	98.8	98.4	90.3
Employment	Both partners employed	84.6	85.7	85.2	59.1
	One partner employed	14.0	13.3	14.0	30.1
	Not employed	1.4	1.0	0.8	10.8
Pregnancy-related stress	No stress	62.1	63.6	56.0	43.0
.09	Some stress	35.5	34.5	40.0	45.2
	Frequent stress	2.4	1.8	4.0	11.8
Psychosocial stress	No stress	70.9	72.3	65.2	53.8
1 by chrosocial seress	Some stress	26.9	25.8	31.2	39.8
	Frequent stress	2.2	1.9	3.6	6.5
Social support	High level of support	48.7	49.0	50.0	37.6
	Moderate level of support	49.1	48.8	48.0	59.1
	Low level of support	2.2	2.2	2.0	3.2
Abreacting as coping	Never last month	58.9	61.1	47.6	38.7
	Sometimes last month	32.7	31.7	36.8	45.2
	Often last month	8.4	7.2	15.6	16.1
Eating/smoking/drinking as coping	Never last month	88.4	89.3	89.2	59.1
	Sometimes last month	8.6	7.9	7.2	26.9
	Often last month	3.3	2.8	3.6	14.0
Lifestyle knowledge	High	61.2	62.0	59.8	48.4
Elicotyle knowledge	Moderate	31.5	31.0	34.8	35.5
	Low	7.3	7.1	6.0	16.1
Pregnancy knowledge	High	54.3	56.7	45.2	29.0
rregiminey knowledge	Moderate	18.0	18.0	16.0	23.7
	Low	27.6	25.3	38.8	27.6
Alcohol last week	No	99.4	99.6	99.2	96.8
Breakfast	7 days a week	93.5	94.4	91.2	79.6
Vegetables	7 days a week	45.3	47.4	36.4	22.6
Fruit	7 days a week	57.8	59.3	53.2	37.6
Snacks	Max 3 days a week	79.4	80.4	72.0	78.5
Physical activity	5 days a week or more	28.1	27.8	28.4	35.5
Folic acid use	Yes	63.7	66.9	47.2	36.6
Adverse neonatal outcome	> 0 adverse outcome	18.5	18.8	15.2	21.5
Adverse maternal outcome	> 0 adverse outcome	13.2	12.8	16.8	10.8
Adverse maternal outcome	> 0 auverse outcome	13.4	12.0	10.0	10.0

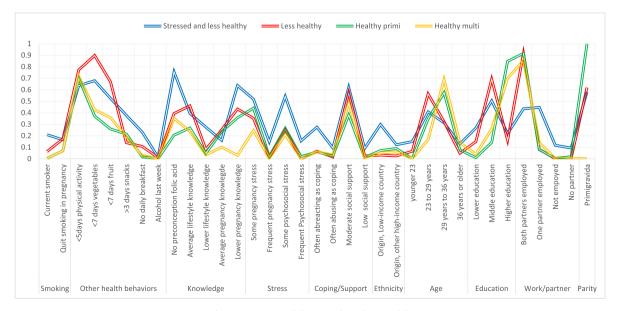


Fig. 1. Outcomes of the LCA: four-class model.

Table 2
Likelihood of adverse neonatal and maternal outcomes for the four classes identified in the LCA; for the total group of women, for only primigravida women, and for only multigravida women.

	Stressed and less healthy %n, reference		Less healthy %n, OR (95%)		Healthy primi %n, OR (95%)		Healthy multi %n, OR (95%)	
Total group, $n = 2226$	205	494		629		898		
Perinatal mortality	0.5	0.4	0.87 (0.17-11.51)	0.5	0.98 (0.10-9.34)	0.7	1.38 (0.17-11.51)	
Small for gestational age	7.4	5.7	0.76 (0.40-1.46)	5.6	0.75 (0.40-1.39)	6.7	0.91 (0.51-1.64)	
Low birth weight < 2500 g	4.5	3.3	0.73 (0.32-1.68)	4.3	0.97 (0.45-2.10)	1.8	0.39 (0.17-0.90)	
Apgar score < 7	3.4	1.8	0.52 (0.19-1.43)	3.3	0.97 (0.41-2.33)	1.6	0.45 (0.18-1.13)	
Premature < 37 weeks	4.4	5.5	1.26 (0.58-2.73)	6.2	1.44 (0.69-3.03)	3.0	0.68 (0.32-1.47)	
Hospitalization	7.3	7.5	1.02 (0.55-1.89)	11.9	1.70 (0.96-3.03)	4.5	0.60 (0.33-1.10)	
Birth defects	6.3	5.9	0.92 (0.47-1.79)	7.3	1.16 (0.62-2.19)	4.7	0.73 (0.39-1.39)	
Adverse neonatal outcome, $> 0$	22.0	20.4	0.90 (0.61-1.33)	25.4	1.19 (0.82-1.72)	16.3	0.70 (0.48-1.01)	
Postpartum hemorrhage	8.3	4.9	0.56 (0.30-1.07)	5.6	0.69 (0.38-1.25)	5.0	0.59 (0.33-1.05)	
Gestational diabetes	4.9	2.0	0.40 (0.17-0.98)	1.7	0.35 (0.15-0.83)	2.0	0.40 (0.18-0.89)	
Hypertension	6.3	9.9	1.60 (0.85-3.03)	10.0	1.63 (0.88-3.03)	3.8	0.59 (0.31-1.14)	
Adverse maternal outcome, $> 0$	20.1	17.2	0.82 (0.54–1.23)	17.3	0.86 (0.58–1.27)	11.9	0.55 (0.37-0.82)	
Primigravida, $n = 1047$	117	309		629				
Perinatal mortality	0.0	0.3	Too small	0.5	Too small			
Small for gestational age	6.8	4.9	0.71 (0.29-1.72)	5.6	0.81 (0.37-1.79)			
Low birth weight	4.3	4.3	1.00 (0.35-2.86)	4.3	1.01 (0.38-2.68)			
Apgar score < 7	3.4	2.3	0.66 (0.19-2.30)	3.3	0.98 (0.33-2.92)			
Premature < 37 weeks	5.1	6.8	1.36 (0.54-3.46)	6.2	1.23 (0.51-2.97)			
Hospitalization	8.5	9.1	1.06 (0.50-2.25)	11.9	1.46 (0.73-2.90)			
Birth defects	6.0	7.1	1.20 (0.50-2.87)	7.3	1.25 (0.55-2.84)			
Adverse neonatal outcome, $> 0$	23.9	23.3	0.96 (0.58-1.57)	25.4	1.10 (0.70-1.73)			
Postpartum hemorrhage	8.5	4.5	0.51 (0.22-1.17)	5.6	0.68 (0.33-1.40)			
Gestational diabetes	5.1	1.9	0.37 (0.12-1.16)	1.7	0.33 (0.12-0.92)			
Hypertension	8.5	12.9	1.57 (0.76-3.25)	10.0	1.20 (0.60-2.41)			
Adverse maternal outcome, $> 0$	22.2	19.1	0.83 (0.49-1.38)	17.3	0.76 (0.48–1.23)			
Multigravida, $n = 1171$	88	185				898		
Perinatal mortality	1.1	0.5	0.47 (0.03-7.60)			0.7	0.58 (0.07-4.89)	
Small for gestational age	8.0	7.1	0.86 (0.33-2.25)			6.7	0.82 (0.36-1.86)	
Low birth weight	4.7	1.6	0.34 (0.07-1.55)			1.8	0.37 (0.12-1.14)	
Apgar score < 7	3.4	1.1	0.30 (0.05-1.86)			1.6	0.44 (0.13-1.58)	
Premature < 37 weeks	3.4	3.2	0.94 (0.23-3.87)			3.0	0.88 (0.26-2.96)	
Hospitalization	5.7	4.9	0.84 (0.28-2.59)			4.5	0.77 (0.30-2.00)	
Birth defects	6.8	3.8	0.54 (0.18-1.64)			4.7	0.67 (0.28-1.61)	
Adverse neonatal outcome, > 0	19.3	15.7	0.77 (0.40-1.49)			16.3	0.81 (0.47-1.41)	
Postpartum hemorrhage	8.0	5.4	0.66 (0.27-1.79)			5.0	0.61 (0.27-1.39)	
Gestational diabetes	4.5	2.2	0.46 (0.11-1.89)			2.0	0.43 (0.14-1.29)	
Hypertension	3.4	4.9	1.44 (0.38-5.44)			3.8	1.11 (0.33-3.68)	
Adverse maternal outcome, $> 0$	17.0	13.5	0.76 (0.38–1.51)			11.9	0.66 (0.37-1.18)	

were classified into this group. These women also scored lower on knowledge regarding lifestyle and pregnancy and had stress levels similar to the healthy primigravida women. They were more often between 23 and 29 years old. The last class included most of the current smokers and can be considered the less healthy, more stressed class (9% of the women). Compared to the other classes, these women in particular had higher pregnancy-specific and psychosocial stress scores and most often reported lower levels of social support and higher use of negative coping mechanisms for dealing with stress. Folic acid use was less than in the other classes, and women in this class scored the lowest on lifestyle- and pregnancy-related knowledge. They more frequently had a non-Dutch origin, were younger than 23 years old, only attained a lower or average level of education, had no or just one paid job in the household, or had no partner.

In Table 2, the two latent class models are regressed against the neonatal and maternal outcomes of 2226 women that could be linked to the National Perined database. The group with healthy primigravida women most frequently had at least one adverse neonatal outcome. Being classified in the less healthy, more stressed group was in particular related to adverse maternal outcomes. Differences were most prominent when comparing the unhealthy and stressed group to the healthy multigravida women. Looking at the specific outcomes, compared to the less healthy, more stressed group, the other groups were less likely to develop diabetes during pregnancy. The less healthy, more stressed group was also more likely to have a child with a low birthweight compared to the healthy multigravida group. In the separate

analyses for primigravida or multigravida women these differences in low birth weight and pregnancy diabetes were no longer statistically significant.

#### 3. Discussion and conclusion

The main purpose of this study was to explore whether classes of pregnant women could be identified based on smoking and other health behaviors, and psychosocial and socio-economic characteristics. We identified four different groups of pregnant women. Two groups in which women hardly smoked, had a relatively healthy lifestyle and a higher level of education; one with first pregnancies and the other with subsequent pregnancies. The group of women pregnant for the first time had less knowledge about pregnancy and had more pregnancyrelated stress than the group of women pregnant of a subsequent child. A third, less healthy group frequently quit smoking during pregnancy, but had lower scores on physical activity and eating behaviors. Overall they had similar levels of psychosocial stress and social support as the higher-educated, healthy women. The last group, the less healthy and more stressed group, contained most of the current smokers. These women also scored less favorably on other health behaviors and scored least favorable on nearly all psychosocial, and socio-economic characteristics. Women classified in this last group had less favorable maternal outcomes, in particular gestational diabetes.

This study confirms that the vast majority of pregnant women in The Netherlands do not smoke during pregnancy (Lanting et al., 2009).

The latent classes we found are quite similar to classes found in other studies: even when not including the same combination of variables, the other studies also arrive at a categorization into groups with lower and higher risk (Pei et al., 2017; Petherick et al., 2017). The current study distinguishes two potential higher risk groups based on their health behaviors and/or psychosocial and socio-economic characteristics. The group with the highest risk contained relatively high rates of smokers and is also characterized by less health knowledge, lower levels of social support, higher levels of psychosocial and pregnancy-related stress, avoidant coping mechanisms and higher rates of adverse socioeconomic circumstances. These findings confirm the results of other studies relating smoking to stress and lower levels of social support and pregnancy-specific knowledge (Riaz et al., 2018; Powers et al., 2013) (Passey et al., 2014; Fulford et al., 2013; Bai et al., 2018). Women with lower levels of education have been found to prepare themselves less for pregnancy (Goossens et al., 2018).

Lower birth weight and small for gestational age have consistently been shown to be related to smoking during pregnancy (Kramer, 1987). Although, in current study the less healthy, more stressed women more often had a child with a low birthweight than the healthy multigravida women, rates did not differ from the other women. Overall, in the less healthy, more stressed group, adverse neonatal outcomes did not differ from the other groups. One explanation might be that we only included smoking behavior at the start of pregnancy. Smoking habits might have changed during the course of pregnancy. Quitting smoking has been found to influence neonatal outcomes (Larsen et al., 2018; Jaddoe et al., 2008).

Maternal outcomes, in particular pregnancy diabetes, were less favorable in this less healthy, more stressed group of women. Other studies have already found a relationship between stress and gestational diabetes (Hosler et al., 2011) and between the co-occurrence of different unhealthy behaviors and gestational diabetes (Badon et al., 2017; Zhang et al., 2014; Ruiz-Gracia et al., 2016). The relationship between adverse maternal outcomes was not found for the group of women that more often quit smoking but adhered least to the Dutch eating and physical activity norms. Their psychosocial wellbeing was similar to that of the healthy non-smoker groups and they were less likely to have lower levels of education or be part of an ethnic minority. This fuels the hypothesis that it is the combination of unhealthy behaviors and adverse psychosocial and socio-economic circumstances that leads to adverse maternal outcomes. Such a combination of physical, psychological and social conditions might emphasize the relevance of a syndemic approach to understanding adverse outcomes during pregnancy and tackling related problems. The syndemics discussion states that public health efforts have generally focused on single health problems, neglecting the interaction between co-occurring health problems and the involvement of contexts of social or health inequity in the causal pathways that leads to exacerbated burdens of disease (Singer et al.,

A strength of the current study is that we combined health behaviors and psychosocial and socio-economic characteristics in the LCA. It is, to the best of our knowledge, one of the first studies to do this: other studies have limited themselves to health behavior indicators. A

limitation of the current study is that the included variables are based on self-report: women may have underreported socially undesirable behaviors, such as smoking. Furthermore, the study sample might be subject to selection bias due to the exclusion of women with insufficient Dutch language skills or a lack of willingness to participate in the study. Women with unhealthy behaviors might have decided not to complete a questionnaire about lifestyle and psychosocial problems. Nevertheless, we expect that without this selection bias, the found latent classes would only be more pronounced.

The BIC indicated that a four-class model fitted the data best, while the entropy indicator suggested that a three-class model is better at distinguishing the classes. We have chosen to present the four-class model, as the BIC is better at selecting the correct number of classes than the entropy (Tein et al., 2013). Additionally the four-class model makes the most theoretical sense. This is confirmed by the increased risk of adverse maternal outcome in the group with the highest risk. Future studies are needed to replicate these analyses and confirm the findings of our study.

#### 3.1. Implications

Baron and colleagues showed that little information was provided to pregnant women about many pregnancy-relevant health behavior topics during their intake in primary midwifery care. Women who did not take folic acid supplements, who smoked or who had a partner who smoked were generally given some information, but mostly basic explanations and only occasionally more extensive explanations (Baron et al., 2017). The current study showed, however, that some women have a combination of unhealthy behaviors and adverse psychosocial characteristics. A basic explanation might not be sufficient to change these women's behaviors and increase their psychosocial wellbeing. A more comprehensive approach is needed to improve perinatal outcomes in these higher-risk pregnancies.

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# Authors' contributions

MC conceptualized and designed the study, carried out the analyses, drafted the initial text, revised concept versions, and approved the final version as submitted.

NM and BB conceptualized and designed the study, supervised the analyses, critically reviewed and revised concept versions, and approved the final version as submitted.

MR and JvL conceptualized the study, participated in the interpretation of the data, reviewed and revised concept versions for important intellectual content, and approved the final version as submitted.

Appendix 1. Fit indicators of the different models in the LCA

	Model	Log-likelihood	Resid. df	BIC	cAIC	Likelihood-ratio	Entropy
1	Model 1 class	-31,850.79	2419.00	63,982.60	64,018.60	26,107.46	_
2	Model 2 classes	-31,070.09	2382.00	62,710.02	62,783.02	24,546.06	0.622
3	Model 3 classes	-30,723.44	2345.00	62,305.53	62,415.53	23,852.75	0.827
4	Model 4 classes	-30,494.84	2308.00	62,137.14	62,284.14	23,395.55	0.783
5	Model 5 classes	-30,358.19	2271.00	62,152.67	62,336.67	23,122.25	0.762

#### References

- Aagaard-Tillery KM, Porter TF, Lane RH, Varner MW, Lacoursiere DY. In utero tobacco exposure is associated with modified effects of maternal factors on fetal growth. Am. J. Obstet. Gynecol.. 2008;198(1):66.e1-6.
- Badon, S.E., Enquobahrie, D.A., Wartko, P.D., Miller, R.S., Qiu, C., Gelaye, B., et al., 2017. Healthy lifestyle during early pregnancy and risk of gestational diabetes mellitus. Am. J. Epidemiol. 186 (3), 326-333.
- Bai, G., Raat, H., Jaddoe, V.W.V., Mautner, E., Korfage, I.J., 2018. Trajectories and predictors of women's health-related quality of life during pregnancy: a large longitudinal cohort study. PLoS One 13 (4), e0194999.
- Baron, R., Martin, L., Gitsels-van der Wal, J.T., Noordman, J., Heymans, M.W., Spelten, E.R., et al., 2017. Health behaviour information provided to clients during midwifeled prenatal booking visits: findings from video analyses. Midwifery 54, 7-17.
- Curry, M.A., Burton, D., Fields, J., 1998. The prenatal psychosocial profile: a research and clinical tool. Research in nursing & health 21 (3), 211-219.
- Fulford, B., Bunting, L., Tsibulsky, I., Boivin, J., 2013. The role of knowledge and perceived susceptibility in intentions to optimize fertility: findings from the international fertility decision-making study (IFDMS). Human reproduction (Oxford, England) 28 (12), 3253-3262.
- Goossens, J., Beeckman, D., Van Hecke, A., Delbaere, I., Verhaeghe, S., 2018. Preconception lifestyle changes in women with planned pregnancies. Midwifery 56,
- Green, J.M., Kafetsios, K., Statham, H.E., Snowdon, C.M., 2003. Factor structure, validity and reliability of the Cambridge Worry Scale in a pregnant population. J. Health Psychol. 8 (6), 753-764.
- Guardino, C.M., Schetter, C.D., 2014. Coping during pregnancy: a systematic review and recommendations. Health Psychol. Rev. 8 (1), 70-94.
- Hamilton, J.G., Lobel, M., 2008. Types, patterns, and predictors of coping with stress during pregnancy: examination of the revised prenatal coping inventory in a diverse sample. J. Psychosom. Obstet. Gynaecol. 29 (2), 97-104.
- Hauck, Y., Ronchi, F., Lourey, B., Lewis, L., 2013. Challenges and enablers to smoking cessation for young pregnant Australian women: a qualitative study. Birth (Berkeley, Calif) 40 (3), 202-208.
- Hosler, A.S., Nayak, S.G., Radigan, A.M., 2011. Stressful events, smoking exposure and other maternal risk factors associated with gestational diabetes mellitus. Paediatr. Perinat. Epidemiol. 25 (6), 566-574.
- Ickovics, J.R., Kershaw, T.S., Westdahl, C., Magriples, U., Massey, Z., Reynolds, H., et al., 2007. Group prenatal care and perinatal outcomes: a randomized controlled trial. Obstet. Gynecol. 110 (2 Pt 1), 330-339.
- Jaddoe, V.W., Troe, E.J., Hofman, A., Mackenbach, J.P., Moll, H.A., Steegers, E.A., et al., 2008. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. Paediatr. Perinat. Epidemiol. 22 (2), 162–171.
- Jesse, D.E., Graham, M., Swanson, M., 2006. Psychosocial and spiritual factors associated with smoking and substance use during pregnancy in African American and White low-income women. Journal of obstetric, gynecologic, and neonatal nursing: JOGNN/NAACOG, 35 (1), 68-77.
- Kramer, M.S., 1987. Determinants of low birth weight: methodological assessment and meta-analysis. Bull. World Health Organ. 65 (5), 663-737.
- Lanting, C.I., Buitendijk, S.E., Crone, M.R., Segaar, D., Bennebroek Gravenhorst, J., van Wouwe, J.P., 2009. Clustering of socioeconomic, behavioural, and neonatal risk factors for infant health in pregnant smokers. PLoS One 4 (12), e8363.
- Lanting, C.I., van Wouwe, J.P., van den Burg, I., Segaar, D., van der Pal-de Bruin, K.M., 2012. Smoking during pregnancy: trends between 2001 and 2010. Ned. Tijdschr. Geneeskd, 156 (46), A5092.

Lanza, S.T., 2012. Introduction to latent class analysis for behavioral research. Ann. Behav. Med. 43, S3-S.

- Larsen, S., Haavaldsen, C., Bjelland, E.K., Dypvik, J., Jukic, A.M., Eskild, A., 2018. Placental weight and birthweight: the relations with number of daily cigarettes and smoking cessation in pregnancy. A population study. Int. J. Epidemiol. 47 (4),
- Lobel, M., Cannella, D.L., Graham, J.E., DeVincent, C., Schneider, J., Meyer, B.A., 2008. Pregnancy-specific stress, prenatal health behaviors, and birth outcomes. Health psychology: official journal of the Division of Health Psychology, American Psychological Association. 27 (5), 604–615.
- Meader, N., King, K., Moe-Byrne, T., Wright, K., Graham, H., Petticrew, M., et al., 2016. A systematic review on the clustering and co-occurrence of multiple risk behaviours. BMC Public Health 16, 657.
- Nylund, K.L., Asparoutiov, T., Muthen, B.O., 2007. Deciding on the number of classes in latent class analysis and growth mixture modeling: a Monte Carlo simulation study. Struct Equ Modeling 14 (4), 535-569.
- Passey, M.E., Sanson-Fisher, R.W., D'Este, C.A., Stirling, J.M., 2014. Tobacco, alcohol and
- cannabis use during pregnancy: clustering of risks. Drug Alcohol Depend. 134, 44–50. Pei, L., Zeng, L., Zhao, Y., Wang, D., Yan, H., 2017. Using latent class cluster analysis to screen high risk clusters of birth defects between 2009 and 2013 in Northwest China. Sci. Rep. 7 (1), 6873.

#### Perined Available from: https://www.perined.nl/.

- Petherick, E.S., Fairley, L., Parslow, R.C., McEachan, R., Tuffnell, D., Pickett, K.E., et al., 2017. Ethnic differences in the clustering and outcomes of health behaviours during pregnancy: results from the Born in Bradford cohort. Journal of public health (Oxford, England) 39 (3), 514-522.
- Powers, J.R., McDermott, L.J., Loxton, D.J., Chojenta, C.L., 2013. A prospective study of prevalence and predictors of concurrent alcohol and tobacco use during pregnancy. Matern. Child Health J. 17 (1), 76–84.
- Ramaswamy VD, W.S.; Reibstein, D.J.; Robinson, W.T. An empirical pooling approach for estimating marketing mix elasticities with PIMS data. Mark. Sci.. 1993;12(1).
- Riaz, M., Lewis, S., Naughton, F., Ussher, M., 2018. Predictors of smoking cessation during pregnancy: a systematic review and meta-analysis. Addiction 113 (4), 610-622
- Ruiz-Gracia, T., Duran, A., Fuentes, M., Rubio, M.A., Runkle, I., Carrera, E.F., et al., 2016. Lifestyle patterns in early pregnancy linked to gestational diabetes mellitus diagnoses when using IADPSG criteria. The St Carlos gestational study. Clinical nutrition (Edinburgh, Scotland) 35 (3), 699-705.
- Singer, M., Bulled, N., Ostrach, B., Mendenhall, E., 2017. Syndemics and the biosocial conception of health. Lancet 389 (10072), 941-950.
- Smedberg, J., Lupattelli, A., Mardby, A.C., Nordeng, H., 2014. Characteristics of women who continue smoking during pregnancy: a cross-sectional study of pregnant women and new mothers in 15 European countries. BMC pregnancy and childbirth 14, 213.
- Statistics UIf, 2012. International Standard Classification of Education ISCED 2011. Motreal, Ouebec, Canada, vol. 2012.
- Tein, J.Y., Coxe, S., Cham, H., 2013. Statistical power to detect the correct number of classes in latent profile analysis. Struct Equ Modeling 20 (4), 640-657.
- Yali, A.M., Lobel, M., 1999. Coping and distress in pregnancy: an investigation of medically high risk women. J. Psychosom. Obstet. Gynaecol. 20 (1), 39-52.
- Zhang, C., Tobias, D.K., Chavarro, J.E., Bao, W., Wang, D., Ley, S.H., et al., 2014. Adherence to healthy lifestyle and risk of gestational diabetes mellitus: prospective cohort study. BMJ 349, g5450.
- van Zwicht, B.S., Crone, M.R., van Lith, J.M., Rijnders, M.E., 2016. Group based prenatal care in a low-and high risk population in the Netherlands: a study protocol for a stepped wedge cluster randomized controlled trial. BMC pregnancy and childbirth 16 (1), 354.