

Original articles

Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly?

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Summary

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In this paper, we review the evidence bearing on socio-economic disparities in pregnancy outcome, focusing on aetiological factors mediating the disparities in intrauterine growth restriction (IUGR) and preterm birth. We first summarise what is known about the attributable determinants of IUGR and preterm birth, emphasising their quantitative contributions (aetiological fractions) from a public health perspective. We then review studies relating these determinants to socio-economic status and, combined with the evidence about their aetiological fractions, reach some tentative conclusions about their roles as mediators of the socio-economic disparities. Cigarette smoking during pregnancy appears to be the most important mediating factor for IUGR, with low gestational weight gain and short stature also playing substantial roles. For preterm birth, socio-economic gradients in bacterial vaginosis and cigarette smoking appear to explain some of the socio-economic disparities; psychosocial factors may prove even more important, but their aetiological links with preterm birth require further clarification. Research that identifies and quantifies the causal pathways and mechanisms whereby social disadvantage leads to higher risks of IUGR and preterm birth may eventually help to reduce current disparities and improve pregnancy outcome across the entire socio-economic spectrum.

Introduction

Among the most robust findings in perinatal epidemiological research are the large socio-economic disparities in such key pregnancy outcomes as perinatal and infant mortality, low birthweight (LBW), intrauterine growth restriction (IUGR) and preterm birth.^{1–5} LBW has long been a popular focus for studies of pregnancy outcome because of its strong association with fetal and infant mortality and both short- and long-term morbidity. LBW is an unsatisfactory outcome for epidemiological studies, however, because birthweight is determined by both duration of gestation and the rate of fetal growth, and thus LBW can occur because an infant is born either too early (preterm birth) or small for his/her gestational age (SGA, which is often used as a proxy for IUGR).¹

It is now recognised that the determinants of gestational duration (and of its left-hand tail, preterm birth) are quite different from the determinants of fetal

growth (and IUGR).¹ The health consequences also differ considerably. Preterm birth (especially when extreme, i.e. < 28 weeks) is associated with high rates of mortality and of severe ophthalmological, neurocognitive and pulmonary morbidity.^{6–8} When extreme, IUGR can cause short-term metabolic derangements and even neonatal death.⁹ Less extreme IUGR is primarily associated with mild, long-term deficits in growth and neurocognitive performance,^{10,11} although Barker and colleagues have reported long-term associations with chronic adult diseases, such as hypertension, type 2 diabetes and coronary heart disease.^{12,13} For all these reasons, it is preferable to separate preterm birth and IUGR when considering the relationship of socio-economic status (SES) to pregnancy outcome.

Differences in prevalence of preterm birth and IUGR among countries differing in level of socio-economic development provide a striking illustration of dispa-

rities in both of these outcomes. In a now classic paper, Villar and Belizan¹⁴ reported data from 11 different regions in developed countries and 25 in developing countries. Most of the differences in LBW rates between developed and developing countries appear to be attributable to an increased prevalence of IUGR, rather than preterm birth, with relative risks of 6.6 and

2.0 respectively.¹⁴ Similar results were reported in a recent WHO Collaborative Study.¹⁵

Even within developed countries, however, preterm birth and IUGR are consistently more frequent among the socially disadvantaged. Table 1 summarises population-based data from several such countries. It is perhaps unsurprising to find such disparities in the

Table 1. Population-based evidence of socio-economic disparities in occurrence of preterm birth (PTB) and intrauterine growth restriction (IUGR)

| Population ^{Ref} | Year(s) | Socio-economic measure | Category | PTB (%) | IUGR (%) |
|------------------------------|---------|--------------------------|-------------|------------------|------------------|
| Canada ¹⁶ | 1986 | Income quintile | 5 | 7.4 | 12.1 |
| | | | 4 | 6.6 | 10.6 |
| | | | 3 | 6.1 | 9.7 |
| | | | 2 | 5.6 | 8.6 |
| | | | 1 | 5.7 | 8.0 |
| Czech Republic ¹⁷ | 1989–91 | Maternal education | Primary | 8.4 | |
| | | | Vocational | 4.4 | |
| | | | Secondary | 3.6 | |
| | | | University | 3.5 | |
| Finland ¹⁸ | 1985–86 | Maternal education | ≤ 8 years | 6.2 | |
| | | | > 8 years | 4.3 | |
| | | Occupational SES group | IV | 5.6 | |
| | | | III | 4.8 | |
| Quebec ¹⁹ | 1993 | Maternal education | < 11 years | 7.9 | |
| | | | 11–12 years | 7.1 | |
| | | | 13–15 years | 5.9 | |
| | | | ≥ 16 years | 5.4 | |
| Scotland ²⁰ | 1981–84 | Maternal occupation | Manual | 5.6 | 6.3 |
| | | | Non-manual | 4.6 | 4.6 |
| | | Paternal occupation | Manual | 4.8 | 5.1 |
| Spain ²¹ | 1988 | Paternal occupation | Non-manual | 3.9 | 3.4 |
| | | | Manual | 3.4 ^a | 3.3 ^b |
| Sweden ¹⁷ | 1989–91 | Maternal education | Non-manual | 2.7 ^a | 2.5 ^b |
| | | | Primary | 6.4 | |
| | | | Vocational | 5.5 | |
| | | | Secondary | 4.9 | |
| US Whites ² | 1988 | Income (% poverty level) | University | 4.5 | |
| | | | < 100% | 3.5 | 10.6 |
| | | | 100–199% | 4.7 | 9.8 |
| | | Maternal education | ≥ 200 | 3.4 | 7.4 |
| | | | < 12 years | 4.5 | 11.6 |
| | | | 12 years | 3.9 | 10.0 |
| | | | 13–15 years | 3.8 | 5.6 |
| ≥ 16 years | 2.8 | 7.5 | | | |
| US Blacks ² | 1988 | Income (% poverty level) | < 100% | 12.2 | 16.7 |
| | | | 100–199% | 9.4 | 12.9 |
| | | | ≥ 200% | 7.4 | 15.9 |
| | | Maternal education | < 12 years | 12.0 | 19.8 |
| | | | 12 years | 12.0 | 16.7 |
| | | | 13–15 years | 7.5 | 14.5 |
| ≥ 16 years | 6.7 | 9.3 | | | |

^aPreterm LBW.

^bTerm LBW.

United States,² with its vast differences between the rich and the poor. But the poor fare poorly even in countries such as Canada,^{16,19} Sweden,¹⁷ Finland,¹⁸ Scotland,²⁰ and Spain,²¹ with lesser degrees of poverty and with universal access to high-quality prenatal and other medical care. As also shown in Table 1, rates of adverse pregnancy outcomes generally rise with increasing socio-economic disadvantage. The rise, albeit monotonic, is not necessarily linear; it is often steepest at the lower end of the social scale. This review will focus on the increased risk of preterm birth and IUGR among the poor and poorly educated, rather than on gradients in these outcomes among the non-poor and the better educated.²²⁻²⁴ The causal pathways that we discuss may therefore not be generalisable across the entire socio-economic spectrum.

In many multiracial countries, disparities in pregnancy outcome according to SES are often closely paralleled (and hence confounded) by disparities according to racial and ethnic origin. Lower gestational age-adjusted birthweight and/or higher IUGR rates have been reported among Blacks in the US,^{2,25} aborigines in Australia,^{26,27} Asians in the UK,^{28,29} and both Blacks and Asians in the Netherlands.³⁰ Although slower fetal growth in some racial groups may be partly explained by true biological (genetic) differences,³¹ much of it is probably linked to socio-economic disadvantage among these racial groups. Interestingly, some other minority groups do not exhibit the same phenomenon; these include American Indian groups^{32,33} and Chinese immigrants³¹ in Canada, North African immigrants in Israel³⁴ and the Netherlands³⁰ and Mexican immigrants in the US.³⁵ Despite their socio-economic disadvantage relative to the predominant racial/ethnic groups, fetal growth rates in these minority groups actually exceed those in the general majority population. More specifically, these low-SES groups show gestational age-adjusted birthweight distributions shifted somewhat to the right relative to the distributions dominant in their respective countries, and/or correspondingly lower rates of IUGR. For some migrant groups, this paradox appears to be explained by the tendency of recent migrants to retain the more favourable nutritional and behavioural (e.g. non-smoking) characteristics of the country they have migrated from, and thereby avoid the elevated risks found in non-migrants with similar socio-economic disadvantage. For preterm birth, most of the evidence on the effect of racial/ethnic origin comes from the US, where Black-

White differences in risk of preterm birth are substantial and persist after adjustment for (measured) socio-economic differences.^{2,36} Here too, however, Black immigrant groups (from Africa or the Caribbean) appear to be at least partly protected from the increased risk.^{37,38}

Thus, the evidence suggests the potential for both confounding and modification of SES effects by racial/ethnic origin. Some immigrant groups appear to be relatively 'protected' from the adverse effects of poverty on pregnancy outcome. But even when confounding or effect modification by race/ethnicity is strong, low SES is generally associated with increased risks of both preterm birth and IUGR within racial/ethnic groups (e.g. among US-born Blacks).²

In the remainder of this paper, we will review the evidence bearing on the causal pathways by which socio-economic disadvantage leads to increased risk of these adverse pregnancy outcomes. SES is a complex construct generally used to define social inequality, usually measured by income, occupation and/or educational attainment.^{23,24,39,40} Education is the dimension of SES that most strongly and consistently predicts health, especially for women and their children.⁴¹ For example, maternal and paternal education were the strongest predictors of adverse reproductive outcome in one recent study.² A low level of education limits a person's access to jobs and other social resources (especially in industrialised countries), which in turn limits his/her capacity to integrate within society and thereby increases the risk of subsequent poverty.

The recent epidemiological literature has highlighted controversies about studies of individuals vs. studies of populations,⁴²⁻⁴⁴ and this debate is relevant to how socio-economic disparities in health (including pregnancy outcomes) are conceptualised. The conceptual model that serves as the basis of our review explicitly acknowledges the existence of causal pathways, i.e. aetiological factors that operate 'upstream' or 'downstream' relative to one another, rather than simultaneously acting, independent determinants. Society-level determinants, such as poverty or income inequality, are considered as antecedent to individual-level exposures and behaviours. In applying this conceptual model, we do not wish to imply an overly simplistic, 'linear' model of causality. Where the available data permit, therefore, we also consider interacting factors in addition to independently acting ones. We take it as given that variations in risk of

preterm birth or IUGR within populations are at least partly explained by ('downstream') exposures or behaviours that can be measured at the level of individuals. In other words, it is the individuals within a society who are exposed to its socio-economic conditions and whose reactions and responses to those conditions alter their risk of adverse pregnancy outcome. Thus, our primary focus is on causal pathways that explain within-population risks that vary according to ('upstream') socio-economic differences. We caution therefore that variations between populations (e.g. between developed and developing countries, or between socio-economically homogeneous developed countries and those with large social class differences) may not share the same causal explanations. Elucidating the latter pathways may require ecological or multilevel studies.^{42,43}

According to our conceptual model, having less money or education probably has no direct effect on the rate of fetal growth or the duration of gestation. In other words, socio-economic disadvantage operates 'upstream'; it leads ('downstream') to unhealthy behaviours, exposure to stress and psychological reactions to stress that increase the risk of IUGR or preterm birth. Such exposures are the mediating variables that are the focus of our review. Those mediators most frequently mentioned in the literature are maternal anthropometry and nutrition (height, prepregnancy body mass index and energy balance, i.e. gestational weight gain); cigarette smoking; genital tract infection and inflammation; cocaine and other drug use; physically demanding work during pregnancy; the quantity and quality of prenatal care; and stress, anxiety, depression and other psychosocial factors.^{1,41} As we argue below, however, the evidence for some of these mediators is weak, while several others that appear to be biologically plausible have not been explored.

In order for a factor to be an important mediator of socio-economic disparity in preterm birth or IUGR, it must satisfy two important statistical requirements: (1) the mediating factor must have a sizeable aetiological fraction (population attributable risk) for the adverse outcome (preterm birth or IUGR) under consideration; and (2) it must be strongly associated with SES, i.e. it should be far more prevalent among the poor than among the socio-economically advantaged. In the following section, we will summarise what is known about the attributable causes of IUGR and preterm birth, focusing on their quantitative importance from a

public health perspective. In the subsequent section, we will review studies bearing on the associations of these 'downstream' determinants with SES and, combined with the available evidence bearing on their aetiological fractions, reach some tentative conclusions about their roles as mediators. In the final section, we summarise these conclusions and suggest some priorities for future research.

Bibliographic methods

Literally thousands of epidemiological studies have been published relating potential risk factors to either IUGR or preterm birth on the one hand, or to SES on the other. The bibliographic methods we used to search the English- and French-language references published before 1985 are detailed in a previous meta-analysis.¹ For references published since 1985, we used a monthly computerised search of MedLine (again with restriction to publications in English or French) based on the following medical subject headings and logic: infant, premature; or infant, low birthweight; or birthweight; or infant, small-for-gestational-age; or fetal growth retardation; or gestational age; or labour, premature.

A mere listing of the references located by this search, even without a description or critical discussion, would exhaust both the reader and the permissible page limit of this review. Thus, although our search methods have been thorough, many references have been omitted from the text and bibliography. Our review makes no claim therefore to be 'systematic'.^{45,46} Instead, we have relied heavily on previously published reviews and meta-analyses of the many pertinent associations, both by us¹ and others.^{47,48} In other words, we have attempted to be comprehensive but not exhaustive. In particular, we have tried to strike a balance between efficiency and unbiasedness by briefly summarising the available evidence for associations that are well established, while restricting more detailed review and methodological comments to those associations that appear to be more controversial.

Aetiological determinants of IUGR and preterm birth

Much is known about the attributable causes of IUGR. Those for which aetiological roles are well established are depicted schematically in Fig. 1 for a developed country setting such as the United States, in which approximately 25% of the women smoke cigarettes

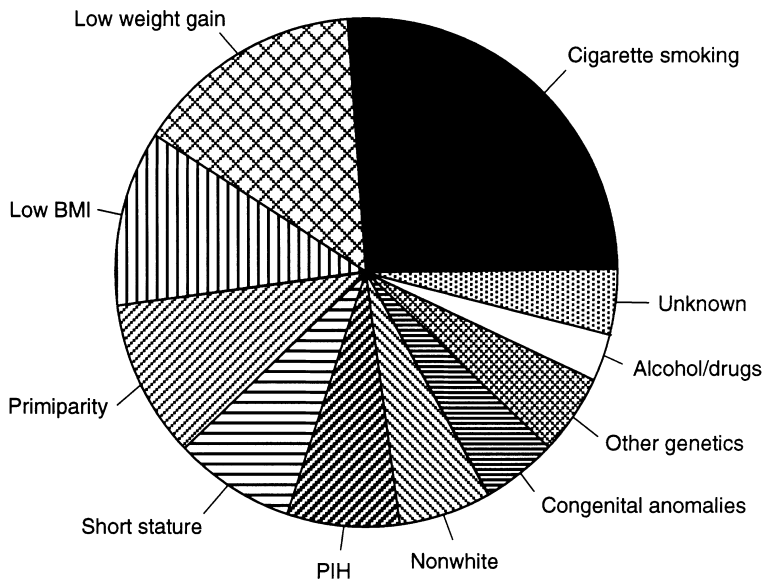


Figure 1. Aetiological determinants of IUGR in a developed country in which 25% of the women smoke during pregnancy and a substantial minority are non-white.

during pregnancy and a substantial minority are non-white. In this pie diagram, the size of the pie slice corresponding to each causal determinant is a rough indication of its importance (in terms of aetiological fraction) relative to the other determinants shown in the pie. It is an updated version originally based on a meta-analysis of the English- and French-language literature published between 1970 and 1984.¹ The diagram should be interpreted in relative terms only; because the determinants shown are not mutually exclusive, any given woman may have more than one of them. Thus, the total aetiological fraction of all the determinants of IUGR is far less than the 90% or so suggested by the diagram,⁴⁹ and the figure should not be construed as showing that almost all is known about the causes of IUGR.

In this type of setting, the risk factors with the highest relative risks are pregnancy-induced hypertension (PIH) and cigarette smoking. Because cigarette smoking is so much more prevalent than PIH, however, cigarette smoking is associated with a much higher aetiological fraction. Other factors with high aetiological fractions (representing somewhat lower relative risks but high prevalences) include low gestational weight gain (partially, but not exclusively, reflecting low energy intake), low prepregnancy body mass index (BMI), primiparity, short maternal stature and non-white racial/ethnic origin. Although primiparity, short maternal stature and non-white racial/ethnic origin are associated with reduced fetal growth, opinions differ as to whether such reduced growth qualifies as true growth 'restriction', in the pathologi-

cal sense, or merely reflects constitutional differences with no adverse consequences for the fetus or infant. Whether the reduced fetal growth associated with these factors increases the risk of fetal/infant mortality or morbidity is an important subject for future research. We demonstrated recently, for example, that 'IUGR' in offspring of short mothers is associated with reduced risk of late fetal death.⁵⁰

Congenital anomalies⁵¹ and genetic factors, such as low paternal height and weight and familial/inter-generational proclivities for IUGR, are associated with relatively small slices of the aetiological pie.¹ High levels of alcohol consumption (two or more drinks per day)^{52,53} and the use of marijuana or cocaine⁵⁴⁻⁵⁶ may also restrict fetal growth, but their aetiological fractions are quite low, owing to low prevalences of exposure. The effect of high caffeine consumption (> 300 mg/day) is more controversial; although such consumption is highly prevalent, its corresponding relative risk is at most only modestly elevated.⁵⁷⁻⁶⁰ Finally, vigorous leisure time aerobic exercise that continues into the third trimester may be associated with a slightly increased in risk of IUGR,⁶¹ although the small number of women engaging in vigorous exercise during this critical period of fetal growth strongly suggests that it is not an important mediating variable from a population perspective.

In a developing country setting in which pregnant women do not smoke cigarettes, the pie diagram would look quite different because of the vastly different prevalence of exposure to the various determinants. Thus, the 'slice' corresponding to cigar-

ette smoking would disappear, while the slices corresponding to low weight gain, low prepregnancy BMI and short stature would increase considerably.¹ In addition, malaria would occupy a substantial slice in those settings where the disease is endemic.¹ The racial/ethnic composition of the country would also affect the appearance of the pie.

Figure 2 shows a comparable pie diagram for the well-established attributable causes of preterm birth, for the same developed country as depicted in Fig. 1. This pie looks quite different from the IUGR pie. Numerous recent studies and reviews have focused on the potential role of genitourinary tract colonisation, infection and inflammation as causes of preterm birth.⁶²⁻⁷² The most consistent associations and highest risks for preterm birth have been reported with bacterial vaginosis, with the majority of relative risks reported between 1.5 and 2.5, but ranging as high as 6.9.^{65,68-71,73} The evidence is particularly strong for early preterm birth (< 32 weeks), when upper genital tract infection/inflammation (chorioamnionitis) is frequently present.^{68,72}

Multiple (twin and higher order) births account for the second-largest slice of the preterm pie. Despite representing only about 2% of all births, half of twins and almost all higher order multiples are born before 37 weeks.⁷⁴ Moreover, the increasing use of infertility treatments has increased the multiple birth ratio and contributed substantially to the recent temporal increase in preterm birth.⁷⁴⁻⁷⁷

Cigarette smoking is a non-negligible cause of preterm birth, but the size of its 'slice' is quite a bit

smaller than for IUGR.¹ Because both pies pertain to the same population, the prevalence of smoking is also the same; the difference in aetiological fractions reflects the lower relative risk of smoking for preterm birth (approximately 1.3) than for IUGR (2.5). A second major difference concerns the importance of factors related to maternal anthropometry or nutrition. The results of the recent WHO Collaborative Study¹⁵ are consistent with earlier evidence in suggesting a modest increase in risk (RR=1.3) of preterm birth among women with prepregnancy BMI in the lowest quartile. As with cigarette smoking, therefore, the size of its slice of the pie is much smaller for preterm birth than for IUGR. Although there is some controversy about whether women who are short or have low weight gains during pregnancy are at increased risk of preterm delivery, available evidence suggests that the effects of these maternal anthropometric factors, if they exist at all, are much smaller than their effects on IUGR.^{15,78,79}

Epidemiological studies of strenuous work and physical activity during pregnancy have focused on preterm birth; most have reported that prolonged standing or strenuous activity at work is associated with a modest increase in risk.⁸⁰⁻⁸⁵ Only a small fraction of employed women are exposed to these strenuous conditions at work,⁸⁴ however, and the aetiological fraction associated with such work is therefore small. Physically demanding domestic work may make a larger, albeit unrecognised, contribution.^{86,87}

Other determinants of preterm birth are those for which few preventive interventions are available, in

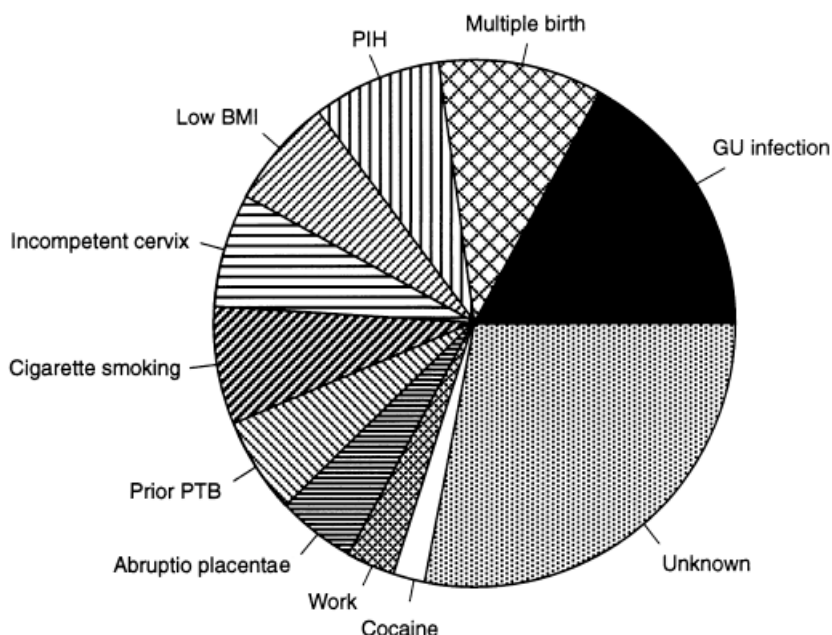


Figure 2. Aetiological determinants of preterm birth in a developed country in which 25% of the women smoke during pregnancy and a substantial minority are non-white.

terms of either public health policy or clinical care: PIH, incompetent cervix, history of prior preterm birth (PTB) and abruptio placentae. Cocaine use is the one modifiable factor besides cigarette smoking with a recognised impact on the risk of preterm birth, but it carries only a small aetiological fraction.^{1,45,56,88} An important message from Fig. 2 is the large pie slice associated with 'unknown cause.' As with IUGR, the determinants of preterm birth are not mutually exclusive and, thus, the aetiological fraction for all the determinants is far less than Fig. 2 suggests. In other words, most cases of preterm birth occur without any known cause.

Because Figs. 1 and 2 are based only on those factors with widely acknowledged (i.e. relatively non-controversial) aetiological roles, they do not summarise all the evidence bearing on causal determinants of IUGR and preterm birth. In particular, several determinants currently under active study may soon have their places in the two pies, and these too need to be considered in terms of their potential roles in mediating socio-economic disparities in adverse pregnancy outcomes. They include prenatal care, psychosocial factors and micronutrients.

Prenatal care

The quantity and quality of prenatal care has been a popular subject for investigation by epidemiologists and clinical researchers over the last decade. Observational studies have reported strong associations between late entry into prenatal care, or the gestational age-adjusted number of prenatal care visits, and the occurrence of preterm birth.^{1,89-91} Comparisons of participants and non-participants in special preterm birth prevention programmes have also yielded impressive results.^{92,93} In contrast, virtually all randomised trials of prenatal care, including those of 'intensive' prenatal care for women at high risk of preterm delivery, have had disappointingly negative results.⁹⁴⁻⁹⁶

Why this discrepancy between the encouraging results of observational studies and the disappointing findings of randomised trials? Consider the components of routine prenatal care: weighing, blood pressure measurement, urinalysis, abdominal palpation, cervical examination and (perhaps) advice about nutrition and smoking reduction. None of these components has shown convincing evidence of benefit. Even though maternal undernutrition and cigarette smoking are important causal determinants of IUGR,

their association with preterm birth is much weaker. Moreover, there is no evidence that routine advice (i.e. to the degree provided in routine prenatal care) to improve nutrition⁹⁷ or reduce smoking⁹⁸ during pregnancy is actually successful in improving pregnancy outcome. Thus, the association between the timing or number of prenatal care visits and the risk of preterm birth may have less to do with what is gained from the visits than with confounding psychological differences between women who initiate prenatal care early and visit their obstetrician, family physician or midwife on a regular basis and women who do not.

Psychosocial factors

The belief that stress and maternal psychological factors can affect the course and outcome of pregnancy can be traced to Biblical times: 'And his daughter-in-law, Phinehas' wife, was with child, near to be delivered; and when she heard tidings that the ark of God was taken, and that her father-in-law and her husband were dead, she bowed herself and travailed; for her pains came upon her'.⁹⁹ It has been only recently, however, that social scientists and epidemiologists have considered this area worthy of serious investigation. Associations have been reported between preterm birth and stressful life events, anxiety, depression, stressful work, physical abuse and low levels of social support.¹⁰⁰⁻¹⁰⁷ As summarised by Hoffman and Hatch,¹⁰⁸ however, the evidence is mixed; several recent studies have not found associations between preterm birth and psychosocial factors (especially with stressful life events).

The inconsistent results may be attributable to the many ways of identifying stress. Most studies have relied on checklists of stressful life events. Several recent studies have reported associations between preterm birth and perceived stress, thus underlining the key role of stress appraisal.^{106,107} In fact, it has been suggested that 'daily hassles' and other chronic stressors might be better predictors of health problems than more dramatic, but less frequent, life events.^{108,109} These chronic stressors include environmental factors, such as poor and crowded housing conditions, unemployment and other severe financial problems, as well as interpersonal factors, such as living without a partner, and domestic violence. According to some recent evidence, it is cumulative, 'lifecourse' exposure to adverse socio-economic environments that may have the largest impact on health.^{23,110,111} Some

investigators have hypothesised that the chronic stress of racial discrimination may partly explain the aforementioned racial disparities in preterm birth.¹¹²

Two recent reports suggest that the effects of stress (perceived stress and anxiety) may be mediated by cortisol-induced positive feedback-mediated increases in placental secretion of corticotropin-releasing hormone (CRH),^{113,114} which can stimulate uterine contractility by potentiating the effects of oxytocin (perhaps via prostaglandins) or by fetal cortisol or androgen-induced oestriol synthesis.^{114–116} Alternatively, chronic stressors may increase the risk of preterm birth indirectly via psychological distress, and especially via the development of a depressive self-concept.^{117–121} The depressive self-concept includes depressed affect about one's current state, dissatisfaction with life, as well as a sense of hopelessness^{122,123} and a lack of optimism about the future.¹²⁴ Furthermore, the depressive self-concept contributes to heightened stress appraisal in response to daily 'hassles'. This creates a vicious cycle, whereby stress appraisal reinforces the depressive self-concept. The depressive self-concept may contribute to the release of stress hormones, such as placental CRH, lead to changes in sexual practices or otherwise enhance susceptibility to genital tract infection and inflammation, or promote the use of cigarettes, cocaine and other drugs that increase the risk of preterm birth.¹²⁵

The depressive self-concept captures an important cognitive-affective intrapsychic construct, but it is also important to consider a motivational construct implicated during pregnancy. Commitment represents the motivation to be pregnant, have a baby and engage in behaviours that facilitate the achievement of that goal. It encompasses and incorporates both the intendedness and wantedness of a pregnancy.¹²⁶ Low pregnancy commitment has also been associated with cigarette smoking and the use of alcohol and street drugs.^{127,128} Generally, commitment appears to be associated with healthy behaviours during pregnancy.¹²⁹

Whereas the depressive self-concept and low pregnancy commitment may increase the risk of preterm birth, social resources may be a moderating (buffering) factor.^{130,131} These social resources include the size of one's social support network, the degree of social integration and the availability and receipt of support when needed. Especially significant is the presence and quality of an intimate relationship (i.e. relationship status and relationship quality). Previous research has found that these resources can act as a stress

buffer, reducing the effects of chronic and severe stressors on intrapsychic factors mediating adverse health outcomes.^{130,131} Although randomised trials of providing social support have yielded uniformly negative results,¹³² the type of intimate support required to reduce perceptions and reaction to stress may not be possible to provide through experimental manipulation.¹⁰⁸

Several methodological problems limit the inferences that can be drawn from previous studies linking maternal psychosocial factors to preterm birth. First, as mentioned earlier and as emphasised by Hoffman and Hatch,¹⁰⁸ chronic stressors have been relatively ignored in favour of stressful life events, anxiety and depression. Secondly, several early studies ascertained exposure to psychosocial factors retrospectively (i.e. after delivery), with considerable potential for recall bias. In other words, women who delivered prematurely may have been more likely to report the occurrence of prior anxiety or stressful events. Thirdly, many studies have assessed psychosocial factors individually or only a few at a time, thus ignoring the cumulative effect of the multiple adverse factors to which disadvantaged women are often exposed. Fourthly, because of the large number of psychological factors that may be implicated and the even larger number of potential confounders, sample sizes have often been insufficient to detect moderate psychosocial effects. Fifthly, the majority of published studies have been based on individual hospitals or small communities, raising questions about sample selection and, thus, the generalisability of the findings. Finally, to our knowledge, none of the studies on maternal psychological factors have controlled for the effects of genital tract infection/inflammation.

Micronutrients

The major micronutrients that have been investigated with respect to IUGR and preterm birth are iron, folate, calcium, zinc and long-chain fatty acids. For all these, observational studies have suggested substantial associations in the expected direction. But methodological problems in these studies, especially measurement issues (dietary recall or blood measurements that may be affected by haemodilution and/or timing during pregnancy) and uncontrolled or residual confounding, hinder confident inferences of causality. Because intakes of many micronutrients are highly intercorrelated both with one another and

with macronutrient (e.g. energy) intakes, their effects can be rigorously evaluated only in the context of randomised supplementation trials. Even though randomised trials and overviews of randomised trials of these micronutrients do not support the results of the observational studies,^{133–138} previous trials are often characterised by limited sample sizes and/or low prevalence of nutrient deficiencies, both of which may have reduced the likelihood of detecting true effects. Although the available evidence does not support an aetiological role for micronutrients in either IUGR or preterm birth, there is ample room for large trials in populations with low dietary or vitamin supplementary intakes, and for observational studies of genetic, lifestyle or other nutritional factors that may increase the effects of (i.e. interact with) low intakes.

Which determinants mediate the socio-economic disparities?

Table 2 summarises the available evidence concerning associations between SES and the determinants of IUGR or preterm birth. In this section, we will attempt to combine that evidence with evidence reviewed in the previous section (on aetiological fractions) to reach some tentative conclusions about the role of these determinants in mediating the socio-economic disparities.

Maternal anthropometry

In industrialised countries, maternal stature is known to be associated with SES, although the direction of cause and effect is far from certain.¹³⁹ Socio-economic differences in stature may therefore explain a modest portion of socio-economic disparities in IUGR. In contrast, at least in the US, BMI is inversely associated with economic status; in other words, BMIs are higher among women of low SES.¹⁴⁰ Thus, unless the US is atypical in this respect, BMI cannot explain the disparities in either IUGR or preterm birth observed in developed countries. In developing country settings, however, chronic undernutrition in early childhood leads to high prevalences of short stature and, thus, its mediating role is likely to be more important in such settings. Moreover, undernutrition is more prevalent among women from more unfavourable socio-economic backgrounds, and low prepregnancy BMI could therefore be partly responsible for the high IUGR rates seen among the poor in many developing countries.¹⁵

Again in the US, gestational weight gain has also been reported to vary by SES; low weight gains appear to be more common in women with low educational attainment, whereas high weight gains are more prevalent among the highly educated.¹⁴¹ Given the large aetiological fraction associated with low gesta-

Table 2. Associations between aetiological determinants of intrauterine growth restriction (IUGR) or preterm birth (PTB) and socio-economic status (SES)

| Potential mediator (outcome) | Association with low SES | References |
|---------------------------------------|---|---------------------|
| Anthropometry/nutrition (IUGR) | Short stature more common | 139 |
| | Low prepregnancy BMI less common | 140 |
| | Low gestational weight gain more common | 141 |
| Micronutrients (IUGR and PTB) | Low intakes more common | 78,142–146 |
| Cigarette smoking (IUGR and PTB) | More frequent and heavier smoking | 78,147,148 |
| Substance use/abuse (IUGR and PTB) | Cocaine use more common | 151,152 |
| | Marijuana use more common | 54,154 |
| | High alcohol consumption more common | 155–157 |
| | High caffeine consumption more common | 58,158,159 |
| | Narcotic use more common | 160 |
| Work/physical activity (IUGR and PTB) | Prolonged standing and strenuous work more common | 83,161–163 |
| | Vigorous leisure time exercise less common | 164–166 |
| Prenatal care (PTB) | Inadequate initiation and frequency of care more common | 90,91,167,168 |
| Bacterial vaginosis (PTB) | More common | 65,66,69,73 |
| Multiple birth (PTB) | Less common | 75–77 |
| Psychological factors (PTB) | Stressful life events more common | 169–171 |
| | Chronic stressors more common | 117,118,169,172–174 |
| | Unwanted pregnancy more common | 175 |
| | Depression more common | 117–121 |
| | Physical abuse more common | 176,177 |
| | Low levels of social support more common | 107,178 |

tional weight gain, low weight gain may well represent an important mechanism for the increased risk of IUGR among the socio-economically disadvantaged. Because of its modest association with preterm birth, low weight gain is unlikely to be an important mediator of socio-economic disparities in preterm birth.

Micronutrients

Because iron, folate, calcium, zinc and long-chain fatty acids are present in higher amounts in meat, fish, milk, fruits and vegetables, it is not surprising that the intakes of all these micronutrients are lower among the poor.^{78,142–146} Given the weakness of the available evidence linking these nutrients to IUGR or preterm birth, however, their role in explaining the socio-economic disparities in these outcomes remains undocumented. As discussed earlier, large, highly focused randomised trials should help in ruling out or establishing such a role with greater certainty.

Cigarette smoking

In both the US and Sweden, cigarette smoking is both far more prevalent and heavier (i.e. larger number of cigarettes are smoked per day) in women from lower socio-economic backgrounds.^{78,147,148} Moreover, as the adverse effects of smoking in pregnancy have become widely recognised by physicians and the general public, the socio-economic gradient in cigarette smoking has widened.^{78,147} Smoking is probably the most important variable mediating socio-economic disparities in IUGR in developed country settings.¹⁴⁹ We caution, however, that in countries such as the US, cigarette smoking appears to be far more important in explaining the SES gradient in IUGR within racial ethnic groups than between them. The much higher prevalence of cigarette smoking among US Whites than among US Blacks suggests that smoking is a far more important mediator of socio-economic disparities in Whites.¹⁵⁰ Smoking may also play a role in mediating the socio-economic disparity in preterm birth, but its importance as a mediating variable is likely to be far less than for IUGR, because the aetiological fraction of cigarette smoking for preterm birth is much lower (see Figs. 1 and 2).

Substance use/abuse

Although several studies have reported a strong socio-economic gradient in cocaine use,^{151,152} its aetiological

fractions for both IUGR and preterm birth are small, and thus it is unlikely to be an important mediator. In poor, inner-city areas in the US, however, the prevalence of cocaine use during pregnancy may be extremely high¹⁵³ and, in these settings, the mediating role of cocaine use is likely to be more important. Marijuana^{54,154} use and high alcohol^{155–157} and caffeine (> 300 mg/day)^{58,158,159} consumption are also more common among the socio-economically disadvantaged, but these factors have not been shown to have an impact on gestational duration and, as mentioned earlier, their impact on fetal growth appears to be modest at best. Narcotic use is also more common among the poor,¹⁶⁰ but its independent effect on fetal growth or gestational duration is uncertain, and exposure prevalence is low.

Work and physical activity

Although many women from the lowest socio-economic stratum are unemployed, it seems clear that, among women who work during pregnancy, those whose jobs require prolonged standing, walking or other physically demanding tasks tend to be of lower SES than women with more sedentary jobs.^{83,161–163} Given the low proportion of women with such jobs, and its correspondingly low aetiological fraction for preterm birth, it is probably not an important mediator of socio-economic disparities in preterm birth. Physically demanding work in the home (or unreported domestic work in others' homes) may make a more important contribution.^{86,87} Low-SES women are, of course, less likely to engage in leisure time physical activity^{164–166} and, thus, this factor cannot explain the high rates of IUGR among the poor.

Prenatal care

There seems to be little doubt that inadequate prenatal care is associated with socio-economic disadvantage.^{90,91,167,168} This appears to be true even in Canada, despite universal health care insurance.^{90,168} Given the serious doubt about the effects of prenatal care on reducing the risk of preterm birth or IUGR, however, it too seems an unlikely mediator of socio-economic disparities in these outcomes.

Genitourinary tract infection

Bacterial vaginosis is more common among the socially disadvantaged.^{65,66,69,73} Given its strong and consistent association with preterm birth, it could be an important

mediating variable in explaining the higher risk of preterm birth among the socially disadvantaged.

Psychosocial factors

Low-SES pregnant women experience more stressful life events during their pregnancy.^{169–171} Moreover, as we have shown, chronic stressors are embedded within and accrue from the environment of low-SES women.¹¹⁷ Besides obvious links to the chronic stress caused by financial insecurity, poverty is also associated with poor and crowded housing conditions, living without a partner, unsatisfying marital relationships, domestic violence and stressful working conditions.^{117,118,169,172–174} Chronic and acute stressors may impact directly on stress hormones such as CRH,^{113,114} independently of intrapsychic factors. Indeed, it has been observed that some low-SES women may be emotionally 'numbed' (e.g. less reactive to stressful events) by their chronic difficulties.¹⁷⁰ On the other hand, intrapsychic factors may play a key mediating role. The chronically stressful environment of low-SES women is known to contribute to the development of a depressive self-concept.^{117–121} Unintended, unwanted pregnancy is also far more common among low-SES women¹⁷⁵ and has been associated with physical violence.^{176,177} In addition, low-SES women have a more restricted social support network, with social support less available during their pregnancy.^{107,178} Thus, low-SES pregnant women are not only more exposed to both acute (life events) and chronic (difficult life conditions) stressors, but also have less social support to limit the impact of those stressors.

Multiple birth

Racial differences in the occurrence of multiple births are well documented,⁷⁵ but socio-economic differences within races have not been well studied. However, indirect evidence suggests that the recent increase in multiple births attributable to infertility treatment has occurred to a greater extent among higher SES groups^{75–77} and, thus, the increasing contribution of multiples to the overall incidence of preterm birth would actually tend to narrow socio-economic disparities rather than widen them.

Conclusions

Based on the available evidence, leading candidates for quantitatively important (from a population perspec-

tive) mediating factors of socio-economic disparities in IUGR include cigarette smoking, low gestational weight gain and short stature. Alcohol, drugs of abuse, and maternal work and physical activity may explain a small, additional portion of the disparity between socio-economic groups.

For preterm birth, socio-economic gradients in bacterial vaginosis and cigarette smoking probably explain some of the disparity; to a lesser extent, so may cocaine use and prolonged standing or other adverse working conditions. Psychosocial factors may prove to be far more important quantitatively, although their aetiological links with preterm birth require further clarification.

Previous research on socio-economic disparities in pregnancy outcome has tended to focus on one or two factors at a time. Few studies have adequately assessed all the above-mentioned potentially mediating variables, and most have had insufficient sample sizes to do so. Thus, it is not known whether any residual socio-economic disparities remain after accounting (controlling) for factors whose mediating roles are known or strongly suspected. This is a promising area for future research that could point the way towards new aetiological hypotheses for preterm birth and IUGR. To the extent that these hypotheses help to identify hitherto unknown modifiable determinants, such research may help to reduce the high incidence of these adverse outcomes among the socially disadvantaged.

Previous studies have generally assumed that aetiological determinants have similar effects across the socio-economic spectrum, i.e. that their effects are not modified by SES. Future studies with adequate sample sizes should explore such interactions. Interactions should also be sought among those determinants that appear to mediate the effects of socio-economic disparity. Living in poverty leads to an accumulation of multiple chronic stressors, which may synergistically increase the risk of adverse pregnancy outcome to a far greater extent than can be explained by their individual aetiological contributions.

In closing, we emphasise that, in attempting to identify mediators of psychosocial disparities in IUGR and preterm birth, we in no way intend to 'explain away' the disparities. In particular, associations between low SES and adverse pregnancy outcomes are not 'confounded' by the mediating variables. Rather, the mediating variables (by definition) lie on the causal path between low SES and IUGR or preterm birth. Nor do we wish to imply that medical, or even psychological, remedies will provide a 'quick fix' for

socio-economic disparities. Indeed, countries with the lowest rates of IUGR and preterm birth have achieved those low rates not by health care interventions, but rather by reducing the prevalence of socio-economic disadvantage. It may not be possible to eliminate the higher risks of IUGR and preterm birth among the poor without eliminating poverty itself. Nonetheless, knowledge about mediating factors may eventually help to reduce these risks. Perhaps more importantly, such knowledge should provide a better overall understanding of aetiology, an understanding that may help to improve outcomes across the entire socio-economic spectrum.

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