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Social circumstances at the micro and macro level

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Abstract

Background

In several developed countries, the number of births is decreasing while the proportion of preterm births and low birthweight seem to be increasing. In addition to their contribution to the burden of disease in childhood, non-fatal adverse birth outcomes seem to affect individuals' health throughout the life course imprinting health later in life. Thus, women's reproductive life, pregnancy and childbirth represent a critical window of opportunity for effective preventive interventions.

For a long time it is recognised the existence of socioeconomic inequalities in pregnancy-related mortality and morbidity. In the early life, they are intrinsically unfair and are likely to assign individuals to further disadvantage, perpetuating the cycle of inequalities in health. Thus, societal efforts towards the prevention of social inequalities should have a particular focus on the beginning of life.

Individuals' choices and social conditions are shaped by upstream determinants such as the communities where people live, work and grow and the economic and cultural societal background. The assessment of social inequalities in health disregarding upstream determinants will only explain part of the variation in risk of disease within populations. In this context, health care system has considerable potential to attenuate social inequalities in health. Thus, effective public health prevention strategies must identify specific influences of these different social 'layers' on women's reproductive life, pregnancy and birth and the best available data must drive evidence.

In the present thesis we aimed to understand how different spheres of social conditions affect perinatal health in Portugal, a country that faced extraordinary social and cultural changes in the recent decades and is now struggling with the international economic crisis. We focused on understanding the macro socioeconomic influence on perinatal health, as the one based on the communities, health care and individual transmission of disadvantage. When analysing the national trends of adverse birth outcomes, no plausible explanation for a substantial increase in preterm between 2006 and 2009 was found. Thus, we also evaluated if this change was reflecting real variations in prevalence.

Specific objectives and main results

In paper I we aimed to compare trends in singletons preterm and low birthweight as recorded in vital statistics and in a hospital database. For the period 2004-2011, we used data of 801,783 singletons collected in the basis of civil registration and of 21,392 singletons registered in the electronic birth dataset from S. João Hospital Center, in Porto, North of Portugal. The annual prevalence of low birthweight (<2500g), of preterm births (<37 gestational weeks), further categorised by pregnancy duration, were compared. The proportion of low birthweight among moderate-late and very preterm babies and the ratio preterm:low birthweight was also compared. Socio-demographic adjusted prevalence ratios were estimated to compare data sources.

While the national prevalence of preterm births increased from 2004 (5.4%), particularly in 2006-2009 (reaching 7.5% in 2007), and decreased afterwards (2011: 5.7%), the prevalence on the maternity unit remained constant (2004: 6.7%; 2011: 6.4%). Data sources were similar with the exception of the period 2006-2009: independently of maternal characteristics, preterm birth was almost 1.4 times more frequent in the national dataset than in the maternity unit. However, in this period, national low birthweight among preterm babies decreased, pattern not observed in the maternity unit data. Differences were only observed among moderate-late preterm; very preterm and low birthweight trends were similar in both sources.

The influence of macroeconomic context on perinatal outcomes was addressed in two distinct papers. First we aimed to describe how the number of births and fertility patterns and indicators of perinatal mortality and morbidity evolved before and during the period of economic crisis. We also tested the relation between indicators of macroeconomic environment and reproductive and perinatal outcomes (paper II). Subsequently, the 20 years' trends in educational inequalities in preterm birth and low birthweight until 2012 were evaluated (paper III).

In paper II, using aggregated data from the National Statistics between 2000 and 2013, we observed that Portuguese birth rates had a steepest decrease after 2008 (from an annual decrease of 2% before 2009 to 4% to 8% afterwards). Emigration may have influenced these trends since the number of women between 25-34 years decreased 17% in this period. Fertility patterns of resident women changed (as a result of emigration or of different attitudes towards childbearing) otherwise more 15,880 children (+19%) were expected to be born in 2013. Before the economic crisis, improvement of economic indicators (as GDP) was strongly related with decreasing fertility rates (rho=-0.90); after the economic crisis this relation was strongly attenuated. During this period no significant changes were observed in perinatal mortality indicators. However, the prevalence of low birthweight among singletons, stable until 2008, increased 10-12% afterwards. Current economic environment was not related with increasing low birthweight. However, since 2008, women's unemployment rates showed a stronger relation with low birthweight than prior to the economic recession ($rho_{2000\text{-}2008}$=0.82; $rho_{2009\text{-}2013}$=0.97).

In paper III individual data from 2,191,249 singleton live births collected in birth civil registries between 1992 and 2012 were used. Maternal education was used as proxy indicator of socioeconomic position. Age- and parity- adjusted slope index of inequality (SII) and relative index of inequality (RII) were computed to estimate, respectively, absolute and relative educational inequalities in preterm birth and low birthweight.

During the study period, less educated women presented higher prevalence of both adverse outcomes. Until 2000, preterm decline was larger among less educated women (1998-2000: 5.4% (-36%) vs. 4.6% (-25%) in more educated), narrowing relative educational inequalities in this outcome. After 2000, educational inequalities increased and remained stable until 2012 (RII_{2012}: 1.35; 95% CI 1.27-1.44). Very preterm births showed larger educational inequalities than moderate-late preterm births. Low birthweight increased in all education strata, but more educated women presented greater increases [2010-2012: 5.8% (+57%) vs. 7.4% (+39%) in low educated]. Inequalities were greater than for preterm birth. Despite a significant increase in absolute differences with time ($p<0.001$), RII in 2012 (1.71; 95% CI 1.61-1.81) was not significantly different from the one observed in the early 2000's.

The following papers, moving closer to proximal social influences in perinatal outcomes, used data collected at the assembling of a population birth cohort, Generation XXI (G21). Between 2005 and 2006, at five public maternities from Porto Metropolitan Region, women were invited to participate. Structured personal interviews were conducted after delivery to collect data on socio-demographic characteristics, lifestyles, reproductive history and prenatal care. Pregnancy complications and birth related data were retrieved from medical files.

In paper IV we aimed to evaluate the effect of neighbourhood's clustering and socioeconomic characteristics on preterm births and small-for-gestational age babies (SGA: sex-specific weight <10th percentile for each gestational age). To clearer understand the role of neighbourhoods in perinatal outcomes we used data from 6585 women from G21 and also from 3078 women from Pelotas 2004 Birth Cohort Study, in Brazil (birth cohort with similar design and inception to G21). Using indicators at the level of census block groups from both regions, a 3-categories' neighbourhood socioeconomic variable was created by latent class analysis. Maternal addresses were linked to the block groups. Country-specific analyses were conducted and, in Pelotas, were stratified by ethnicity. Mixed effects multilevel logistic regression models, adjusted for individual- and block-level socioeconomic conditions were used.

The prevalence of preterm was 7% in G21 and 15% and Pelotas and SGA accounted for 15% of babies in G21 and 18% in Pelotas. Neighbour-to-neighbour heterogeneity in perinatal outcomes was not found in G21. In Pelotas, even after adjustment for individual- and neighbourhood socioeconomic class, unexplained neighbourhood variability was found for preterm among white women (Median Odds Ratio (MOR): 1.50) and for SGA among black women (MOR: 1.47). Neighbourhood social class did not explain the remaining variance for none of the outcomes.

Paper V aimed to evaluate whether public and private prenatal care users experience similar outcomes, taking into consideration maternal pre-pregnancy social and clinical risk. We evaluated 7325 women that included 4499 public prenatal care users (61%). The odds of inadequate weight gain, continuing to smoke, gestational hypertension, gestational diabetes, caesarean section, preterm birth, low birthweight, and small- and large-for-gestational-age were estimated for public and private providers using logistic regression, stratified by pre-pregnancy risk profile, adjusted for maternal characteristics.

Among low risk women, public care users were more likely than private users to excessive weight gain (OR=1.26; 95% CI: 1.06-1.57) and to be diagnosed with gestational diabetes (OR=1.37; 95%C I: 1.01-1.86). They were less likely to have a caesarean (OR=0.63; 95% CI: 0.51-0.78) and more likely to deliver SGA babies (OR=1.48; 95% CI: 1.19-1.83). Outcomes were similar in high risk women except for preterm and pre-labour caesarean, less frequent in public prenatal care (respectively, OR=0.64 95% CI: 0.45-0.91; OR=0.69 95% CI: 0.49-0.97). The amount of care was not significantly related with risk profile in either case.

In paper VI, we intended to estimate the extent to which differences in SGA according to maternal socioeconomic position and anthropometrics are accounted for childhood background. Among 6893 mothers of singletons, maternal education and marital status were used as indicators of adult socioeconomic position. Adult height (as indicator of previous growth) was classified as <10th, 10th-90th, >90th percentiles. Grandparent's education and childhood social class (created using self-reported assets available to the mother at the age of 12 years) were used to characterise childhood social environment. The adjusted odds of SGA according adult socioeconomic indicators and height were stratified by childhood conditions.

SGA was less likely in taller [vs. 10th-90thpercentile: OR=0.62 (95% CI: 0.46-0.83)], more educated [vs. low: OR=0.77 (95% CI: 0.65-0.90)] and in married women [vs. single: OR=0.64 (95% CI: 0.47-0.86)]. No association was found between childhood social conditions and SGA. The protection provided by maternal education was found in women from deprived childhood backgrounds but not in those with more advantage conditions. Shorter women were more likely to deliver SGA babies but the effect was stronger ($p_{interaction}$<0.001) among those from least deprived childhood conditions.

Finally, we expected to estimate the relation between socioeconomic position and reproductive outcomes. In paper VII, among women who eventually managed to have a child, we aimed to assess the association between individual socioeconomic position and female fertility impairment. This study used data from 7472 women aged 18 or more years, with spontaneous conception and with no male diagnosis of infertility. Education, income and occupation were used as individual indicators of socioeconomic position. Impaired female fertility was defined as women who had unsuccessfully tried to conceive for over a year. Multivariate logistic regression models were fitted to estimate the association between socioeconomic position and impaired female fertility, stratified by gravidity and adjusted for age, pregnancy planning and behavioural characteristics.

Among primigravidae, 7.7% presented impaired fertility and the prevalence was 9.6% in multigravidae. A significant independent social gradient between educational level and female fertility impairment was found among primigravidae (OR (95% CI) vs ≤ 6 schooling years: 7–9: 0.85 (0.54-1.34); 10 – 12: 0.34 (0.21-0.54); ≥13: 0.24 (0.14 to 0.40), p-value for trend <0.001) but not in multigravidae. No other indicator of socioeconomic position was related with impaired fertility.

Conclusions

Despite substantial social, cultural and health care improvements in the last decades in Portugal, we found socioeconomic inequalities in reproductive and perinatal outcomes, albeit of moderate magnitude. The vulnerability associated with lower maternal education makes this population group an important target for preventive strategies aimed at improving overall health. The work in this thesis allowed the identification of other features, beyond individual social conditions, which may contribute to promote or narrow inequalities in reproductive and perinatal health. It reinforces the need to design specific interventions to reduce adverse reproductive outcomes, thus obtaining health gains in future years.

Resumo

Introdução

Em grande parte dos países desenvolvidos o número de nascimentos tem vindo a diminuir. No entanto, a prevalência de partos pré-termo e de baixo peso ao nascimento parece aumentar em alguns destes países. Estes desfechos, para além de contribuírem substancialmente para a morbilidade na infância, parecem ter consequências no curso da vida, contribuindo para a morbilidade na idade adulta. Assim, o período de vida reprodutiva da mulher, a gravidez e o nascimento são importantes janelas de oportunidade para estabelecer estratégias de prevenção.

A existência de desigualdades sociais na mortalidade e morbilidade relacionadas com a gravidez é reconhecida na investigação em saúde perinatal. Nos primeiros anos de vida as desigualdades socioeconómicas são intrinsecamente injustas para o desenvolvimento do potencial da criança e, adicionalmente, aumentam a susceptibilidade para futura desvantagem no curso de vida, perpetuando um ciclo de desigualdades sociais em saúde. Neste sentido, os esforços organizados da sociedade na prevenção de desigualdades sociais em saúde deve ter como prioridade o início da vida.

As condições socioeconómicas individuais e as escolhas consigo relacionadas não são factores isolados, mas modelados por condições socioeconómicas mais distais como as características onde os indivíduos vivem, trabalham e crescem e o contexto sociocultural da sociedade em que estão inseridos. A avaliação do efeito das desigualdades sociais em saúde negligenciando os seus determinantes distais apenas explicará parte da variação do risco de doença nas populações. Também a organização dos sistemas de saúde poderá ter um importante papel na atenuação das desigualdades sociais em saúde. Neste enquadramento, o conhecimento da forma de como estes diferentes níveis sociais afectam a saúde reprodutiva da mulher, a gravidez e o nascimento é fundamental para o delineamento de estratégias de saúde pública efectivas e deve ser assegurado que a evidência é gerada com base nos melhores dados disponíveis.

Nesta tese, pretendemos perceber de que forma diferentes esferas sociais afectam a saúde perinatal em Portugal, país que, nas últimas décadas, enfrentou mudanças socioculturais substanciais e, mais recentemente, se depara com importantes mudanças relacionadas com a crise económica internacional. Focámos as influências socioeconómicas nos desfechos perinatais a um nível macro, bem como ao nível das comunidades de residência, dos cuidados de saúde e da transmissão geracional da desigualdade. Ao avaliar as tendências temporais dos desfechos adversos da gravidez não foi possível encontrar uma explicação plausível para o aumento de partos pré-termo observado apenas no período entre 2006 e 2009; como tal, avaliámos também se esta mudança reflectiu uma variação real na prevalência deste desfecho.

Objectivos específicos e principais resultados

No **artigo I** desta tese pretendeu-se comparar a evolução temporal da prevalência de recém-nascidos pré-termo e com baixo peso ao nascimento entre as estatísticas vitais e os dados clínicos de uma maternidade. Para o período entre 2004 e 2011, foram utilizados dados de 801.783 nados-vivos (gestação de feto único) recolhidos no âmbito do registo civil e daqueles registados na base de dados electrónica do Hospital de S. João, no Porto (n=21.392). Em cada ano, comparou-se a prevalência de baixo peso ao nascimento (<2500g), de nascimentos pré-termo (<37 semanas de gestação), divididos posteriormente de acordo com a idade gestacional, bem como o rácio pré-termo:baixo peso ao nascimento. Foram estimadas razões de prevalência entre as duas fontes de dados ajustadas para o perfil sociodemográfico materno.

Observou-se que, enquanto a prevalência nacional de nascimentos pré-termo aumentou desde 2004 (5,4%), particularmente em 2006-2009 (máximo em 2007: 7,5%) e diminuiu após esse período (2011: 5,7%), a prevalência hospitalar manteve-se constante (2004: 6,7%; 2011: 6,4%). No entanto, a prevalência nacional de baixo peso em crianças pré-termo diminuiu no período de 2006-2009, padrão não observado nos dados hospitalares. As diferenças entre as fontes de dados apenas foram observadas entre os partos pré-termo moderado-tardio (32-36 semanas de gestação). Diferenças significativas entre as fontes de dados, independentemente das características maternas, apenas foram observadas no período 2006-2009 e unicamente para os nascimentos pré-termo.

A influência do contexto macroeconómico nos desfechos perinatais foi abordada em dois artigos. Inicialmente pretendeu-se descrever de que forma o número de nascimentos, taxas de fertilidade e os indicadores de mortalidade e morbilidade perinatal evoluíram nos períodos pré- e pós-crise económica (**artigo II**). Testou-se ainda a relação entre indicadores macroeconómicos e os desfechos reprodutivos e perinatais. Seguidamente avaliaram-se 20 anos de evolução de desigualdades educacionais nos nascimentos pré-termo e com baixo peso até 2012 (**artigo III**).

No **artigo II**, utilizando dados agregados fornecidos pelo Instituto Nacional de Estatística para os anos entre 2000 e 2013, verificou-se que o número de nascimentos sofreu uma diminuição mais acentuada após o ano 2008 (passando de uma diminuição anual de 2% antes de 2009 para 4% a 8% após essa data). A emigração pode ter influenciado esta tendência, uma vez que o número de mulheres residentes entre os 25 e os 34 anos de idade diminuiu 17% neste período. Os padrões de fecundidade nas mulheres residentes modificaram-se (como resultado da emigração ou da disponibilidade/vontade para ter filhos), caso contrário, em 2013, seriam esperadas mais 15.880 nascimentos (+19%). Antes da crise económica a melhoria de indicadores económicos (como o PIB) mostrava-se fortemente relacionada com a diminuição de fertilidade (rho=-0.90); após 2009 esta relação atenuou-se. Durante este período não se verificaram diferenças nos indicadores de mortalidade perinatal. No entanto, a prevalência de baixo peso ao nascimento em fetos únicos – estável até 2008 – aumentou 10 a 12% depois deste ano. A evolução do PIB não se relacionou com a ocorrência de baixo peso ao nascimento. Após 2008, a taxa de desemprego entre as mulheres mostrou uma relação mais forte com este desfecho do que no período prévio à crise económica ($rho_{2000\text{-}2008}$=0.82; $rho_{2009\text{-}2013}$=0.97).

No **artigo III** foram utilizados dados individuais de 2.1191.249 nascidos vivos (fetos únicos) recolhidos nos registos civis de nascimento entre os anos 1992 e 2012. A escolaridade materna foi utilizada como indicador de posição socioeconómica. Para quantificar as desigualdades educacionais relativas e absolutas nos nascimentos pré-termo e com baixo peso, foram estimados dois indicadores de desigualdade ajustados para a idade e paridade, *slope index of inequality* (SII) e *relative index of inequality* (RII), respectivamente.

A prevalência de ambos os desfechos foi mais elevada entre as mulheres menos escolarizadas em todos os momentos considerados. No entanto, até o ano 2000, as desigualdades nos nascimentos pré-termo atenuaram-se, resultado de uma maior diminuição da prevalência nestas mulheres (1998-2000: 5,4% (-36%) vs. 4,6% (-25%) entre as mais escolarizadas). Após esta data, as desigualdades educacionais nos partos pré-termo aumentaram mantendo-se depois estáveis até 2012 (RII_{2012}: 1,35; IC 95% 1,27-1,44). Verificaram-se desigualdades mais acentuadas entre nascimentos muito pré-termo (<32 semanas de gestação). A frequência de baixo peso ao nascimento aumentou em todos os estratos de escolaridade, embora as mulheres mais escolarizadas apresentassem um aumento mais acentuado [2010-2012: 5,8% (+57%) vs. 7,4% (+39%) nas menos escolarizadas]. As desigualdades educacionais neste desfecho foram mais elevadas do que as observadas nos nascimentos pré-termo. Apesar de um aumento significativo na desigualdade absoluta (p<0,001), o RII em 2012 (1,71; IC 95% 1,61-1,81) não foi significativamente diferente do observado nos primeiros anos do novo século.

Nos artigos seguintes, aproximando-nos das influências proximais dos desfechos perinatais, foram utilizados dados recolhidos no recrutamento da coorte de nascimentos de base populacional Geração XXI (G21). Entre os anos 2005 e 2006 foram convidadas a participar as mulheres com nados-vivos nascidos em cinco maternidades públicas da Área Metropolitana do Porto. Após o parto foram realizadas entrevistas pessoais estruturadas no sentido de recolher dados sociodemográficos, de estilos de vida, história reprodutiva e cuidados pré-natais. Através dos processos clínicos recolheu-se informação sobre complicações na gravidez e dados relacionados com o nascimento.

No artigo IV, pretendeu-se avaliar o efeito das condições socioeconómicas da área de residência nos nascimentos pré-termo e leves para a idade gestacional (LIG: peso ao nascimento <percentil 10, específico para o sexo e semana de idade gestacional). No sentido de melhor perceber o efeito das vizinhanças nos desfechos, utilizaram-se dados de 6585 mulheres da coorte G21 mas também de 3078 mulheres da coorte de nascimentos 2004 de Pelotas, no Brasil (coorte com desenho de estudo e início semelhantes aos da coorte G21). Considerando indicadores fornecidos pelos Censos de ambas as regiões (anos 2001 e 2000, respectivamente), agregados ao nível da secção estatística, foram identificadas 3 classes socioeconómicas da área de residência através de modelos de análise de classes latentes. Os endereços maternos foram georreferenciados e ligados à secção correspondente. A análise foi realizada para cada país e, em Pelotas, foi estratificada por etnia materna. Foram utilizados modelos de regressão logística multinível com efeitos fixos e aleatórios ajustados para as características socioeconómicas individuais e ao nível da secção.

A prevalência de pré-termo foi de 7% na G21 e 15% em Pelotas, enquanto 15% dos bebés G21 e 18% de Pelotas foram classificados como LIG. NA coorte G21 não foi encontrada heterogeneidade entre as áreas de residência nos desfechos. Em Pelotas, independentemente das características individuais e da secção, verificou-se existir variabilidade entre vizinhanças nos nascimentos pré-termo entre as mulheres brancas (*Median Odds Ratio* (MOR): 1,50) e o mesmo aconteceu nos LIG entre as negras

(MOR: 1,47). As características socioeconómicas da área de residência não explicaram a variabilidade nas vizinhanças.

O **artigo V** teve como objectivo avaliar se as mulheres que utilizam cuidados pré-natais públicos, apesar de apresentarem um perfil socioeconómico mais desfavorável, têm desfechos obstétricos semelhantes àquelas que utilizam cuidados de saúde privados. Foram avaliadas 7325 mulheres, incluindo 4499 que utilizaram cuidados pré-natais públicos (61%). Através de modelos de regressão logística foram estimados os *odds* de ganho de peso inadequado na gravidez, não cessação tabágica, complicações hipertensivas, diabetes gestacional, cesariana, parto pré-termo, baixo peso ao nascimento, LIG e GIG (grandes para a idade gestacional), de acordo com o tipo de prestador de cuidados (público ou privado), estratificados para o risco de complicações pré-concepcional e ajustados para características sociodemográficas maternas e planeamento da gravidez.

Entre as mulheres de baixo risco, as que utilizaram cuidados pré-natais públicos, quando comparadas com as que utilizaram cuidados privados, apresentaram mais frequentemente ganho de peso excessivo (OR=1,26 IC 95%: 1,06-1,59) e diabetes gestacional (OR=1,37 IC 95%: 1,01-1,86). Tiveram menos frequentemente parto por cesariana (OR=0,63 IC 95%: 0,51-0,78) e apresentaram menor risco de um nascimento LIG (OR=1,48 IC 95%: 1,19-1,83). OS desfechos foram semelhantes entre as mulheres com elevado risco de complicações pré-concepcional, excepto no que diz respeito a partos pré-termo e cesariana electiva, desfechos menos frequentes entre as utilizadoras de cuidados públicos (respectivamente: OR=0,64 IC 95%: 0,45-0,91; OR=0,69 IC 95%:0,49-0,97). A quantidade dos cuidados não se relacionou significativamente com o perfil de risco em ambos os prestadores de cuidados.

No **artigo VI** pretendeu-se estimar de que forma as diferenças nos recém-nascidos LIG relacionadas com a altura materna (como indicador do seu crescimento) e com as características socioeconómicas na vida adulta reflectiam contexto social materno na infância. Entre 6893 mulheres a escolaridade e estado marital maternos foram utilizados como indicadores de posição socioeconómica na idade adulta. A altura materna foi classificada de acordo com os percentis 10 e 90 da distribuição da amostra. A classe social na infância foi definida utilizando a escolaridade dos avós maternos e a disponibilidade de diferentes recursos aos 12 anos de idade. A probabilidade de ter uma criança LIG de acordo com a posição socioeconómica adulta e a altura materna foi estimada em modelos ajustados para a idade e número prévio de gravidezes e estratificada pela classe social na infância.

A probabilidade de ter uma criança LIG foi menor entre as mulheres mais altas (vs. p10-90: OR=0,62 IC 95%: 0,46-0,83), mais escolarizadas (vs. menos escolarizadas: OR=0,77 IC 95%: 0,65-0,90) e nas mulheres casadas (vs. sem companheiro: OR=0,64 IC 95%: 0,47-0,86), mas não se relacionou com o contexto social na infância. A protecção relacionada com o aumento da escolaridade materna foi observada nas mulheres provenientes de classe baixa mas não entre as que tiveram melhor ambiente socioeconómico na infância. A protecção conferida por uma estatura mais elevada foi mais acentuada (valor de p para a interacção <0,001) entre as mulheres provenientes de uma condição social favorável.

Finalmente pretendeu-se avaliar a relação entre as condições socioeconómicas e os desfechos reprodutivos prévios à gravidez. No **artigo VII**, estimou-se a associação entre diferentes indicadores de posição socioeconómica e comprometimento da fecundidade da mulher (designado infertilidade). Incluíram-se 7472 mulheres adultas, cuja gravidez ocorreu espontaneamente e que não declararam um diagnóstico médico de infertilidade do companheiro. A escolaridade, rendimento e ocupação maternos foram considerados como indicadores de posição socioeconómica. As mulheres que declararam estar mais de um ano a tentar engravidar sem sucesso foram classificadas como tendo infertilidade. A sua associação com os indicadores socioeconómicos foi estimada através de modelos de regressão logística, estratificados pelo número prévio de gravidezes e ajustados para a idade, planeamento da gravidez e estilos de vida.

A prevalência de infertilidade entre as primigesta foi de 7,7% e de 9,6% entre as multigesta. Verificou-se existir uma relação estatisticamente significativa, independente das características maternas e com efeito dose-resposta, entre a escolaridade e a infertilidade em primigestas [OR (IC 95%) vs. ≤6 anos de escolaridade – 7 a 9 anos: 0,85 (0,54-1,34); 10 a 12: 0,34 (0,21-0,54); ≥13: 0,24 (0,14 to 0,40), valor de p para a tendência <0.001], mas não em multigestas. Nenhum outro indicador socioeconómico se relacionou significativamente com a infertilidade.

Conclusões

Apesar da melhoria nas condições sociais, culturais e de prestação de cuidados de saúde observada em Portugal nas últimas décadas, verificámos que as desigualdades socioeconómicas nos desfechos perinatais persistem, embora com moderada magnitude. A vulnerabilidade associada a uma menor escolaridade materna torna este grupo populacional um importante alvo de estratégias preventivas, visando a melhoria global da saúde da população. O trabalho desenvolvido nesta tese permitiu a identificação de outras características, para além das condições sociais individuais, que se revelam importantes para o agravamento ou atenuação das desigualdades na saúde reprodutiva e perinatal. Reforça ainda a necessidade de delineamento de intervenções específicas para a diminuição de desfechos reprodutivos adversos, obtendo assim, ganhos em saúde nos anos futuros.

1. Introduction

1.1. Reproductive and perinatal health indicators

The importance of monitoring and studying reproductive life is somewhat reflected in the extensive use of reproductive and perinatal outcomes as indicators of societal development and well-being. Particularly perinatal, maternal and infant deaths have been valuable to characterise populations' health status and to serve as proxies for the success of public health strategies and of improvements in care [1].

Chronic diseases are not frequent among childbearing women because of their young ages. Therefore, women at reproductive ages belong to a particularly healthy group of individuals for whom low incidence of pathological outcomes is expected, even if undiagnosed diseases become revealed during pregnancy [2]. However, the way childbearing women act in the society has huge impact on the population growth and on its economic improvement. High values of perinatal mortality indicators, although with their own specificities and causal features, reflect not only medically determined factors, but also economic and sanitary resources, such as the availability of effective health care to deal with the increased risk that pregnancy and labour may induce [3]. Pregnancy and childbirth represent a critical window of opportunity for providing effective interventions to prevent adverse maternal and child health outcomes.

Two of the eight Millennium Development Goals - worldwide countries' agreement in 2000 on efforts to meet the needs of the world's poorest until 2015 - are related with the reduction of child mortality (goal 4 including infant and under-five mortality and children measles immunization[1]) and with the improvement of maternal health (goal 5) [4].

In the European setting perinatal health has substantially improved in the last decades and disparities are thought to have become narrower. This called for a set of quantitative data that could reflect the current needs of those countries. However, no standardised tools for monitoring and comparing perinatal health status and perinatal health care in Europe were available in the beginning of the XXI century [5]. The EURO-PERISTAT project, integrating 29 European countries and a broad and articulated team of obstetricians, paediatricians, midwives, epidemiologists and statisticians, developed an indicator set for describing and monitoring perinatal health. Consensus processes identified potential indicators after scientific literature review. Subsequently to the analysis of the availability and feasibility of the proposed indicators from routine data sources, a final set of indicators was created. It aimed to provide standardised data not only on mortality but also on infant and maternal health status, risk factors and health care provision [6]. Up to the present, comparable data were already provided for the years 2000, 2004 and 2010, allowing the understanding of regional differences and time trends. Most of the European data described in the following section on perinatal indicators were driven by this work.

We opted to describe in more detail traditional indicators of reproductive behaviour, mortality and morbidity, placing the Portuguese trends in context with the reported estimates in Europe and in other countries with different social backgrounds. To understand the trends of adverse pregnancy outcomes and their social inequalities one must consider how maternal and health care characteristics have evolved in time. We will explore them further ahead when describing the specificities of the Portuguese social context.

[1] Under-five mortality rate and measles immunization are indicators used worldwide although more relevant in the developing countries. We will focus on infant mortality and references to these indicators will be made when appropriate.

1.1.1. Reproductive behaviour

The registry of the population's number of births and deaths goes back centuries ago [7]. Population crude birth rate (generally defined as the number of live births per 1000 inhabitants) or the total fertility rate (children per woman: the average number of children a hypothetical cohort of women would have at the end of their reproductive period if they were subject during their whole lives to the fertility rates of a given period and if they were not subject to mortality) essentially reflect the social environment of a population and are shaped by social norms and economic conditions, contraception practices, women's participation in the labour market and change in values and attitudes towards childbearing [8]. Thus, fertility levels vary substantially in the world; low income countries, despite the huge decline in the past half-century, still present higher rates (2.7 children per woman in 2005-2010) than high income countries (1.7 children per woman in 2005-2010) [9]. European rates are below the average fertility level that is described as necessary in the developed countries to maintain population size in the absence of migration (2.1 children per woman) [10] and Portugal is one of the top 10 countries in the world with the lowest rates (1.3 children per woman in 2012) [11]. The number of births in the country has been declining since the 1960's. Between 1965 and 1995, it declined, on average, 2% per year (210,299 live births in 1965 and 107,097 in 1995), increased 2.3% per year until 2000 (120,008 live births) and fell again 2% per year until 2008. Since then, the number of live births has been declining almost 5% annually (in 2013 82,787 children were born) [11] (Figure 1).

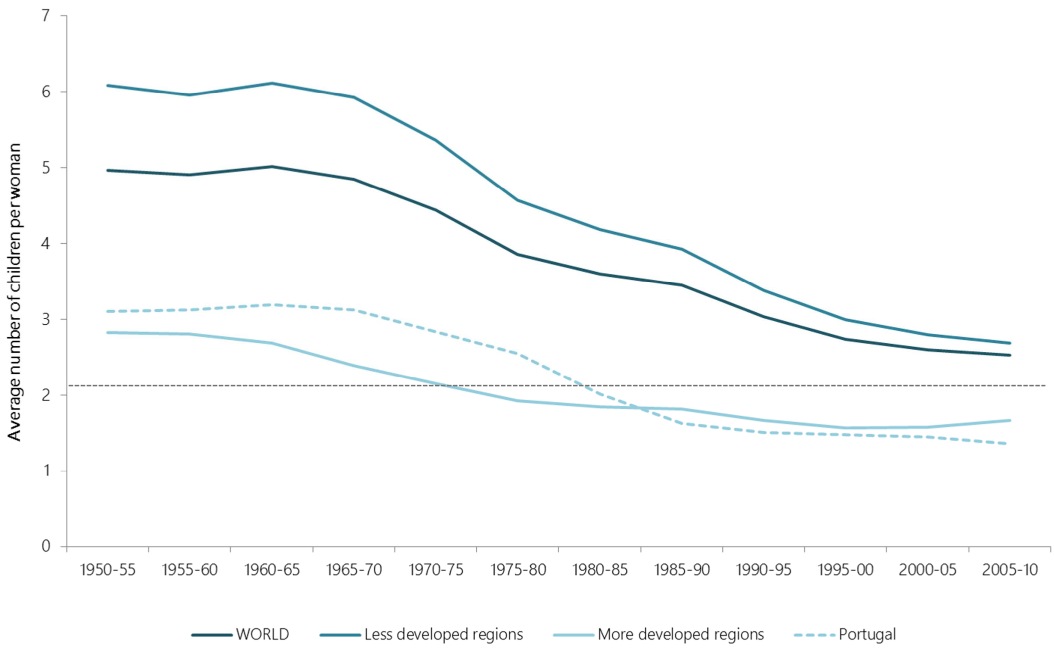

Figure 1 – Total fertility rates (children per woman) according to region between 1950 and 2010
(Horizontal line represents the replacement fertility level in the developed countries – 2.1 children per woman) (adapted from the United Nations online database [9])

By means of an increasing life expectancy, these values impose important challenges to societies' economic pattern and sustainability, as the population over 65 years is expected to correspond to 27% of the total European population in 2050 (34% in Portugal) [9]. In recent years life expectancy at birth in developed countries has been increasing about 2% every 5 years. However, improvements had been much larger during the XX century [9]. Currently, the increase is mainly the result of better management of pathologies that occur at older ages but, most of the increment in the previous decades was attributed to the huge decline in mortality in the first year of life [3]. Between 1950 and 2010, life expectancy at 60 years increased 5 years in developed countries (and not very differently from the rest of the world), while at birth, the increase was of 12 years. In Portugal the difference was even more pronounced: increased 5 years at the age of 60 and 19 years at birth [9].

1.1.1.1. Infertility

Reproductive health is a recognised predictor of women's health later in life. Conditions associated with female reproductive ability and the occurrence of complications during pregnancy may function as markers of underlying chronic diseases [12,13]. Childbearing choices, namely the delaying of childbirth may alter the course of some conditions, such as breast cancer [14]. Therefore, fertility impairment, the most common health concern among young adults [3], may also be a surrogate for future health. We mentioned above fertility rates in a demographic perspective as the number of children per childbearing woman. Clinically, the term fertility is used to represent fecundity, which is the ability to conceive, rather than the actual production of a baby [3]. Definition of infertility is not straightforward and is attributed to the couple, increasing the difficulty of ascertainment. Sterility, meaning couples with total inability to conceive, is a rare phenomenon of about 5% prevalence [3]. Infertility is a term used to characterise couples who have difficulties to conceive but that will eventually achieve a recognised pregnancy. It is defined as incapacity to achieve pregnancy after one year of unwanted non-conception with unprotected intercourse in the fertile phase of the menstrual cycles. Sub-fertile couples are those that conceive between 6 and 12 months [15]. The prevalence of this phenomenon is heterogeneous and seems to be around 10-15%, but varying between 3% and 39%. This may result from different age distributions of the considered population (as fertility significantly decline with increasing women's age) but also because of different numerator and denominator definitions (as planned pregnancies, first time pregnancies or expected to be, married women, etc.) [16,17]. Infertility is related with fecundability which represents the probability of a couple to conceive in one menstrual cycle. Time-to-pregnancy, a surrogate of fecundability, is often used in large epidemiologic studies, reinforcing the concept that infertility is not a dichotomy but a continuum. One of the main difficulties when assessing infertility and time-to-pregnancy is the ability of couples to report the exact duration of their intention to conceive (misclassification increases with increasing interval between data collection and the index pregnancy) [18]. Added to this are the heterogeneous sexual practices among those that are trying to get pregnant and the large proportion of unplanned pregnancies for whom is virtually impossible to assess time-to-pregnancy [19]. Also, assuming that the latter represent couples with no fertility impairment is a misleading inference.

The decreasing birth rates in several developed countries raised the question of a possible decline in human fertility, allegedly as a result of a decline in semen quality. However, conflicting results have been presented [20,21]. Apart from semen quality, several female factors are implied in the ability to conceive and, part of them, is socially patterned. Female ability to conceive is known to be age-dependent. After the age of 31 years, monthly fecundity rate significantly declines and, after 37 years, the deterioration is more accentuated [22]. The childbirth delay observed in most developed countries may have contributed to the increasing prevalence of fertility impairments [23]. Childbearing postponement has also contributed to the increased use of infertility treatments [22], although financial, psychosocial and ethical reasons make the uptake of such treatments socially-patterned: couples who seek for medical advice account for approximately less than 50% of infertile couples and are older, more educated, married and with higher income [23].

One of the recognised preventable reasons for female infertility relates with sexually-transmitted infections, such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. As *Chlamydia trachomatis* (and *N. gonorrhoeae*) urinary infection is frequently asymptomatic, is often undiagnosed and, consequently, inadequately treated. In these situations it can lead to pelvic inflammatory disease (PID) which might affect reproductive function [24]. Infection rates, also frequently socially-patterned, have declined in the last century, contributing to the decrease in fertility impairment [3]. However, for the recent years, increasing number of new cases has been reported in several regions (more 4% of C. *trachomatis* and more 21% of *N. gonorrhoeae*), although it may reflect increasing infection rates but also the increasing number of tested individuals. Even so, in the European setting, the incidence and prevalence of these sexually transmitted infections seem to be decreasing in childbearing women between 2005 and 2008 [25,26].

More recently there has been growing evidence on the effect of obesity, smoking behaviours and environmental exposures on impaired capacity to reproduction, although the magnitude of the association does not seem to be strong [3].

Besides biological factors, first of all, the decision to have children reflects the social environment of a population and is shaped by the social norms and economic conditions, contraception practices, women's penetration in the labour market and change in values and attitudes towards childbearing [23]. These have been the most studied factors when assessing the effect of social conditions on fertility. However, downstream from the decision to reproduce, among those that try to get pregnant, part of the determinants of infertility are socially-patterned and the reduction of inequalities may contribute to the ability of women to achieve their desired reproductive potential and contribute to better health later in life. Also, as fertility impairments are related with child's health, mediated by the adverse effect of the described risk factors but also by the use of medically assisted techniques, understanding and acting on the social differences in fertility may contribute to improve the health of the next generation.

1.1.2. Infant and maternal mortality

Infant mortality (deaths occurring from birth to 364 days of life) is divided into subtypes according to the period when it occurs. Early neonatal mortality corresponds to deaths from birth to 6 days of life, late neonatal mortality from 7 to 27 days and post-neonatal mortality refers to deaths from 28 to 364 days of life [27]. All the rates are calculated by dividing the number of deaths by the number of live children born in the same year. Prematurity-related complications contribute to 35% of neonatal deaths worldwide, followed by intrapartum-related events (23%), sepsis or meningitis (13%) and congenital anomalies (9%) [28]. In developed countries, prematurity-related complications and congenital anomalies are the major causes of neonatal deaths [29]. As they are intrinsically related with the existence of on-site intensive neonatal units, neonatal mortality rates are usually used as an indicator of suboptimal care [30,31]. Post-neonatal deaths are more related with external causes as sudden infant death syndrome and infections, showing stronger relation with social conditions than neonatal deaths. Sudden infant death syndrome has become rare at the end of the XX century (much related with successful public health campaigns to avoid prone sleeping in infants [32]) while pneumonia and diarrheal diseases are the leading causes of infant deaths in countries, or time periods, with high infant mortality rates [7,28,32].

However, and considering the increased viability of preterm infants in the neonatal period and the improvements in neonatal care, high-risk babies remain at considerable risk of dying in the post-neonatal period [30].

In less developed countries post-neonatal deaths usually predominate among infant deaths while the opposite occurs in the developed countries: more than half of all infant deaths occur in the early neonatal period, 13% in the late neonatal period and 34% after the first 28 days of life [3].

During the past century, infant mortality and under-five child mortality rates showed huge decline worldwide. In less developed countries, the fall was more accentuated after the establishment of the Millennium Development Goals in 2000 [33]. Among high income countries, the decline was more pronounced until the 1950's. In the 1920's, the United States post-neonatal mortality rates became lower than neonatal ones and in 1940's corresponded to about half of neonatal deaths. In other countries, such as in Portugal, this pattern occurred a few decades later [3]. In fact, the Portuguese infant mortality decline in the past 60 years is a well-known history of success. In the beginning of the second half of the previous century, Portuguese rates were 1.4 times the Spanish ones and almost 5 times higher than the infant mortality in Sweden (Figure 2). From 94 infant deaths per 1000 live births in 1950, Portuguese infant mortality decreased to 2.7 deaths per 1000 live births in 2013, being one of the lowest rates in the world [9,11]. Most of the decline until the 1980's was observed in post-neonatal infant mortality. It parallels the implementation of a structured vaccination plan in 1965 and the improvement in living conditions that happened since the sixties and were boosted by the 1974 Portuguese revolution that ended with almost 50 years of dictatorship. In 1979 the National Health Service was launched and, in 1980 the first neonatal intensive care units were created in the country [34]. The access to prenatal care became universal and part of a structured perinatal health care referral system. The proportion of hospital deliveries increased (8% in 1950; 61% in 1975; 85% in 1985 and 99% in 1995), contributing to an important decline in neonatal deaths, particularly in the early neonatal period [11,34]. In 2013, 1.9 deaths per 1000 live births occurred in the neonatal period, particularly in the early period (1.2 deaths per 1000) [11].

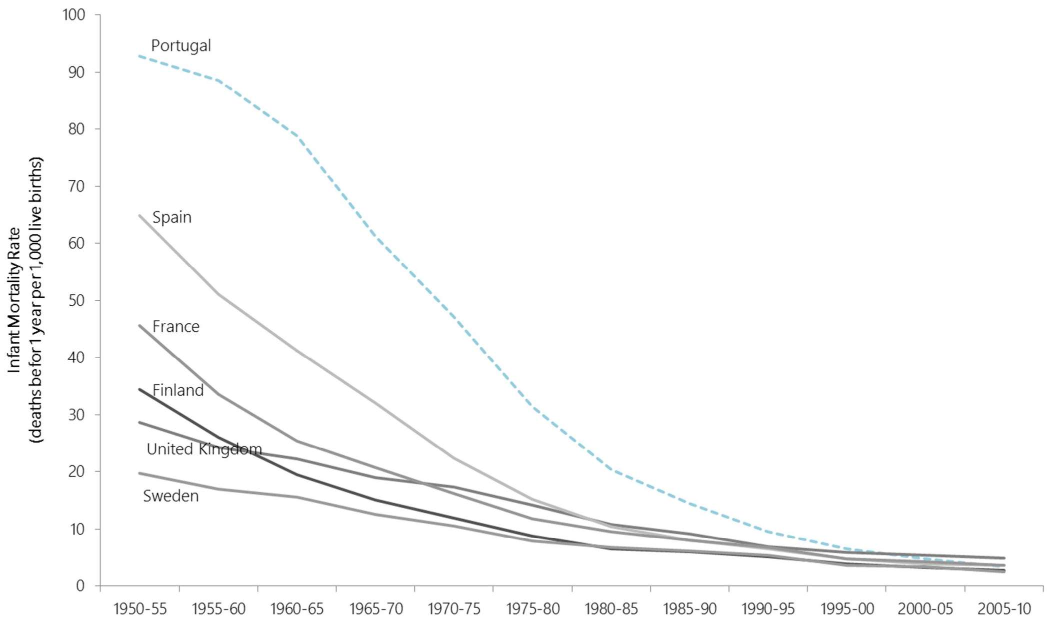

Figure 2 - Infant mortality rate between 1950 and 2010 in Portugal and other European countries
(adapted from the United Nations online database [9])

Together with newborn and child mortality indicators, maternal deaths are sentinel events that raise questions about the administration of effective care and the avoidance of substandard care [35].

A maternal death is defined as the "death of a of a woman while pregnant or within 42 days of the termination of pregnancy, irrespective of the duration and site of the pregnancy, for any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes" [9]. This implies pregnancy to be a causal factor in death which may be difficult to ascertain. It can either have a direct effect (complications of pregnancy, childbirth or postpartum) or indirect effect (exacerbation of a pre-existing condition).

The Millennium Development Goal 5 aims at reducing the maternal mortality ratio (the number of maternal deaths per 100,000 live births) by three quarters between 1990 and 2015, and achieving universal access to reproductive health by 2015 [4]. When compared to the evaluation of newborn and child health trends, the monitoring of maternal mortality has been much more difficult to implement and estimates show larger differences depending on the assessment method [36,37]. Several countries still lack complete and accurate vital registration systems with good attribution of cause of death, often misclassified to other causes [36-38]. The difficulty in maternal mortality ratio estimation is highlighted by the results of *ad hoc* surveys and inquiries conducted in developed countries with good civil registration systems: they have shown comparatively larger numbers of maternal death conveying that official estimates are usually underestimated [30,39].

Based on the latest available publication, when compared to under-five mortality rate, a slower annual fall of 1.3% in maternal mortality ratio was observed between 1990 and 2013. However, the annual rate of change was accelerated since 2003, achieving a 3.3% annual decrease in the past year [37]. Worldwide ratios vary considerably: while developed countries presented in 2013 a mortality ratio of 12.1 deaths per 100,000 live births, the estimate in developing settings is of about 232.8 per 100,000 live births [37]. In Europe, using a 5-year period to minimise the variation related to the small number of deaths, maternal mortality ratio varied from 2.5 per 100,000 live births in Italy and 2.6 in Austria and Estonia to 24.5 in Latvia and 21.0 in Romania in 2006-2010 [30]. Portugal presented 5.8 maternal deaths per 100,000 live births and was one of the few countries with available enhanced registration systems, reporting the maternal mortality ratio to be almost 12 per 100,000 live births in 2003-2007 [30,40]. Portuguese estimates dramatically fell between 1960 and 1985 (from 115.5 deaths per 100,000 live births to 10.7 in 1985). After this period, the rates continued to decline but at a much slower velocity [41].

Haemorrhage is the main cause of death worldwide followed by hypertensive disorders [37,42]. Despite the observation that the contribution of each cause varies according the development of regions, this pattern is observed in Europe and other developed countries.

Worldwide disparities in maternal, neonatal and post-neonatal mortality rates are still notorious. Even in the European setting – showing very low rates that continue to decline – discrepancies are observed, which highlights that there is still place for improvement and reinforces the utility of continuing to monitor mortality trends [30]. Still, efforts directed to the survival of high risk babies and mothers (more than to the prevention and management of high risk pregnancies) imposed an increased burden of perinatal morbidity in several countries [43]. More children survive to prematurity and congenital anomalies contributing to higher costs borne by healthcare systems and families [44] and also to the burden of disability [45] and long-term morbidity that is associated with complications stem in in the perinatal period. In the recent years, the increasing research on the early origins of adult chronic diseases highlights the importance of monitoring perinatal outcomes and respective risk factors [46].

1.1.3. Perinatal morbidity

Much of the research on adverse pregnancy outcomes is based on proxy outcomes of mortality and severe morbidity. Children born too soon and those with low birthweight are at increased risk of death but also of long term morbidities such as cardiovascular, respiratory and neurodevelopmental diseases [45,46]. On the opposite end of the distribution, the excessive fetal growth (traditionally defined as macrossomia) or post-term birth also produce increased risk of adverse outcomes [3]. In this section we will focus mainly on the lower extremes and on excessive fetal growth since post-term births, due to the advances in obstetrical practices, are rare in developed countries [30].

Maternal morbidity and behavioural risk factors for these outcomes, such as pre-eclampsia, smoking and weight gain during pregnancy are also associated with women´s morbidity later in life [47,48]. In addition, the burden of perinatal adverse health behaviours and outcomes seems to be socially-patterned [49]. Aiming to reach health equity, perinatal health surveillance must focus not only on the more severe events such as death, but also on morbidity indicators and on the non-medical factors that contribute to the burden of disease [30]. Understanding the aetiology of these outcomes and their main risk factors is essential to inform the design of interventions to decrease child’s mortality and disability later in life. Also, strategies towards their prevention will also impact women’s health throughout their life course [12].

The association between social disadvantage and adverse pregnancy outcomes is one of the most consistent findings in the literature [50-54]. It is frequently reported to be mediated by risk factors such as smoking, body mass index or pregnancy related complications. However, despite the provided knowledge, inequalities remain pervasive in time and significant associations are still found after controlling for individual characteristics [51], imposing further detailed explanation. Also, other social environment characteristics beyond individual features impact pregnancy outcomes and contribute to burden of disease. The way how prenatal care is structured within countries and its potential role in the prevention of these outcomes, through early access, amount or content is not clear. These aspects will be explored in further sections of this work.

1.1.3.1. Definition and assessment issues

Preterm birth is defined as the birth before 37 completed gestational weeks. Routine indicators on preterm births often distinguish preterm in terms of the gestational age when they occur: 34-36 gestational weeks (late preterm or near term), 32-33 gestational weeks (moderate preterm) and before 32 gestational weeks (very preterm). Very preterm births are defined as extremely preterm if occurring before 28 gestational weeks [50,55]. At 24 gestational weeks 50-70% of babies are estimated to survive outside the uterus [56] and so, before that, a preterm delivery is, in several countries, classified as a miscarriage. However, this lower limit is not consensual since viability changed over time and the limits for resuscitation practices vary considerably across and within countries. Because of that preterm estimates, particularly when analysed by gestational age, are likely to depend on these factors and the trends will also reflect changes in practices [30]. The precise duration of gestation should consider the time between conception and delivery. Although delivery is a very well recognised milestone, the exact moment of conception is not easily accessed. Indirect methods of dating pregnancy are currently used which brings additional variation to population-based estimates. The first day of last menstrual period (LMP) has long been used to date pregnancy. Since the 18th century, Naegele's rule is applied to estimate the date of delivery: add 1 year and 7 days to the first day of the LMP and subtract 3 months [57]. However, this rule is based on the assumptions that the menstrual cycle lasts 28 days and that ovulation occurs in the 14th day of the cycle. The first assumption is only true for half or less than half of women [58,59] and only about 30% of women present their fertile window between the 10 and 17 days of the menstrual cycle [60]. Also, most women are not able to report the exact day of their LMP, particularly those with unplanned pregnancies and those that enter late in prenatal care. Finally, irregular bleeding or bleeding in early pregnancy is likely to change the perception of the LMP. Gestational age based on LMP is likely to be biased and may originate shorter or longer pregnancies [61,62]. However, when compared to the ultrasound-based estimates, it seems that it overestimates the true gestational age, leading to lower prevalence of preterm and higher prevalence of post-term [63]. Ultrasound-based gestational age is reported to be the gold-standard if performed early in pregnancy [57]. It is based on fetal biometry, particularly the crown-rump length or the bi-parietal diameter. Besides the natural inter-individual heterogeneity that might affect the accuracy of pregnancy dating, after 20-24 gestational weeks fetal growth introduces additional variation. Between 7-13 weeks, gestational age measurement may vary 3 to 5 days, increasing to 1 week until the 20th gestational age and to 2 to 3 weeks after this period [61]. Some studies evaluated the benefit of using a combined measurement of ultrasound and last menstrual period gestational age if discrepancies did not exceed 7 to 14 days. Some found that the algorithm including LMP would not affect the final estimate [64] while others reported that including LMP would produce a worse estimate than ultrasound data alone [65]. The worldwide variation on the access and routine use of ultrasounds make this estimation method more likely to produce biased estimates. However, as it has been used in clinical practice in several countries, vital statistics data from these settings are likely to be ultrasound-based. When no LMP or ultrasound-based data are available, gestational age is estimated based on the neonatal assessment of newborn physical and neuromuscular maturity [61]. Some scoring systems are available; the Dubowitz score has been the most frequently used.

In Portugal, despite no national guidelines for the assessment method to be adopted, ultrasound-based gestational age is becoming more frequently used. Until 1994 pregnancy duration registered in birth certificates was explicitly based on the LMP. Since then, no reference is made to the method used to record pregnancy duration. Usually, ultrasound-based dating is the preferential method if ultrasound was performed until the 20th gestational week, which seems to happen to the majority of women that become pregnant in Portugal [66].

Child size at birth is an important indicator of perinatal health. An abnormal size at birth may be a proxy indicator of in-utero insults and is a good predictor of later morbidity [67]. Direct methods to estimate fetal growth imply ultrasonography measurements limiting their availability. Despite the increasing use of ultrasounds in the last 20 years, and the fact that their accuracy has improved, advanced methods are not available in more deprived settings and depend on the health care professionals experience and on access to prenatal care. Thus, birthweight is the most widely used and reliable measure of fetal growth, available within most vital statistics [67], although it seems to have a much weaker relation with subsequent mortality than reported in the past [3]. Low birth weight (<2500g) is frequently divided in very low birthweight (<1500g) or extreme low birthweight (<1000g). On the opposite tail of the distribution, macrosomia is usually defined as 4000g or above or 4500g or above. In addition to being a predictor of future chid health, low birthweight is an integrated measure of maternal nutrition, health status and poor prenatal health care.

Until the 1960's, a newborn with less than 2500g at birth was considered premature [68]. In 1963, Lubchenko et al. showed the existence of newborns that do not achieve their growth potential and, to distinguish the pathological condition of growth restriction from the one related with short pregnancy duration, established the first reference curves using data from birthweight and gestational age of thousands of live births [69]. After that, several reference and standard growth curves were created [70-73]. Standard curves [72] use a restricted sample of healthy pregnancies under a framework of comparison with optimal growth while reference curves [71,73] have a descriptive purpose and consider all population live births [67]. Fetal growth curves are created using large samples of live births and the cut-offs for poor or excessive weight at each gestational age are estimated taking into consideration sex-specific birthweight distribution. Usually, small-for-gestational age (SGA) babies are defined as those with birthweight below the 10th percentile for gestational age and LGA as those above the 90th percentile. The 3rd percentile is also often used to reflect severe growth restriction. However, cross-sectional data do not represent growth in time. Particularly among preterm births, biases are more likely to occur since preterm babies are smaller in size than fetuses of the same gestational age that remain in-utero [74]. In fact it is possible to classify as SGA babies that are constitutionally small. In addition, newborns with adequate birthweight for gestational age may be growth restricted if they were redisposed to be larger [3]. Even so, data at birth remain the widely accepted best sources for creating growth curves for the assessment of infant size at birth [49,74].

1.1.3.2. Preterm birth

Preterm estimates have been routinely reported in several publications. Recently, worldwide prevalence of preterm is estimated to be 11%, ranging from 5% in several European countries to 18% in some African countries [75]. As mentioned above, countries' gestational age specificities on the registry of live and stillbirths are likely to limit international comparisons [55]. In Europe, disparities are much smaller. In 2010 preterm rates varied from 5% in the Nordic countries to 10% in Cyprus. Among singleton pregnancies, rates ranged from 4% to 8% presenting similar geographical pattern [30].

Several reports show increasing preterm prevalence over time [54,76]. Part of the possible increase is related with the growing number of multiple pregnancies associated with reproductive assisted technologies, older maternal age and the lowered threshold for indicated preterm births [30,77]. As so, increases are mainly attributed to moderate-late preterm births rather to very preterm that remained stable in the last years, accounting for around 1% of all live births. Across Europe, trends in the overall preterm prevalence vary substantially (Figure 3) [30].

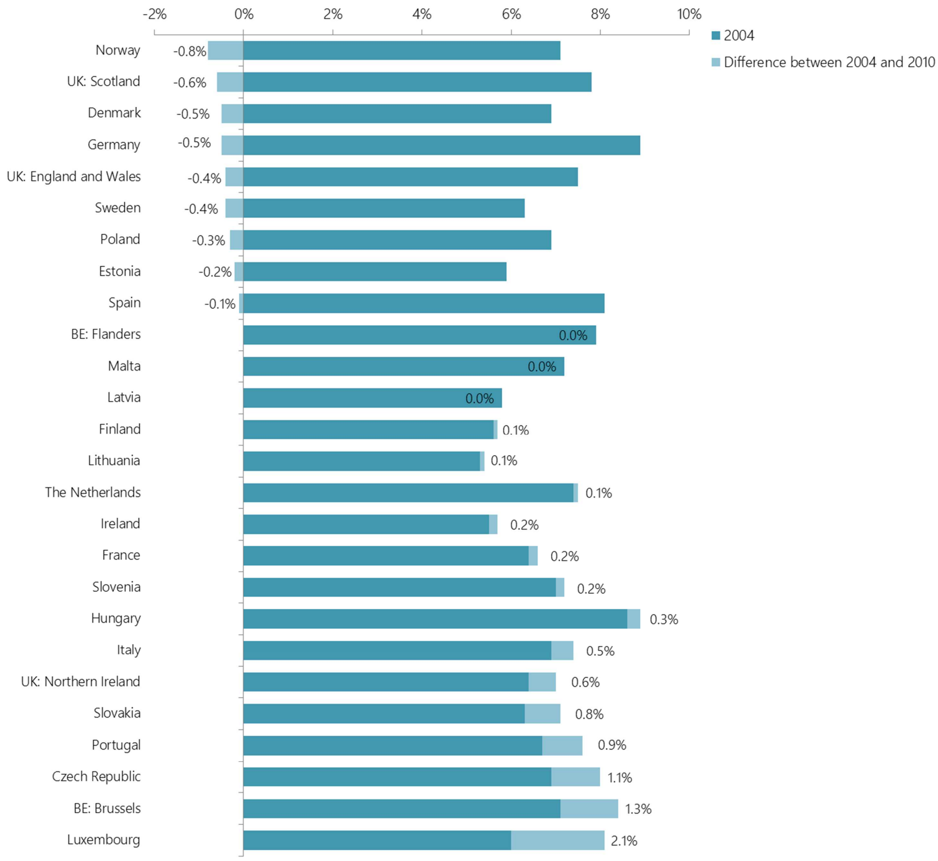

Figure 3 - Percentage of preterm live births in 2004 and difference between 2010 and 2004 in European countries (adapted from the European Perinatal Health Report [30])

Between 1996 and 2008, several European countries showed declining preterm rates suggesting that the above-mentioned increasing trend could have inverted. However, in some other countries the rates are still increasing. Countries that faced declines in preterm were those that also presented more restrictive policies related to the use of assisted reproductive technology, such has elective single embryo transfer. In contrast, those with lower proportions of elective single embryo transfer, as Portugal, presented increasing multiple births and increasing preterm births [77].

In Portugal (Figure 4), after a decline from 9% in the 1990's to 6% in 2000 preterm rates started to increase slightly afterwards. In 2013 almost 8% of live births were preterm. The Portuguese preterm pattern is not easy to explain since an abnormal increase was observed between 2006 and 2009 and after that, it resumed to levels similar to those observed before that period [11].

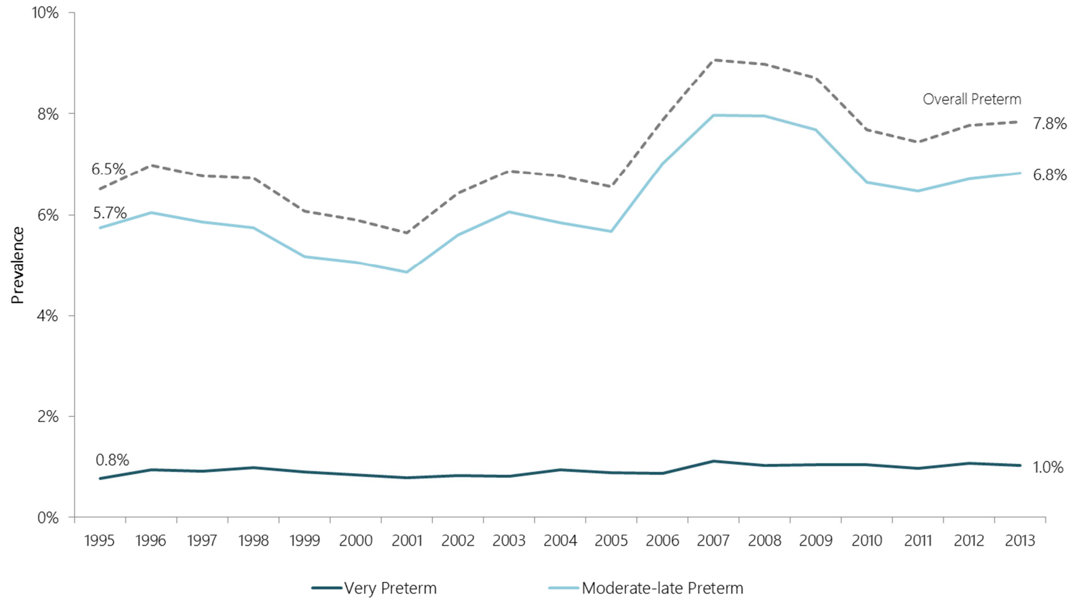

Figure 4 - Portuguese trends in preterm births between 1995 and 2013
(based on the National Statistics online database [11])

1.1.3.2.1. Aetiology of preterm birth

Preterm birth is a complex phenomenon and its multifactorial aetiology and mechanisms are not yet well understood [50,55,61,78]. Traditionally, most efforts have been directed to increase the survival of children born too soon [79], due to an apparent ineffectiveness of prevention and prophylactic strategies to decrease preterm deliveries [80]. Also, the increasing preterm rates observed in several countries contribute to make preterm birth a major public health concern.

As previously reported, preterm deliveries can be classified according to the period of pregnancy when they occur. Underlying this classification are different causal mechanisms and different levels of newborns' care to improve prognosis. A preterm birth comes about spontaneously or after elective procedures. Spontaneous preterm can occur after preterm labour with intact chorioamniotic membranes or subsequent a preterm premature rupture of the membranes (PPROM) [55,81,82].

Medically indicated preterm birth (by induction of labour or elective caesarean) contributes to around 30% of all preterm births [50] but its burden increases with increasing gestational age and is higher in more developed countries [83]. An earlier induced labour depends on medical judgment about the risks of continuing pregnancy and the risks of delivery before term: it occurs under the assumption that the newborn will have better prognosis outside than if it remained in-utero. The most common indications are pre-eclampsia and other severe hypertensive disorders and fetal indications, like severe growth restriction or fetal distress. Iatrogenic preterm is reported to be among the major causes (together with the rising multiple births) to the worldwide increase of preterm rates [50,77]. However, it also contributes to decrease the risk of stillbirth and children morbidity [84]. Although there is no universally accepted number needed to treat (i.e. the number of iatrogenic deliveries that would be necessary to prevent one stillbirth), it seems that medically indicated late preterm births do not increase the population rates of neonatal mortality or morbidity [85].

Term and preterm spontaneous labour pathways do not seem to significantly diverge and it appears that labour in preterm deliveries is triggered by pathologic insults [56]. Spontaneous preterm labour is a major contributor to preterm deliveries (around 45%) and seems to result from an early activation of the normal labour process, frequently as a result of intrauterine infection. A role of the fetus in the preterm activation of labour has also been proposed [50]. PPROM (apparently a result of similar mechanisms that lead to spontaneous preterm labour) is responsible for around 25%-40% of preterm deliveries and is defined as the rupture of the fetal membranes before 37 gestational weeks and before the onset of labour [50,78]. Although term premature rupture of membranes (PROM) and onset of labour are events usually close in time, the PPROM may be at a greater distance from the onset of labour. Thus, as the fetal membranes act as barriers to infection, PPROM leads to an increased probability of infection and subsequent preterm labour and fetal and maternal complications [86]. Even so, there is insufficient evidence on the advantages of induction delivery over expectant management of women with PPROM [87].

Infection is an important contributor to spontaneous preterm births before 30-32 gestational weeks, by activating the pro-inflammatory cascade and producing mediators that stimulate labour inducers as prostaglandins [88]. Intrauterine infection is the risk factor with the strongest causal evidence and potential for prevention. Also, bacterial vaginosis, genital tract infections and systemic infections (such as malaria, HIV or syphilis) have been reported to increase the likelihood of spontaneous preterm [78]. A very preterm birth is also a major risk factor for a subsequent preterm delivery and for long-term morbidity. After 32 gestational weeks, the risk of mortality and morbidity decreases but, as 60-70% of preterm births occur at these gestational ages, particularly between 34 and 36 weeks, perinatal mortality and morbidity attributable to moderate-late preterm is large [89]. Moderate and late preterm are less likely to be related with infection status but with uterine overdistension, caused by an increased uterine volume subsequent to multiple pregnancies, macrossomia or hydramnios [78]. Multiple pregnancies have 10 times higher risk of preterm delivery than singleton and 17% to 27% of preterm births in Europe were, in 2008, attributable to multiple births [77]. Hypertensive disorders that lead to compromise of the vascular function of the placenta and result in ischemia, stress (via endocrine, immunologic or inflammatory processes) and other immunologically mediated processes have also been reported as triggers of preterm labour [61,88].

Several risk factors are thought to be related with preterm labour. Thus, the knowledge on the main determinants of these processes may be useful in the identification of women at higher risk [49,50,52,54,61].

Beyond non-modifiable risk factors, as ethnicity (African-Americans present a two-fold increased risk) [90], other maternal risk factors present potential for prevention [50,52,54,61,78]. Multiple pregnancies, although not directly modifiable may be limited by policies directed to reproductive assisted conception practices, namely the restriction in the number of transferred embryos [77,91].

One of the major, also not directly modifiable risk factor is the occurrence of a previous preterm delivery, particularly at earlier gestational ages, and after spontaneous preterm labour [50]. A previous medically-indicated preterm birth also increase the risk of a subsequent preterm birth, probably because the underlying causes of the first preterm birth, such as maternal hypertensive and metabolic disorders, are also likely to persist in subsequent pregnancies. In multipara, a short inter-pregnancy interval (below 6 months) is associated with 2 to 3 times higher risk of preterm delivery independently of other maternal characteristics [92] and even for those who had delivered a first term baby [93]. An insufficient time necessary to resolve the inflammatory status associated with the previous pregnancy or the persistence of genital infections are possible mechanisms that explain the association [50,92,93]. In Europe, 40% to 60% of pregnancies are among women with a previous delivery [30] which reinforces the opportunity to reduce preterm. Portugal is one of the countries with the lowest prevalence of multiparous women but still represented 47% of all births in 2010 [30].

Maternal lifestyles and indicators of nutritional status are also associated with preterm delivery. Smoking seems to be related with placental damage and the impairment of the uroplacental blood flow, inducing an inflammatory response. Via fetal growth restriction and, consequently, increasing the likelihood of medically-indicated preterm, or via systemic inflammation, triggering spontaneous preterm, smoking in pregnancy is one of the most important preventable preterm risk factor [50,94]. Taking into consideration potential confounders, smoking-related relative risk of preterm birth is modest (1.2-1.6) and weaker than of fetal growth restriction, but consistent across studies, presenting a dose-response relationship. Smoking cessation also seems to be associated with longer gestations, even in subsequent pregnancies [94]. These factors argue in favour of a causal relation with preterm. The attention focused on smoking cessation seems to have declined its prevalence during pregnancy, although more than 10% of women still smoke during pregnancy [30].

The relation between maternal body mass index (BMI) and preterm birth is not as consistent. Most studies report a dose-response protective effect of BMI on the occurrence of preterm, while others showed inverse results [95]. The controversy is probably related with the different aetiologies of preterm deliveries and different pathways whereby body mass index acts. The increased risk of spontaneous preterm in low BMI women seems to be consensual [50,61] but, for severe degrees of obesity ($\geq$35 kg/m^2), the risk seems to be the same as for normal weight women (BMI 18.5–24.9 kg/m^2). Contrarily, obese women (BMI $\geq$30 kg/m^2) have higher risk of elective preterm than women with normal weight. Obese women are more likely to develop pre-eclampsia and gestational diabetes which might explain the relation [50,96].

Vaginal bleeding driven by placental abruption (premature separation of the normally implanted placenta from the uterus) and placenta praevia (abnormal placental implantation in the lower part of the uterus) [27] is also associated with higher risk of preterm birth [49].

One of the possible reasons for the increasing trends in preterm birth is related with childbearing postponement that, as described, is increasing particularly in more developed settings. Women are delivering at older ages which encompass a greater risk of maternal and fetal mortality and morbidity. However, the association is not consistent in the literature, probably resulting from insufficient control for potential confounders and also from the heterogeneity in preterm mechanisms [50]. Extreme age groups seem to be the high-risk ages for preterm. The relation between teenage pregnancies and subsequent preterm is probably related with social factors, while older age may be related with higher likelihood of maternal chronic conditions, such as hypertension or diabetes, conception-related complications such as infertility and non-spontaneous pregnancy and pregnancy-induced complications [97].

Also, other behavioural and psychological features may be related with preterm birth. Stressful life events, anxiety, depression, stressful work, physical abuse and low levels of social support, have been found to be associated with preterm, although not consistently [51]. The relation is probably mediated by corticotrophin-releasing hormone that activates earlier labour [78]. Other stress-related mediators have been evaluated, such as cortisol, adrenocorticotrophic hormone and catecholamines, although with inconsistent results [98].

Other maternal socio-demographic characteristics have been associated with the increased risk of preterm births. Work-related conditions, associated with high physical demands, are socially patterned and single women and those with low socioeconomic status are at increased risk of preterm. These aspects, as referred, will be explored later in this work.

1.1.3.3. Fetal growth restriction and excessive fetal growth

As mentioned above, low birthweight is traditionally used as a proxy of fetal growth restriction. However it comprehends different etiologic components as it may be also reflect preterm birth. It presents larger geographical disparities than preterm. Most of the differences between developed and developing countries appear to be the result of an increased prevalence of growth restriction, rather than preterm birth [99]. In Europe low birthweight ranged from 3% in Iceland and 10% in Cyprus. As observed in Figure 5 a clear geographic pattern was observed: the Nordic and the Southern European countries, particularly Portugal and Spain, presented the lowest and highest prevalence estimates, respectively.

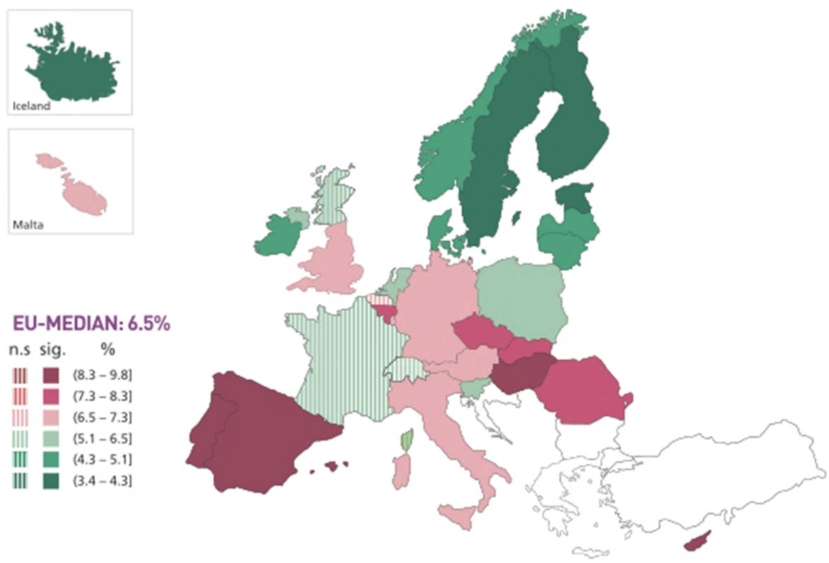

Figure 5 - Map distribution of live births with low birth weight (<2500 grams) in 2010
(from the European Perinatal Health Report [30])

Also, while some countries present declining or stable rates, in others low birthweight seems to be increasing. Portugal is part of the latter group of countries with a 9% increase in low birthweight prevalence between 2004 and 2010 (from 7.6% to 8.3%) [30]. In fact, as presented in Figure 6, a relatively steady increase has been observed in the country since the 1990's, partially related with the increasing number of multiple pregnancies, since low birthweight among singletons remained relatively stable in the first 8-9 years of the XXI century (6%) [11].

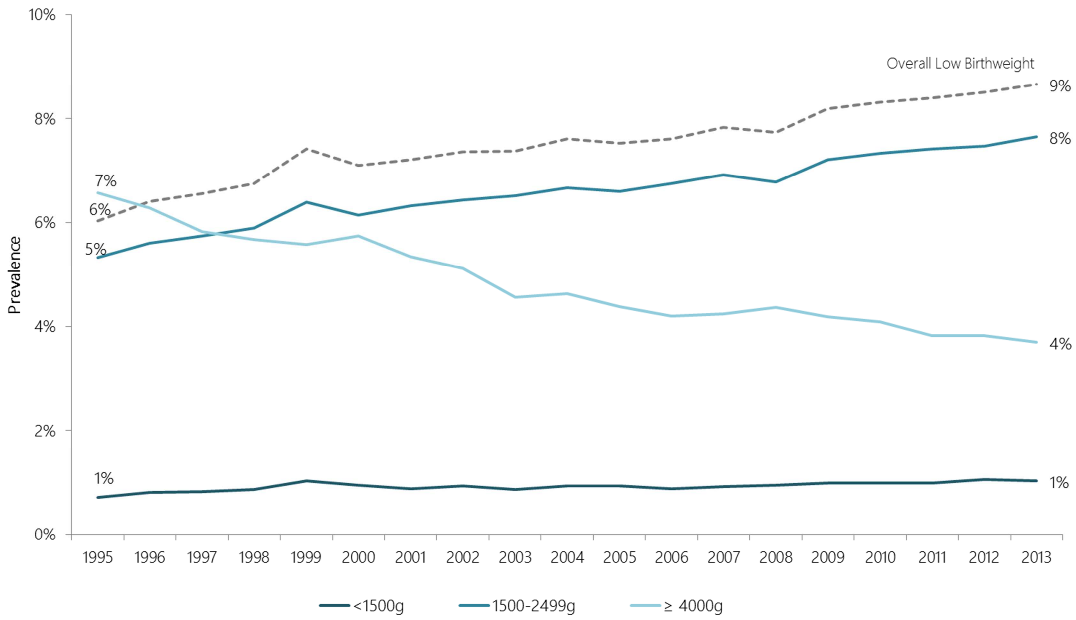

Figure 6 - Portuguese trends in birthweight between 1995 and 2013
(based on the National Statistics online database [11])

1.1.3.3.1. Aetiology of fetal growth restriction

The antagonistic selection for a large neonatal brain and a narrow, bipedal-adapted birth canal in human evolution poses a problem for childbirth. Some argue that there was an evolutionary adaptive process to restrict fetal growth in late pregnancy [100,101]. However, intrauterine growth restriction (IUGR) is an important contributor to perinatal morbidity, infants' growth and adult chronic diseases [102].

In the first weeks of pregnancy, growth is mainly about an increase in cell number. After the 16th gestational week and until the 32nd, parallel to hyperplasia, fetal growth is characterised by hypertrophy, in which cells and organs increase in volume and differentiate. After this period, hypertrophy is the major contributor to growth [2]. Growth is dependent on maternal nutritional provision, placental transfer and genetic potential [2]. Thus, insults to each of these components are likely to influence fetal development, inducing structural and functional alterations that may continue throughout adult life [103].

Placental structure and hormone secretion, together with maternal hormone release, have an important role on fetal growth regulation [67]. Abnormalities in placenta size, shape and morphology are observed in smoking women and in other pathological conditions associated with growth restriction. Moreover, the metabolic changes of pregnancy, mediated by several steroid and protein hormones are intrinsically related with growth [104]. Placental lactogens and growth hormone ensure constant mobilization of maternal nutrients to the fetus but induce maternal insulin resistance, particularly after 24 gestational weeks, increasing the risk of gestational diabetes and, consequently of large-for-gestational age (LGA) babies. In the presence of maternal malnutrition or other pathologic conditions inducing placental insufficiency, a decrease in hormone secretion and interaction with insulin-like growth factors, particularly insulin-like growth factor-I (IGF-I), may lead to growth restriction [105]. Current research has been evaluating the role of adipokines, hormones secreted in the adipose tissue, such as leptin, adiponectin, ghrelin or resistin, although their role in fetal growth is still being elucidated [2].

The main IUGR risk factors are well established and the most important are related with maternal characteristics [106].

Smoking is the risk factor of larger magnitude, since smokers have more than double the risk of delivering a restricted infant due to reduced oxygen release to the fetus, induced uterine vasoconstriction and interference with fetal oxidative metabolism [106,107]. As such, its effect is stronger in late pregnancy and increases with increasing number of cigarettes smoked per day. In populations with high prevalence of pregnancy smokers, cigarette consumption is the major preventable determinant of low birthweight and growth restriction (for smoking prevalence of 20% and 40%, population attributable risk varies from 22% to 36%, respectively). Currently, as mentioned above, smoking prevalence seems to have decreased in most countries (around 10-15%) [30] but smoking elimination would still contribute to more than 10% decrease in the occurrence of growth restriction [108].

Maternal age seems to present a U-shaped relation with growth restriction and birthweight: women younger than 20 or 25 and over 40 are at higher risk of delivering a growth restricted newborn [109]. This relation may be explained by socio-demographic and lifestyle-related determinants, such as maternal parity, maternal stature and weight, gestational nutrition and cigarette, alcohol, or drug use. Independently of these factors, low birthweight among teenage pregnancies may result from gynaecological immaturity and competition for nutrient between the mother and the fetus [110]. The effect of older ages is not completely understood and may reflect chronic pathological conditions that affect fetal growth and also the higher frequency of grand multiparity (usually more than 4 previous deliveries). However grand multiparity is more likely to be associated with excessive fetal growth than with growth restriction because of the higher incidence of gestational diabetes [111]. The highest parity-related risk of restricted birth size is found among nulliparous women (women expecting to deliver for the first time) and grand multiparae, although more consistent results have been found for nulliparity. The independent causal effects of age and parity are difficult to disentangle and, while age may be reflecting parity, the relation may be on the other way around. Also, some studies reported an age-parity interaction in which multiparity increases the risk of adverse outcomes among younger women, but has no effect on those between 20-34 years and decreases the risk in older mothers [106]. The population-level impact of grand multiparity is low and is declining since having more than two or three deliveries is becoming a rare phenomenon [30]. Among multiparae, a previous adverse pregnancy outcome, such as a SGA infant, also seems to increase the risk of subsequent IUGR. Part of this association seems to be related with recurrent risk factors. With the exception of maternal short stature, most recurrent determinants are potentially modifiable such as underweight, weight gain and smoking habits [112].

Women's height, reflecting an interaction between genetic potential and social circumstances from infancy to adult life, inversely relates with birthweight and fetal growth. Women of short stature have smaller organs and there may be area constraints for fetal growth. Also, these women are more likely to have lower weight and nutritional intake which might act as confounders for the observed association [106,113]. Maternal nutrient intake and weight gain are strong predictors of fetal growth explained by the availability of glucose, protein and other nutrients [106,114]. Maternal pre-pregnancy BMI, as proxy indicator of nutritional status, is directly associated with birthweight: underweight women are at increased risk of low birthweight and fetal growth restriction than those with normal or overweight. Maternal obesity and excessive glycaemia relates with macrosomia but severe obesity also increases the risk of restriction, possibly mediated by weight loss during pregnancy or by increased risk of preeclampsia [106]. Due to the striking evidence that obesity is rising in most countries [43], further research on the potential damage effects on birth outcomes is of particular importance. Recently, new guidelines on pregnancy glucose cut-offs to diagnose gestational diabetes were released, after hyperinsulinemia and consequent excessive fetal growth being found in women with glucose levels below the traditional threshold for diabetes [115]. Maternal insufficient weight gain during pregnancy, by reflecting a deficient supply of nutrients to the fetus is also associated with infant underweight. However, weight gain may interact with pre-pregnancy nutritional status and underweight women with adequate weight gain seem to have better outcomes [116].

Most of the risk factors of adverse birth outcomes overlap. Thus, the reduction of their frequency is expected to have a large impact on infants' health. Moreover, most of the determinants of adverse pregnancy outcomes are socially-patterned and may result from a cycle of disadvantage throughout women's life that might be perpetuated in generations, imposing effective strategies towards its reduction.

1.2. Social inequalities and reproductive outcomes

1.2.1. Underlying concepts of health disparities, inequalities and inequity

One can express social disadvantage to enclose the unfavourable social, economic or political conditions that some groups of the population experience assuming their relative position in the social hierarchy [117,118]. It is often driven by disparities in income, wealth and education but may also be reflecting gender, race/ethnic or sexual orientation. Social gradient in health would occur if these social differences are translated into variations in health indicators.

In the United States, the concept 'health disparities' was traditionally used to define racial or ethnic differentials in health (assuming biological or cultural roots instead of socially-driven ones) while inequalities in health typically refer to variations related with socioeconomic conditions. In the European setting, the terms are often used interchangeably, assuming that social disadvantage is the root for health inequalities [119]. However, strictly speaking, health disparities or health inequalities refer only to differentials in health that are not necessary driven by societal arrangements or norms.

However, the term health inequality has been used to refer of differences in health across social groups, unless otherwise specified, although as a descriptive term. In addition to that descriptive nature, inequity [120] embodies a moral judgment of these differences: it assumes that the differential in health driven by the social structure is unfair and unjust. As Margaret Whitehead defined in the 1990's [inequity] *refers to differences which are unnecessary and avoidable but, in addition, are also considered unfair and unjust. So, in order to describe a certain situation as inequitable, the cause has to be examined and judged to be unfair in the context of what is going on in the rest of society* [121].

The concept of health equity, an absence of unjust health disparities between social groups, became then more comprehensive, including also the unfair inequalities in the social determinants of health [122]. It is also recognised that certain health disparity is inequitable "if it is systematically associated with social disadvantage in a way that puts an already disadvantaged social group at further disadvantage" [123]. This explicitly assumes that some feature in the social hierarchy is causally related with health outcomes or their determinants. These features, the circumstances wherein individuals born, grow, live and work, are defined as the social determinants of health [120]. The term refers to any nonmedical factors influencing health, exerting a direct physiological effect or mediated by behaviours and attitudes related to health. Traditionally, individual-related socioeconomic characteristics, such as education, income or occupation have been used as measures of social determinants, based on the evidence that those at the lowest ranks are more likely to present adverse health outcomes, including perinatal outcomes [51,124-126].

With the increased interest in the field, the knowledge and public health interventions, social inequalities in health would be expected to narrow, which is not observed. The conceptual models used to explain how individual social determinants affect health have failed to acknowledge that these factors are not isolated but are shaped by upstream determinants, such as the conditions where individuals live and work and, even more upstream, the societal economic and social resources that influence individuals' choices [127]. As Kramer et al. highlight [51], exposures and behaviours measured at the level of individuals can only partly explain the variation in risk within populations. Also, even populations similar in their development indices and social structure may not share the same causal pathways.

It is currently acknowledged that intervening at these upstream factors, the fundamental causes, will significantly improve individuals' health and reduce social inequalities in health [127].

Again, societal efforts on the reduction of inequities in health do not intend to eliminate natural differentials in health, but the ones that are driven from unfair allocation of resources, health care access, use or adequate treatment and also from restricted option to choose and adopt health behaviours. In this framework, policies addressing inequities in health are based on two fundamental principles: a) inequalities imply injustice and unfairness and b) improving health in disadvantaged individuals will promote the improvement of the overall population health status. Pursuing health equity [120,121], is the commitment for assessing social justice in health.

In 2005 the WHO created the Commission on Social Determinants of Health. Part of the recommendations for action are directed to the life course and to the early years assuming that: a) women are at particularly vulnerable positions, result of the interaction between social determinants and gender inequity; b) social inequalities are usually perpetuated in time and are transmitted to the next generations; c) ensuring a good start of life, including the guarantee of women's decision on their reproductive life and healthy pregnancy resulting in healthy child, will impact population health [128].

1.2.2. How individual socioeconomic conditions affect perinatal outcomes

Socioeconomic position refers to the social and economic factors that influence what positions individuals or groups hold within the structure of a society [129]. It aggregates resource-based and prestige-based concepts. The first relates with social and material resources while the latter is related with individuals' rank in the social hierarchy [120]. Thus, it includes concepts of "social class" and "socioeconomic status" that are often used interchangeably, although they reflect distinct theoretical frameworks. Social class assumes that social groups arise from interdependent relationships based on people's structural location within the society. It is premised on the structural location within the economy, related to employment conditions and respective relationships [118,120]. Socioeconomic status, in turn, arises from the idea of hierarchy or ranking, often using reputational measures. Traditionally it is defined ranking job titles according society members perception of prestige [118].

Karl Marx and Max Webber were two sociologists stated as the reference for the theoretical basis of social structure and social classes [118]. Marx defined individuals according their relation to "the means of production". Social classes were driven by the ownership of assets and employment conditions and working relations, based on forms of exploitation. Webber suggested that social hierarchical stratification represents several dimensions beyond the social class based on individuals' means of production. In addition, prestige and status – as a result of property but also assessed from other sources, such as skills and intellectual ability – impact social stratification and influence life chances.

Currently, several indicators are used to define socioeconomic position (SEP), implying different theories, concepts and mechanisms, even though these are often related. There is no single best indicator; the relation of each one with health is depending on the time, setting and objective under study [129,130]. In the United States, education, income and wealth are indicators that traditionally have been used and shown to be associated with health, while in the European setting occupation has been widely used, particularly in the United Kingdom [131].

We will, first, briefly describe the most used individual SEP indicators, focusing on those that are more often related with women's social conditions and their effect on health. Then, the evidence on the relation between SEP and perinatal and reproductive outcomes is presented.

1.2.2.1. Individual indicators of socioeconomic position (SEP)

Education is a traditionally used indicator based on the Webber's social theory and represents the knowledge-related assets that individuals acquire [129]. It represents the transition from childhood to adulthood and, because of that, may reflect parental socioeconomic conditions. It is a stable indicator in adulthood, not influenced by health constraints, although childhood morbidity may affect the educational attainment later in life leading to health selection [132]. Better education is related with increasing health knowledge and healthy behaviours [127] and is a predictive measure of better jobs, income and housing conditions. In young adulthood, education is often the preferred indicator because of the age-dependent trajectory that income and occupation follow, resulting in peak achievements only in the mid-age [131]. Probably because of that, education is the social indicator that most strongly and consistently predicts pregnancy outcomes [51]. When evaluating the effect of education on health, one must take into consideration setting-specific characteristics, since the association depends on the global educational level of the population, the cohort under evaluation and societal changes in formal education policies and in cultural beliefs [133]. For International and time trends comparisons the International Standard Classification of Education (ISCED) is often used, aggregating the number of completed schooling years in the highest academic level achieved [134]. However, neither number of years of education nor levels of attainment reflect the quality of the educational experience which may be important when analysing the effect of education in health [131].

Income is an indicator that reflects material resources and its association with health is essentially related with the individuals' monetary ability to assess better housing conditions, health-related behaviours as dietary patterns, physical activities and health care. A direct effect on health may also be observed by the sense of control and perception of social advantage with increasing income. Usually income presents a dose-response relationship with different outcomes. Even though it may not remain constant in time, it may reflect an accumulation of resources during individuals' life. In women, a particular difficulty relates with those that do not have a regular source of income and depend on the partner's earnings. It is common to use the household income to better ascertain what available resources exist in a family, although they may not be equally distributed. It is useful to understand the effect of actions such as welfare, taxation and other fiscal policies on different socioeconomic groups. As defined by the OECD, "household income consists of all receipts, whether monetary or in-kind (goods and services), that are received by the household or by individual members of the household at annual or more frequent intervals, but excludes windfall gains and other such irregular and typically one-time receipts". It is evident that household income depends on the number of individuals in the family. Thus, for welfare purposes and based on economic theories, it is frequent to divide the household income by a function of the household size, in which adults and children have different weights. This division assumes that welfare is equally distributed in the household [135] which changes in time, populations and according women's role in a family. Even for women working outside home, is frequent to observe lower incomes in women when compared to the men sources of remunerations. In many settings income may be considered a sensitive question with higher likelihood of non-response and misclassification which limits its ability to discriminate differentials in health outcomes.

Occupation based measures may reflect distinct concepts and underlying mechanisms that affect health status. As mentioned above, it may symbolize the idea of status, according the position of the occupation in the prestige ranking. It also represents the pathway to income and living standards, hierarchical relations and stressful processes that individuals are exposed to, working autonomy and job expectations. All these features may contribute to explain mortality and morbidity gradients observed throughout the years. Several occupational schemes have been purposed and their use as a proxy indicator of SEP in health research must take into account the theoretical approaches used in their creation and what they represent. One of the accepted classification schemes, the International Standard Classification of Occupations (ISCO) was created at the mid-XX century by the International Labour Organization (United Nations), to address the need for an international standard classification of occupations [136]. Basically it was created to help countries improve their labour administration as well as the quality, reliability and comparability of their labour statistics. As the labour context is dynamic and occupational structures differ in time, schemes are updated in a regular basis to meet labour market demands. Most recent update was conducted in 2008 (ISCO-08). In this classification, a job is defined as a set of tasks and duties which are (or can assigned to be) carried out by one person (including an employer or self-employed). An occupation is defined as a set of jobs whose main tasks and duties are characterised by a high degree of similarity. Jobs are classified by occupation in major (10), sub-major, minor and unit groups, on the basis of the skill level required to fulfil the tasks and duties of that occupation. Each country should attempt to convert their classification schemes to ISCO-08 system. The Portuguese Classification of Occupations 2010 is a result of that adaptation (previous version was from 1994). One of the main limitations of occupational schemes is the exclusion of the unemployed, students or those working at home. Thus, it may underestimate social differences, particularly among women. Also, occupational structures are mainly based on men's job distribution. Although we observed an increase of women in the labour market, the existing schemes might not be appropriate to capture women's occupational positions [131].

In women, marital status is traditionally used as a proxy indicator of individual SEP, since it is strongly associated with circumstances that relate with SEP. Historically, married women were attributed the partner's socioeconomic conditions and marriage was seen as a route for social prestige. It has been consistently reported the protective effect of marriage in health, mediated by improving financial conditions, health information, buffering stress or improving health behaviours, although it has been reported that this association is overestimated [137].

1.2.2.2. Individual SEP and pregnancy outcomes

Globally, women in more deprived socioeconomic position are at increased risk of delivering a preterm, growth restricted or low birthweight infant [53]. This is a clear and recognised relation although it may reflect diverse constructs that affect health differently. Several systematic reviews have been published on a regular basis. In 1987, Kramer [106] evaluated almost 1000 studies published up to 1984 referring to the determinants of intra-uterine growth restriction and preterm, including the role of socioeconomic conditions on these outcomes. In 2000, the same author updated the available evidence, focusing on the socially-patterned relations and the potential mediators to explain them [51]. Ten years later, Blumenshine et al. [53] published a systematic review addressing socioeconomic disparities (including area level indicators, discussed in the next section) in birth outcomes including studies published from 1999 to 2007. Interestingly, but nonetheless alarmingly, the results and conclusions do not significantly change from the oldest to the more recent review. Despite years of intense research on this topic, women in the bottom of the social hierarchy remain at greater risk of adverse pregnancy outcomes than those at the top.

Among the latest studies, most have been conducted in the United States and in Europe. Among the latter, samples from the United Kingdom and from the Nordic countries were the basis for most research. SEP has been mainly addressed by the use of maternal education (followed by area-level measures). Research from the United Kingdom was essentially conducted using area-level deprivation indices. Occupational status, almost only assessed in Europe, and area-based measures were most frequently associated with adverse birth outcomes. However, only two studies used education, income and occupation simultaneously (from the United States and Germany). In the United States only income was observed to be independently associated with low birthweight. Education, but not occupational level, was significantly associated with birthweight and preterm in Germany, whereas income effects were significant in East Germany only. When evaluating the effect of SEP according ethnicity or race, results varied but the effect seemed to be more pronounced among black women. In these situations, SEP seems to be more consistently related with preterm than with other outcomes such as low birthweight or SGA [53].

For public health interest, the mediating factors between SEP and pregnancy outcomes must be seen according to their aetiological fractions, relating the magnitude of the association with such outcomes and their socially-related prevalence (Figure 7). So, even though some characteristics are related with both preterm birth and IUGR, their contribution to explain socioeconomic disparities is necessarily dependent on the magnitude of the association.

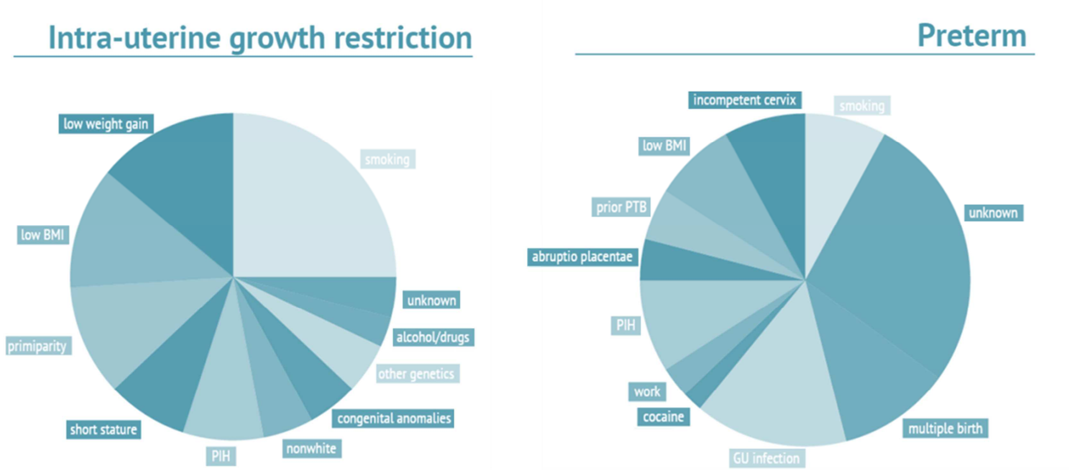

Figure 7 - Aetiological determinants of Intra-uterine growth restriction (IUGR) and preterm in a developed country where 25% of women smoke (adapted from Kramer et al. 2000 [51])

One of the major contributors to explain inequalities relates with the social gradient in smoking during pregnancy [51,53]. As previously described, smoking is particularly important to explain IUGR inequalities. Despite the socially pervasive decrease of smoking prevalence at the end of the previous century, women with higher SEP presented larger declines [94]. This pattern widened social inequalities in smoking consumption and, consequently, in pregnancy outcomes [52]. Several studies found that, independently of the SEP indicator used, socially-advantaged pregnant women are more likely to stop smoking [138]. However, this relation is not only mediated by an increased attention towards healthier pregnancy but also because women in disadvantage positions are more likely to have a smoking partner, limiting cessation during pregnancy [138]. Smoking will have a more pronounced role as a mediator of socioeconomic conditions in settings with higher consumption prevalence. In a study in Finland, where almost 16% of women were smokers in the beginning of pregnancy, smoking contributed to 40-50% of the excess SGA risk among women with low SEP [139]. In a national perinatal survey in the nineties, 19% of Portuguese mothers were pre-pregnancy smokers and 12% smoked during pregnancy [140], while the prevalence in 2005 was 23% and 13%, respectively (personal communication). For the same period we found similar results in the Porto Metropolitan Region: 23% of mothers were pre-pregnancy smokers and 11% were still smoking at the end of pregnancy [141]. Women with basic schooling were more likely to be pre-pregnancy smokers than those with high school or more (26% vs. 16%) and, among smokers, women with lower educational level were less likely to stop smoking during pregnancy (41% vs. 61%), even after taking into consideration potential confounders.

Contrarily to smoking, women obesity and overweight have increased in the past decades. In several developed countries educational inequalities in overweight remained large but relatively stable in the past 15 years, particularly in women, with those in more deprived conditions to present higher rates of obesity [142]. In this perspective one would expect to observe a decrease in SEP-related inequalities in pregnancy outcomes, particularly in IUGR, since higher body mass seem to be a protective factor of low birthweight and preterm birth [51,143]. As disparities are still observed, it seems that BMI is a minor contributor to the observed differences. However, obese women are four times more likely to develop gestational diabetes mellitus and two times more likely to develop pre-eclampsia compared with women with a healthy BMI [96]. The social influence of maternal anthropometry on pregnancy outcomes is, however, conflicting. If, on the one hand, low SEP women are protected via body fat (although with higher risk of macrosomia), on the other hand, they are at increased risk (particularly of preterm birth) via low stature, probably a result of childhood socioeconomic deprivation and under nutrition. Under nutrition in childhood may also explain part of the underweight in adulthood that is observed among more deprived women. This relation, described as typical of developing countries, may still be reflected on pregnancy outcomes in countries that recently faced significant social improvements, such as Portugal. Beyond pre-pregnancy anthropometry, weight gained during pregnancy is a strong predictor of adverse outcomes, particularly IUGR. Lower than recommended weight gain is more likely to be present among women in a more disadvantaged condition and, consequently, contributes to the increase in IUGR in this group.

For preterm births, and particularly early preterm, bacterial vaginosis has been the major contributor to explain inequalities: it seems to be more frequent among disadvantaged women [144]. Chronic stressors have been extensively evaluated in the literature but inconsistent results have been obtained. Their role in explaining social inequalities would be related with housing conditions, unemployment or other financial hardships [145] but also with socially-patterned social networks like single motherhood and domestic violence. Intimate partner violence during pregnancy was previously assessed in the Portuguese setting. Those affected showed a three-fold risk of preterm birth and violence was more frequent among women with lower educational level and lower income [146]. Unplanned pregnancies, being more frequent among women with lower SEP, contribute to explain the social gradient in pregnancy outcomes, possibly mediated by the stress that pregnancy induces, by the inadequate care and adoption of healthier lifestyles [147].

Unemployment, more frequent among women with lower SEP, is strongly related with preterm birth [148,149]. Also, the association between work related characteristics and preterm and fetal growth restriction seems to be mediated by the physically demanding occupations that women with low SEP are more likely to attain as opposed to women in a more advantageous socioeconomic position. In addition, job control explains part of the inequalities in birth outcomes. In the 1980's, maternal working conditions differences contributed to 14-20% to 20-46% of Swedish class differences in low birthweight and preterm, respectively (particularly early preterm) [150]. The relation between working conditions and pregnancy outcomes is difficult to ascertain because of the changes that women frequently adopt after pregnancy [148]. Also, reverse causation is very likely to occur, since longer pregnancy leaves may result from pregnancy complications or preterm labour threats [149].

The knowledge on the potential mediators of these relations has increased in the last decades and several public health actions were launched towards the reduction of socioeconomic inequalities in birth outcomes, focusing on individual features and behavioural modification. However, other contextual socioeconomic characteristics are upstream determinants and may interact with individual socioeconomic characteristics, contributing to occurrence of adverse pregnancy results. Also, more recently, literature suggests that the relation between adult SEP and health is a result of childhood social experiences. Several studies, reporting significant associations of childhood exposures with maternal smoking [151] and birth outcomes [152,153], even after adjustment for adult socioeconomic factors, have provided evidence of the childhood influence on the persistence of socioeconomic inequalities in birth outcomes.

1.2.3. The importance of contextual influences

At the end of the XX century, McMichael [154] suggested that modern epidemiology had failed to explain the determinants of population health because of the proximate constraints of the research priorities:

1. *The preoccupation with proximate risk factors*
2. *The focus on individual-level versus population- level influences on health*
3. *The typically modular (time-windowed) view of how individuals undergo changes in risk status*
4. *The, as yet, unfamiliar challenge of scenario-based forecasting of health consequences of future, large-scale, social and environmental changes.*

It seems clear that individuals' health reflects their own biological background, experiences and interaction with others and with the society [155]. In addition to an approach centred on the evaluation of individual risk factors, societal constructs of disease have been incorporated in research aiming at understanding the fundamental causes of disease, defined by Geoffrey Rose as the *causes of the causes* [156]. Having this framework in mind, one can move towards fundamental causes, assuming health behaviours and stressful events to be shaped by individual social characteristics in connection with the community where people live and work, the health care system, social norms and economic development [157-159]. As much as one may desire to believe in total individual free will, assuming that unhealthy lifestyles depend only on individual management, this simplistic approach is likely to be translated into unsuccessful interventions to change population risk factors. Different levels of socially-related circumstances, as Glass and McAtee [158] suggest, are physiologically incorporated (embodied [120]) in two interrelated axis: time and the societal and biologic hierarchies (Figure 8).

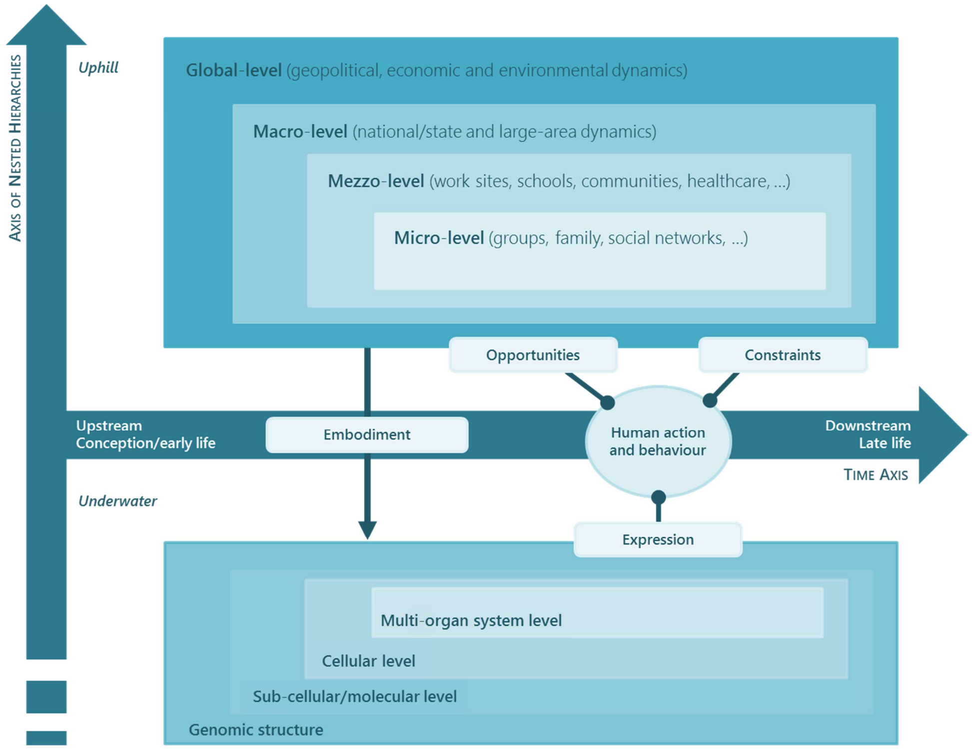

Figure 8 – Adapted from Glass and McAtee [158] **conceptual approach of the society-behaviour-biology nexus in multidimensional space**

Adopting the ecological framework, it seems clear that disentangling individual and aggregated should be achieved through assuming a hierarchical conceptual model. The understanding of social determinants of health imposes the use of data from international comparisons, from within-country differences, from individuals and from biological processes.

Among the proximal non-individual characteristics that might influence health is the social environment where people live. Several studies, almost all from the United States, have assessed the effect of the place of living on birth outcomes [160-162], which seems to be related with the social conditions and resources that allow or restrict individuals to live their lives while promoting or damaging health [160,162]. Social environment (measured by socioeconomic composition, cohesion and related attributes) is likely to influence health through chronic stress, social support and coping strategies. The availability of goods and services, such as the access of healthy products and health care facilities may shape the timely admission to quality health care and adequate nutritional intake during pregnancy. The exposure to environmental toxicants and pollution is also likely to be related with birth outcomes [160]. These conceptual domains are often clustered being difficult to extricate their independent effects. Several individual variables and composite scores have been used to characterise neighbourhoods and most relied on measures of socioeconomic position and social resources, such as community average income, education, age distribution, housing characteristics and crime and violence [163]. Although most literature reported neighbourhood deprivation to have a weak to moderate effect on preterm, low birthweight or IUGR, the results vary according to racial/ethnic backgrounds [164,165]. More recently, some studies have evaluated the influence of place of residence on behaviours known to affect birth outcomes such as weight gain [166] or smoking during pregnancy [167]. These approaches highlight the importance of taking into consideration the individual-community relations when designing prevention strategies. The US Healthy Baby Second-Hand Smoke Study showed that, beyond addressing individual characteristics, interventions integrating the differences at the level of social networks, health care and community increased the effectiveness of smoking cessation programs [168].

Moving further in the multidimensional space, individuals' health and health behaviours respond to more upstream determinants, such as government policies, practices and political and economic development. Norms and policies towards behavioural change do not seem to have same levels of effectiveness in lower socioeconomic groups [157]. Such is the case of anti-smoking policies that, despite have reduced the overall proportion of smoking individuals, have resulted in widened inequalities [52].

By using aggregated data, underlying factors that relate with health are brought out. Wilkinson and Pickett considered the level of income inequality in each country (the gap between the poorest and the richest) in relation to several health outcomes. Although causal inference should be taken carefully, the analysis showed that larger inequalities, beyond crude countries' income, seem to be related with poor health outcomes [169]. But even in high income settings with less poverty and universal access to care, such as the Northern European countries, social inequalities in several outcomes have been observed [124], namely in birth outcomes [170,171]. On the other side of the ranking and regardless the political controversies, Cuba is an example of how equality and strong public health surveillance systems may lead to high-standard pattern of health. Although considered a country with fewer resources, Cuba is a comparatively equal country with several health indicators on top of the international rankings. Infant mortality rate is the second lowest of the American continent only surpassed by the Canadian rates. In the early 1990's, following the economic retraction, low birthweight rates increased but, even before economic recovery, rates returned to the previous levels by the public health actions on nutritional supplementation programs for pregnant women [172].

Economic patterns may be particularly important when addressing the contextual effects of birth outcomes. The mechanisms underlying this relation are diverse and may act by affecting different levels of the causal pathway, such as individual, familial and community social circumstances [173,174]. As suggested by Zilko (Figure 9), the changes induced may lead to worse nutrition, adoption of unhealthy coping strategies, decreased access to care and attention to health issues, as well as directly increasing stress [173].

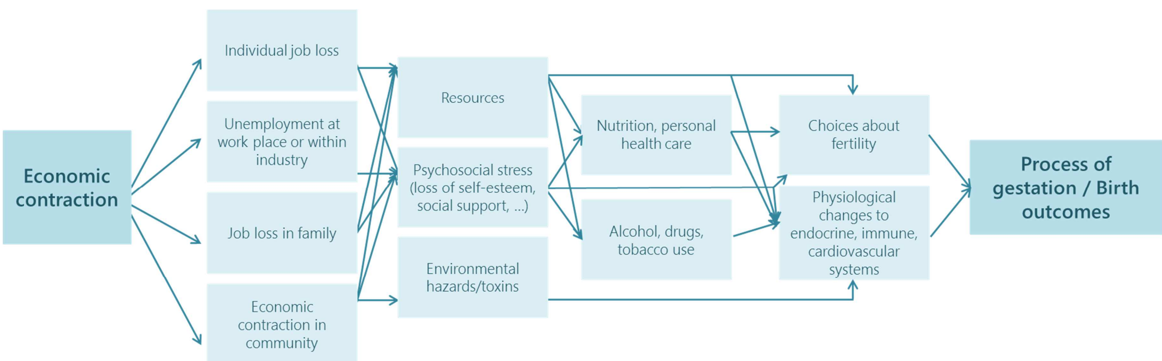

Figure 9 - Plausible mechanisms connecting economic contractions to gestational outcomes

(adapted from Zilko [173])

However, during periods of economic contraction, ecological analyses have also suggested that higher levels of unemployment may increase the time for leisure and socialising activities and lower levels of substance use, particularly among those who do not experience major economic hardship as a result of the recession [175]. If the 'negative' exposures are more likely to be experienced by those in the bottom of social hierarchy, inequalities in health are more likely to be magnified. Recently, 20 years data from the US, showed that alcohol consumption during pregnancy, but not smoking behaviours or weight gain, increased as result of economic contraction [176].

The individual adoption of different childbearing practices, towards the decreasing number of children, may result in a process of positive health selection, by which those women who get pregnant have a better social and health profile and, consequently, child health will be improved [177]. It is also possible, however, that socially advantaged women are more likely to control their fertility practices leading to an increase of births among those in lower social positions that experience more adverse exposures.

Thus, the impact of recession periods and, globally, of macroeconomic contexts, are heterogeneous and their effects on widening or narrowing inequalities may differ throughout time and between countries. Strong welfare states, ruled by the principle of equality of opportunities and equitable distribution of wealth, may attenuate the individuals' adverse experiences [174]. But even in countries with similar societal patterns, economic contraction or growth may differently affect birth outcomes [170,178].

1.2.4. Life course perspective

The approaches trying to understand how social and biological exposures during gestation, childhood, adolescence and adulthood contribute to health over time have emerged and are the basis of life course epidemiology [179]. Studies from Barker and colleagues in the 1980's, evaluating the effect of birthweight on the development of chronic diseases later in life [102], substantially contributed to the rising interest in the field. When evaluating the influence of social conditions on health, an approach centred in the life course is essential as social environment affect health throughout the course of people lives, like reflected in the Glass and Mctee society-behaviour-biology nexus [158].

Different theoretical mechanisms have been suggested to explain how early factors affect later health, varying on the importance attributed to the moment of exposure, the amount and duration of exposure and its interaction with other individual experiences. The life course approach recognises that the social gradient that is found in several outcomes may result from different processes [118]. Barker's model was based on the theory of fetal programming, according to which insults that occur at critical periods during fetal development are directly associated with the occurrence of chronic diseases later in life [46,102]. If so, social inequalities in adult disease may be reflecting social inequalities in birth outcomes. Other indirect mechanisms were also proposed. Early exposures are likely to accumulate over the life course, being the accumulation of risk, and not early exposure itself, that relates with disease occurrence [180]. However, the probability of risk exposure at different moments may be random or clustered as result of a previous social environment. In fact, another conceptual model suggests that early environment is likely to influence subsequent life trajectories, which, in turn, will influence health [181]. This chain of risk may be broken if one considers the possibility of social mobility. Social mobility hypothesis suggest that mobile individuals, i.e., those that change their social conditions in relation to their parents (intergenerational mobility) or in relation to their own adulthood SEP (intragenerational) may be at different risk of disease [133]. Social mobility is intrinsically dependent on societal opportunities or constraints. The importance and ability of individuals to climb the social hierarchy depends on the cultural and political features of each society and on the time period under evaluation. As a consequence, its implication on health is likely to be heterogeneous. Disentangling the mechanisms that underlie social gradients in health is particularly difficult because they are closely interrelated and because mechanisms are not mutually exclusive and may operate simultaneously [182,183].

Therefore, the approach to health inequalities is not only focused on improving health conditions of those in the poorest circumstances but also on acting early in life [128]. Poor childhood social circumstances, traditionally measured by parents' education or occupation and by housing characteristics [131], may be related with poor health by different mechanisms. The relation between maternal childhood adversity and birth outcomes, as previously mentioned, is also acknowledged [152,153,184]. Globally, childhood origins are likely to shape adult destinations. Individuals raised in families of more deprived conditions are more likely to be in a more disadvantage position later in life. This relation may be mediated by lower investment in children education, by greater community and societal barriers to educational success or by the adoption of mechanisms of self-affirmation that do not rely on the success at school but leave individuals more vulnerable to later disadvantage [185]. Early motherhood is such an example related with persistent disadvantage in adulthood [186]. Disentangling the effect of previous and current socioeconomic conditions is, however, particularly difficult. Traditionally, the independent effect of childhood conditions and later outcomes is assessed by treating current SEP as a confounder of the association and so, estimating adjusted coefficients. However, the strong mediating role of adult SEP may lead to spurious results.

Childhood social adversity may also be related with the acquisition of adverse health behaviours such as smoking and dietary patterns which, in turn, increase the risk of pre-conceptional and pregnancy adverse lifestyles [151]. Moreover, a disadvantaged social environment in childhood is related with exposure to insults that directly affect children's health [185]. The relation of low birthweight with chronic diseases may be reflecting this relation. It is acknowledge that women born low birthweight are also more likely to deliver a low birthweight child [187,188], although the mechanism is not entirely known. However, maternal low birthweight may act as a surrogate of adversity in childhood which is also related with subsequent growth. Women (and men) from poor social circumstances seem to grow more slowly and, on average, are shorter than those from advantage environments [189]. Although the relation between social conditions and individuals stature is not new [190], the hypothesis that adverse childhood conditions affect not only women's health in adulthood but also her offspring's health has been recently acknowledged [191,192].

It is possible that inequalities in birth outcomes result from an interaction between childhood social environment, growth and adult socioeconomic conditions. The extent to which processes of upward social mobility can overcome previous experiences are not entirely known. In the United States a decreased risk of offspring low birthweight among upward mobile mothers was observed in whites but not in blacks [193], suggesting that upward mobility may, itself, not be sufficient in specific contexts.

Childhood conditions, through their effect on subsequent generations highlight the importance of understanding, at each context, its mechanisms. As population health does not result only from personal choices, but from the contexts where individuals are born, raised and age, the need for countries commitment on ensuring a good start to life is reinforced [128,194].

1.3. Prenatal Care

In the 1920's prenatal care was recognised as an important strategy to ensure that women would go through pregnancy with minimum risk and would deliver under the most favourable obstetrical conditions. In opposition to the general idea that child's health was a postnatal concern – assuming that fetus development was independent of maternal health – some studies reported that child birthweight was related with maternal general conditions, particularly the hardships that she was exposed while pregnant [195]. Since then, prenatal care was established as a tool to monitor women's well-being and to ensure children a good start, aiming at the reduction of child mortality and morbidity, namely preterm and low birthweight. European (and particularly English) based models for prenatal care, including 12-16 visits were created and most of them remain as the structural basis for current practices [196]. Screening methods evolved with technology and were integrated in routine care, in addition to the existing measurements to evaluate pregnancy course [197].

Prenatal care is supposed to initiate early in pregnancy and, if possible, a pre-conceptional visit should be conducted for planning the future pregnancy and initiation of folic acid supplementation. Early initiation allows a correct dating of gestational age, early screening of possible underlying conditions, healthy lifestyles promotion and the assessment of women's social environment to identify possible constraints or facilitators of optimal pregnancy course. There is evidence that early initiation in care is related with a decrease risk of pregnancy complications and adverse birth outcomes.

The optimal prenatal care model is difficult to ascertain; most research evaluated the effectiveness of prenatal care assuming that timely access and the amount of care were the major contributors for successful prevention of adverse birth outcomes [198]. With this framework in mind, several indices were developed to measure prenatal care adequacy. One of the most used was the Kotelchuck modified version of the Kessner Index, the Adequacy of Prenatal Care Utilization Index (APNCU). This index, integrates the trimester of prenatal care initiation and the proportion of visits conducted in relation to what was recommended for the gestation length. In addition to the adequate, intermediate and inadequate resulting categories, this index includes the category adequate plus to refer to women receiving more than the recommended number of visits. This category was created to minimise the problem that high risk pregnancies are more likely to have more prenatal care visits, resulting in a positive association between the number of visits and the occurrence of adverse birth outcomes [199]. However, in settings where women may overuse prenatal care, the adequate plus category is a mixture of high risk and low risk pregnancies. More recently, some authors are trying to incorporate the content of care (such as ultrasound blood pressure measurements and blood screening) as important components of adequacy [200].

The effectiveness of implemented protocols is still controversial, and the association between prenatal care adequacy and adverse birth outcomes is far from being established. The underlying characteristics of women using prenatal care adequately, such as socioeconomic and clinical profiles, are likely to bias the estimated association and are a major limitation of the observational studies [201]. Several studies found that an increasing number of prenatal care visits was associated with a decreased risk of preterm and low birthweight [201]. However, few randomised controlled trials exist because of the emotive and ethical dilemma related with pregnancy, where the denial of care is out of question. Among seven trials, no evidence of an increased risk of adverse outcomes was found with an alternative routine protocol with a reduced number of visits for low risk pregnant women, although the absolute difference in the number of visits was small [198].

Timely access to care does not depend only on maternal will to attend care, but also on the structure and organisation of prenatal care, which is also dependent on the structure of health care systems. Increasing access to prenatal care, particularly by those in less privileged conditions is a public concern and, in the last decades, the proportion of women entering late in care significantly decreased in most countries. In the 1990's, European women used to start prenatal care earlier than in the United States and to have fewer visits during pregnancy [202], suggesting that universal access to prenatal care and established financial incentives could be facilitators of adequate pregnancy care. However, even among European countries, some barriers still exist at the end of the 1990's. At this time, a less favourable socio-demographic profile and aspects related with the organization of health care were significant barriers to attendance. In Portugal, unmarried women and those with unplanned pregnancies were more likely to enter late in care [203]. Another study found that, at this time, almost 20% of Portuguese women entered late in prenatal care and 15% had inadequate care during pregnancy. Late entrance and inadequacy of prenatal care were significantly associated with subsequent preterm and low birthweight deliveries, even taken into consideration maternal social profile [204]. However, 10 years later, we found that the prevalence of late care users had decreased to half (11%) and inadequate care was rare (4%) [141,205].

Despite the increased access to prenatal care observed in Portugal and in most countries, the trends in adverse non-fatal pregnancy outcomes have evolved in the opposite way [206]. As previously mentioned, most countries witnessed growing rates of preterm birth and low birthweight which increases the doubt on the efficacy and effectiveness of prenatal care. One of the questions relates to the medicalization of care, as observed at birth with the increasing use of labour induction techniques and caesarean deliveries. If prenatal care is becoming more medicalised, are the opportunities to modify lifestyles being left behind? These aspects may be intrinsically related with models of prenatal care provision, such as differentials between public and private settings, and also with the choice of providers: midwives, general practitioners and obstetricians may have meaningfully different approaches to care.

The other fundamental question relates with the equity in care. The first recommendation of the Commission on Social Determinants of Health is about the provision of "adequate social and health protection for women, mothers-to-be, and young families" [128]. It is not known if the public sector expenditure in universal programs of prenatal care is being able to decrease inequalities in pregnancy outcomes. Care should be delivered according the needs and specificities of low and high risk women, particularly those with worse social profile. Women with worse social profiles are more likely to be exposed to adverse risk factors and would probably need different levels of care and more visits than those with similar clinical conditions but more advantageous social circumstances. Equity in health implies that, in practice, access, quality and acceptability of care are guaranteed for all [123].

1.4. The Portuguese context

Over the past 50 years, the Portuguese society faced substantial social, cultural and economic changes, contrasting with the stagnant period of the beginning of the XX century. After being established as a republican state in 1910, Portugal was governed by a dictatorship between 1926 and 1974, the longest in the Western European setting. Since 1960, after joining the European Free Trade Association, Portugal longed for living standards and development indicators similar to those that were gradually attained by several developed countries. Economy rose after the 1974 revolution and was boosted with the integration in the European Union in 1986. After that, economic growth was intensified but slowed down to alarming levels after the incorporation in the Economic and Monetary Union and the consequent adoption of the Euro currency. As happened in some other countries, the 2008 international financial crisis was deeply felt in the country and, in 2011, Portugal received external assistance from the European Financial Stabilisation Mechanism.

Before this recent period of significant changes, the Portuguese society was characterised by very low levels of education. In 1970 more than 25% of the population over 10 years of age was illiterate, a proportion that decreased to 5% in 2011 (7% in women). Four years of formal education became compulsory for both sexes in 1960 and, in 1964, increased to 6 years, although only effectively assured in the late 1970's. In 1986, compulsory education increased to 9 schooling years and in 2009 up to 12 or up to the age of 18. Despite these increases Portugal is still one of the least educated countries in Europe. In 2011 about 50% of men and 60% of women between 25-34 years had attained upper secondary education. These figures are below the European ones and even far below the rates among older individuals in some of those countries [207]. Both secondary and tertiary education levels were more common among women than men, contrasting with a small proportion of women that achieved higher education in the 1960's. While less than 1% of resident women had tertiary education in 1960, in 2011 the proportion was 17% (and around 30% in the ages 30-34 years). Women delivering in Portugal seem to present a slightly higher education than the female population with the same age: in 2010 31% of delivering women between 15 and 44 years had tertiary education whereas this proportion was 26% in the total female population [11].

With increasing education, women's role in the Portuguese labour market also changed. Employment rate increased to almost 70% in 2008 (higher than the average in the European Union), corresponding to 50% of the active working population (39% in 1974). Not only the proportion of working women is higher than the average of the European countries, but the full-time employment rates are also higher (91% IN 2013) [208]. Since 2008, however, employment rates decreased reaching, in 2013, 62% of the female population. Despite large penetration in labour market Portuguese women still earn around 20% less than men for the same occupation skills [209], highlighting gender inequalities. Together with the overall mobility to higher levels of education also mobility in the socio-professional structure has occurred. For the same professional places, more qualifications are needed. However, the distance between position in the social hierarchy and employment and education opportunities seem to remain similar, which implies that no relative differences were observed despite the overall social mobility due to changes in education [210]. This pattern, however, is distinct for men and women, with latter presenting much higher upward mobility [211].

The increasing penetration of women in the labour market was also accompanied by changes in the structure of Portuguese families. The number of marriages decreased and the age at first marriage increased, particularly among women (from 25 years in 1960 to 30 years in 2013). The average number of individuals per family decreased from almost 4 in 1970 to 2.6 in 2011 [209]. As previously described, fertility rates have been declining since the sixties. Contrarily to other countries, in which parenthood postponement has been a crucial factor in fertility trends, in Portugal the pattern was somehow different. Women's age at the first child decreased until the early 1980's (from 25.0 years in 1960 to 23.5 in 1983) and only after that time started to increase (29.7 years in 2013). In terms of parents' support to combine work and family, in 1976, the Portuguese Constitution attributed 90 days of maternity leave. In 2003 it changed to 120 days (90 of which compulsory) and included a paternity leave. Since 2009, the mother has 120 days of maternity leave paid 100% that can be postponed until 150 days (paid 80%). Currently, Portugal is one of the few countries in the world with paternity leaves longer than 14 days (20 days of leave with the first 10 mandatory). Parental leave can be shared until 180 days [212]. Due to the current fertility rates and the economic constraints, new incentive birth policies are been discussed in the national parliament.

Simultaneously to the significant changes in the socio-demographic profile of the population in the last decades, substantial improvements in the access to health care also took place. In 1979 the National Health Service was launched, guaranteeing universal access to health care and health protection. In 1974, 94 medical doctors per 100,000 residents were available, while in 2012 the rate was of 418 per 100,000 residents. The investment was particularly relevant for general practitioners that correspond to 18% of all medical specialities [209]. The primary health care sector was extended, also increasing the proximity to the population and ensuring high coverage of prenatal care services.

Maternal and child health have been the cornerstone of the Portuguese public effort to improve population health (Figure 10).

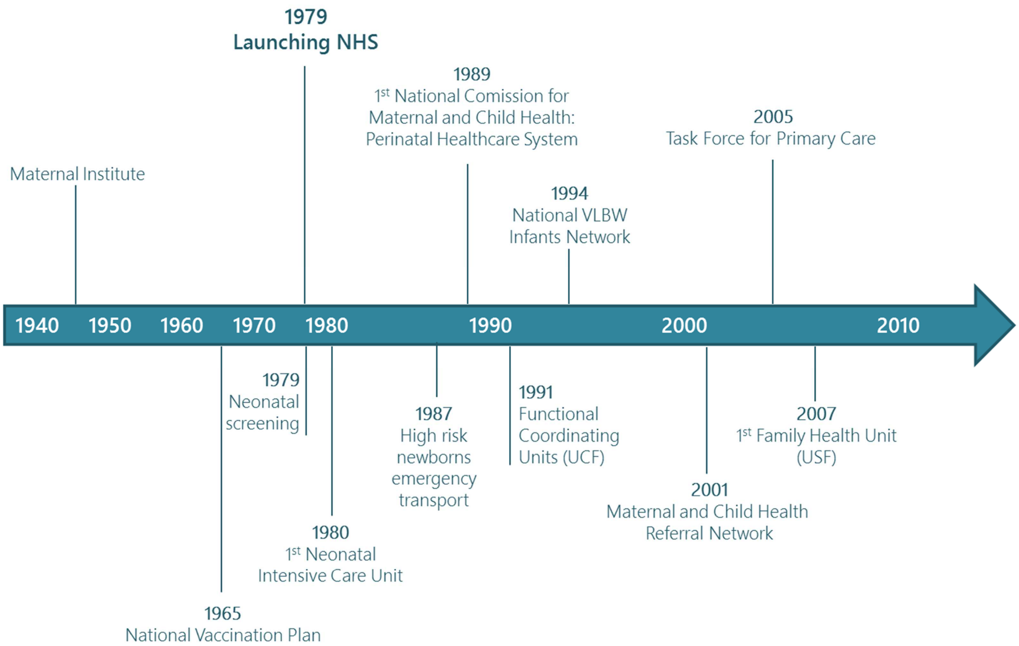

Figure 10 - Milestones in the Portuguese Maternal and Child Health Care Organization

In 1980 the first neonatal intensive care unit was created. In 1989, the establishment of the first commission on maternal and child health steered the Maternal and Child Health National Program. Since 1990, among other interventions, the program recommended the closure of maternity units with less than 1500 deliveries per year, the creation of functional coordinating units ("Unidades Coordenadoras Funcionais") between hospitals and primary health care centres, the setting up of special training in neonatology and the classification of hospitals as level I, II (with perinatal support) and III (with differentiated perinatal support). In 2001 was organised the Maternal and Child Health Referral Network establishing the link between primary health care centres, level II maternity units and level III hospitals [213]. In 2005, the Task Force for Primary Care was created aiming at launching the reform on primary health care. Within this work, health care centres were re-designed and the first Family Health Unit (USF) was created in 2007. These units are multidisciplinary, with organizational, functional and technical independence, and intend to provide better access, quality and continuity of care, increasing satisfaction of both patients and professionals [214].

In 2010, 90% of children born in facilities with more than 1500 deliveries per year (32% with more than 3000) and 93% of very preterm babies were delivered in level III units (differentiated perinatal support is now available at private clinics although contributing with less than 1% to all very preterm births) [30].

Pregnant women and children are entitled to free care at all the levels of care. Even so, in 2007 around one fourth of the population had other source of health insurance, provided by health subsystems or voluntary insurance [214]. Hospital deliveries increased from 15% in the 1960's to 99% in the 1990's but the prevalence of deliveries in private settings also increased, which currently contribute to 13% of all Portuguese births. Despite high rates of public hospital-based births, private prenatal care, provided by obstetricians, seems to be frequent as has happened with other medical specialities, mainly among more educated and wealthier women [215].

Concomitantly with the increasing trends in hospital-based births, the prevalence of caesarean also increased, representing 36% of all deliveries in 2010 (and reaching 67% in private settings) [30]. Portugal also presents high rates of vaginal instrumental deliveries (15% in 2010) and the highest European prevalence of episiotomy (73% in 2010) [30]. These figures contribute to making birth in the Portuguese setting highly medicalised and question about the contribution of non-medical factors to the increasing rates of obstetric intervention.

The increasing prevalence of caesarean deliveries precluded the achievement of the National target (24.8%) defined in the 2004-2010 National Health Plan. The plan evaluation report showed important improvements on several health goals, namely through the decreasing trends of perinatal mortality and of teenage pregnancies that account for less than 5% of all live births. However, other birth-related priorities remain a public concern. Preterm and low birthweight live births seem to be increasing and did not reach the 2010 targets of 4.9% and 5.8%, respectively. The proportion of women delivering at 35 years and over increased to 22% in 2010 but government targets were of 14.6% of all deliveries at this time [30,216]. The negative impact of these indicators on pregnant women and child health highlight the importance of monitoring these trends, and of investigating how these differences may be the result of inequalities in care. The evaluation of the previous National Health Plan also pointed out existing gaps in the Portuguese Health System to address health inequalities, namely those that are driven from socioeconomic disparities [216].

The Portuguese society remains profoundly unequal, with large social disparities between those at the more privileged conditions and those that remain in the bottom. Previous work recognised socioeconomic conditions to influence birth outcomes in the Portuguese setting [108,149], but several questions are still unsolved, namely those regarding the evolution of inequalities, their response to social changes and the role of other than individual features in these outcomes.

2. Objectives

The aim of this thesis is to understand how different spheres of social conditions affect reproductive and perinatal health in Portugal, a country that faced extraordinary social and cultural changes in the recent decades. Using national vital statistics and population-based research data we addressed three specific areas:

1. Macro socioeconomic influences in the frequency of adverse perinatal outcomes:

   1.1 To evaluate the accuracy of vital statistics in recent years comparing the evolution of preterm and low birthweight between official National data source and a hospital database;
   1.2 To describe how Portuguese reproductive and perinatal health indicators have evolved in the recent economic crisis;
   1.3 To assess the national trends in educational inequalities in preterm birth and low birthweight from 1992 to 2012;

2. Neighbourhoods and health care influences in pregnancy-related behaviours and outcomes:

   2.1. To estimate the effect of neighbourhood clustering and socioeconomic characteristics on preterm and small-for-gestational age births in urban areas from Portugal and Brazil;
   2.2. To evaluate whether public and private care users experience equality of pregnancy outcomes, taking into consideration maternal pre-pregnancy risk profile and social characteristics;

3. Individual socioeconomic circumstances influence on reproductive and perinatal outcomes considering previous social environments:

   3.1. To estimate the extent to which differences in small-for-gestational age according to maternal socioeconomic position and anthropometrics are explained by childhood social background;
   3.2. To estimate the relation between women's socioeconomic position and the occurrence of fertility impairment;

3. Participants and methods

This work was based in different data sources. The first three objectives (1.1-1.3) used the Portuguese vital statistics that collects data as part of the civil registration process; the first objective (1.1) also considered electronic birth data from a maternity unit in Porto, Portugal. All the other objectives were answered using data collected at the assembling of a population-based birth cohort in the North of Portugal: Generation XXI birth cohort (G21). Objective 2.1 also used data a Brazilian birth cohort study from Pelotas, Rio Grande do Sul: the 2004 Pelotas Birth Cohort Study.

3.1. Generation XXI (G21)

Generation XXI is a birth cohort study assembled during 2005 and 2006 in the Porto Metropolitan Region. The recruitment and follow-up evaluations are of the responsibility of the University of Porto Medical School and Institute of Public Health. It was established as a multi-purpose prospective population-based cohort that aims to chart the growth and development of children born at the dawn of the new millennium, and to address scientific questions as well as policy concerns.

The cohort comprises 8647 children (8495 mothers), born between April 2005 and August 2006 in the Porto Metropolitan Region (Figure 11) [217,218]. Recruitment was conducted at five public maternity units, responsible for 95% of the deliveries in the region at that moment. All resident women, delivering a live birth with more than 23 gestational weeks were eligible to be included. Among those invited (not all eligible mothers were invited due to logistic constraints, namely the availability of human resources: in these circumstances, women were invited in a basis of first come, first served), 8% of the mothers refused to participate. In all, 70% of the eligible mothers accepted to participate and to be followed. Within G21, a subgroup of participants (n=320 children, 313 mothers) was recruited prenatally when pregnant women went to their first hospital antenatal appointment at two of the included units (up to the 13th gestational week). Besides the evaluations conducted in all participants, these were also evaluated at each trimester [219]. After birth, children were re-evaluated at 4 and 7 years of age. Subgroups of participants were examined at 6, 15 and 24 months.

All the phases of the study complied with the Ethical Principles for Medical Research Involving Human Subjects expressed in the Declaration of Helsinki [220]. The study was approved by the University of Porto Medical School/ S. João Hospital Centre ethics committee and a signed informed consent according HelsinkiDeclaration was required for all participants.

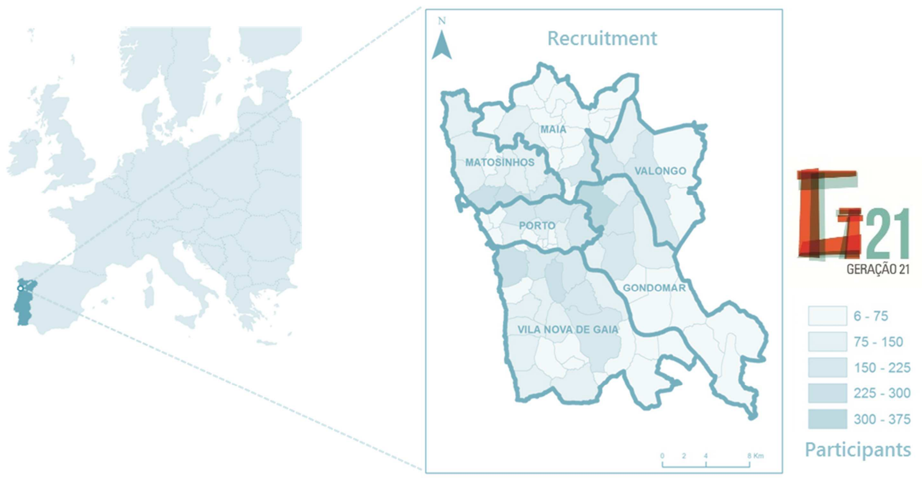

Figure 11 - Generation XXI participants' ditribution

At birth, participants were face to face interviewed between 24 and 72 hours after delivery by trained interviewers. Data were collected using standardised questionnaires on maternal socio-demographics, obstetric and gynaecologic history, planning and occurrence of the current pregnancy, prenatal care, lifestyles before and during pregnancy. Pregnancy complications, delivery- and newborn-related data were retrieved from the medical files by the same interviewers using standard forms. They also performed more detailed measurements of the newborns as well as of their parents (i.e. weight, height and head circumference) using standardised methods.

3.2. 2004 Pelotas Birth Cohort Study

Pelotas is a city located in the southern state of Rio Grande do Sul, Brazil. It has nearly 330,000 inhabitants and most deliveries occur in hospital facilities (>98%). The 2004 Pelotas Birth Cohort Study (Figure 12) is the third initiated in the city, after the assembling of the 1982 and the 1993 cohort studies [221]. Following the previous studies, 2004 birth cohort was conducted aiming to assess maternal, neonatal and child health characteristics, to evaluate the magnitude of changes in health status and its determinants and to address emerging health and developmental problems.

All births occurring in the city of Pelotas, from 1 January to 31 December 2004, were enrolled (n=4231). Eligible mothers included those living in the urban area of Pelotas according to the 1982 boundaries (part of the original city later became a separate municipality). They were interviewed soon after delivery using a standardized questionnaire and were measured with calibrated equipment. Subsequent follow-ups were carried out at 3 months, 1, 2, 4 and 6 years. The study protocol was approved by the Medical Ethics Committee of the Federal University of Pelotas and written signed consent form was required for all women.

At birth, as part of the socio-demographic characterisation, data on parents' age, household income, parent's education, occupation and employment were gathered. Women's obstetric history, prenatal care and pregnancy lifestyles and complications were also collected. Birth-related data, as pregnancy duration, birthweight or mode of delivery were retrieved from medical files.

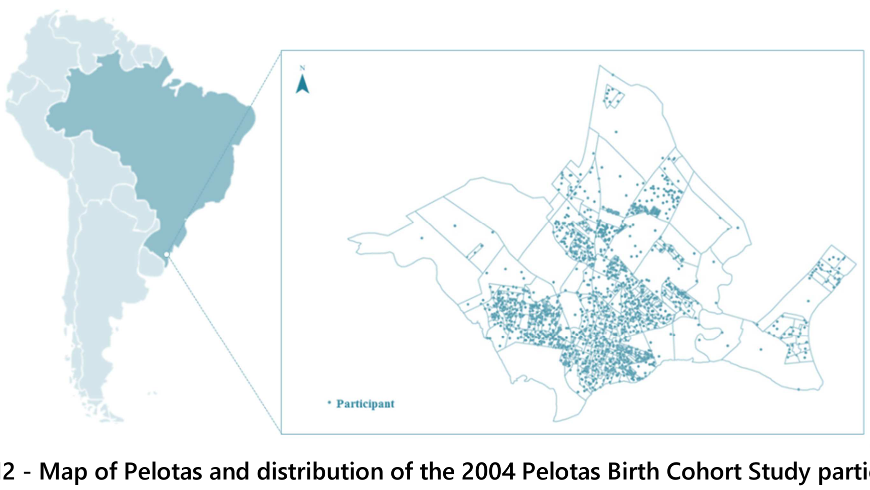

Figure 12 - Map of Pelotas and distribution of the 2004 Pelotas Birth Cohort Study participants

3.3. Vital Statistics and electronic birth data

Portuguese data on live births are routinely provided since 1935 [128]. Civil registration process is compulsory for all births occurred in Portugal. Since 2007, maternity units are equipped with an official from civil registry allowing the immediate birth registry. Since 2010, officials have direct access to the electronic forms for the birth registry.

In the birth certificates data on the child, mother and the father are collected. Parents provide their nationality, civil status, place of residence, highest academic level and occupation. Some data regarding women's earlier obstetric history are also collected as the number of previous live births, fetal deaths and miscarriages. For the index pregnancy, data on the number of fetus, pregnancy duration and birth assistance (from medical doctor, nurse, other or none) is registered. Child-related data include the sex of the baby, nationality and birthweight.

Birth certificates' forms were updated regularly in time. Changes allowed the inclusion of some variables, as the parents' nationality (only included in 1994) and the change of others, namely the information on pregnancy duration. Figure 13 presents parts of the most recent forms (1979 until now) used in the Portuguese birth registry regarding birthweight and pregnancy duration. Contrarily to birthweight that, for a long time is recorded as a continuous variable in grams, the registry of pregnancy duration changed in time. Between 1979 and 1993 the date of LMP or the number of completed gestational weeks was collected. Between 1994 and 1998, pregnancy duration was recorded as the number of completed weeks. Between 1998 and 2006 gestational age was no longer registered as a continuous variable but aggregated as less than 22, 22-27; 28-31; 32-36; 37-41 or more than 41 weeks. Although expiration date was December 2006 we were informed that only in 2010-2012 a new form was adopted. In 2010, birth registry started to be conducted in electronic forms that collected pregnancy duration as the number of completed gestational weeks. Methodological documents refer gestational age to be calculated according to the LMP although, in practice, ultrasound-based gestational age is routinely used [11].

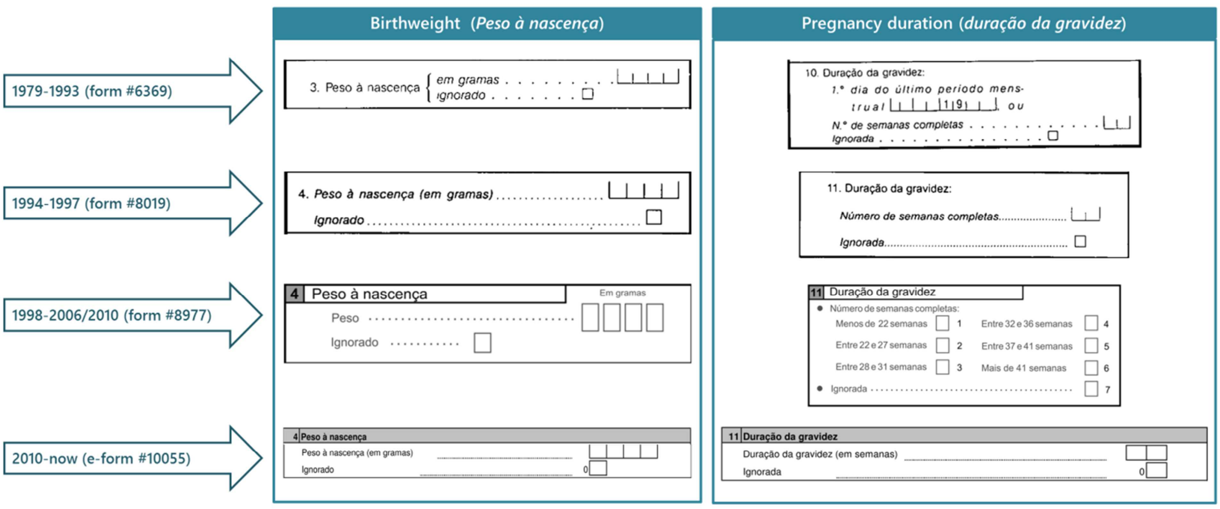

Figure 13 – Frames of the birthweight and pregnancy duration variables used in the Portuguese birth certificate forms (adapted from the Demographic Statistics at the National Statistics digital library [11])

Registry data is sent to the National Institute of Statistics that provide online summary tables with aggregated data and annually publishes a detailed report. Academic institutions are allowed to request individual data on the basis of submission of a protocol to conduct scientific research. Data are provided in anonymous datasets and researchers sign a confidentiality statement.

Although electronic medical records are being increasingly used in the Portuguese hospital context, they were not available at the time of conducting this work. However, in 2002, the Department of Gynecology and Obstetrics from S. Joao Hospital Centre (CHSJ), in the north of Portugal, designed a specific software designed *Obscare*. This software resulted in an electronic medical database that includes, in addition to socio-demographic characteristics of the parents and birth data collected as the one described for the civil registration, clinical data from the point of admission at the maternity through discharge after delivery. Data regarding prenatal care and the course of pregnancy is collected, as all medical diagnoses and procedures and newborn-related data referring to the moment of birth.

The summary of the studies' design conducted in the current work is presented in Figure 14:

PAPER	I	II	III	IV	V	VI	VII
DESIGN	Time-trend analysis	Ecological approach	Time-trend analysis	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional
MAIN EXPOSURES	Source of data	Time; GDP, women's unemployment rate	Time	Neighbourhood social class	Prenatal care provider	Education, marital status, height	Education, income, occupation
MAIN OUTCOMES	Preterm birth and Low birthweight	Live births, perinatal mortality indicators, Low birthweight	Educational inequalities in preterm birth and low birthweight	Preterm birth, SGA	Smoking, weight gain, preeclampsia, gestational diabetes, Preterm birth, SGA, LGA, caesarean	SGA	Infertility
STRATIFICATION	Year of birth			(Pelotas 2004: ethnicity)	Pre-pregnancy risk of adverse birth outcomes	Childhood social class, grandparents' education	Parity
DATA COLLECTION	2004-2011	2008-2013	1992-2012	2005/2006 + 2004	2005/2006	2005/2006	2005/2006
DATA SOURCE	Vital Statistics + *Obscare*	Vital statistics	Vital Statistics	G21 + Pelotas 2004	G21	G21	G21
SAMPLE SIZE	801,783 + 21,392		2,191,249	6,585 + 3,078	7,325	6,893	7,472

Figure 14 - Simplified diagram of study design and methodological characteristics of the included studies

GDP: Gross Domestic Product; SGA: Small-for-gestational age; G21: Generation XXI

4. Results

4.1. Valuing vital statistics: the case of preterm birth trends in Portugal

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(under review)

Authors' contributions: Sofia Correia was responsible for study design, analysis and interpretation of data, and first draft of the manuscript; Teresa Rodrigues interpreted the data and revised the manuscript critically for important intellectual content; Nuno Montenegro contributed to the acquisition of data and revised the manuscript critically for important intellectual content; Henrique Barros was responsible for study concept, interpreted the data and revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

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Conflict of interest: The authors report no conflict of interest.

ABSTRACT

OBJECTIVE: Using the national vital statistics, the Portuguese National Health Plan predicts that 14% of live births will be preterm in 2016. Prediction was based on preterm rise from 5.9% in 2000 to 8.8% in 2009. However, the same source showed a decline in preterm in 2010 and onwards. To assess if national preterm trends were plausible, we aimed to compare the evolution of preterm and low birthweight (LBW) between vital statistics and a hospital database.

DESIGN: time-trend analysis

SETTING: National birth certificates and maternity unit electronic data

SAMPLE: 801783 and 21392 data on singletons born between 2004 and 2011.

MAIN OUTCOME MEASURES: preterm (<37 gestational weeks) and LBW (<2500g)

METHODS: Annual prevalence, LBW prevalence among preterm sub-categories and ratio preterm:LBW were compared. Adjusted prevalence ratios were estimated to compare data sources.

RESULTS: While the national prevalence of preterm increased from 2004 (5.4%), particularly in 2006-2009 (7.5% in 2007), and decreased afterwards (2011: 5.7%), the prevalence on the maternity unit remained constant. Data sources were similar with the exception of the period 2006-2009: preterm was almost 1.4 times more frequent in the national than in the maternity unit. However, in this period, national LBW among preterm babies decreased, pattern not observed in the maternity unit data. Differences were only observed among moderate-late preterm.

CONCLUSIONS: The Portuguese preterm prevalence seems biased between 2006 and 2009, suggesting early term babies to be misclassified as preterm. Civil registration systems need innovative monitoring strategies to guarantee data quality to support effective public health strategies.

Key words: Preterm, Vital statistics; trends; low birthweight

BACKGROUND

Preterm related complications are the leading cause of neonatal mortality and contribute to child morbidity and long-term complications [1]. The Global Action Report on preterm birth calls for prevention to be accelerated [2]. Time trend analyses are of particular importance to direct and monitor public health interventions, despite difficulties in the registration of gestational age [3]. Most high income countries have reliable data available [4] some of which report continuous improvement over time [5]. A recent systematic review evaluated the quality of perinatal health databases regarding several conditions, procedures and outcomes. Authors found that hospital discharge databases are, in general, more accurate than birth data but birth registers showed high accuracy when considering preterm birth or low birthweight [6]. Still, due to the significant investment that prevention entails, one must assure that decisions are based on the best quality data.

Recently, in a time-trend analysis of preterm rates in several European countries using data from vital statistics, Portugal appeared as the third country with the highest increase in preterm births (7.0% in 1996, 5.9% in 2000, 6.8% in 2004 and 9.0% in 2008), while some countries managed to maintain or reduce their estimates [7]. Using the same data source, the WHO evaluation of the Portuguese National Health Plan 2004-2010 referred that preterm rate was one of the five indicators (among 64) worsening their performance between 2004 and 2008 [8]. Moreover, based on the increase of preterm from 5.9% in 2000 to 8.8% in 2009, the National Health Plan 2012-2016 anticipated (using exponential regression analysis) that preterm rate will reach 14% of all newborns in 2016 and targeted a rate reduction of 11% as one of the priority strategies [9]. However, in 2010 the rates of preterm birth decreased to 7.7% and remained relatively constant afterwards. Low birthweight showed a small and linear increase since 2000 (7.1% to 8.3% in 2010), not following the preterm pattern [10]. The preterm birth and low birthweight rates among singletons were similar to the ones mentioned above (Figure 1) which suggests that the increasing rates of multiple pregnancies [10] do not explain this pattern.

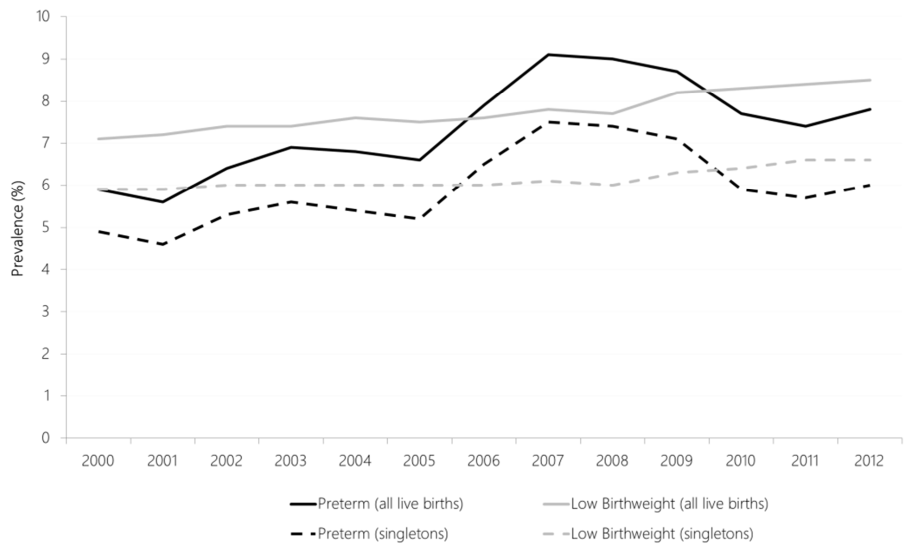

Figure 1 – Preterm birth and low birthweight rates between 2000 to 2012 in Portugal (from vital statistics, 2014 [10])

Additionally, during that period we are unable to detect changes in maternal risk factors, namely socio-demographic characteristics and in clinical obstetrical practices that would consistently explain the observed trend in preterm [10, 11]. Thus, the official preterm rates released from 2006 to 2009 lack a plausible clinical explanation and, unless random variation occurred, they suggest that predictions and subsequent prevention strategies may have been designed in the absence of good quality data.

We hypothesized that local time trends in preterm and low birthweight would follow the national pattern even if actual rates are different according to differentiation of care. Thus, aiming for a better understanding of Portuguese perinatal indicator trends and reinforcing that assuring data quality in birth registration is vital to ensure adequate utility of perinatal health indicators, we compared the national trend in preterm and low birthweight with the ones from a large university maternity unit in the North of Portugal that has a stable and quality assured registration process.

METHODS

National data on live births, routinely recorded in the birth certificates was anonymously provided by the National Statistics Institute for 2004 to 2011. Data are registered in the civil registration process that covers virtually 100% of births. Birth certificates include maternal and paternal socio-demographics (age, education, employment and occupation, marital status), maternal obstetric history (previous pregnancies and deliveries) and delivery and newborn data (health care assistance, single or multiple pregnancy, newborn gender, birthweight and duration of pregnancy). Most Portuguese maternity units do not have electronic medical records, particularly for the period considered. However, the department of obstetrics from S. Joao Hospital Centre (CHSJ), in the north of Portugal, developed specific software, designed *Obscare*, which has resulted in an electronic medical database (since 2002), providing data from the point of admission to the antenatal clinic, through delivery until discharge. In addition to the data collected at the birth registration, this database collects women's clinical history previous to conception, during pregnancy and post-natal and all the pre-labour, delivery and post-natal procedures. Anonymous data from all deliveries at CHSJ during the study period were obtained.

Both data sets were provided anonymously and no record linkage was possible. National data are provided by the National Statistics Institute on the basis of submission of a protocol to conduct scientific research by agreement between this entity and the author's academic institutions. Researchers signed a confidentiality statement and only Correia S accessed the dataset. The procedures were in accordance with the ethical standards of the Helsinki Declaration and national regulation (Law 46/2007). The study was approved by the ethics committee from the Institute of Public Health University of Porto (CE14020, 11 July 2014).

Duration of pregnancy was recorded in birth certificates as a categorical variable up to 2009 (<22; 22-27; 28-31; 32-36; 37-41; >41 gestational weeks) and, from 2010, is registered by week. Preterm was defined as a gestational age less than 37 weeks. Very preterm was defined if less than 32 gestational weeks and moderate-late if between 32 and 36 gestational weeks. In both systems, birthweight is recorded as a continuous variable. Low birthweight was further classified as below 2500g.

Women delivering singleton live births with complete data on birthweight and gestational age at birth were included: 801 783 women from the civil registration (99.7% of all live births in the registry) and 21 392 from the maternity unit (94.6%). For each data source we estimated the annual prevalence of preterm, moderate-late and very preterm births, as well as of low birthweight of term and preterm sub-categories. For each year, the ratio between preterm prevalence and low birthweight prevalence was estimated. In order to understand the reasons for possible differences in trends we also compared the annual proportions of older (≥ 35 years), less educated (≤ basic schooling), unemployed and primiparas (women with no previous deliveries) according to the data source. Obstetrical interventions are not registered in birth certificates. Thus, the maternity unit prevalence of caesarean deliveries was compared with national estimates using data from the annual hospital inquiries conducted by the National Statistics and from the General Directorate for Health [11]. Annual preterm and low birthweight prevalence ratios (PR and respective 95% confidence intervals (95% CI)) were estimated by Poisson regression to compare data sources, using the maternity unit as the reference class. Prevalence ratios were adjusted for maternal age, education, employment status and parity to minimise the confounding effect of maternal characteristics. Civil registration does not include the hospital of birth. Sensitivity analyses were performed restricting the civil registration data for resident women from the Porto Metropolitan region (n=101 858), the catchment area for CHSJ. All the results are available upon request.

RESULTS

While the national prevalence of preterm birth among singletons increased since 2004, particularly between 2006 and 2009 (7.5% was the highest prevalence recorded in 2007), and decreased in 2010 and 2011, the maternity unit study did not present the same pattern. After a decrease from 2005 to 2006 (6.6% to 5.2%), the prevalence remained constant up to 2010. Between 2006 and 2009, the ratio preterm:low birthweight increased from around 0.9 to 1.23 in the national data, while it remained constant in the maternity unit. National low birthweight rates were lower for all the considered years but the trends were similar to those observed using the maternity unit data (Table 1).

Table 1 – National and maternity unit prevalence of preterm, low birthweight (LBW) and maternal risk factors for singleton live births between 2004 and 2011

	Year of birth							
	2004	2005	2006	2007	2008	2009	2010	2011
National data								
n	*105,930*	*106,074*	*102,156*	*99,416*	*100,455*	*96,018*	*98,015*	*93,719*
Preterm (%)	5.4	5.2	6.5	7.5	7.4	7.0	5.9	5.7
Low birthweight (%)	6.0	6.0	6.0	6.1	6.0	6.3	6.4	6.6
Ratio Preterm:LBW	0.90	0.87	1.08	1.23	1.23	1.11	0.92	0.86

		Year of birth							
		2004	2005	2006	2007	2008	2009	2010	2011
≥ 35 years (%)		15.6	16.2	17.3	18.1	19.1	20.2	21.6	23.7
≤ basic schooling (%)		52.3	49.8	47.5	46.3	44.7	42.6	40.2	37.0
Unemployed (%)		6.9	7.8	9.9	11.6	10.9	12.8	12.8	12.6
Primiparas (%)		54.1	54.3	54.3	54.0	53.9	54.3	53.3	53.6
Cesarean deliveries (%)		33.1	34.7	35.1	35.4	36.0	36.7	36.3	35.8
Maternity unit data									
	n	*2,712*	*2,598*	*2,426*	*2,486*	*2,745*	*2,750*	*2,918*	*2,757*
Preterm (%)		6.7	6.6	5.2	5.5	5.5	5.4	5.7	6.3
Low birthweight (%)		7.4	7.2	6.4	6.4	7.0	7.4	7.4	7.3
Ratio Preterm:LBW		0.90	0.92	0.81	0.86	0.78	0.73	0.77	0.86
≥ 35 years (%)		16.1	17.4	19.7	19.7	19.7	21.3	22.2	23.5
≤ basic schooling (%)		51.6	47.2	47.7	47.2	45.4	41.8	38.9	38.8
Unemployed (%)		11.5	13.4	14.0	14.1	15.3	15.7	17.1	16.6
Primiparas (%)		56.5	56.8	56.6	58.2	59.2	59.1	59.2	56.0
Cesarean deliveries (%)		27.5	29.5	26.8	27.4	28.7	27.9	27.4	29.7

The trends of maternal characteristics were similar in both settings. As observed in Table 1, the prevalence estimates of older age and of less educated women were almost the same throughout the years. Despite higher prevalence of primiparas and unemployed women and lower prevalence of caesarean deliveries in the maternity unit, the trends were similar.

In Figure 2 we present the prevalence of very preterm and moderate-late preterm according to the data source. Very preterm rates were similar in both data sources. Moderate-late preterm was less frequent in the national data in the first and the last years. From 2006 to 2009 the estimates were around 30 to 40% higher than in the maternity unit.

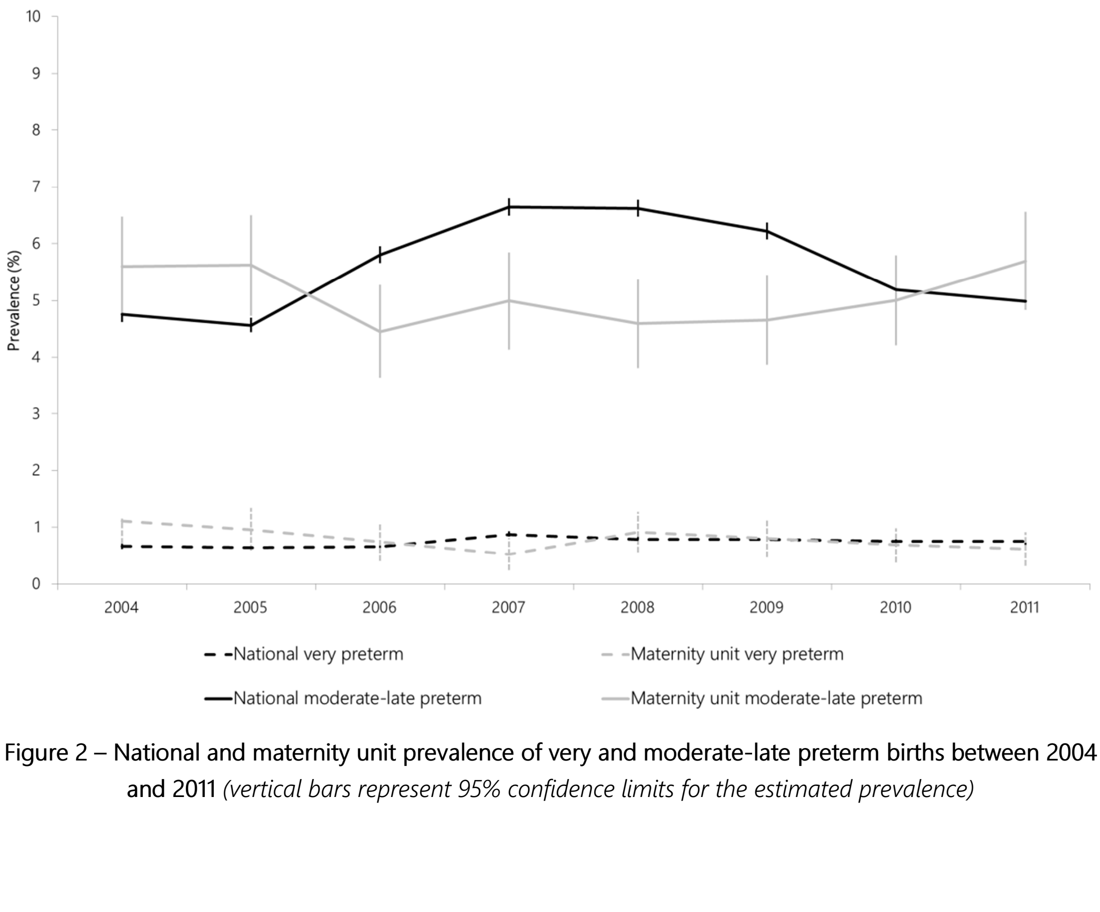

Figure 2 – National and maternity unit prevalence of very and moderate-late preterm births between 2004 and 2011 *(vertical bars represent 95% confidence limits for the estimated prevalence)*

However, in this period, among moderate-late preterm babies, the national prevalence of low birthweight decreased and was 24% to 40% lower than the one reported in the maternity unit. No differences were found for low birthweight among very preterm babies (Figure 3).

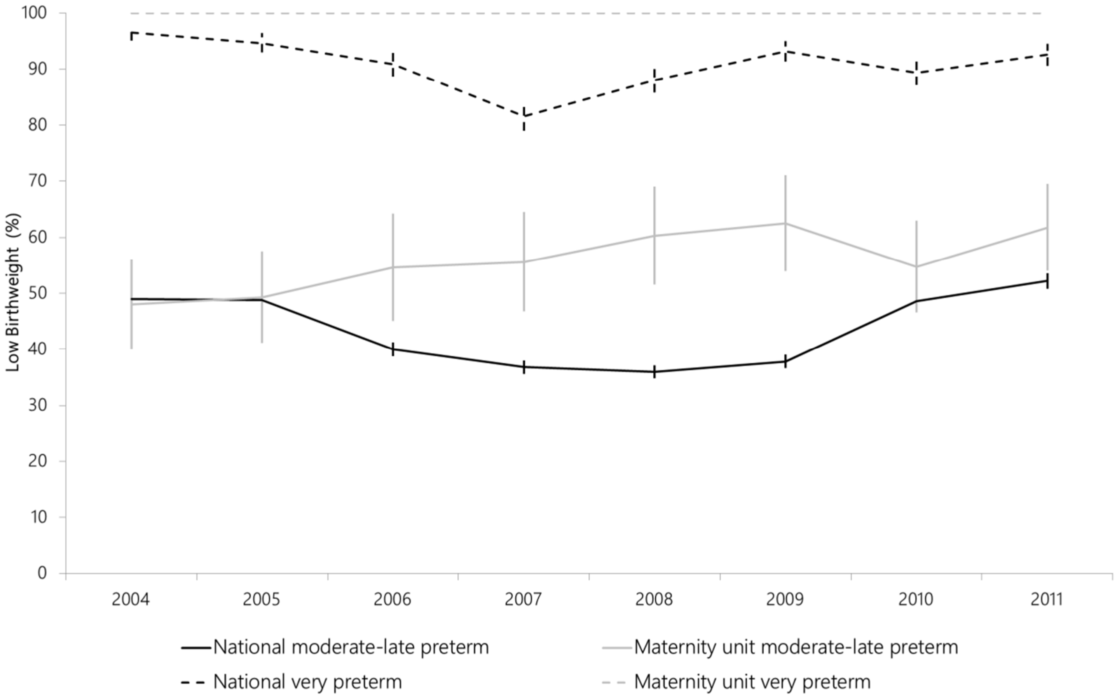

Figure 3 - National and maternity unit prevalence of low birthweight between 2004 and 2011 among preterm babies by gestational age categories

(vertical bars represent 95% confidence limits for the estimated prevalence)

Independently of maternal characteristics the singletons' preterm birth and low birthweight estimates were similar in both data sources in the years 2004, 2005, 2010 and 2011. During the period 2006-2009, national preterm was almost 1.4 times higher in the national statistics than in the maternity unit but no differences were found for low birthweight (Table 2).

Table 2 – Annual relation between adverse birth outcomes and the data source, taking the maternity unit as reference

	Year of birth							
	2004	2005	2006	2007	2008	2009	2010	2011
Prevalence Ratios [a] (95% CI)								
Preterm								
Crude	0.81 (0.70,0.94)	0.79 (0.68,0.92)	1.24 (1.04,1.48)	1.36 (1.15,1.61)	1.35 (1.15,1.58)	1.28 (1.09,1.51)	1.04 (0.89,1.22)	0.91 (0.78,1.06)
Adjusted [b]	0.85 (0.73,1.00)	0.82 (0.70,0.97)	1.37(1.14,1.66)	1.44 (1.21,1.72)	1.40 (1.18,1.65)	1.33 (1.12,1.58)	1.10 (0.94,1.29)	0.99 (0.80,1.23)
Low birthweight								
Crude	0.82 (0.71,0.94)	0.83 (0.72,0.96)	0.94 (0.80,1.10)	0.96 (0.82,1.12)	0.86 (0.74,0.99)	0.86 (0.75,0.99)	0.86 (0.75,0.99)	0.90 (0.78,1.03)
Adjusted [b]	0.84 (0.73,0.98)	0.85 (0.73,1.00)	0.97 (0.82,1.15)	1.01 (0.86,1.19)	0.88 (0.76,1.02)	0.90 (0.78,1.05)	0.92 (0.80,1.06)	0.99 (0.81,1.20)

[a] Reference class: maternity unit; [b] Adjusted for maternal age, education, employment status and parity

COMMENTS

Using one large maternity unit as the comparison, this study found similar national low birthweight trends but a different pattern for preterm rate. Differences were observed for the years 2006 to 2009 and mainly for moderate-late preterm.

Despite the difficulties in the gestational age appraisal, namely its accuracy and standardized methods of estimation [5, 12, 13], we do not expect that the observed differences would be influenced by the assessment heterogeneity. First, because civil registration process uses the data registered in the medical forms and so, the estimation process is probably the same in vital statistics and in the maternity unit dataset. Second, because ultrasound-based gestational age is the recommended estimation method since 2001 and is expected to have been widespread in most settings in 2004 and onwards. Thus, a degree of registry error may have influenced the estimates. Birth certificate forms have periodical changes to include new variables or change the existing ones. Regarding pregnancy duration, up to 1994, gestational age was recorded as a continuous variable (by week) and based on the last menstrual period. Since 1994 no reference to the method of estimation was present in the forms. Between 1998 and 2006, the new form imposed gestational age registration to be categorized, affecting its precision but increasing the validity of data. In 2006-2007, the use of electronic civil registration forms was implemented. However, the forms used in the period 2007-2009 (in 2010 gestational age was recorded again as a continuous variable) are not available and we do not know how gestational age was registered. We assume it was recorded as a categorical variable, although any potential error on the definition of each category is not possible to ascertain.

The distinct pattern observed for low birthweight suggests that the observed national increase in preterm birth rate may be a data artefact. The overall low birthweight trends were similar in both data sources suggesting that maternity unit data is reflecting national trends, despite higher estimates because of its differentiated level of care (CHSJ is one of the largest maternity units in the country classified as level III – differentiated perinatal care hospital). Also, the ratio preterm:low birthweight remained constant in the maternity unit data (varying between 0.77 and 0.92) and, nationally, in the periods before and after 2006-2009 (varying between 0.86 and 0.92). The national increase in 2006-2009 (varying between 1.08 and 1.23) suggests record errors. Finally, the prevalence of low birthweight among preterm babies decreased from 54% in 2005 to 41-45% in the period 2006-2009 and increased again to 54% in 2010. Thus, a systematic error in 2006-2009 on the classification of early term babies as preterm, who were not low birthweight, may explain why national preterm rate increased but low birthweight among preterm decreased in this period.

Apart from a registry error, we could only accept the observed national preterm trend as true if significant changes in the social profile and maternal characteristics, in the obstetrical protocols (mainly those related to iatrogenic preterm delivery) or in the referral of cases had occurred.

Maternal characteristics did not explain the results. As observed in this study, women delivering at S. João Hospital Center were similar to the country pregnant population. Despite presenting a higher prevalence of unemployed and primiparas, the trends regarding age, education, unemployment and parity were similar to the ones observed using civil registration data. Although we do expect other maternal characteristics (such as smoking habits, weight gain or pregnancy complications) to present trends congruent with the national preterm pattern, no perinatal database is available in the country to allow such comparisons.

According to what we have previously found for the induction procedures among level III hospitals from the Porto Metropolitan Region [14], country variation in obstetric practice is expected. However, induction practices are more likely to vary for term babies which will decrease the impact on the preterm prevalence. We do not have national data on induction techniques and we can only compare the caesarean trends. Although national caesarean rates were higher than the ones observed at S. João Hospital Center, particularly since 2005, the difference remains consistent for all years considered and the pattern does not change for the years 2006 and 2009, not explaining the differences in preterm birth rates.

The higher national preterm prevalence between 2006 and 2009 could also be explained if more preterm pregnancies had been referred from the S. Joao Hospital Center to other maternity units during this period. Maternal and neonatal health care services were restructured in 2006 which resulted in the closure of delivery units with less than 1500 deliveries per year, in the increase of high risk in-uterus transfers (not only after birth) and in the creation of more highly differentiated perinatal facilities. So, these changes are more likely to have affected the very preterm estimates than the moderate-late preterm estimates and are likely to affect the estimates since that date and not only for the period 2006-2009. Finally, we only considered singleton live births, excluding one of the possible reasons for the increasing rates of preterm birth [15].

This analysis has the limitation of comparing all Portuguese births with only one maternity unit (2.7% of all deliveries) that might be significantly different from the rest of the country. However, the parallel trend in all the other characteristics besides preterm strengthens the results and increases the validity of the study. In the sensitivity analysis we considered only women living in the Porto Metropolitan Region, which comprises the catchment area for this maternity unit, and similar results were obtained (data not shown). Although women from the Porto Metropolitan Region might have delivered at one of the four other maternity units serving the area, similar results would have been expected if we could have linked the datasets.

These results have important implications when used to inform public health strategies towards a reduction in preterm birth rate and suggest caution should be urged when comparing and interpreting differences observed in preterm birth rates between different countries. National routine data are used by different national and international entities that monitor perinatal health, such as the World Health Organization [16] or European health information projects [17] reinforcing that one must assure its high quality.

The overall preterm birth rate seems to be increasing and, in fact, did not reach in 2010 (7.7%, 5.9% in singletons) the goal of the National Health Plan 2004-2010 (4.9%). The preterm birth rate is no longer expected to reach 14% in 2016 as forecast by the National Health Plan 2012-2016, a forecast that had been based on official trend data published for the years 2000-2009. The National Plan 2012-2016 had also targeted a reduction to a preterm birth rate of 11%. Our results indicate that this target can now be considered overly conservative. Our results are also relevant to re-define methods of data gathering and reporting. Perinatal datasets or data linkage processes are useful to timely validate the estimates using also clinical data. Civil registration systems, of undoubted value

[6, 18], need innovative monitoring strategies to guarantee high quality health indicators to support effective public health strategies.

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4.2. Reproductive and perinatal health after the economic crisis in Portugal

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Periods of economic contraction may induce changes in reproductive patterns and also influence maternal behaviour, fetal and neonatal health [1]. Several European countries, particularly those that sought for financial assistance from the European Financial Stabilisation Mechanism, have been reporting a severe decline in the birth rate during the recent economic crisis [2, 3].

Contrarily to Greece and other countries that presented increasing birth rates before the crisis [4], in Portugal, the number of live births has been declining on average by 2% per year since the end of the 1970's (with an exception of a small increase at the end of the 1990's, partly attributed to an increase of immigrants [5]). The steepest decline however, has been observed in recent years. After 2008, the annual decrease was, on average, 4.5% and peaked in 2013 with the lowest ever number of live births for a century – 82,787 (21% fewer than in 2008) (Table 1).

Table 1 – Demographic, mortality and morbidity indicators in Portugal between 2000 and 2013

Year	Childbearing women (n) [a]	Live births (n)	GFR (/1000 women) [b]	Mortality indicators			Low birthweight [f]	
				Fetal mortality [deaths (rate)] [c]	Neonatal mortality [deaths (rate)] [d]	Infant mortality [deaths (rate)] [e]	All live births [n(%)]	Singletons [n(%)]
2000	2618375	120008	45.93	692 (5.73)	410 (3.42)	662 (5.52)	8485 (7.1)	6857 (5.9)
2001	2621836	112774	43.04	659 (5.81)	332 (2.94)	567 (5.03)	8097 (7.2)	6493 (5.9)
2002	2622505	114383	43.62	587 (5.11)	391 (3.42)	574 (5.02)	8386 (7.4)	6709 (6.0)
2003	2617788	112515	42.94	506 (4.48)	304 (2.70)	466 (4.14)	8272 (7.4)	6505 (5.9)
2004	2606964	109298	41.84	423 (3.86)	282 (2.58)	420 (3.84)	8290 (7.6)	6377 (6.0)
2005	2594476	109399	42.06	432 (3.93)	242 (2.21)	384 (3.51)	8204 (7.5)	6380 (6.0)
2006	2584204	105449	40.72	414 (3.91)	224 (2.12)	349 (3.31)	8012 (7.6)	6170 (6.0)
2007	2573785	102492	39.74	376 (3.66)	213 (2.08)	353 (3.44)	8017 (7.8)	6110 (6.1)
2008	2559524	104594	40.75	341 (3.25)	216 (2.07)	340 (3.25)	8008 (7.7)	6080 (6.0)
2009	2544248	99491	38.99	379 (3.79)	245 (2.46)	362 (3.64)	8124 (8.2)	6096 (6.3)
2010	2522955	101381	40.01	332 (3.26)	169 (1.67)	256 (2.53)	8416 (8.3)	6306 (6.4)
2011	2494438	96856	38.61	294 (3.03)	230 (2.37)	302 (3.12)	8135 (8.4)	6186 (6.6)
2012	2457261	89841	36.29	327 (3.63)	198 (2.20)	303 (3.37)	7644 (8.5)	5753 (6.6)
2013	2421288	82787	33.94	245 (2.95)	161 (1.94)	244 (2.95)	7165 (8.7)	5442 (6.8)

[a] Number of resident women aged between 15 and 49 years
[b] GFR (General Fertility Rate) – number of live births per 1000 childbearing women´
[c] Fetal deaths (compulsory registry at or after 24 gestational weeks) expressed per 1000 live births plus stillbirths
[d] Death of live births up to 28 days after birth expressed per 1000 live births
[e] Death of live births up to 365 days after delivery expressed per 1000 live births
[f] Prevalence of low birthweight excludes missing values for birthweight (<1%)

Several factors play a role in understanding this decrease. Part of the decline seems to reflect emigration of women of childbearing age (15-49 years), particularly those between 25-34 years: when compared to resident women in 2008, a 17% decrease was observed in 2013. Based on the general fertility rate formula (number of live births divided by the number of women of childbearing age), we would have expected 4,000 additional births in 2013 if the resident population remained as the one observed in 2008. Within emigrating residents, most (64% in 2012 [6]) are individuals with the citizenship of the Member State to which they are migrating (return migration), which may also explain the decrease in the number and in the proportion of foreign women delivering in the country (10,238 in 2008 to 7,405 in 2013). Together with the emigration of national and foreign women in reproductive ages, personal behaviours towards childbearing seem to have changed in the last years. Even with a reduced resident population, if the general fertility rate remained constant to the one observed in 2008 (40.8/1000 rather than 33.9/1000 in 2013), 15,880 more children (+19%) would have born (appendix). Until 2008, improvement of economic indicators (as GDP) was strongly related with decreasing fertility rates (rho=-0.90); after the economic crisis this relation was strongly attenuated and it is possibly moving in the opposite direction (rho=0.44), although GDP has not significantly changed since then (Figure).

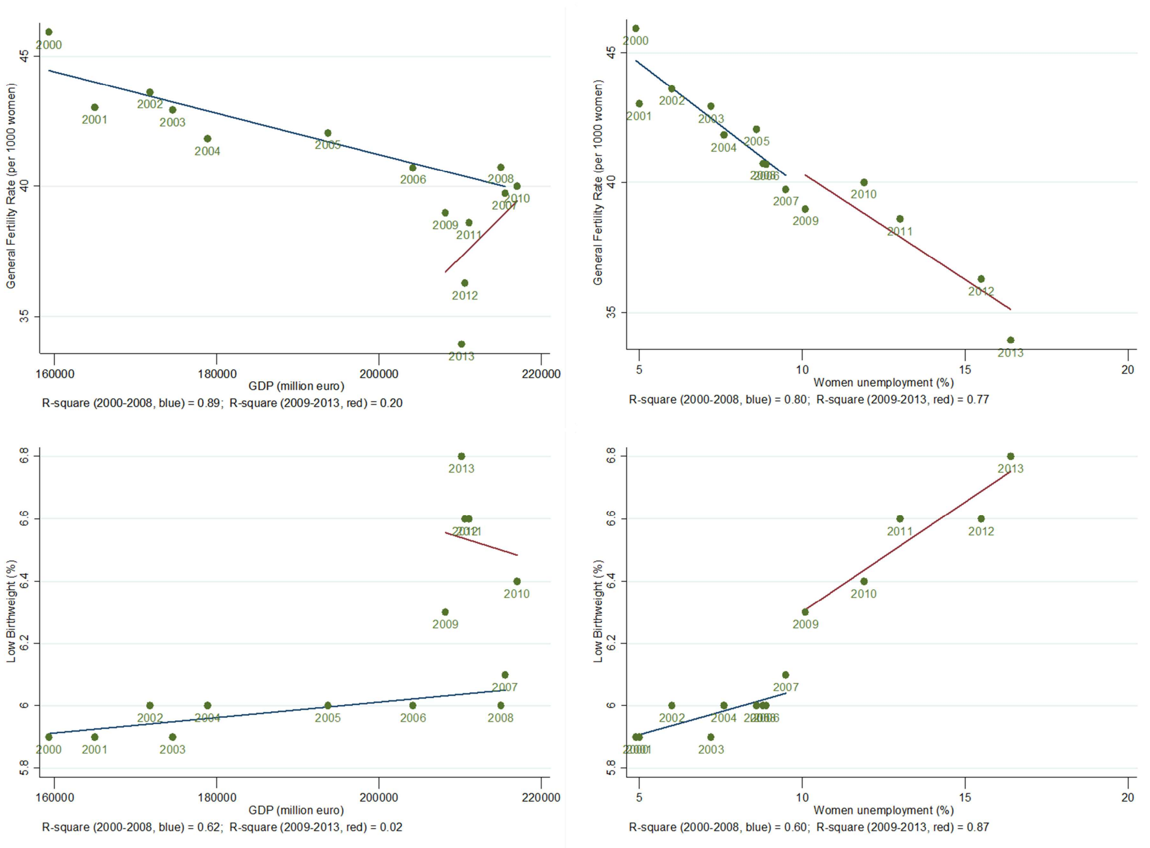

Figure – Fertility rate and low birthweight by the national Gross Domestic Product and by the proportion of unemployed women in Portugal between 2000 and 2013

Parallel to the long-term societal impact of such dramatic reduction in the birth rate, mortality indicators and fetal and children's health are likely to be compromised. Following the massive decline in the Portuguese maternal and infant mortality during the last 40 years, an annual average decline in perinatal mortality of about 5% has been observed since 2000. In 2013 the rates were below the ones prior to the economic crisis (Table 1).

Regarding babies at risk, as observed in the Table 1, Portuguese overall low birthweight (<2500g) rate has steadily increased by 21% since 2000 (7.1% in 2000 and 8.6% in 2013). Part of the increase was related with multiple pregnancies since a constant incidence rate among singletons was observed until to 2008 (5.9%-6.1%). Afterwards, it has been increasing and reached 7% in 2013 (more 12% than in 2008). Maternal age did not fully explain this change: a constant annual 5% increase in older mothers (≥35 years) has been observed since the 2000's (13% in 2000, 19% in 2008 and 26% in 2013) and the prevalence of low birthweight increased mostly among younger women (below 35 years). Therefore, it seems that economic contraction has been followed by changes in the nutritional and behavioural patterns. Current economic environment does not seem to be related with increasing low birthweight (rho=-0.15). However, since 2008, women's unemployment seems to show a stronger relation with low birthweight than prior to the economic recession (Figure, rho2000-2008=0.82; rho2009-2013=0.97).

In summary, in Portugal we are observing an unfavourable combination of fewer births accompanied by a higher proportion of babies at increased risk, as measured by low birthweight. Even so, mortality patterns remain declining, which may underlie a buffering effect of the National Health Service. It is therefore crucial that further monitoring of perinatal indicators and subsequent research of possible implicated macro socioeconomic features is undertaken.

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Appendix file

Estimation of the predicted number of live births

The calculation was based on the formula:

General fertility rate (GFR) =

(Number of Live births / Number of childbearing women)*1000 childbearing women

1. **General population**

   a) **Number of childbearing women kept constant as the 2008 estimates**

Year	Observed			Predicted No. Live births	Predicted-Observed (%)
	Live Births (n)	GFR (/1000 women)	Childbearing women (n)		
2008	104,594	40.75	**2,559,524**		
2009	99,491	38.99	*2,544,248*	99,796	305
2010	101,381	40.01	*2,522,955*	102,407	1,026
2011	96,856	38.61	*2,494,438*	98,823	1,967
2012	89,841	36.29	*2,457,261*	92,885	3,044
2013	82,787	33.94	*2,421,288*	86,870	**4083 (+4.9%)**

(Predicted number of Live births = GFR/1000 * Number of childbearing women 2008)

   b) **General fertility rate (GFR) kept constant as the 2008 estimates**

Year	Observed			Predicted No. Live births	Predicted-Observed (%)
	Live Births (n)	GFR (/1000 women)	Childbearing women (n)		
2008	104,594	**40.75**	2,559,524		
2009	99,491	*38.99*	2,544,248	103,678	4,187
2010	101,381	*40.01*	2,522,955	102,810	1,429
2011	96,856	*38.61*	2,494,438	101,648	4,792
2012	89,841	*36.29*	2,457,261	100,133	**10,292**
2013	82,787	*33.94*	2,421,288	98,667	**15,880 (+19.2%)**

(Predicted number of Live births = GFR_{2008}/1000 * Number of childbearing women)

2. By maternal age (for 2013)

c) Number of childbearing women kept constant as the 2008 estimates

Age	Observed			Childbearing women in 2008 (n)	Predicted No. Live Births	Predicted-Observed (%)
	Live Births (n)	GFR (/1000)	Childbearing women (n)			
15-19	2808	10.65	267655	283674	3021	213 (+8%)
20-24	9254	32.86	279329	300409	9871	617 (+7%)
25-29	20050	66.9	294052	360022	24085	4035 (+20%)
30-34	28833	79.79	354864	419088	33439	4606 (+16%)
35-39	17908	42.36	419465	406154	17205	-703 (-4%)
40-44	3680	9.07	407787	398779	3617	-63 (-2%)
45-49	193	0.5	398136	391398	196	3 (+1%)

(Predicted number of Live births = GFR/1000 * Number of childbearing women 2008)

d) General fertility rate (GFR) kept constant as the 2008 estimates

Age	Observed			GFR in 2008 (/1000)	Predicted No. Live Births	Predicted-Observed (%)
	Live Births (n)	GFR (/1000)	Childbearing women (n)			
15-19	2808	10.65	267655	16.17	4328	1520 (+54%)
20-24	9254	32.86	279329	47.33	13221	3967 (+43%)
25-29	20050	66.9	294052	79.67	23427	3377 (+17%)
30-34	28833	79.79	354864	86	30518	1685 (+6%)
35-39	17908	42.36	419465	42.01	17622	-286 (-2%)
40-44	3680	9.07	407787	7.82	3189	-491 (-13%)
45-49	193	0.5	398136	0.44	175	-18 (-9%)

(Predicted number of Live births = GFR_{2008}/1000 * Number of childbearing women)

4.3. Educational inequalities in preterm birth and low birthweight in Portugal: a time trend analysis from 1992 to 2012

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ABSTRACT

BACKGROUND: It is well recognised the effect of contextual socioeconomic environment on birth outcomes. Thus, we aimed to evaluate any social impact of the recent economic crisis, analysing the trends in educational inequalities in preterm and low birthweight in Portugal.

METHODS: We used individual data of 2,191,249 Portuguese singletons between 1992 and 2012. Preterm birth and low birthweight were defined, respectively, as bellow 37 weeks of gestation and bellow 2500g. Age- and parity- adjusted absolute (SII) and relative (RII) indices of inequality with 95% confidence intervals were estimated for each 3-years intervals.

RESULTS: During the study period, less educated women presented higher prevalence of both adverse outcomes. Until 2000, preterm decline was larger among less educated women (-36% vs. -25% in more educated), narrowing relative inequalities. The educational gap increased in 2001-03 but remained stable until 2012 (RII=1.35; 95%CI 1.27-1.44). Very preterm births showed larger educational inequalities than moderate-late preterm births.

Low birthweight increased in all education strata, especially in more educated women (+57% vs. +39% in low educated). Absolute and relative educational inequalities in low birthweight were larger than in preterm. Despite a significant increase in absolute differences with time ($p<0.001$), relative inequalities in 2012 (RII=1.71; 95% CI: 1.61-1.81) were not significantly different from the early 2000's.

CONCLUSION: Educational inequalities in adverse birth outcomes declined during the economic growth in the 1990's. After increasing again in the early XXI century, inequalities remained stable and no evident effect of recent economic crisis was observed.

Keywords: Education; preterm; low birthweight; trends; inequalities

INTRODUCTION

Preterm birth and low birthweight (LBW) are two major predictors of newborns' health [1]. The frequency of preterm birth has been reported to be increasing in several settings [2], although a decline was observe in some European countries during the last 15 years [3]. Similar trends were observed in LBW [4-6]. In Portugal preterm birth and LBW have been increasing reaching, respectively, 7.8% and 8.6% of all live births in 2013 [7].

Socially deprived women are at increased risk of delivering preterm or LBW babies. Smoking, nutritional factors and health care uptake have been described as possible reasons for social inequalities in birth outcomes [8] but time and space persistent inequalities suggest that other features may be involved. Thus, given the lifelong impact of preterm and LBW [9] and its potential to prevention, monitoring social inequalities in these outcomes is of outstanding importance. There is limited evidence on the time-trends of social inequalities in perinatal morbidity and how this change reflects country-specific macroeconomic characteristics. During the latest 20 years of the 20th century, educational gap in preterm did not change in Norway [10], but seems to have decreased in New Zealand [11]. In Scotland, inequalities in birthweight decreased in the eighties and increased in the nineties [6] while no changes were observed in relation to preterm [12].

In periods of economic crisis, health and health equity may be impaired [13] by individual constraints and societal changes [14]. However, it is also possible that positive selection into pregnancy (i.e., social distribution of those who become pregnant moves towards the right, to the top of the hierarchy) and the availability of health care services result in similar or better perinatal health outcomes and in a reduced social gap [13, 14]. During the 1980's recession, Danish inequalities in fetal growth increased but no changes were observed in Finland or Sweden [15] contributing to the inconsistent findings in the associations between economic contraction and birthweight [16].

Over the past 50 years, Portugal faced impressive socioeconomic and cultural changes. After the 1960's, and particularly after the democratic revolution in 1974, living conditions improved and the number of compulsory schooling steadily increased. The National Health Service was launched, providing universal free access to care for mothers and children [17]. Although Portugal remains one of the less educated countries in Western Europe, health indicators are similar to or better than most European and OECD countries.

Recently, economic recession almost doubled women unemployment (16% in 2013 and much more in younger women). In addition, larger permanent migration rates were observed (3/1000 in 2012 vs. 1/1000 in 2008) as a steepest decline in birth rates [18].

Given the social impact of economic growth and of the recent recession in Portugal, we aimed to evaluate the national trends in educational inequalities of singleton preterm and LBW from 1992 to 2012.

METHODS

This study used anonymous individual data of all live births from 1992 and 2012, based on the Civil Registration and provided by the National Statistics Institute. Civil Registration is compulsory and all births are included. Demographic data is provided by the parents and newborns' related information (as birthweight and gestational age) is retrieved from medical forms. Civil Registration is carried by administrative staff and, since 2007, it can be done at maternity facilities [7].

The level of recorded aggregation of maternal education differed in time. In this study, education was categorised as: low (basic schooling or less); intermediate (secondary level) and high (university degree or further education) [19]. Maternal age at birth is recorded as a continuous variable. Parity is recorded as the number of previous deliveries; women were classified as: primiparae (no previous deliveries), with one, two and three or more previous deliveries. Birthweight is recorded as a continuous variable and LBW was classified as below 2500g. Duration of pregnancy was recorded as a categorical variable from 1999 and 2009. Thus, small-for-gestational age (as a proxy indicator of intra-uterine growth restriction) was not possible to ascertain; instead, LBW among babies born at term (≥37 gestational weeks) was considered. Preterm comprised pregnancies with less than 37 weeks and it was further classified as very preterm (<32 weeks) and moderate-late preterm (32-36 weeks). For the current analysis all women delivering single live births, with data on the above mentioned variables (n=2,191,249) were considered (99% of 2,220,189 eligible). To minimise random errors, analyses were performed in three years intervals, resulting in seven time periods.

For each time period the proportions of women younger than 20 and over 34 years, with low, intermediate and high education level, employed and primiparae were calculated. The prevalence of preterm and LBW was estimated according maternal education. Percentage changes in the prevalence were calculated in relation to the beginning of the studied period as: ($_{\text{prevalenceeach period}}$ – $\text{prevalence}_{1992\text{-}94}$)/$\text{prevalence}_{1992\text{-}94}$). To assess what the preterm and LBW rates would be if age and parity distributions remained as the observed in 1992-1994, for each period and education class, logistic regression models were fitted including maternal age, squared maternal age and parity. Predicted probability was estimated according to the models' equations using the observed coefficients times the 1992-1994's mean maternal age, mean squared age and mean prevalence of each parity class.

Time trend inequalities in preterm and LBW were assessed estimating absolute (slope index of inequality (SII)) and relative (relative index of inequality (RII)) measures of inequality [20, 21]. Categories of education were ordered from the highest to the lowest and women in each category were assigned a score (fractional rank from 0 (highest education) to 1 (lowest education)) based on the midpoint of the cumulative distribution. Preterm and LBW were then regressed on the score using binomial regression adjusted for maternal age, squared maternal age and parity. SII is the slope of the resulted regression line and reflects the difference in the outcome between women in the extremes of educational hierarchy. RII results from the ratio between the slope and the prevalence of the outcome in the population. It is interpreted as the odds ratio (OR) of the outcome between the highest and the lowest educational level [20]. SII and RII were calculated for each time period; a linear test for trend was used to evaluate whether inequalities changed over time.

RESULTS

Preterm and LBW prevalence according maternal education are presented in Table 1; the percentage changes taking as reference 1992-94 are plotted in Figure 1. Higher prevalence of both outcomes was found in less educated women in all time periods.

Table 1 – Preterm and low birthweight prevalence according maternal education between 1992 and 2012

Time Periods	Education level	Preterm						Low birthweight (<2500g)			
		Overall (<37weeks)		Very (<32 weeks)		Moderate-late (32-36 weeks)		Overall		Among babies at term (≥37 weeks)	
		n	%	n	%	n	%	n	%	n	%
1992-1994	Low	18,308	8.4	1,502	0.7	16,806	7.7	11,601	5.3	7,139	5.6
	Intermediate	5,466	6.8	427	0.5	5,039	6.2	3,569	4.4	2,087	2.8
	High	1,539	6.1	99	0.4	1,440	5.7	933	3.7	548	2.3
1995-1997	Low	14,208	6.3	1,761	0.8	12,447	5.5	12,678	5.6	7,122	3.4
	Intermediate	2,857	5.3	358	0.7	2,499	4.6	2,458	4.6	1,229	2.4
	High	1,800	4.7	211	0.6	1,589	4.2	1,509	4.0	811	2.2
1998-2000	Low	11,782	5.4	1,690	0.8	10,092	4.6	13,600	6.2	7,877	3.8
	Intermediate	3,578	5.2	456	0.7	3,122	4.5	3,803	5.5	2,058	3.1
	High	2,373	4.6	280	0.5	2,093	4.1	2,465	4.8	1,311	2.7
2001-2003	Low	10,274	5.4	1,297	0.7	8,950	4.7	12,284	6.5	6,392	3.6
	Intermediate	3,772	5.0	454	0.6	3,318	4.4	4,265	5.7	2,122	3.0
	High	2,977	4.6	331	0.5	2,646	4.0	3,123	4.8	1,513	2.4
2004-2006	Low	9,586	6.1	1,153	0.7	8,433	5.4	10,463	6.7	5,522	3.8
	Intermediate	4,258	5.4	487	0.6	3,771	4.8	4,468	5.6	2,300	3.1
	High	4,002	5.1	416	0.5	3,586	4.6	3,947	5.1	1,927	2.6
2007-2009	Low	10,222	7.8	1,230	0.9	8,992	6.9	9,003	6.9	4,524	3.7
	Intermediate	5,580	7.0	606	0.8	4,974	6.3	4,529	5.7	2,200	3.0
	High	5,710	6.8	559	0.7	5,151	6.2	4,564	5.4	2,226	2.8
2010-2012	Low	6,515	6.4	905	0.9	5,610	5.5	7,609	7.4	3,830	4.0
	Intermediate	4,665	5.7	621	0.8	4,044	5.0	5,090	6.2	2,489	3.2
	High	4,984	5.6	548	0.6	4,436	4.9	5,221	5.8	2,579	3.0

When compared to 1992-1994, in 1998-2000 preterm decreased 36% in less educated (from 8.4% to 5.4%) and 25% in highly educated women (from 6.1% to 4.6%). It increased afterwards, particularly since 2004. In 2010-2012, 6.4% of low educated (more 19% than in 1998-2000) and 5.6% of high educated women (more 22% than in 1998-2000) delivered a preterm baby. Intermediate and high educated women seem to be similar until 2003. If delivering women presented the mean age and parity distribution of those in 1992-1994, similar prevalence estimates would be found (2010-2012: 6.1%, 5.5% and 5.3% in low, intermediate and high education, respectively). For all periods, differences in preterm according education were more evident in very preterm than in moderate-late preterm.

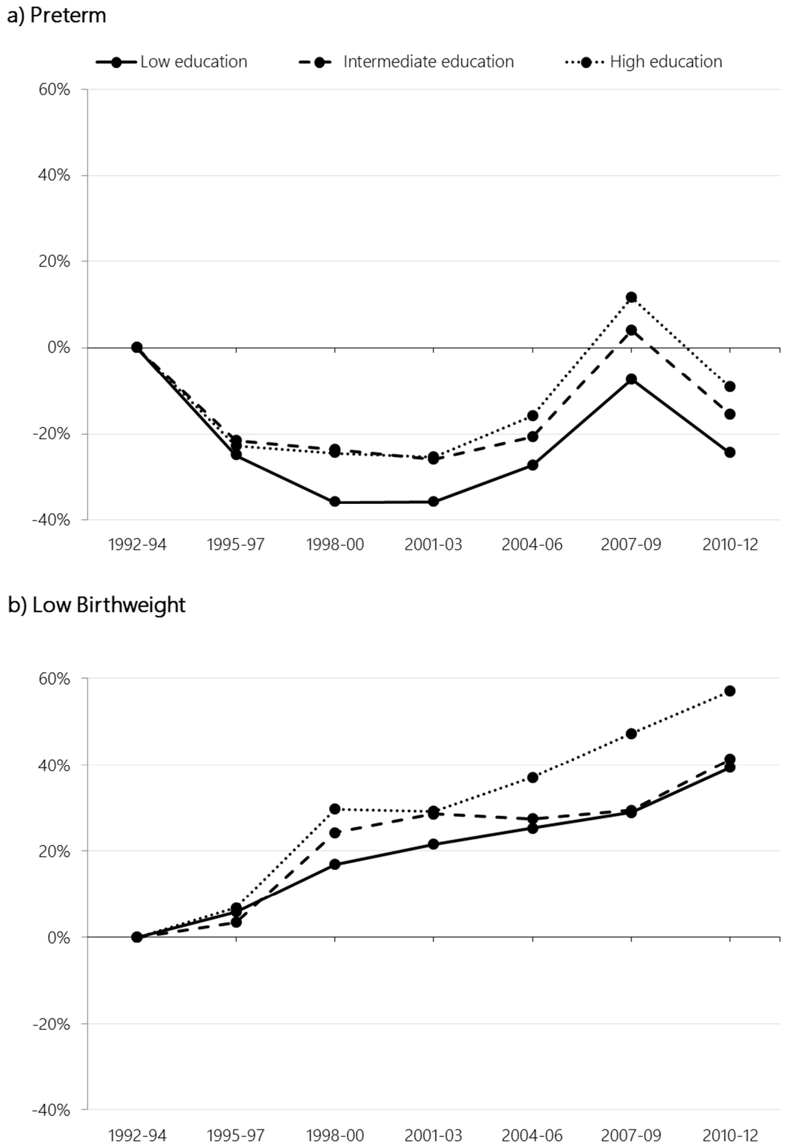

Figure 1 - Change in the prevalence of preterm (PT) and low birthweight (LBW) according to maternal education taking as reference 1992-1994.

LBW increased in all education strata. Since 1992-1994, increase was larger in more educated women (57% increase: 3.7% 1992-1994 to 5.8% in 2010-2012 vs. 40% in less educated: 5.3% to 7.4%). Among babies born at term, LBW was relatively constant: 3.3% in 1992-1994 to 3.4%in 2010-2012. However, among more educated women, it increased around 30% from 1992-1994 (2.3%) to 2010-2012 (3.0%). Among less educated, after a decrease in 1995-1997, it increased 17% until 2010-2012 (3.4% to 4.0%). The predicted overall LBW prevalence estimates in 2010-2012 would be similar in low educated (7.4%), slightly lower in intermediate (6.0%) and 28% lower in high educated women (4.2%).

Trends in maternal characteristics are presented in Table 2. A marked increase in maternal education was observed. The prevalence of highly educated was, in the last years, 4 times the one observed in the beginning of the 1990's (33% vs. 8%). An increase in the prevalence of older mothers was also observed (≥35 years: from 9% in 1992-94 to 23% in 2010-12). More pronounced increases in maternal age were observed among highly educated, particularly since 2006. Low educated women presented the higher prevalence of teenage mothers and the lowest proportions of employed and primiparae in all time-periods. The percentage decrease of employed women in 2010-2012, when compared to 2007-2009, was more evident among low educated (-13%) followed by intermediate (-7%) and more educated (-2%).

Table 3 shows age- and parity-adjusted inequality trends in preterm and LBW. In 1992-1994, women in the bottom of the education hierarchy were almost 50% more likely to deliver a preterm than those in the top [RII=1.47 (95% CI 1.39-1.55)], but educational gap decreased until 1998-2000 [RII=1.08 (1.02-1.16)]. In 2001-2003 relative inequalities increased and remained stable until 2012 [RII=1.35 (1.27-1.44)]. Relative educational inequalities were larger in very preterm deliveries than in moderate preterm, particularly since 2007. At this time, relative inequalities in very preterm showed a larger increase while inequalities in moderate-late preterm remain stable.

Despite presenting a similar pattern, more pronounced inequalities were observed for LBW and particularly among babies born at term (Table 3). Differences between the extremes of educational hierarchy (SII) significantly changed with time ($p<0.001$) and varied between 1.7% (95%CI: 1.38-2.01) in 1992-94 and 3.6% (3.19-3.95) in 2010-2012. Although no significant changes were observed in LBW relative inequalities with time ($p=0.133$), women in the bottom of the educational hierarchy were, in 2010-2012, almost two times more likely of a LBW [RII=1.71 (1.61-1.81); among babies born at term: RII=1.82 (1.68-1.99)].

Table 2 – Women characteristics according maternal education in Portugal from 1992 to 2012 (single live births)

	Period						
	1992-1994 (n=323,574)	1995-1997 (n=316,792)	1998-2000 (n=338,948)	2001-2003 (n=329,964)	2004-2006 (n=313,978)	2007-2009 (n=294,104)	2010-2012 (n=273,889)
All singleton live births (n=2,191,249)							
<20 years (%)	8.1	7.1	6.4	5.9	5.1	4.5	3.8
≥35 years (%)	9.1	10.5	12.5	14.4	16.4	19.2	23.2
Employed (%)	54.6	60.7	67.6	71.6	72.0	73.3	70.1
Primiparous (%)	53.5	53.4	54.3	54.5	54.2	54.1	53.5
Low education (n=1,239,967)	67.2	71.0	64.4	57.4	49.9	44.3	37.3
<20 years (%)	10.1	9.1	8.8	9.0	9.0	9.0	8.9
≥35 years (%)	9.0	10.0	11.7	13.8	15.7	17.2	19.5
Employed (%)	44.1	52.4	58.8	62.2	60.0	59.4	51.8
Primiparous (%)	49.3	50.1	49.7	48.0	46.6	46.0	43.6
Intermediate education (n=519,814)	25.0	17.0	20.5	22.8	25.3	27.0	29.8
<20 years (%)	5.2	4.0	3.6	3.2	2.3	2.1	1.8
≥35 years (%)	7.9	9.0	10.8	11.7	13.5	16.0	19.4
Employed (%)	70.8	72.6	76.22	77.6	77.2	77.4	72.3
Primiparous (%)	62.2	63.7	64.1	64.2	62.2	60.4	58.2
High education (n=431,468)	7.8	12.1	15.2	19.8	24.8	28.6	32.9
<20 years (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
≥35 years (%)	13.8	15.6	18.1	18.9	20.6	25.0	30.8
Employed (%)	93.2	92.6	93.1	92.1	91.0	91.2	89.0
Primiparous (%)	59.5	58.2	60.3	62.3	61.5	60.7	60.4

Table 3 – Time trend in absolute and relative educational indices of inequality in adverse pregnancy outcomes

	Preterm			Low Birthweight (<2500g)	
	Overall (<37 weeks)	Very preterm (<32 weeks)	Moderate-late preterm (32-36 weeks)	Overall	Among babies at term (≥37 weeks)
SII [a]					
1992-1994	2.88 (2.48-3.27)	0.26 (0.16-0.37)	2.63 (2.25-3.01)	1.70 (1.38-2.01)	1.56 (1.30-1.83)
1995-1997	1.73 (1.37-2.09)	0.17 (0.04-0.29)	1.56 (1.23-1.90)	2.18 (1.84-2.51)	1.73 (1.48-1.98)
1998-2000	0.40 (0.08-0.72)	0.18 (0.07-0.30)	0.21 (-0.09-0.50)	1.94 (1.61-2.27)	1.75 (1.49-2.01)
2001-2003	1.00 (0.69-1.32)	0.23 (0.12-0.33)	0.78 (0.49-1.07)	2.69 (2.36-3.02)	1.78 (1.54-2.03)
2004-2006	1.52 (1.19-1.84)	0.26 (0.15-0.37)	1.24 (0.94-1.57)	3.06 (2.73-3.40)	2.21 (1.96-2.47)
2007-2009	1.77 (1.38-2.15)	0.46 (0.33-0.59)	1.31 (0.94-1.67)	3.08 (2.73-3.43)	1.84 (1.57-2.11)
2010-2012	1.68 (1.32-2.04)	0.47 (0.34-0.60)	1.21 (0.86-1.54)	3.57 (3.19-3.95)	2.04 (1.75-2.32)
RII [a]					
1992-1994	1.47 (1.39-1.55)	1.50 (1.22-1.85)	1.47 (1.38-1.56)	1.42 (1.32-1.52)	1.71 (1.56-1.88)
1995-1997	1.37 (1.28-1.47)	1.29 (1.05-1.57)	1.39 (1.29-1.49)	1.55 (1.44-1.67)	1.94 (1.75-2.14)
1998-2000	1.08 (1.02-1.16)	1.39 (1.16-1.67)	1.04 (0.97-1.12)	1.36 (1.28-1.44)	1.70 (1.56-1.85)
2001-2003	1.22 (1.15-1.30)	1.47 (1.22-1.77)	1.19 (1.11-1.27)	1.54 (1.45-1.63)	1.83 (1.68-1.99)
2004-2006	1.31 (1.24-1.39)	1.56 (1.30-1.87)	1.28 (1.20-1.37)	1.63 (1.53-1.72)	2.02 (1.86-2.20)
2007-2009	1.28 (1.21-1.35)	1.82 (1.54-2.15)	1.23 (1.16-1.30)	1.61 (1.52-1.71)	1.77 (1.63-1.93)
2010-2012	1.35 (1.27-1.44)	1.92 (1.60-2.29)	1.28 (1.20-1.37)	1.71 (1.61-1.81)	1.82 (1.68-1.99)

SII – Slope index of inequality (represents the percentage difference in each outcome between the extremes in education);
RII – Relative index of inequality (represents the odds ratio in each outcome between the extremes in education);
[a] Adjusted for maternal age, squared maternal age and parity

DISCUSSION

In this study we found that educational inequalities in preterm birth and LBW declined in Portugal during the 1990's but increased again in the XXI century without significant impact of the 2009 economic crisis.

To the best of our knowledge, no time trend analysis of socioeconomic inequalities in birth outcomes including data from the recent period of economic crisis is available for comparison. Though, the magnitude of educational gap in birth outcomes in Portugal was found to be similar to what was previously described in other countries and historical moments [12, 22, 23].

Although educational inequalities in preterm declined in the nineties, they increased afterwards and, in 2010-2012, reached levels similar to the late 20th century. Some studies suggest that the gap between the most and the least deprived women is not increasing because preterm is increasing among the latter, as a result of a rise in maternal age and in iatrogenic preterm [11, 24]. Our results are in accordance with this pattern only for the recent years. The narrowing gap in the nineties seems to result from a greater decrease in preterm in less educated than in highly educated women; only for the period 2007-2012 the increase was greater among more educated. Differences do not seem to be explained by maternal age since it increased similarly according education levels. Despite a slightly larger increase of older mothers among more educated after 2007, predicted estimates (if maternal age and parity profile remained stable) were similar to the observed ones. Unemployment is also associated with an increased risk of preterm [25]. Employment among low educated increased 33% in the 1990's while no changes occurred in highly educated women (almost all women were employed at the beginning of the 1990's). However, adjustment for employment status only attenuated the differences, which remained significant and presented similar pattern (supplementary table S1).

In 1994 almost 20% of Portuguese pregnant women entered late in care and, for 15%, prenatal care was inadequate. Inadequate care was associated with maternal social conditions and with subsequent preterm deliveries [26]. However, 10 years later, the prevalence of late care users has halved (11%) and inadequate care was rare (4%) [27, 28]. The increasing access to care in the late 20th century is a plausible explanation for the greater decrease of preterm births among less educated. However, although it could be a consequence of effective preventive care, it is reasonable to reflect improvements in pregnancy duration assessment, namely of the widespread use of more accurate methods [29]. Obstetric intervention also rose since 2000 and caesarean deliveries have been increasing particularly in more privileged women, both in private and public settings [30]. Although this change is probably attributed to interventions among term babies, it might have contributed to an increase in late preterm prevalence among more educated.

Greater educational gap was observed for very preterm. Despite the small impact on the overall inequalities in preterm, our results suggest that disparities might be increasing which calls for future monitoring. These results are in accordance to what has been described elsewhere, explained by the uninterrupted higher likelihood of vaginal infection in women exposed to more deprived social conditions, particularly since childhood [11, 12, 23]. As women are becoming more educated, the ones that remain in the bottom of the education scale are more likely to be the more deprived from all. Also, a steepest increase in inequalities in very preterm was observed after 2006 while no changes were found for moderate-late preterm.

In the last 15 years, delivering women in Portugal are more educated that the general childbearing female population but the educational time-trend distribution seems to be similar. When comparing 2013 with 2008 (pre-crisis period, data not shown) we observed that no educated women decreased in similarly in the general population and among delivering women (28% and 27%, respectively). However, the increase of highly educated women was larger in the general population than among pregnant women (more 39% vs. 22%) [18]. This suggests a less than expected frequency of highly educated pregnant women in the recent years. In addition, educated women who become pregnant may be those in the top end of the distribution increasing educational gap, particularly noticed in the most adverse outcomes as very preterm. Due to its universal and free essence, we do not expect increasing barriers to care in recent years. However, it could be useful to understand its role, namely among more vulnerable women.

LBW slightly increased in time and educational inequalities in this outcome presented a pattern similar to the one observed in preterm. However, only part of inequalities is reflecting disparities in preterm: first, because the educational gap was wider than in preterm, second because even larger inequalities in LBW were found among babies born at term, reflecting larger educational inequalities in fetal growth restriction. This may be explained by the stronger association between fetal growth restriction and socially-related maternal behaviours, such as pregnancy smoking or nutritional factors [8]. Although we do not have data on smoking trends in pregnancy, a recent systematic review found an increase in smoking among Portuguese women from 1988 to 2008, particularly in the first 10 studied years and in women bellow 50 years [31]. Women from more deprived social conditions are more likely to smoke during pregnancy [27] which can contribute to the observed educational gradient [15, 22]. The gap between most and least educated women could even be larger because an increase in LBW was more pronounced in the former. This may be the result of the increase in maternal age: in 2010-2012 LBW was almost 30% higher than it was expected if women presented the age and parity distribution observed in the 1990's. Also, LBW may have decreased in less educated women as a result of the rise in gestational diabetes [32], more likely to occur in this group of women than in more educated [8] and associated with heavier babies. Even absolute differences between the highest and the lowest educated women increased until 2010-2012, part is attributable to the overall increase in LBW prevalence, since relative inequalities had not significantly changed.

Overall, preterm and LBW showed similar patterns of educational inequality: a decrease up to 2000 and a slight increase afterwards that remained stable in recent years. These trends follow the pattern of economic growth in the country, suggesting that macroeconomic environment might impact education disparities in birth outcomes. Between 1986 (when Portugal entered the European Economic Community) and 1999 intense economic growth was observed. Since then, growth rates were much lower and fell in 2008-2009 with the economic crisis, with huge impact on labour market and population well-being. However, it seems that the implementation of the Euro might had safeguarded the country from a deeper impact of the crisis [33]. Although the similarities between economic and perinatal patterns may be an artefact, analogous parallel trends were previously observed in Finland in the beginning of the 1990's [23] and in other Nordic countries [15]. We cannot, however, clearly define what macroeconomic features impact social inequalities in birth outcomes and to what extent the universal access to healthcare might have influenced this relation and buffered its effects.

Portuguese birth registration covers the entire population, making selection bias unexpected. Also, only 1% of births were excluded because of missing data. Gestational age missing values decreased from 2% in 1992-1994 to 0.2% in 2010-2012 (birthweight from 0.4% to 0.1%). Thus, it is unlikely that results would be different if missing cases were included. The use of birth certificates in time-trend analyses may introduce bias because of changes in data accuracy [34]. The validity of LBW classification is not questioned since birthweight assessment is unlikely to have significantly changed during the studied 20 years. However, gestational age is more prone to error, depending on the timing of prenatal care and on the estimation method [29]. Large inequalities in preterm in the beginning of the 1990's may reflect the higher likelihood of more educated women to have pregnancy duration more accurately estimated as a result of the higher likelihood to early entrance in care and to the access to more sophisticated prenatal care. As the general population access to high-quality care improved over time, inequalities in pregnancy duration assessment are likely to have decreased. Particularly since 2000, ultrasound-based estimations became routinely used and a social gradient in its use is very unlikely. The main limitation of using Portuguese data from civil registration is the lack of behavioural-related characteristics or clinical data, such as smoking, pregnancy complications or infection status, not registered in the birth certificates. Models were fitted considering maternal age and parity that, although are possible mediators of the relation between education and birth outcomes, allow for estimates independent of the distribution of these characteristics in time.

In this study, rather than using area-based measures, we considered individual education as a proxy indicator of socioeconomic position, which increased the validity of social characterisation. Education only captures part of the components of socioeconomic disadvantage but it is known to be the most valuable indicator at early adult life, less likely to change during women's childbearing age and useful to comparisons [35]. Also, the use of inequality indexes is a major advantage of the current study. Traditional measures, as relative risks or odds ratio, represent pairwise comparisons (i.e. do not take into consideration all education categories of the distribution) and are not sensitive to different distributions of education in time. SII and RII take into account all groups in the educational hierarchy and not only those in the extremes and are sensitive to different distributions of education in time [21].

Conclusion

Despite a significant improvement in the educational profile of women delivering in Portugal, this study confirmed that inequalities in adverse birth outcomes remain. As inequality parallels the trends in economic growth during most of the considered period, an effect of macroeconomic environment is suggested, particularly in preterm. However, recent economic crisis was not reflected in larger educational inequalities in birth outcomes, probably because it uncovered unfavourable economic conditions, namely those resulted of the monetary changes that joining the euro currency might have boosted.

Further analyses should monitor the trends, since recession may be revealed in the following years. Public health strategies addressing prevention of preterm births and fetal growth restriction should integrate individual and contextual features in order to promote gains in health. Selection into pregnancy in periods of economic contraction might explain larger educational inequalities in the most severe birth outcomes as very preterm deliveries.

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SUPPLEMENTARY FILE

Table S1 - Time trend in absolute and relative educational indices of inequality in pregnancy outcomes (further adjustment for employment status)

	Preterm			
	Overall	Very preterm	Moderate-late preterm	Low Birthweight
SII *				
1992-1994	1.39 (0.99-1.80)	0.24 (0.13-0.36)	1.14 (0.75-1.53)	1.29 (0.97-1.61)
1995-1997	0.93 (0.56-1.29)	0.14 (0.01-0.26)	0.79 (0.44-1.13)	1.83 (1.49-2.17)
1998-2000	0.11 (-0.21-0.43)	0.12 (0.01-0.24)	0.21 (-0.09-0.50)	1.58 (1.25-1.92)
2001-2003	0.76 (0.45-1.07)	0.18 (0.07-0.29)	-0.03 (-0.33-0.27)	2.32 (1.99-2.65)
2004-2006	1.36 (1.03-1.70)	0.25 (0.14-0.36)	0.58 (0.29-0.88)	2.76 (2.43-3.10)
2007-2009	1.61 (1.22-2.01)	0.42 (0.29-0.56)	1.11 (0.79-1.42)	2.76 (2.40-3.11)
2010-2012	1.51 (1.14-1.88)	0.46 (0.33-0.60)	1.19 (0.82-1.56)	3.25 (2.86-3.63)
RII *				
1992-1994	1.27 (1.20-1.34)	1.47 (1.19-1.82)	1.26 (1.18-1.33)	1.35 (1.25-1.45)
1995-1997	1.23 (1.15-1.32)	1.24 (1.01-1.52)	1.23 (1.14-1.33)	1.51 (1.40-1.63)
1998-2000	1.03 (0.96-1.10)	1.29 (1.07-1.55)	1.00 (0.93-1.07)	1.35 (1.27-1.43)
2001-2003	1.17 (1.10-1.25)	1.36 (1.13-1.64)	1.15 (1.07-1.23)	1.53 (1.44-1.62)
2004-2006	1.28 (1.20-1.36)	1.53 (1.27-1.84)	1.25 (1.17-1.33)	1.62 (1.53-1.72)
2007-2009	1.26 (1.19-1.32)	1.75 (1.47-2.07)	1.20 (1.14-1.28)	1.59 (1.50-1.68)
2010-2012	1.32 (1.24-1.40)	1.88 (1.56-2.26)	1.25 (1.17-1.34)	1.67 (1.57-1.77)

* Adjusted for maternal age, squared maternal age, parity and employment status (employed vs. unemployed)

SII – Slope index of inequality (represents the percentage difference in each outcome between the extremes in education hierarchy)

RII – Relative index of inequality (represents the odds ratio in each outcome between the extremes in education hierarchy);

4.4. The effect of neighbourhood socioeconomic context in birth outcomes: results from Generation XXI (Portugal) and 2004 Pelotas (Brazil) birth cohorts.

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ABSTRACT

BACKGROUND: We aimed to evaluate the effect of neighbourhood's clustering and socioeconomic characteristics on preterm and small-for-gestational age (SGA) births in urban areas from Portugal and Brazil.

METHODS: This study considered 6585 women from Generation XXI (G21), Portugal and 3078 women from 2004 Pelotas Birth Cohort Study, Brazil. Preterm (<37 GW) and SGA (sex-specific weight <10thpercentile for each GW) births were considered according the birth medical records. Individual characteristics were self-reported and maternal addresses were linked to the census block groups and respective 3-category socioeconomic class, created using latent class analysis. Country-specific analyses were conducted and, in Pelotas, data were stratified by ethnicity. Multilevel logistic regression models, adjusted for individual- and block-level socioeconomic conditions were used. Neighbour-to-neighbour unexplained heterogeneity was measured using median odds ratio (MOR). The effect of block socioeconomic class was assessed using 80% interval odds ratio (IOR).

RESULTS: The prevalence of preterm and SGA was, respectively, 7% and 15% in G21 and 15% and 18% in Pelotas. Neighbourhood heterogeneity was not found in G21 birth outcomes. In Pelotas it was observed for preterm among white women (MOR=1.50) and for SGA in blacks (MOR=1.47), even after adjustment for individual-level characteristics. Neighbourhood social class did not explain the remaining variance for none of the outcomes.

CONCLUSIONS: An independent area-level effect on preterm and SGA was found beyond individual characteristics for specific ethnic groups in Brazil but not in Portugal. The influence of neighbourhood context may be explained by other social and organizational resources than neighbourhood social class.

INTRODUCTION

An individual-level approach has traditionally been used to describe the relation between social circumstances and perinatal health and low maternal education, income or other measures of socioeconomic disadvantage commonly relate with increased risk of adverse outcomes [1, 2]. Differences in smoking or diet patterns and the unequal availability or uptake of health care services are referred as possible mediating mechanisms. However, individual characteristics have not fully explained the observed social inequalities in perinatal outcomes [1, 3].

Research on the influence of upstream social determinants on reproductive outcomes has increased, taking the premise of the ecological frameworks wherein individuals' behaviour is shaped by personal factors and by their interaction with the communities and with public policies [4]. The effect of neighbourhood deprivation on birth outcomes was assessed in some studies, mostly from the United States [5-10]. Despite the heterogeneity in the measurement of social context and in the analytical approaches, a weak-to-moderate effect of neighbourhood deprivation on the increasing risk of adverse perinatal outcomes, particularly preterm and reduced birthweight. Contextual influences, independently of individual socioeconomic profile, seem to differ according maternal ethnicity, suggesting that social environment may be a particularly interesting target for preterm and low birthweight prevention interventions [11, 12].

Recently, population-based birth cohorts have been used to compare the effect of social deprivation on women's and children's health across countries. Pelotas, in South Brazil, showed weaker social inequalities when compared to the United Kingdom and, while inequalities in health care access and utilization seemed to have decreased over the time, the opposite was observed in relation to health behaviours and pregnancy outcomes, such as smoking or preterm birth [13]. Differences between middle and high-income countries may reflect the level of epidemiological, nutritional and life-style transitions in which contextual socioeconomic characteristics may differently contribute to attenuate or increase disparities. In the past half century Portugal lived impressive improvements in health indicators, result of huge changes in the political, social and cultural context. However, adverse pregnancy outcomes as low birth weight and preterm seem to be increasing [14].

Portugal and Brazil are two interesting settings beyond economic or development characteristics. Individuals share a common genetic and historical ground since Portuguese settled in Brazil for colonial purposes in the XVI century and onwards. Even after independence in 1822, and during the XIX and XX centuries, Portuguese migration to Brazil was frequent and characterised by long duration and endogamous practices [15].

The evaluation on how social conditions, particularly neighbourhood deprivation, differently affect individuals' health, might contribute to a clear understanding of social determinants of health.

In this framework, and making use of Generation XXI and 2004 Pelotas Birth Cohort Study (Portuguese and Brazilian birth cohorts, respectively) we intended to evaluate the effect of neighbourhood clustering and respective socioeconomic characteristics on preterm and small-for-gestational age babies.

METHODS

We used data from two population-based birth cohorts recruited at similar points in time in Porto Metropolitan Region (Portugal) and Pelotas (Brazil).

Generation XXI (G21) includes 8647 children born between April 2005 and August 2006 at five public maternity units (8% refused to participate). A subgroup of women was recruited during pregnancy if prenatal care started before 14th gestational week at two of the referred hospitals and so were excluded from the present analysis (n=313). Due to logistic constraints and to increase follow-up participation, after the first months of recruitment inclusion criteria were restricted to mothers living at six municipalities from Porto Metropolitan Area in the North of Portugal (Gondomar, Maia, Matosinhos, Porto, Valongo and Vila Nova Gaia) [16, 17]. The region has about 1 million inhabitants and comprises urban and suburban areas. The study was approved by the Ethics Committee from the University of Porto Medical School/Hospital S. João and a written signed consent form was obtained from all women.

2004 Pelotas Birth Cohort Study is the third birth cohort recruited in Pelotas, a region of about 330,000 inhabitants in Southern Brazil. Detailed methodology has been previously described [18]. Briefly, all live births between January and December 2004, to mothers living in the urban area of Pelotas and in Jardim America (an urban district contiguous with Pelotas) (n=4231, 99% of all eligible) were included. The study protocol was approved by the Medical Ethics Committee of the Federal University of Pelotas and written signed consent form was required for all women.

In both studies women were evaluated immediately after delivery in face-to-face interviews using standardised questionnaires and comparable questions. Data on maternal socio-demographics, reproductive history, prenatal care and lifestyles was collected. Subsequent follow-up evaluations were conducted for both groups; consequently mothers provided their address and other contacts.

Outcome measures

Preterm was classified as birth before 37 gestational weeks. In Pelotas 2004, gestational age was estimated based on the last menstrual period (LMP) and, when not available, on ultrasound or Dubowitz score. In G21, ultrasound gestational age was considered and, if no data available (15%), the one based on the last menstrual period. SGA was classified using Kramer et al. [19] reference curves considering the sex-specific birthweight below the 10th percentile for each gestational age.

Individual characteristics

Maternal ethnicity was available only for Pelotas 2004 (G21 was not allowed to question women about their ethnicity but migrants accounted for less than 4% of women) and was measured using mothers self-reported skin colour as proxy indicator. The question options were white, brown, black, Asian and indigenous. Women reported their age at the time of delivery, the number of completed schooling years, working condition (employed vs. unemployed during pregnancy in Pelotas and at the moment of birth in G21) and their marital status: living with partner (married or not) or single. Household monthly income, including salaries and other sources of income, was questioned in categories of 500€ in G21 and as a continuous variable in Pelotas 2004. Therefore, the distribution of income in Pelotas was aggregated to reflect the G21 distribution. Lower income (<500€ in G21) corresponded to Brazilian income equal or smaller than R$240. The upper class of more than 2000€ corresponded to more than R$1400. Women were asked about pregnancy planning and about the number of previous deliveries (further classified as primiparae (first delivery) or multiparae (≥1 previous deliveries)). Women were asked about the number of cigarettes smoked before pregnancy and were further classified as smokers (smoking at least 1 cigarette per day) and non-smokers. While for G21 the preconception period referred to the previous 3 months, for the Pelotas cohort it considered the 6 previous months. Maternal body mass index (BMI) was calculated using self-reported pre-pregnancy weight and measured height, whenever possible. Gestational age at first prenatal care visit was asked in weeks in G21 and in months in Pelotas 2004. Late prenatal care was considered if first appointment occurred after the 12th gestational week or after the 3rd month, respectively.

Neighbourhood socioeconomic environment (SEE_N)

Area-level characteristics were based on aggregated data provided by the 2000 (Brazil) and 2001 (Portugal) National Census. Data was aggregated at the level of census block groups (further designed as neighbourhoods or blocks). A neighbourhood socioeconomic environment (SEE_N) was created since some country differences in the collected indicators were observed. The set of indicators used for each country and the detailed description of the resulting socioeconomic class is available in the supplementary file 1.

We opted to follow the strategy used by Alves et al. using Porto city blocks [20]. It was used a set of variables reflecting three distinct socioeconomic dimensions: age composition, education/occupation and housing characteristics. For Brazilian data, the same indicator used in the Portuguese characterisation was tested whenever possible, otherwise a similar indicator to reflect the same construct or one that would better reflect Pelotas social reality was used. Taking into consideration aspects as heterogeneity, correlation between indicators and reliability, a final set of indicators was achieved (described in Table 1).

Neighbourhoods were characterised fitting latent class analysis models to assess homogenous groups regarding socioeconomic characteristics. The number of latent classes was achieved considering the Bayesian information criterion (BIC), the Akaike information criterion (AIC), entropy and interpretability. Better fit was indicated by smaller AIC and BIC values and entropy values closer to 1.0. The number of classes was achieved when an increase of classes did not improve the overall fit of the model or decreased interpretability. Because most variables did not present a Gaussian distribution, they were categorised in tertiles. Table 1 summarises the characteristics of the final SECN in both regions and the included indicators in each setting.

Maternal addresses were used to link women to the respective neighbourhood. Using the streets network from each country – with information on initial and final numbering for each street segment – home position was estimated by interpolation on each street segment.

Data analysis

For the current analysis all women delivering single fetus, recruited at birth from the six municipalities in the Porto Metropolitan Area (n=7329) and from Pelotas (excluding women from Colonia Z3, a rural area, n=4114) were eligible. For 556 and 879 women from Porto and Pelotas, respectively, it was not possible to link maternal address to city blocks, were living in blocks with less than 10 residents or for which it was not possible to assess the neighbourhood SEC. Among the remaining women, those with missing data in the outcomes or confounding variables were also excluded. Finally, in the Pelotas cohort, Asian and Indigenous women were also excluded because of the small number of participants (n=68). The final sample included 6585 women from G21 and 3078 from Pelotas. Pelotas 2004 analyses were conducted separately for white (1956, 63%), brown (636, 21%) and black women (486, 16%).

Analyses were conducted separately for each country. Initially, the distributions of each outcome according individual characteristics and SEE_N were compared. Then, the analysis was conducted considering a two-level hierarchical structure of data in which individuals are clustered in the neighbourhoods. The questions are a) whether two women who have similar individual profiles but live in different neighbourhoods have the same probability of delivering preterm and SGA babies and b) if the variability is explained by differences in the SEE of the neighbourhood. A set of individual-level (level 1) explanatory variables were considered and a cluster-level (level 2) explanatory variable, neighbourhood SEE, was also used in the analysis.

Three different multilevel logistic regression models were fitted in order to measure both individual and neighbourhood socioeconomic conditions according the methodology proposed by Oakes [21]. The first model, an empty model, was performed for assessing neighbourhood effects, i.e., neighbourhood-to-neighbourhood differences in the odds of preterm or SGA. The second model was adjusted for the individual variables that may be related with the option to live in the neighbourhood or are potential confounders of the association (age (linear, quadratic and cubic terms) and education as continuous variables, work status, marital status and pregnancy planning as dichotomous variables). Income was also tested but was removed from the models because of it was highly correlated with maternal education and was not statistically significant (α=10%). The third model included the SECN. When neighbourhood variability was not fully explained by the individual confounders, models were further adjusted to potential mediators as late prenatal care, smoking during pregnancy and BMI (model 4).

The association between the variables at individual level (fixed effects) and each outcome were reported as odds ratios (ORs) and respective 95% confidence intervals (95%CI) which are interpreted as the ORs for within-neighbourhood comparisons. The neighbourhood unexplained heterogeneity at each model was quantified using the variance and its proportional variation was estimated taking model 1 as reference. For easier interpretability and outcomes' comparability, neighbourhood unexplained heterogeneity was also assessed using Median Odds Ratio (MOR). The effect of the cluster-level variable was quantified using 80% interval odds ratios (IOR) [22, 23]. MOR is interpreted as an odds ratio and is computed as the ratio between the persons (similar in terms of all the characteristics included in the models) living in blocks with higher probability to the outcome and the ones with the lower probability. It is always higher than one and the higher the value, the higher the cluster variability. IOR integrates the fixed effects and the random variation at the area-level. The larger the interval the higher the neighbourhood variability; if it includes the value one it is assumed that the effect of the neighbourhood social class is not significant. [22]

Cross-level interactions were considered, i.e., the effects of individual-level predictors were allowed to vary across neighbourhoods. Models were fitted including the slopes of the associations between the individual socioeconomic variables and pregnancy outcomes at the neighbourhood level but no significant effects were observed. Because of the small number of participants in each neighbourhood, sensitivity analyses were conducted excluding the blocks with less than 5 participants. Logistic multilevel models were conducted by means of generalised linear-mixed effects models using maximum likelihood estimation based on Laplace approximation, from R version 3. The statistical significance of covariates was calculated using the Wald test. All tests were two-tailed and a significance level of 5% was defined.

RESULTS

Census blocks characterisation

G21 women were living in 1266 blocks (87% of the total), with a median number of households of 314 (interquartile range (IQR): 263.25-370) per block and 722 median number of residents (IQR: 574-913). The final sample resulted in a median of 3 participants per neighbourhood (IQR: 2-5). In Pelotas, participants were distributed by 395 blocks, with 233.5 (IQR: 172.5-282.0) and 741 (IQR: 533.25-930.75) median number of households and residents, respectively. A median number of 6 participants per block were obtained.

Neighbourhood socioeconomic classes presented similar distribution of most indicators in both settings (Table 1). Class 3 is characterised by lower proportions of young individuals and high prevalence of old and high educated individuals and of large households. Class 1 is on the opposite socioeconomic spectrum although more marked differences were found in Pelotas than in Porto (e.g. 85% and 42% of blocks classified as class 1 in Pelotas and in Porto Metropolitan Region, respectively, showed a distribution of illiteracy in the third tertile).

Table 1 - Proportion of blocks in each tertile of the selected indicator for Porto Metropolitan Region (Portugal) and Pelotas (Brazil), considering the blocks included in the analysis

Porto Metropolitan Region

		Blocks distribution (tertiles [cut-off %])	Class 1 (n=310, 25%)	Class 2 (n=657, 52%)	Class 3 (n=299, 24%)
Age composition	Proportion of individuals aged less than 15 years (%)	1st [7.30-27.51]	34.8	1.2	88.0
		2nd [27.52-37.16]	56.1	33.3	12.0
		3rd [37.17-72.48]	9.0	65.4	0.0
	Proportion of individuals aged 65 or more years (%)	1st [0.88-10.41]	6.1	63.8	2.0
		2nd [10.42-16.20]	49.7	34.7	19.4
		3rd [16.21-54.41]	44.2	1.5	78.6
Education, occupation, income	Proportion of illiterate individuals (%)	1st [3.33-10.78]	6.1	14.9	87.3
		2nd [10.79-14.31]	51.0	37.3	12.4
		3rd [14.32-34.15]	42.9	47.8	0.3
	Proportion of individuals with completed high school or more (%)	1st [0.00-4.45]	65.8	34.1	0.3
		2nd [4.46-10.19]	33.9	38.7	28.4
		3rd [10.20-43.23]	0.3	27.2	71.2
	Proportion of individuals unemployment	1st [0.00-4.18]	19.0	40.5	33.1
		2nd [4.19-5.61]	26.1	36.4	38.1
		3rd [5.62-14.87]	54.8	23.1	28.8
Housing characteristics	Proportion of rented households (%)	1st [0.00-16.18]	0.0	59.8	16.7
		2nd [16.19-30.11]	25.8	35.6	39.5
		3rd [30.12-96.26]	74.2	4.6	43.8
	Proportion of houses with 4 rooms or less (%)	1st [5.11-40.53]	2.6	39.7	49.2
		2nd [40.54-51.13]	19.4	41.2	33.4
		3rd [51.14-93.27]	78.1	19.0	17.4
	Proportion of old* buildings (%)	1st [0.00-72.80]	3.5	64.4	4.0
		2nd [72.81-88.98]	44.8	31.8	30.4
		3rd [88.99-100.0]	51.6	3.8	65.6

Pelotas

	Blocks distribution (tertiles [cut-off %])	Class 1 (n=128, 32%)	Class 2 (n=137, 35%)	Class 3 (n=130, 33%)
Proportion of individuals aged less than 15 years (%)	1st [6.62-20.74]	0.0	18.4	81.5
	2nd [20.75-26.48]	13.3	69.1	16.9
	3rd [26.49-42.56]	86.7	12.5	1.5
Proportion of individuals aged 65 or more years (%)	1st [1.01-5.81]	72.7	12.5	13.1
	2nd [5.82-9.90]	26.6	54.4	19.2
	3rd [9.91-45.43]	0.8	33.1	67.7
Proportion of illiterate individuals (%)	1st [0.00-2.71]	0.0	10.3	88.5
	2nd [2.72-6.69]	15.6	73.5	11.5
	3rd [6.70-20.00]	84.4	16.2	0.0
Proportion of individuals with completed high school or more (%)	1st [0.00-0.94]	85.9	16.2	0.0
	2nd [0.95-4.79]	13.3	79.4	3.8
	3rd [4.80-28.41]	0.8	4.4	96.2
Proportion of individuals with ≤ 2 National minimum wages (%)	1st [0.77-10.94]	0.0	8.1	93.8
	2nd [10.95-17.09]	13.3	76.5	6.2
	3rd [17.10-27.34]	86.7	15.4	0.0
Proportion of rented households (%)	1st [0.00-6.70]	71.9	19.1	5.4
	2nd [6.71-17.12]	25.8	56.6	21.5
	3rd [17.13-50.78]	2.3	24.3	73.1
Proportion of houses with ≥2 bathrooms (%)	1st [0.00-8.67]	78.1	10.3	9.2
	2nd [8.68-19.34]	21.9	67.6	10.8
	3rd [19.35-59.88]	0.0	22.1	80.0

* Constructions with more than 15 years (construction date until 1985)

Portuguese and Brazilian sample characterisation

As presented in table 2, delivering women in Portugal were significantly different from those delivering in Pelotas. G21 women were older, more educated, more likely to have a partner, to be working during pregnancy, to be primiparae and to have planned the index pregnancy and to enter earlier in care. Despite large socio-demographic differences, the proportion of smokers and of overweight/obese women was slightly lower than the one found in Pelotas. In Pelotas, ethnic groups had also a different socioeconomic profile, reflected in most variables. As an example, white women presented higher educational and income levels, followed by brown and black women (>12 years: 16.0%, 4.9% and 1.6%, respectively; R$>1400: 20.8%, 9.4%, 4.1%, respectively).

There was an aggregation of women according SECN and a gradient of individual socioeconomic profile. Both in G21 and Pelotas, women living in class 3 neighbourhoods were more likely to be older, more educated, with higher monthly income. In Pelotas neighbourhoods seem to be more homogeneous than in G21, since more marked differences were observed.

Preterm accounted for 7% and 15% of all live births from G21 and Pelotas 2004, respectively. SGA was also more frequent in Pelotas (18% vs. 15%). Preterm and SGA did not significantly varied according SECN in none of the evaluated groups. However, in Pelotas, white women living in class 1 neighbourhoods presented higher prevalence of preterm (14.6% vs. 11.8% in SEC2 and 10.4% in SEC3, p=0.074). SGA was also more frequent in SEC1 of brown women (17.0% vs. 15.0% in SEC2 and 6.8% in SEC3, p=0.058).

Table 2 – Generation 21 and Pelotas 2004 women characteristics and adverse birth outcomes according the neighbourhood socioeconomic class

	G21 (n=6585)				Pelotas (n=3078)												
						White				Black				Brown			
	Overall	Class1 (n=1439)	Class 2 (n=4175)	Class3 (n=971)	Overall	All	Class1 (n=782)	Class 2 (n=705)	Class3 (n=469)	All	Class1 (n=273)	Class 2 (n=171)	Class3 (n=42)	All	Class1 (n=348)	Class 2 (n=200)	Class3 (n=88)
Age (years)																	
<20	**5.6**	8.3	4.8	4.6	**18.4**	16.5	22.0	14.9	9.8	21.4	20.9	24.6	11.9	22.2	22.7	22.0	20.4
20-34	**78.3**	76.6	79.7	75.0	**68.1**	69.0	65.1	70.5	73.4	66.5	67.8	64.3	66.7	66.4	65.8	66.5	68.2
≥ 35	**16.1**	15.2	15.5	20.4	**13.5**	14.5	12.9	14.6	16.8	12.1	11.4	11.1	21.4	11.5	11.5	11.5	11.4
			<0.001					<0.001				0.195				0.994	
Education (years)																	
≤ 4	**7.6**	9.5	7.2	6.7	**14.1**	11.2	19.4	8.4	1.9	17.5	24.2	8.8	9.5	20.4	27.3	14.0	8.0
5-8	**24.4**	28.1	24.7	17.2	**39.7**	35.4	50.5	32.5	14.7	50.2	51.6	53.2	28.6	45.0	46.3	48.5	31.8
9-11	**24.2**	26.8	24.2	20.5	**34.7**	37.4	27.0	46.8	40.5	30.7	23.4	36.8	52.4	29.7	24.1	33.0	44.3
≥12	**43.8**	35.6	43.9	55.6	**11.4**	16.0	3.1	12.3	42.9	1.6	0.7	1.2	9.5	4.9	2.3	4.5	15.9
			<0.001					<0.001				<0.001				<0.001	
Monthly income																	
<500€ | R$≤240	**7.2**	10.8	5.9	7.8	**10.3**	7.6	12.2	5.6	3.0	16.8	19.6	15.2	5.6	14.4	18.3	9.8	9.5
500-1000€ | R$241-480	**32.5**	38.0	32.1	26.4	**27.9**	23.0	34.3	20.8	7.9	38.9	41.1	40.6	19.4	35.6	43.7	29.9	17.6
1001-1500€ | R$481-895	**28.6**	26.7	29.8	26.4	**29.9**	31.2	35.7	34.2	19.0	29.0	31.0	26.1	27.8	26.4	24.6	32.3	20.3
1501-2000€ | R$896-1400	**15.7**	12.5	16.8	15.6	**15.8**	17.4	11.9	22.7	18.3	11.2	5.9	13.8	33.3	14.2	8.4	20.7	21.6
>2000€ |R$>1400	**15.9**	12.0	15.4	23.8	**16.0**	20.8	5.8	16.8	51.8	4.1	2.3	4.4	13.9	9.4	4.9	7.3	31.1
			<0.001					<0.001				<0.001				<0.001	
Single marital status	**6.3**	8.9	5.2	7.5	**16.0**	12.9	13.4	12.9	11.9	26.8	25.3	29.2	26.2	17.6	19.0	16.5	14.8
			<0.001					0.749				0.653				0.577	
Working in pregnancy	**77.4**	73.3	78.5	78.9	**41.5**	46.0	32.9	49.5	62.5	37.2	32.2	43.3	45.2	31.1	27.9	31.5	43.2
			<0.001					<0.001				0.034				0.021	
Primiparae	**56.2**	54.1	57.0	55.9	**41.0**	42.9	36.4	42.7	54.2	37.4	31.1	43.3	54.8	37.6	35.1	38.0	46.6
			0.158					<0.001				0.002				0.135	
Planned pregnancy	**66.2**	61.2	68.4	64.6	**44.6**	49.3	45.0	52.3	52.0	32.1	34.4	28.6	31.0	39.6	38.2	39.5	45.4
			<0.001					0.008				0.441				0.463	
Pre-pregnancy smokers	**27.5**	31.3	25.6	30.5	**31.6**	28.9	32.5	27.8	24.7	35.8	39.6	31.6	28.6	36.8	39.7	36.5	26.1
			<0.001					0.010				0.138				0.063	
Overweight/obese (>25.0Kg/m^2)	**30.6**	30.1	31.6	27.3	**33.9**	33.2	35.3	33.1	30.3	34.7	38.0	28.7	39.5	35.5	38.4	33.3	28.4
			0.037					0.205				0.133				0.186	
Late prenatal care	**11.6**	15.4	10.3	11.8	**27.6**	21.7	30.2	20.0	10.3	41.8	46.3	37.9	28.6	34.9	37.8	34.2	25.3
			<0.001					<0.001				0.042				0.089	
Preterm	**6.8**	7.1	6.7	7.0	**14.6**	12.6	14.6	11.8	10.4	19.1	20.9	15.8	21.4	17.1	18.1	17.5	12.5
			0.844					0.074				0.384				0.454	
Small-for-gestational age	**14.9**	14.2	15.0	15.0	**17.5**	17.5	19.7	15.9	16.4	21.0	23.8	17.5	16.7	14.9	17.0	15.0	6.8
			0.755					0.120				0.222				0.058	

[a] The total number of women with data in lower than the overall sample; [b] For G21, 10% of women were not included because did not want to report or did not know the monthly income

Multilevel approach to neighbourhood variation

In table 3, the summary results of the multilevel analyses are presented. No neighbourhood-to-neighbourhood variation was found in preterm or SGA neither in G21 nor in brown women from Pelotas 2004. Among Brazilian white women, moderate neighbourhood heterogeneity was found (MOR1=1.54) in preterm, but almost no changes were observed after the inclusion of individual socioeconomic characteristics (MOR2=1.51) or neighbourhood SEC (MOR3=1.50). When including late prenatal care, smoking and body mass index, unexplained heterogeneity slightly decreased (MOR4=1.45). Among blacks, neighbourhood heterogeneity was observed for SGA (MOR1=1.86) and part was explained by the individual socioeconomic characteristics (MOR2=1.68). Although SECN contributed to decrease the unexplained heterogeneity (MOR3=1.59), did not explain neighbourhood variations in SGA since IOR was large and included the value 1.

The individual effects on preterm and SGA are presented in table 4. The odds ratio represents the odds within neighbourhoods. None of the included characteristic was found to be related with preterm and only marital status was significantly associated with SGA in Porto (OR=1.35; 95% CI: 1.03-1.76).

When including potential mediators, within neighbourhoods, late prenatal care was significantly associated with preterm among white women in Pelotas (OR=1.53; 95% CI 1.06-2.23) and decreasing BMI decreased the odds of SGA among black women.

Table 3 – Summary results of the intercept models for both cohorts (Pelotas 2004 stratified by maternal ethnicity)

	Variance	% Explained variance	Median Odds Ratio	80% Interval Odds Ratio SEC_N (vs. class1)	
				Class 2	Class 3
Preterm					
Generation XXI					
Empty model	0.000	Reference	1.00	-----	-----
Adjusted for confounders [a]	0.000	NA	1.00	-----	-----
Pelotas 2004					
White					
Empty model	0.163	Reference	1.47	-----	-----
Adjusted for confounders [a]	0.151	8.9%	1.45	-----	-----
Adjusted for confounders + SEC_N	0.147	11.9%	1.44	0.44-1.77	0.43-1.72
Adjusted for confounders + SEC_N + mediators [b]	*0.152*	*24.8%*	*1.45*	*0.44-1.81*	*0.43-1.79*
Black					
Empty model	0.000	Reference	1.00	-----	-----
Adjusted for confounders [a]	0.000	NA	1.00	-----	-----
Brown					
Empty model	0.000	Reference	1.00	-----	-----
Adjusted for confounders [a]	0.000	NA	1.00	-----	-----
Small-for-gestational age					
Generation XXI					
Empty model	0.001	Reference	1.03	-----	-----
Adjusted for confounders [a]	0.006	-4%	1.07	-----	-----
Adjusted for confounders + SEC_N	0.008	-6%	1.09	0.94-1.31	0.96-1.34

	Variance	% Explained variance	Median Odds Ratio	80% Interval Odds Ratio SEC_N (vs. class1)	
				Class 2	Class 3
Pelotas 2004					
White					
Empty model	0.000	Reference	1.00	-----	-----
Adjusted for confounders [a]	0.000	NA	1.00	-----	-----
Black					
Empty model	0.423	Reference	1.86	-----	-----
Adjusted for confounders [a]	0.297	29.8%	1.68	-----	-----
Adjusted for confounders + SEC_N	0.239	43.5%	1.59	0.31-1.84	0.36-2.11
Adjusted for confounders + SEC_N + mediators [b]	0.179	57.7%	1.50	0.36-2.11	0.41-1.89
Brown					
Empty model	0.000	Reference	1.00	-----	-----
Adjusted for confounders [a]	0.000	NA	1.00	-----	-----

SEC_N - Neighbourhood Socioeconomic Class
[a] Adjusted for confounders: maternal age, education, marital status, employment, pregnancy planning and parity
[b] Adjusted for confounders, Neighbourhood Socioeconomic Class, late prenatal care, pre-pregnancy body mass index and smoking in pregnancy

Table 4 – Association between individual and neighbourhood socioeconomic characteristics and birth outcomes (fixed effects) in Generation XXI and maternal ethnic groups from Pelotas 2004

	Odds Ratio (95% CI) [a]			
	G21 (n=6585, 1266 blocks)	Pelotas 2004		
		White (n=1956, 387 blocks)	Black (n=486, 216 blocks)	Brown (n=636, 270 blocks)
Preterm				
Age	1.00 (0.99-1.02)	1.00 (0.98-1.02)	0.97 (0.93-1.01)	0.96 (0.77-1.18)
Squared age	-	-	-	1.01 (1.00-1.01)
Education	1.00 (0.98-1.03)	0.96 (0.91-1.00)	0.90 (0.83-0.99)	0.73 (0.58-0.91)
Squared education	-	-	-	1.02 (1.01-1.04)
Marital status (single vs. with partner)	1.13 (0.76-1.67)	0.87 (0.54-1.40)	0.72 (0.41-1.26)	0.79 (0.44-1.41)
Working (yes vs. no)	0.90 (0.71-1.14)	1.20 (0.87-1.64)	0.97 (0.57-1.64)	1.08 (0.66-1.76)
Pregnancy planning (yes vs. no)	0.91 (0.74-1.13)	1.23 (0.91-1.66)	0.81 (0.48-1.37)	0.82(0.52-1.28)
Small-for-gestational age				
Age	0.98 (0.97-1.00)	0.99 (0.97-1.01)	0.96 (0.92-1.00)	1.02 (0.99-1.06)
Education	0.98 (0.96-0.99)	1.11 (0.95-1.29)	0.94 (0.85-1.03)	0.94 (0.87-1.01)
Squared education	-	0.99 (0.98-1.00)	-	-
Marital status (single vs. with partner)	1.35 (1.03-1.76)	1.23 (0.88-1.74)	1.21 (0.69-2.11)	0.57 (0.29-1.13)
Working (yes vs. no)	1.15 (0.97-1.37)	0.80 (0.61-1.03)	0.95 (0.54-1.66)	0.68 (0.39-1.17)
Pregnancy planning (yes vs. no)	1.00 (0.85-1.16)	1.07 (0.84-1.36)	1.74 (1.04-2.94)	1.05 (0.67-1.67)

[a] Adjusted for maternal age, education, marital status, employment, pregnancy planning and Neighbourhood Socioeconomic Class. The fixed effect of neighbourhood SEC was not presented because does not have practical interpretation

DISCUSSION

This study shows that neighbourhood variation in pregnancy outcomes is not a consensual feature in all settings and ethnic groups. In Porto Metropolitan region, no clustering effect was observed for preterm or small-for-gestational age births. In Pelotas, a cluster effect was present in preterm within white women, while neighbourhood heterogeneity in SGA was only observed in black residents. Neighbourhood-to-neighbourhood disparities were beyond individual characteristics and were not explained by the contextual socioeconomic class.

This study used large population-based studies from two different settings which contribute to reinforce two main principles of research on contextual social determinants. First, the operationalization of neighbourhood contextual variables is striking and setting-specific. Second, disparities vary between and within settings.

We found that in Porto the composition of census group blocks is much more heterogeneous than in Pelotas. Census group blocks presented similar mean number of residents, but it is possible that, within groups, smaller clusters would be found. Women socio-demographic characteristics are more uniformly distributed and neighbourhood social class does not seem to distinguish such clear niches as in Pelotas. Our knowledge on this setting makes us to believe that it reflects true context variation. More homogenous results would be observed at the level of city blocks [20] but our sample is distributed in a large geographical space with more than 70% of the city smaller blocks having only one participant, which would limit our analysis. Also, it is reasonable to admit that the effect of social context does not restricts to immediate neighbourhood but also to the surrounding ones in which women spend their daily lives [24].

We based the analysis in the conceptual framework that neighbourhood socioeconomic composition would be related to birth outcomes because of different availability of social support and of goods and services (as health care or leisure time facilities), adaptation of coping strategies or exposure to chronic stress [7]. The lack of association between neighbourhood disadvantage and perinatal outcomes could result from inaccuracy of the obtained social class variable. It is possible that other variables would be useful to reflect the theoretical construct of socioeconomic class. We tested other indicators (such as mean per capita income, sanitation structures, attractiveness index) that did not reveal to increase the ability to socially discriminate neighbourhoods. Also, we intended to have a comparable set of indicator in both settings. Moreover, the individual maternal socioeconomic distribution across neighbourhoods' social class adds in favour of the good quality of this indicator. Other aspects related with violence, crime or social organization are important to explain the contextual effect on perinatal outcomes but represent other theoretical constructs [6] that we were no able to evaluate in this analysis. Thus, neighbourhood variation may be the result of different features of neighbourhood social environment that act beyond socioeconomic characteristics.

The operationalization of neighbourhood characterisation has other limitations that must be referred. We opted to use a geographical division of the neighbourhoods that is used for administrative purposes which may not adequately capture the social context and traditionally underestimates the relation between neighbourhood social class and perinatal outcomes. Also, we explored the relation of contextual effects on birth outcomes not taking into consideration the length of time women have lived in the neighbourhood [24]. In addition, pregnancy-induced mobility to different residences may limit the availability to causal inference on this association.

The non-randomization of individuals in neighbourhoods may be problematic and social selection may be an important limitation to interpret the results. We have adjusted the models for the background factors that may be related with people moving to or residing in their neighbourhoods, as purposed by Oakes, which may decrease selection bias [21].

Our results showed weak to no association between individual socioeconomic characteristics and birth outcomes. These results should be interpreted carefully since they represent within neighbourhood variations. Absence of statistical significance can be the result of the relatively small mean number of participants per neighbourhood.

In G21 study, no contextual variation was observed in pregnancy outcomes. These results contradict some previous studies reporting an increased rate of preterm and SGA with increasing neighbourhood deprivation [12, 25]. Heterogeneity in the place of residence may be a plausible explanation. Also, although the prevalence of adverse health behaviours, such as smoking, varies according neighbourhood social class, no clear gradient is observed and the frequency is relatively high in the entire sample which decreases potential cluster variation.

Additionally, the high proportion of early beginning in care (almost 90% of women begun prenatal care in the first trimester) may have attenuated potential differences. It would be useful to evaluate in which extent the universal and free health care service for pregnant women buffers contextual and individual socioeconomic effects on adverse birth outcomes.

In Pelotas preterm births seem to vary across neighbourhoods among white women while SGA showed neighbourhood-to-neighbourhood variation among the black ones. Ethnic differences were previously observed in the use of prenatal care, with quality of care to be consistently higher among white and high socioeconomic status women than among black and poor women [26]. Individual characteristics only explained 9% of the clustering in preterm and neighbourhood social class did not change the overall contextual variation. Also, despite not considering the components of prenatal care, further adjustment for late beginning of care only explained 3% of the differences in preterm among white women. Still, white women with similar individual socio-demographic profile living in neighbourhoods of higher prevalence of preterm showed a 45% increased risk of delivering a preterm than those living in neighbourhoods with lower propensity to preterm. This may reflect groups of white women living in neighbourhoods with high black density, since preterm was more frequent among black women. Racial disparities in preterm seem to result from higher infection rates and higher exposure to stressful events [27]. If the underlying reasons for exposure are contextual-patterned, understanding their specific features could be useful to address contextual variability among white women, particularly because segregation patterns are not as the same as in other settings and may have different influences in perinatal health [28].

Small-for-gestational age showed a different pattern with neighbourhood effects only detected among black women. Previous research found birthweight to vary according neighbourhood socioeconomic conditions in black women and not in whites or Latinas [11]. Neighbourhood social environment are thought to influence SGA babies by influencing the availability of resources that promote healthier lifestyles [7]. However, the variability across neighbourhoods was not attenuated after the adjustment for smoking behaviours or body mass index. Black women were the ones with higher prevalence of individual socioeconomic disadvantage, adverse lifestyles and late entrance in care. We cannot reject the possibility of residual confounding of individual socioeconomic characteristics may be reflected in the unexplained heterogeneity.

If a true effect of neighbourhood social environment in preterm and SGA does exist, it seems that other characteristics such as segregation, violence and crime or the availability and distance to grocery stores should be explored in these settings. Moreover, specific social organization of deprived neighbourhoods may lead to better outcomes while other conditions act in the opposite direction. Other resources like health care systems or neighbourhood-specific organizations may offset adverse exposures related to neighbourhood deprivation, requiring further research [5]. Especially in the Pelotas social context, special attention should be addressed to understanding neighbourhood variability in birth outcomes among white and black women.

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SUPPLEMENTARY FILE 1

Area-level characteristics were based on aggregated data at the statistical level of census block groups (the smallest level in Pelotas and the second smallest in Porto) provided by the 2000 (Brazil) and 2001 (Portugal) National Census. In Portugal, neighbourhoods from the city of Porto have already been socioeconomically characterised and the detailed description of the procedures can be found elsewhere [1]. We followed the same approach using a set of variables that reflect three distinct socioeconomic dimensions: age composition, education/occupation and housing characteristics.

Porto Metropolitan Region

Starting with 11 indicators, 3 presented floor or ceiling effects (more than 30% of sectors with the minimum or the maximum value), (aging index, attractiveness and primary sector activities). Within the same construct the correlation between indicators was tested and none was excluded since (correlation lower than 80%). The final set included 8 indicators showed a Cronbach's alpha of 0.69.

Pelotas

In Pelotas, Brazil, we opted to use the same strategy for selection of indicators. We have begun with 13 indicators to reflect the same constructs used in the Portuguese definition (age, education, occupation and housing) plus the proportion of female-headed households. Whenever possible the same indicator used in the Portuguese characterisation was tested, otherwise an indicator reflecting the same construct was tested or one that would better reflect Pelotas social reality was used (e.g. proportion of houses with two or more bathrooms).

After testing floor or ceiling effects, we excluded 6 indicators because of large asymmetries (aging index, proportion of individuals with high income, mean per capita income, proportion of households with three or more bathrooms, proportion of households with basic sanitation, proportion of households with septic tanks). Because of the possible correlation between variables representing the same theoretical construct, we opted to select only one of the variables if the correlation was larger than 80%. This only happened for mean number of schooling years and illiteracy proportion and, after fitting the models and calculating the cronbach's alfa, the mean number of schooling years was excluded and a final set of 7 indicators was used. The components of final set of indicators showed cronbach's alpha ranging from 0.69 to 0.93.

Table 1: Definition of the variables selected to characterize neighborhoods

A priori construct	Indicator	Porto	Pelotas	Type of indicator	Numerator (or definition if mean)	Denominator
Age	Young individuals	Yes	Yes	Proportion	Number of families with an individual aged 15 years or less (PT) Number of individuals aged 15 years or less (BZ)	Number of resident families (PT) Number of residents (BZ)
	Old individuals	Yes	Yes	Proportion	Number of residents at 65 years old or above	Number of residents
Education or occupation	Illiteracy	Yes	Yes	Proportion	Number of persons that cannot read or write	Number of residents aged ≥10 years
	High education	Yes	Yes	Proportion	Number of persons with upper secondary level of education or more (PT) Number of persons with 12 or more years of education (BZ)	Number of residents

A priori construct	Indicator	Porto	Pelotas	Type of indicator	Numerator (or definition if mean)	Denominator
	Unemployment	Yes	NA	Proportion	Number of persons unemployed	Number of residents aged 15 or more years
	Income	NA	Yes	Proportion	Number of persons with two or less National minimum wages	Number of residents
Building characteristics	Rented households	Yes	Yes	Proportion	Number of rented households	Number of households
	House size	Yes	Yes	Proportion	Number of households with or less rooms (PT) Number of households with two or more bathrooms (BZ)	Number of households
	Old buildings	Yes	NA	Proportion	Number of buildings constructed until 1985 (with more than 15 years)	Number of buildings

NA – Not Available;

Some indicators did not present a Gaussian distribution; consequently, all the variables were categorized in tertiles. Neighbourhoods with less than 10 residents per block were excluded. Further ahead, the rural region of Colonia was excluded because of the small number of participants (n=33)

For both datasets, neighborhoods were characterized fitting latent class analysis models to assess homogenous groups regarding socioeconomic characteristics. The number of latent classes was achieved considering the Bayesian information criterion (BIC), the Akaike information criterion (AIC), entropy and interpretability (collins). Better fit was indicated by smaller AIC and BIC values and entropy values closer to 1.0. The number of classes was achieved when an increase of classes did not improve the overall fit of the model or decreased interpretability. The analysis resulted in three socioeconomic classes for each country. At each class was calculated the probability of a block classified as belonging to that class to be in the 1st, 2nd or 3rd tertile of the selected indicator.

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4.5. Assessing the effect on outcomes of public or private provision of prenatal care in Portugal

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ABSTRACT

OBJECTIVE: To evaluate whether public and private prenatal care users experience similar outcomes, taking into consideration maternal pre-pregnancy social and clinical risk.

METHODS: We studied 7,325 women who delivered single newborns at five public maternity units in Porto, Portugal. Health behaviors and prenatal care were self-reported; pregnancy complications and delivery data were retrieved from medical files. The odds of inadequate weight gain, continuing to smoke, gestational hypertension, gestational diabetes, caesarean section, preterm birth, low birthweight, and small- and large-for-gestational-age were estimated for public and private providers using logistic regression, stratified by pre-pregnancy risk profile, adjusted for maternal characteristics.

FINDINGS: 38% of women used private prenatal care. Among low-risk women, public care users were more likely to gain excessive weight (OR = 1.26; 95% CI: 1.06–1.57) and be diagnosed with gestational diabetes (OR = 1.37; 95% CI: 1.01–1.86). They were less likely to have a caesarean (OR = 0.63; 95% CI: 0.51–0.78) and more likely to deliver small-for-gestational-age babies (OR = 1.48; 95% CI: 1.19–1.83). Outcomes were similar in high-risk women although preterm and pre-labor caesarean were less frequent in public care users (OR = 0.64 95% CI: 0.45–0.91; OR = 0.69 95% CI: 0.49–0.97). The amount of care was not significantly related to risk profile in either case.

CONCLUSIONS: Public care users experienced similar outcomes to those using private care, despite higher pre-pregnancy disadvantage. Low-risk women need further attention if narrowing inequalities in birth outcomes remains a priority.

Key words: prenatal care; health care provider; pregnancy complications; birth outcomes

INTRODUCTION

Strategies to expand quantity, quality and access to prenatal care services were designed during the past half-century to reduce inequalities in birth outcomes [1]. Despite an increase in coverage and the improvement in mortality indicators, low birthweight and preterm births have been rising in several countries, including Portugal [2-4]. Prenatal care should generally be tailored by pregnancy risk, and more care does not guarantee a favourable outcome. For low-risk women, a small number of visits is enough to ensure appropriate screening or treatment interventions, keeping costs affordable; high-risk pregnancies need an adaptation or scaling up of care [5].

Most research focusing on the effect of healthcare setting on pregnancy outcomes is conducted in the United States [6, 7] or in low-income countries [8, 9]. Despite improvements in prenatal care use, programs remained centred on specific disadvantaged populations and the evidence regarding universal health services is scarce and out of date.

Since the launch of the Portuguese National Health Service (NHS) in the early 1980s, the government has guaranteed universal free access to healthcare for all pregnant women and the coverage is high [10]. Also, more than 90% of all deliveries occur in the NHS. Low-risk pregnancies are followed at primary healthcare centres, by general practitioners, working as gatekeepers to public hospitals where differentiated care is provided. However, alternative or complementary private prenatal care with a gynaecologist or obstetrician is frequent, covered by out-of-pocket payment or voluntary/employer health insurance schemes. Despite the extensive offer, at the end of the twentieth century, barriers to care were observed, resulting in social inequalities in its use and in subsequent pregnancy outcomes [11, 12].

Universal healthcare services are moving closer to private solutions in several countries, so it is important to understand if and how public services are able to narrow social inequalities.

In a country where free prenatal care is universally available, we aimed to evaluate whether public and private care users experience equality of pregnancy outcomes, taking into consideration maternal pre-pregnancy risk profile and social characteristics.

METHODS

This cross-sectional study used baseline data from Generation XXI, the Portuguese birth cohort [13, 14]. In 2005-2006, at five public maternity units in the Porto Metropolitan Area, in the north of Portugal, resident women delivering live births were invited to take part. The sample includes 92% of women invited. Women (n=8,495) were evaluated up to 72 hours after delivery in face-to-face interviews using detailed standardized questionnaires. Pregnancy complications and peri-partum data were retrieved from medical records. The study was approved by the ethics committee of the University of Porto Medical School/Hospital S. João and a written signed consent form was obtained from all participants.

Prenatal care provider and components

Women were asked about the type of prenatal care used, with options offered being primary healthcare centre (always public), out-patient clinic at a public hospital, or private care. There are two major reasons for private care users to use prenatal care in public hospitals as well: pregnancy complications and because care after the 36th gestational week is offered to all women in the hospital where delivery will occur. Providers were further classified as public (primary healthcare centre and/or public hospital) or private (exclusive or with public). Almost 70% of public users and 72% of private users used only one type of facility. The characteristics of women using each type of healthcare provider can be found in the Supplementary file, Table S1. Women self-reported their gestational age at the first visit and the total number of visits. They also provided the number of routine biochemical tests (blood count, glucose, screening tests for infections), ultrasounds and whether they had received the biochemical aneuploidy screening [plasma protein A (PAPP-A), free-β human chorionic gonadotrophin (free hCGβ)], amniocentesis or chorionic villus sampling.

Maternal characteristics

Women were asked about their marital status, number of years of formal schooling, employment status and occupation (classified on the National Occupation Classification Scale [15]), and their household monthly income using €500 categories. Migration status was assessed using the women's and their parents' country of birth and age on arrival in Portugal [16]. Women were asked the number of previous pregnancies (none; 1; ≥2) and whether they had planned the current pregnancy.

Smoking status 3 months before conception and at each trimester was reported, including the number of cigarettes per day. Pre-pregnancy weight was reported and height was measured or obtained from the women's identity card registry. Body mass index (BMI) was calculated as "weight (kg)/(height2) (m)" and grouped as <18.5; 18.5–24.9; 25.0–29.9; ≥30.0 kg/m2.

Maternal pre-pregnancy risk profile was dichotomized as low and high, based on characteristics before the current pregnancy. As no national guidelines are available, women were classified according to a local hospital's guidelines (one of the units included) [17]. Indicators were added for characteristics which have been shown to increase the risk of pregnancy complications and adverse outcomes, and which need specialized care [18, 19]. Women considered to be high-risk fulfilled at least one of the criteria of history of fetal death, ≥3 miscarriages, previous gestational diabetes, placental abruption or placenta praevia, previous preterm birth (<37 weeks), low birthweight (<2,500g) or macrosomia (>4500g), previous fetal congenital anomaly, maternal medical diagnosis of HIV, epilepsy, dyslipidaemia, hypertension, diabetes, cancer, cardiac or renal disease, BMI <18.0 kg/m2 or ≥35.0 kg/m2, age <18 or >40 years or smoking >10 cigarettes per day.

Prenatal outcomes

Among smokers (women smoking 3 months before conception), continuation was attributed to those who smoked the same number of cigarettes in the third trimester (vs. women that ceased or reduced). Weight gain during pregnancy was calculated as the difference between the mother's reported weight before delivery and pre-pregnancy weight. Taking in consideration pre-pregnancy

BMI, weight gain was categorized according to the Institute of Medicine (IOM) recommendations as adequate, reduced or excessive [20]. Gestational hypertensive disorders (gestational hypertension or preeclampsia/eclampsia) and diabetes were retrieved from clinical records.

Birth outcomes

Mode of delivery was classified as caesarean or vaginal. Caesareans were also classified as in-labour (vs. vaginal deliveries) or before the onset of labour (vs. vaginal plus in-labour caesareans). Newborns were classified as preterm (<37 gestational weeks), low birthweight (<2,500g), small-(SGA) or large-for-gestational-age (LGA). Gestational age used ultrasound measurements (if performed up to the 20th gestational week) or, if no data available (15%), the last menstrual period. SGA and LGA were defined as the sex-specific birthweight <10th or > 90th percentile for each gestational age [21].

Analysis

Of 8,495 participants in the birth cohort, a subgroup of 313 women was recruited during pregnancy at two of the hospitals included. They were invited if their first prenatal care visit had occurred before 13 gestational weeks. Because of that, they were excluded from this analysis. Eligible women were therefore recruited at birth, delivered a single fetus (137 multiple pregnancies were excluded) and had had prenatal care [23 (0.3%) women had had no care or had begun care after the 36th gestational week] (n=8,022). Women were excluded if had missing data on: source of prenatal care (n=62), variables that made it possible to define pre-pregnancy risk profile (n=319), smoking cessation (n=62), weight gain (n=194), gestational hypertension/eclampsia/diabetes (n=30), mode of delivery (n=1), gestational age (n=10), or age, education or pregnancy planning (n=19). The final sample comprised 7,325 women. When compared with those excluded, those included were more educated, more often married, with a higher monthly income, and more likely to have had a planned pregnancy and used private prenatal care.

Maternal socio-demographics and pre-pregnancy risk profile were compared by care provider (public and private) using chi-square tests. Because prenatal care components and outcomes could vary with pre-pregnancy risk profile, the analyses were stratified by pre-pregnancy risk (interactions (α=10 between pre-pregnancy risk and prenatal care provider were found for smoking continuation, weight gain, gestational diabetes and hypertensive disorders, preterm birth and SGA). Odds ratio (and respective 95% confidence intervals) of each adverse pregnancy outcome by care provider were computed using multivariable logistic regression models.

To minimize selection bias because of case mix, all socio-demographic characteristics, clinical history and delivery hospital were included in the first adjusted model (Model 1). Model 2 was adjusted for potential confounders: parity, pre-pregnancy BMI and pre-pregnancy smoking. Interactions between healthcare provider and each variable were tested. When statistically significant (α=10%), interaction terms were included in the model. Successive models 3 and 4 were adjusted to assess potential mediators of the observed differences. Model 3 included gestational age at the first prenatal care visit and the number of visits. Both variables were removed as no changes in the estimates were observed. Model 4 fitted only for birth outcomes, including prenatal outcomes (smoking in the third trimester, weight gain, gestational diabetes and gestational hypertensive disorders) as possible mediators. The robustness of our results was tested by conducting sensitivity analyses. First, the association between prenatal care provider and birth outcomes was tested excluding women with gestational diabetes and hypertensive disorders. Then women that used more than one type of facility were excluded, i.e., exclusive primary healthcare centre or exclusive public hospital users were compared with exclusive private care users (TableS2). Finally, multivariate imputation via chained equations was used to test whether the exclusion of participants with missing variables led to distinct results (Table S3).

RESULTS

Thirty-eight percent of women (n=2,826) used private prenatal care. Of public care users, 30% and 37% respectively were followed exclusively in primary healthcare and in public hospitals. Public care users were more likely to be younger, less educated, single, migrant (from Brazil or Portuguese-speaking African countries), multigravidae, be unemployed or have unskilled occupations, have lower income and an unplanned pregnancy (Table 1). They more frequently presented a pre-pregnancy high-risk profile (39% vs. 26%) and were more often overweight or obese (34% vs. 24%), smokers (30% vs. 20%) and previously diagnosed with chronic diseases (10% vs. 8%) (Table 2).

Table 1 – Maternal socio-demographic characteristics according the prenatal care provider

	Prenatal Care Provider		
	Public (n=4499)	Private (n=2826)	p-value*
Maternal Age (years)			
<20	351 (7.8)	29 (1.0)	
20-24	987 (21.9)	209 (7.4)	
25-29	1323 (29.4)	911 (32.2)	
30-34	1168 (26.0)	1183 (41.9)	
35-39	553 (12.3)	422 (14.9)	
≥40	117 (2.6)	72 (2.6)	<0.001
Education (schooling years)			
≤5	582 (12.9)	56 (2.0)	
6-8	1393 (31.0)	334 (11.8)	
9-11	1282 (28.5)	435 (15.4)	
12	740 (16.4)	688 (24.3)	
≥13	502 (11.2)	1313 (46.5)	<0.001
Migrant Status			
Portuguese born	4274 (95.3)	2703 (96.5)	
European	37 (0.8)	36 (1.2)	
Portuguese speaking countries [a]	155 (3.5)	49 (1.8)	
Other Migrants	18 (0.4)	13 (0.5)	<0.001
Single women	361 (8.0)	64 (2.3)	<0.001
Working condition			
Employed	2831 (63.1)	2425 (86.0)	
Unemployed	1138 (25.4)	288 (10.2)	
Housewife	363 (8.1)	65 (2.3)	
Student / other	155 (3.4)	43 (1.5)	<0.001
Occupation			

	Prenatal Care Provider		
	Public (n=4499)	Private (n=2826)	p-value*
Non-qualified worker	576 (14.3)	70 (2.6)	
Blue-collar worker	747 (18.5)	179 (6.6)	
Clerical worker	2211 (54.9)	1235 (45.3)	
Managerial-professional worker	496 (12.3)	1243 (45.6)	<0.001
Monthly income (€)			
<500	410 (9.3)	35 (1.3)	
500-1000	1662 (37.7)	437 (15.9)	
1001-1500	1105 (25.1)	737 (26.9)	
1501-2000	447 (10.2)	597 (21.8)	
>2000	284 (6.4)	733 (26.7)	
No answer / Not known	498 (11.3)	203 (7.4)	<0.001
Number of previous pregnancies			
None	2084 (46.3)	1502 (53.1)	
One	1529 (34.0)	915 (32.4)	
Two or more	886 (19.7)	409 (14.5)	<0.001
Planned pregnancy	2729 (60.7)	2233 (79.1)	<0.001

*The number of participants in each category may not add up due to missing data; * Chi-square tests excluded the category "does not know";* [a] Brazil, Angola, Mozambique, Cape Verde, S. Tome and Principe, Guinea Bissau

Table 2 – Maternal pre-pregnancy risk profile according the prenatal care provider

	Prenatal Care Provider		
	Public (n=4499)	Private (n=2826)	p-value
Pregnancy risk classification			
Low-risk	2758 (61.3)	2079 (73.6)	
High-risk	1741 (38.7)	747 (26.4)	<0.001
Body mass index (kg/m^2)			
<18.5	200 (4.4)	99 (3.5)	
18.5-24.9	2775 (61.7)	2045 (72.4)	
25.0-29.9	1047 (23.3)	512 (18.1)	
≥30.0	477 (10.6)	170 (6.0)	<0.001
Pre-pregnancy smoking status			
Never smoker	2698 (60.0)	1900 (67.2)	
Ex-smoker	456 (10.1)	362 (12.8)	
Smoker, ≤ 10 cig/day	663 (14.7)	317 (11.2)	
Smoker > 10 cig/day	682 (15.2)	247 (8.8)	<0.001
Chronic disease	452 (10.0)	241 (8.5)	0.030
Among multigravidae			
Previous fetal deaths	50 (2.1)	20 (1.5)	0.227
Previous miscarriages	504 (21.0)	357 (27.1)	<0.001
Previous preterm birth (<37 weeks)	201 (8.7)	84(6.5)	0.021
Previous low birthweight (<2500g)	194 (8.3)	71 (5.4)	0.002
Previous macrosomia (>4500g)	25 (11)	7 (0.5)	0.102
Previous congenital anomaly	95 (4.0)	36 (2.8)	0.056
Previous placental disorder	34 (1.5)	28 (2.2)	0.124
Previous gestational diabetes	52 (2.2)	39 (3.0)	0.133

The number of participants in each category may not add up due to missing data;

Both low and high pre-pregnancy risk women who opted for public services began care later, and had fewer visits, ultrasounds and routine blood analyses. Private care users reported more visits and ultrasounds, even for similar gestational ages at the beginning of care. Among low-risk early care users (<6 gestational weeks), 52% of women in public and 64% in private settings reported at least 10 visits and differences remained for late care users (>13 gestational weeks): ≥10 visits were reported by 17% public vs. 28% private. Biochemical aneuploidy screening tests were less frequently reported by public care users, as were amniocentesis/chorionic villus sampling among younger women (<35 years), although for those aged ≥35 years no difference was observed (Table 3).

Table 3 – Prenatal care components according prenatal care provider and pre-pregnancy risk profile.

	Low Risk			High Risk		
	Public (n=2758)	Private (n=2079)	p-value	Public (n=1741)	Private (n=747)	p-value
First Prenatal Visit (Gestational Age)						
<6	619 (22.8)	631 (30.7)		351 (20.6)	235 (32.1)	
6-12	1746 (64.4)	1348 (65.6)		1062 (62.2)	453 (61.8)	
≥13	347 (12.8)	76 (3.7)	<0.001	294 (17.2)	45 (6.1)	<0.001
Does not know	*1.4*	*1.1*		*1.9*	*1.6*	
Number of visits						
≥ 10	1136 (41.7)	1123 (54.5)		733 (42.7)	380 (51.8)	
7-9	1216 (44.6)	833 (40.5)		744 (43.4)	307 (41.8)	
3-6	361 (13.2)	103 (5.0)		228 (13.3)	45 (6.1)	
1-2	12 (0.4)	0 (0.0)	<0.001	11 (0.6)	2 (0.3)	<0.001
Does not know	*0.3*	*0.2*		*0.6*	*0.3*	
Number of ultrasounds						
≥7	162 (6.0)	860 (42.5)		131 (7.7)	323 (44.6)	
4-6	1475 (54.5)	674 (33.3)		925 (54.4)	247 (34.1)	
3	912 (33.7)	465 (23.0)		533 (31.3)	142 (19.6)	
0-2	158 (5.8)	23 (1.1)	<0.001	113 (6.6)	13 (1.8)	<0.001
Does not know	*0.7*	*1.2*		*0.8*	*1.5*	
Number of routine biochemical analysis						
≥7	64 (2.4)	60 (3.0)		57 (3.4)	23 (3.3)	
4-6	1005 (38.2)	772 (39.2)		621 (37.3)	290 (41.1)	
3	1312 (49.9)	1035 (52.5)		785 (47.2)	350 (49.6)	
0-2	249 (9.5)	105 (5.3)	<0.001	201 (12.1)	43 (6.1)	<0.001
Does not know	*2.5*	*2.1*		*2.0*	*1.3*	
Biochemical aneuploidy screening *						
Maternal age <35 years	881 (40.7)	1327 (78.4)	<0.001	513 (42.2)	397 (74.5)	<0.001
Does not know	*8.8*	*2.5*		*11.5*	*4.3*	
Maternal age ≥ 35 years	138 (42.3)	149 (51.4)	0.025	92 (30.9)	76 (43.4)	0.006
Does not know	*3.3*	*4.3*		*6.9*	*1.7*	
Amniocentesis / Chorionic villus sampling						
Maternal age <35 years	107 (4.5)	111 (6.3)	0.008	65 (4.7)	38 (6.8)	0.056
Does not know	*0.2*	*0.2*		*0.3*	*0.4*	
Maternal age ≥ 35 years	162 (47.6)	154 (49.8)	0.577	175 (54.4)	104 (58.1)	0.418
Does not know	*0.0*	*0.0*		*0.0*	*0.0*	

** plasma protein A (PAPP-A), free-β human chorionic gonadotrophin (free hCGβ)*

The number of participants in each category may not add up due to missing data. Proportions were calculated excluding women reporting "not know"

Prenatal outcomes

When compared with private care, pre-pregnancy low-risk public users presented higher frequency of excessive weight gain (38% vs. 33%) and of gestational diabetes (7% vs. 4%), while high-risk women were more likely to continue smoking (11% vs. 3%) (Table 4).

Table 4 – Prevalence of pregnancy and birth outcomes according health care provider

	Low Risk			High Risk		
	Public (n=2758)	Private (n=2079)	p-value	Public (n=1741)	Private (n=747)	p-value
Prenatal outcomes						
Smoking continuation [b]	61 (12.8)	26 (10.6)	0.400	92 (10.6)	11 (3.4)	<0.001
Reduced weight gain [c]	689 (25.0)	529 (25.4)	0.191	492 (28.3)	191 (25.6)	0.244
Excessive weight gain [c]	1051 (38.1)	689 (33.1)	<0.001	648 (37.2)	290 (38.8)	0.913
Gestational Diabetes [d]	186 (6.7)	88 (4.2)	<0.001	144 (8.4)	61 (8.3)	0.892
Gestational hypertensive disorders [e]	87 (3.2)	58 (2.8)	0.462	55 (3.3)	34 (4.8)	0.084
Birth outcomes						
Caesarean delivery	883 (32.0)	825 (39.7)	<0.001	607 (34.9)	317 (42.4)	<0.001
Caesarean in labour	567 (23.2)	458 (26.8)	0.009	349 (23.5)	172 (28.6)	0.016
Caesarean before labour	316 (11.5)	367 (17.6)	<0.001	258 (14.8)	145 (19.4)	0.004
Preterm birth	171 (6.2)	131 (6.3)	0.886	144 (8.3)	88 (11.8)	0.006
Low birthweight	164 (6.0)	110 (5.3)	0.329	163 (9.4)	76 (10.2)	0.529
Small-for-gestational-age	396 (14.4)	220 (10.6)	<0.001	330 (19.0)	132 (17.7)	0.450
Large-for-gestational-age	101 (3.7)	74 (3.6)	0.850	83 (4.8)	32 (4.3)	0.598

After adjusting for maternal characteristics (Table 5, model2), excessive weight gain (OR=1.29; 95%CI: 1.06–1.57) and gestational diabetes (OR=1.37; 95%CI: 1.01–1.86) remained significantly different among pre-pregnancy low-risk women. No differences were found after adjustment for prenatal care components (Model3). High-risk women presented similar prenatal outcomes in both settings.

Birth outcomes

Women in public care had lower proportions of caesarean deliveries, both before and during labour. Low-risk women delivered more SGA babies in public care (14% vs. 11%) (Table 4). After adjustment (Table 5, Model2), the differences remained significant: in-labour caesarean OR=0.70 (95%CI: 0.54–0.91), pre-labour caesarean OR=0.62 (95%CI: 0.47–0.2), SGA (OR=1.48; 95%CI: 1.19–1.83). The adjustment for prenatal care components and for pregnancy mediators did not explain the differences (Table 5, Models 3-4). High-risk women attending public care were less likely to have pre-labour caesareans (OR=0.69; 95%CI: 0.49–0.97) and to deliver preterm babies (OR=0.66; 95%CI: 0.48–0.92).

The results of the sensitivity analyses (Tables S2-S3) were similar to those mentioned above. When excluding mixed care users, estimates remained similar or with stronger significant associations. Among high-risk women, preterm and caesarean deliveries were no longer different by healthcare provider. When models were fitted using multiple imputed data, in-labour caesareans among pre-pregnancy low-risk women were no longer different by prenatal care providers.

Table 5 - Effect of prenatal care provider on prenatal and birth outcomes according pre-pregnancy risk profile

	Adjusted Odds Ratio (95% CI): Public vs. Private Health Care provider							
	Pre-pregnancy Low Risk				Pre-pregnancy High risk			
	Models #1	Models #2	Models #3	Models #4	Models #1	Models #2	Models #3	Models #4
Prenatal outcomes								
Smoking continuation [a]	0.65 (0.33-1.25)	0.61 (0.31-1.20)	0.63 (0.32-1.25)	------	1.64 (0.78-3.41)	1.41 (0.66-3.02)	1.36 (0.63-2.97)	------
Reduced weight gain [b]	1.08 (0.90-1.29)	1.10 (0.92-1.32)	1.10 (0.92-1.32)	------	0.98 (0.75-1.28)	0.96 (0.73-1.26)	0.96 (0.73-1.26)	------
Excessive weight gain [b]	1.20 (1.02-1.40)	1.29 (1.06-1.57)	1.29 (1.06-1.57)	------	1.04 (0.82-1.31)	1.12 (0.40-3.11)	1.18 (0.42-3.33)	------
Gestational Diabetes [c]	1.42 (1.05-1.93)	1.37 (1.01-1.86)	1.39 (1.02-1.90)	------	1.18 (0.81-1.73)	1.09 (0.74-1.60)	1.09 (0.74-1.61)	------
Gestational hypertensive disorders [d]	0.97 (0.65-1.46)	1.11 (0.72-1.70)	1.12 (0.73-1.72)	------	0.61 (0.37-1.03)	0.54 (0.29-0.99)	0.53 (0.29-0.98)	------
Birth outcomes								
Caesarean delivery	0.79 (0.69-0.92)	0.63 (0.51-0.78)	0.65 (0.53-0.81)	0.62 (0.50-0.76)	0.94 (0.76-1.16)	0.88 (0.67-1.16)	0.86 (0.65-1.13)	0.89 (0.68-1.17)
Caesarean in labor	0.83 (0.70-0.99)	0.70 (0.54-0.91)	0.72 (0.56-0.94)	0.70 (0.54-0.91)	0.92 (0.71-1.20)	1.08 (0.76-1.53)	1.05 (0.74-1.50)	1.10 (0.78-1.56)
Caesarean before labor	0.78 (0.64-0.95)	0.62 (0.47-0.82)	0.65 (0.49-0.86)	0.61 (0.46-0.81)	0.96 (0.73-1.26)	0.69 (0.49-0.97)	0.68 (0.48-0.95)	0.70 (0.50-0.98)
Preterm birth	0.96 (0.72-1.28)	0.97 (0.73-1.30)	0.87 (0.65-1.17)	0.99 (0.74-1.33)	0.67 (0.48-0.95)	0.68 (0.48-0.95)	0.66 (0.46-0.94)	0.70 (0.49-1.00)
Low birthweight	1.25 (0.92-1.69)	1.29 (0.96-1.75)	1.17 (0.86-1.60)	1.29 (0.95-1.76)	0.80 (0.56-1.12)	0.83 (0.58-1.17)	0.83 (0.58-1.18)	0.90 (0.62-1.30)
Small-for-gestational-age (SGA)	1.44 (1.16-1.78)	1.48 (1.19-1.83)	1.49 (1.20-1.84)	1.47 (1.19-1.82)	0.95 (0.72-1.24)	0.97 (0.74-1.28)	0.96 (0.72-1.26)	0.98 (0.74-1.29)
Large-for-gestational-age (LGA)	0.83 (0.57-1.22)	0.78 (0.53-1.14)	0.77 (0.52-1.14)	0.74 (0.50-1.09)	1.40 (0.85-2.31)	1.30 (0.79-2.15)	1.30 (0.78-2.17)	1.28 (0.78-2.13)

Models #1 - Adjusted for hospital of delivery + maternal age + education + migrant status + marital status + working condition + occupation + income + pregnancy planning + chronic conditions

Models #2 – Models #1 + parity (except for gestational diabetes; interaction with prenatal care provider included for caesarean deliveries models) + pre-pregnancy body mass index (except for smoking continuation and preterm; interaction with prenatal care provider included for excessive weight gain) + smoking before pregnancy (except for caesarean deliveries models, preterm, low birthweight and LGA; interaction with prenatal care provider included for gestational hypertensive disorders)

Models #3– Models #2 + gestational age at 1st visit + number of visits

Models #4 – Models #2 + weight gain (except for pre-labour caesarean) + smoking in 3rd trimester (only for SGA) + gestational hypertensive disorders (except for LGA) + gestational diabetes (except caesarean in labour, preterm, low birthweight, SGA)

[a] within pre-pregnancy smokers; [b] versus adequate weight gain; [c] excluding women with pre-pregnancy diabetes; [d] excluding women with pre-pregnancy hypertension.

DISCUSSION

Women using public prenatal care showed less favourable clinical and social pre-pregnancy characteristics and had less care than women using private prenatal care. Nonetheless, pre-pregnancy high-risk public care users presented outcomes similar to those using private care, while in low-risk pregnancies, only part of the inequalities seemed to be attenuated. Public prenatal care users showed higher rates of pregnancy-related adverse behaviours and an increased likelihood of fetal growth restriction.

Strengths and limitations

All women delivered in public hospitals so the impact of peri-partum context on pregnancy outcomes was attenuated. At the time of recruitment, public hospitals were responsible for 95% of deliveries in the region. We would expect the inclusion of the small group of women delivering in a private setting to increase the differences found in this study, as we predict that these women would be more advantaged, presenting lower prevalence of the most adverse outcomes. Also, caesarean deliveries are more frequent in private than in public hospitals [22].

Our data are from 2005–2006, and changes in prenatal care are likely to have occurred. Primary healthcare was restructured after 2005, resulting in the creation of Family Health Units that, as using a more flexible and multidisciplinary approach [23], might positively impact the quality of care. However, recent policies on cost controls and the economic crisis seem to be negatively affecting access to and use of public care services [24], although prenatal care remains free of charge.

Most outcomes were collected from medical files, so we expect misclassification to be minimal. Misclassification may have occurred in the report of pre- and in-pregnancy smoking habits and weight [25]. However, these characteristics are in accordance with what would be expected for this group of women [13, 26]. However, it is possible that more educated women underreport their smoking consumption, because of social desirability. If so, smoking cessation among private care users would be overestimated and differences between healthcare providers may be attenuated. Other pre-pregnancy characteristics are less likely to be biased.

Prenatal care providers were distinguished by the system of payment. However, healthcare professionals are differently distributed in the public and private sectors. In private settings, care is mainly provided by gynaecologists/obstetricians. In public settings low-risk women are followed by general practitioners in primary healthcare centres and high-risk women referred to hospitals, where specialized care is offered. Differences between sources of care may, therefore, represent different healthcare providers. However, public care is designed assuming that different levels of risk need different levels of specialization. Low-risk pregnancies, followed by general practitioners, are expected to present similar outcomes to those with comparable risk followed by gynaecologists/obstetricians. Unfortunately, to the best of our knowledge, no clinical trial in developed settings has tested this hypothesis.

We did not collect the number or sequence of visits to each prenatal care facility. However, a large proportion of women received care from only one setting, reinforcing our results. When excluding mixed users, similar estimates were observed and significant differences were emphasized (Table S2).

Differences in preterm observed in high-risk women were probably explained by selection bias. Most women delivering preterm (and all delivering very preterm) are transferred to public settings with neonatal intensive care facilities. Preterm delivery was therefore likely to be overestimated among private users, explaining the observed differences.

Another possible limitation of our study was the chosen definition of pre-pregnancy risk. No consensual definitions are available and we opted for the features that are most often reported and so generally agreed to be relevant [17-19]. Most of the characteristics listed were included in our definition, although that excluded factors such as previous pre-eclampsia or severe asthma. Though most are rare conditions, the low-risk group may include some high-risk women.

Finally, causal inference should be drawn carefully due to the observational design of our study. Self-selection of healthcare provider is likely to have occurred, which limits generalizability of the results. However, we have adjusted for a large number of socio-demographic and clinical characteristics that may be related to the decision to use particular healthcare providers, minimizing potential selection bias. Nevertheless, the differences observed may result from uncontrolled variables. We tested propensity score matching (considering all the variables that we used in Models 1 and 2) to control for self-selection to prenatal care provider and similar results were found (data not shown). We conducted several sensitivity analyses to assure the strength of our results. This study therefore seems to be a robust alternative to randomized and quasi-randomized experiments.

Interpretation

Women opting for out-of-pocket private services (disregarding the public offer) show, in general, better social profile and are more likely to plan pregnancy, adopt healthy lifestyles and to be aware of the risk of complications [27, 28]. Prenatal care in Portugal is available at all primary healthcare centres, which are at relatively short distance from residence and each woman is entitled to free care. Thus, the decision to use alternative care seems to be related to the perception of quality or the access to specialized care [12]. Because public prenatal care for low-risk women is offered by general practitioners, private settings are a possible route to access an obstetrician. The observed apparent protection provided by private providers may therefore be a result of differences in women's attitudes and expectations, which we could not fully attenuate by adjusting for social profile and pregnancy planning. This may also explain the higher rates of caesarean deliveries before the onset of labour, which are, as previously described for this cohort, also associated with cultural background [16].

Our results may also be explained by the early initiation of care or the higher number of visits in private settings. However, adjusting for these characteristics did not change the results and we would expect to see the same differences independently of the risk profile, and not only in low-risk pregnancies. Additionally, no data supports the theory that privately-insured women have better results based on the number of visits [29].

We can hypothesize that public providers disregarded preventable adverse health behaviours in alleged low-risk women. Differences were found for weight gain and gestational diabetes and not for smoking. This may reflect the widely-recognized risk of smoking, justifying more efforts regarding smoking cessation [30]. We cannot assess whether the differences in prenatal outcomes reflect time constraints, providers' skills or non-existent clinical guidelines. However, no national guidelines exist on weight gain and IOM recommendations have only recently started to be adopted. Despite the higher likelihood that public care users will gain excessive weight or have impaired glucose metabolism, macrosomia (or excessive fetal growth) was not different. This might reflect either early diagnosis and/or timely treatment, based on the existing referral system to hospitals with perinatal support [31].

High-risk women appeared to have a similar and probably more standardized clinical approach, regardless of the care setting. Health behaviours were possibly addressed more carefully in women with another risk factor than in apparently low-risk ones. Also, other non-behavioural risk factors may contribute to adverse outcomes. Unfortunately, we could not assess the effect of the quality of care, which would be of particular interest as the minimization of risk was not mediated by the amount of care. Differences between public and private providers in prenatal care components do not seem to reflect effectiveness, but rather increased medicalization of care provided by private providers to wealthier and healthier women, which may not always be necessary.

Conclusion

Most public prenatal care users experienced similar outcomes to those from private care. Public care seems to solve the major problems effectively, but only attenuates part of their users' increased social and clinical risk. To further overcome inequalities in birth outcomes, prevention strategies need to incorporate special attention to low-risk women, as well as those at higher risk of problems.

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Supplementary Tables

Table S1 - Maternal socio-demographic and clinical characteristics by prenatal care provider

	Exclusive Public			Public + Private	Exclusive Private
	Only Primary Health Care (n=1339) %	Only Hospital (n=1685) %	Primary Health Care + Hospital (n=1475) %	(n=792) %	(n=2034) %
Maternal socio-demographics					
Maternal Age (years)					
<20	7.3	9.1	6.8	2.2	0.6
20-24	29.3	14.0	24.4	10.6	6.2
25-29	31.4	27.6	29.6	34.3	31.4
30-34	24.8	26.9	26.0	37.1	43.7
35-39	6.0	17.5	12.0	13.0	15.7
≥40	1.1	5.0	1.2	2.8	2.5
Education (schooling years)					
≤5	13.9	12.8	12.3	3.7	1.3
6-8	35.2	26.9	31.7	15.5	10.4
9-11	28.6	26.4	30.8	20.0	13.6
12	14.9	16.8	17.4	25.5	23.9
>12	7.3	17.1	7.9	35.4	50.8
Migrant Status					
Portuguese	94.4	95.4	96.1	95.4	96.9
European	0.8	1.0	0.7	1.0	1.4
Portuguese speaking countries	4.3	3.2	3.0	3.3	1.1
Other Migrants	0.6	0.4	0.2	0.2	0.6
Single women	7.2	7.1	9.8	2.8	2.1
Working condition					
Employed	61.0	64.6	63.3	79.3	88.6
Unemployed	27.4	22.9	26.3	14.7	8.5
Housewife	9.1	7.7	7.6	3.8	1.7
Student / other	2.5	4.8	2.8	2.3	1.2
Occupation					
Non-qualified	16.8	11.6	15.0	4.8	1.7
Blue-collar	22.5	15.3	18.5	8.4	5.9
Clerical	51.5	54.4	58.3	52.6	42.5
Managerial-professional	9.2	18.6	8.2	34.2	49.9
Monthly income (€)					
<500	8.8	9.4	9.6	2.6	0.8
500-1000	40.2	34.9	38.8	21.2	13.9
1001-1500	24.5	23.8	27.1	30.7	25.4
1501-2000	8.9	12.1	9.0	20.0	22.4
>2000	4.4	9.8	4.5	17.7	30.3
No answer / Not known	13.2	10.0	11.0	7.8	7.3
Number of previous pregnancies					
None	46.2	44.2	48.8	56.8	51.7
One	36.4	32.9	33.0	29.3	33.6
Two or more	17.4	22.8	18.2	13.9	14.7
Planned pregnancy	60.6	60.4	61.0	73.2	81.3

Maternal pre-pregnancy risk profile					
Pre-pregnancy high risk	25.9	40.5	31.8	26.4	20.9
Body mass index (kg/m^2)					
<18.50	4.0	4.5	4.8	2.4	3.9
18.50-24.99	63.4	63.2	58.4	69.3	73.6
25.00-29.99	23.4	20.5	26.4	20.7	17.1
≥30.00	9.2	11.9	10.4	7.6	5.4
Pre-pregnancy smoking status					
Never smoker	64.2	59.3	57.0	68.2	66.9
Ex-smoker	9.3	10.6	10.3	13.8	12.4
Smoker, ≤ 10 cig/day	13.9	13.9	16.5	9.0	12.1
Smoker > 10 cig/day	12.6	16.2	16.3	9.1	8.6
Chronic disease	5.8	14.0	9.4	11.1	7.5
Among multigravidae					
Previous fetal deaths	0.8	2.9	2.3	2.1	1.3
Previous miscarriages	16.0	24.7	21.0	26.2	27.4
Previous preterm birth (<37 weeks)	8.0	10.5	7.1	7.2	6.3
Previous low birthweight (<2500g)	9.0	9.0	6.6	6.2	5.2
Previous macrosomia (>4500g)	1.3	1.2	0.7	0.9	0.4
Previous congenital anomaly	2.7	4.3	5.0	4.5	2.2
Previous placental disorder	1.2	1.3	2.1	2.8	2.0
Previous gestational diabetes	1.2	2.2	2.9	4.1	2.6

Table S2 –Sensitivity analyses: effect of prenatal care provider on prenatal and birth outcomes according pre-pregnancy risk profile

	Sensitivity analysis (public vs. private) Adjusted OR (95% CI) [a]	
	Excluding gestational diabetes and hypertensive disorders	Excluding mixed users [b]
LOW RISK		
Prenatal outcomes		
Smoking continuation [c]	-------	0.91 (0.40-2.08)
Reduced weight gain [d]	------	1.15 (0.93-1.44)
Excessive weight gain [d]	-------	1.42 (1.12-1.80)
Gestational Diabetes [e]	------	1.59 (1.06-2.37)
Gestational hypertensive disorders [f]	-------	1.38 (0.80-2.42)
Birth outcomes		
Caesarean delivery	0.64 (0.52-0.80)	0.67 (0.52-0.86)
Caesarean in labour	0.76 (0.58-1.00)	0.71 (0.52-0.97)
Caesarean before labour	0.57 (0.42-0.77)	0.68 (0.49-0.95)
Preterm birth	0.87 (0.63-1.20)	1.06 (0.75-1.50)
Low birth weight	1.34 (0.96-1.87)	1.50 (1.05-2.14)
Small-for-gestational-age (SGA)	1.64 (1.31-2.06)	1.73 (1.33-2.25)
Large-for-gestational-age (LGA)	0.77 (0.50-1.16)	0.73 (0.45-1.17)
HIGH RISK		
Prenatal outcomes		
Smoking continuation [c]	-------	0.79 (0.30-2.11)
Reduced weight gain [d]	------	0.97 (0.69-1.35)
Excessive weight gain [d]	-------	1.37 (0.42-4.41)
Gestational Diabetes [e]	------	1.00 (0.61-1.64)
Gestational hypertensive disorders [f]	-------	0.65 (0.26-1.58)
Birth outcomes		
Caesarean delivery	0.83 (0.62-1.12)	0.90 (0.64-1.26)
Caesarean in labour	1.00 (0.69-1.46)	1.12 (0.72-1.76)
Caesarean before labour	0.65 (0.44-0.94)	0.74 (0.49-1.13)
Preterm birth	0.75 (0.50-1.11)	0.69 (0.45-1.06)
Low birth weight	1.01 (0.67-1.52)	0.85 (0.55-1.32)
Small-for-gestational-age (SGA)	1.00 (0.74-1.35)	0.84 (0.60-1.19)
Large-for-gestational-age (LGA)	1.00 (0.58-1.73)	1.21 (0.65-2.27)

[a] Based on manuscript models #2 – adjusted for hospital of delivery + maternal age + education + migrant status + marital status + working condition + occupation + income + pregnancy planning + chronic conditions + parity (except for gestational diabetes; interaction with prenatal care provider included for caesarean deliveries models) + pre-pregnancy body mass index (except for smoking continuation and preterm; interaction with prenatal care provider included for excessive weight gain) + smoking before pregnancy (except for caesarean deliveries models, preterm, low birthweight and LGA; interaction with prenatal care provider included for gestational hypertensive disorders)

[b] Exclusive primary health care centre or exclusive public hospital vs. exclusive private care users

[c] within pre-pregnancy smokers; [d] versus adequate weight gain; [e] excluding women with pre-pregnancy diabetes; [f] excluding women with pre-pregnancy hypertension

Table S3 – Sensitivity analysis: Effect of prenatal care provider on prenatal and birth outcomes according pre-pregnancy risk profile using multiple imputation *

	OVERALL		Low risk		High risk	
	Complete cases	Multiple imputation	Complete cases	Multiple imputation	Complete cases	Multiple imputation
LOW RISK						
Prenatal outcomes						
Smoking continuation [c]	0.90 (0.54-1.44)	0.94 (0.62-1.43)	0.61 (0.31-1.20)	0.64 (0.36-1.14)	1.41 (0.66-3.02)	1.62 (0.80-3.30)
Reduced weight gain [d]	1.06 (0.91-1.23)	1.02 (0.88-1.17)	1.10 (0.92-1.32)	1.06 (0.89-1.25)	0.96 (0.73-1.26)	0.96 (0.74-1.23)
Excessive weight gain [d]	1.08 (0.39-1.97)	1.60 (1.06-2.42)	1.29 (1.06-1.57)	2.94 (1.65-5.26)	1.12 (0.40-3.11)	0.62 (0.35-1.09)
Gestational Diabetes	1.22 (0.96-1.54)	1.23 (0.99-1.54)	1.37 (1.01-1.86)	1.38 (1.04-1.85)	1.09 (0.74-1.60)	1.05 (0.74-1.49)
Gestational hypertensive disorders	0.89 (0.64-1.24)	0.91 (0.67-1.25)	1.11 (0.72-1.70)	1.16 (0.77-1.76)	0.54 (0.29-0.99)	0.58 (0.32-1.05)
Birth outcomes						
Caesarean delivery	0.72 (0.61-0.84)	0.86 (0.76-0.96)	0.63 (0.51-0.78)	0.82 (0.72-0.94)	0.88 (0.67-1.16)	0.92 (0.76-1.12)
Caesarean in labour	0.82 (0.67-1.01)	0.93 (0.82-1.07)	0.70 (0.54-0.91)	0.91 (0.77-1.95)	1.08 (0.76-1.53)	0.98 (0.76-1.24)
Caesarean before labour	0.65 (0.52-0.80)	0.78 (0.67-0.90)	0.62 (0.47-0.82)	0.74 (0.61-0.88)	0.69 (0.49-0.97)	0.88 (0.68-1.14)
Preterm birth	0.85 (0.68-1.06)	0.74 (0.60-0.91)	0.97 (0.73-1.30)	0.85 (0.65-1.12)	0.68 (0.48-0.95)	0.60 (0.44-0.82)
Low birth weight	1.06 (0.85-1.34)	0.97 (0.79-1.19)	1.29 (0.96-1.75)	1.15 (0.87-1.51)	0.83 (0.58-1.17)	0.80 (0.58-1.10)
Small-for-gestational-age (SGA)	1.26 (1.07-1.49)	1.30 (1.11-1.52)	1.48 (1.19-1.83)	1.48 (1.21-1.80)	0.97 (0.74-1.28)	1.04 (0.81-1.34)
Large-for-gestational-age (LGA)	0.96 (0.71-1.29)	0.88 (0.68-1.16)	0.78 (0.53-1.14)	0.80 (0.56-1.12)	1.30 (0.79-2.15)	1.04 (0.65-1.66)

[*] Multivariate imputation via chained equations. Because of stratification by pre-pregnancy risk (one of the imputed variables), and when subsamples were used (smoking continuation, weight gain caesarean in labour), estimation sample varies across imputations and thus results may be biased

[a] Based on manuscript models #2 – adjusted for hospital of delivery + maternal age + education + migrant status + marital status + working condition + occupation + income + pregnancy planning + chronic conditions + parity (except for gestational diabetes) + pre-pregnancy body mass index (except for smoking continuation and preterm; interaction with prenatal care provider included for excessive weight gain) + smoking before pregnancy (except for caesarean deliveries models, preterm, low birthweight and LGA; interaction with prenatal care provider included for gestational hypertensive disorders)

[c] within pre-pregnancy smokers; [d] versus adequate weight gain

4.6. Small-for-gestational age Portuguese babies: the effect of childhood and adult socioeconomic conditions and maternal anthropometrics

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Small-for-gestational age Portuguese babies: The effect of childhood social environment, growth and adult socioeconomic conditions

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ABSTRACT

Objective. We aimed to estimate the extent to which differences in small-for-gestational age (SGA) according to maternal socioeconomic position (SEP) and anthropometrics are accounted for childhood background.

Methods. Adult mothers of singletons (n = 6893) recruited in 2005/2006 in Porto, Portugal self-reported data on socio-demographics. Grandparents' education and social class were used to characterise childhood social environment. Maternal education and marital status were used as adult SEP indicators. Height was categorised according to the 10th and 90th percentiles. The odds of SGA according to adult SEP and height were stratified by childhood conditions.

Results. SGA (14.5%) was less likely in taller [vs. 10th–90th percentiles: 0.62 (95% confidence interval (CI): 0.46–0.83)], more educated [vs. low: 0.77 (0.65–0.90)] and in married women [vs. single: 0.64 (0.47–0.86)]. No association was found between childhood social conditions and SGA. The protection provided by maternal education was found in women from deprived childhood backgrounds but not in those with more advantage conditions. Shorter women were more likely to deliver SGA babies but the effect was stronger ($p_{interaction} < 0.001$) in those from least deprived childhood conditions.

Conclusions. Sufficient increase in education seems to overcome disadvantage earlier in life. Other pathological processes might impact physical development beyond social influence, having long lasting effects on SGA.

Introduction

Nutritional, behavioural and psychosocial factors are recognised determinants of intrauterine growth restriction (Kramer et al., 2000; Raisanen et al., 2013) which might explain the pervasive social inequalities in this outcome (Mortensen et al., 2008; Blumenshine et al., 2010). For several years, research suggests that more educated women (or those with higher income or socially-advantaged occupations) are more likely to seek prenatal care, to adopt healthier lifestyles during pregnancy and are less likely to be exposed to stressful events (Kramer et al., 2000).

The intergenerational transmission of social conditions and its impact on adult health may reflect a failure of modern societies in the discontinuation of social inequalities in health and emphasise the importance of focusing early in life (Graham and Power, 2004; Marmot et al., 2012). Most evidence suggests that childhood circumstances influence adult socioeconomic conditions and, consequently, adult health. Some authors argue that improving social status (upward mobility) may represent a protective exposure to health while individuals who fall in the social hierarchy may be at increased risk of disease (Poulton et al., 2002). Childhood background is also likely to influence cognitive and physical development and health behaviours' acquisition resulting in health differentials later in life (Graham and Power, 2004).

Childhood social environment has been described to affect pregnancy outcomes, namely the delivery of low birthweight or preterm infants (Astone et al., 2007; Collins et al., 2003, 2009; Colen et al., 2006; Emanuel et al., 1992; Hypponen et al., 2004; Lumey and Stein, 1997). Maternal birthweight and physical growth (possibly reflecting unfavourable early childhood conditions) are known to influence the next generation birthweight. Some studies show that the relation is independent of childhood economic conditions (Collins et al., 2011), others report maternal social environment when in-utero (Emanuel et al., 1992; Hypponen et al., 2004; Lu and Halfon, 2003; Lawlor et al., 2003), together with social trajectories (Colen et al., 2006) to be important to explain forthcoming inequalities.

Over the past 50 years impressive changes in the socioeconomic and cultural context were observed in Portugal. The country faced the longest-standing dictatorship in Europe (1926–1974), a period of nearly inexistent social mobility, of highly illiterate population and high infant mortality rates. After the 1960s, and particularly after the 1974 revolution, social conditions improved, compulsory schooling increased and

Abbreviations: SGA, small-for-gestational age; OR, odds ratio.

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the National Health Service was launched, guaranteeing free universal access to care. After few decades, Portugal remains one of the least educated countries in Europe (Albert and Davia, 2011) but with health indicators similar to or better than the most European countries (Barreto, 2011).

In a context of such transformations it is not known if the association of social conditions with pregnancy outcomes is still reflecting childhood environment.

We aimed to estimate the extent to which differences in small-for-gestational age (SGA) according to maternal socioeconomic position and anthropometrics are accounted for childhood social background.

Methods

This study is based in Generation XXI, a cohort of 8647 newborns recruited in 2005–2006 in Porto Metropolitan Area, north of Portugal (Alves et al., 2012; Larsen et al., 2013). Recruitment occurred at 5 public maternity units, responsible for 95% of all births in the region. During the hospital stay (within 72 h of delivery), resident women delivering live births were invited and 92% of mothers accepted to participate. Data on socio-demographic, lifestyles and pregnancy characteristics were collected in structured face-to-face interviews. Interviewers were part of the project staff, trained by the research team. Regular meetings were taken place to assure inter-observer consistency. Delivery- and newborn-related data were retrieved from medical records by the same interviewers. The study was approved by the University of Porto Medical School/Hospital S. João Ethics Committee and a signed informed consent was required for all participants.

Childhood, growth and adult social conditions

Childhood socioeconomic characteristics were reported by the mothers using their 12 years of age as reference. Three indicators were used as proxies of childhood social environment: grandparents' highest education, childhood social class and family structure. Grandparents' highest academic level was categorised as low (≤primary academic level), intermediate (secondary) and high (>secondary). Social class was previously defined considering maternal recall of grandparents' education and 11 family resources (house ownership, household heating, washing machine, television, telephone, housemaid, family car, bicycle, annual holidays, club membership and association affiliation) (Teixeira, 2013). By using latent class statistical modelling, three categories were obtained representing low/deprived (25%), intermediate (50%) or high/advantaged (24%) social class. Mothers reported if they were living with both, one or none of the grandparents.

Adult mothers' height was used as proxy of physical growth. Height was measured whenever possible, otherwise was copied from identity card. The 10th (<153.0 cm) and 90th (>169.0 cm) percentiles of the sample distribution were estimated to categorise women.

Mothers' education and marital status at delivery were used to characterise adult socioeconomic position. Other indicators were available but were found to be highly correlated with education. Educational achievement was categorised as low (≤primary level), intermediate (lower secondary) and high education (≥upper secondary). Marital status was grouped as married, cohabitant and single.

Small-for-gestational-age

SGA was classified using Kramer et al.'s (2001) reference curves, considering sex-specific birthweight below the 10th percentile for each gestational age. Birthweight is routinely measured within 24 h after delivery. Gestational age is registered in medical files based on the biometric measurement of the ultrasound or, if not performed/available (15%), on the last menstrual period.

Confounding variables

Maternal age and the number of previous pregnancies (gravidity) – 0, 1 and 2 or more – were used as confounders. Pre-pregnancy weight was reported by the mothers and was used as a confounder of the association between height and SGA. Potential mediating variables, such as smoking during pregnancy or pregnancy complications, were excluded from the models. Adjusting for mediators could introduce confounding where none existed before resulting in biased estimates (Robins and Greenland, 1992). Still, their distribution according to education and height is available in Supplementary Table 1.

Data analysis

Women over 20 years, reporting other occupation than being a student and delivering singletons were eligible ($n = 7588$). Those with missing data on the above-mentioned variables were excluded, resulting in 6863 women (Fig. 1). Additionally, 362 mothers were also excluded for the grandparents' education analysis because of unknown data. Included newborns were more likely to have more educated mothers (high: 47% vs. 42%; $p = 0.009$) and less educated grandparents (low education: 65% vs. 60%, $p < 0.001$).

Proportions were compared using Chi-squared test. The association between each childhood socioeconomic indicator and adult education, marital status and height was estimated by fitting logistic regression models and presented as odds ratios (OR and 95% confidence intervals). Maternal age was included as a confounder; for the association between childhood environment and adult education it was included as an interaction term (significant interaction for $\alpha = 10\%$).

The odds of SGA according to each adult and childhood indicator were estimated using logistic regression analysis adjusted for maternal age and gravidity (age and gravidity interactions were also tested). Because no association was found between family structure and adult conditions or between SGA and marital status, subsequent analyses were conducted for the remaining indicators. The association between maternal height and maternal education with SGA was evaluated for each stratum of childhood social environment. To analyse the independent effect of each mechanism, models were mutually adjusted. The association between height and SGA was also adjusted for pre-pregnancy weight. All models showed adequate fit, assessed by the Hosmer–Lemeshow goodness-of-fit test statistic (p-value > 0.05).

Results

In this study 14.5% of the newborns ($n = 997$) were SGA. Almost 47% of the mothers completed upper secondary or higher education level while 31% only achieved primary education. About 2/3 were married and 22% were cohabiting. Almost half were primigravidae and 13% were aged above 35 years. Nearly 68% of the grandparents only achieved primary or lower academic level. In childhood, 1/4 of the mothers were from high social class and 85% were living with both parents (Table 1). More educated and taller mothers were more likely to be primigravidae, married, and normal/underweight and to use private prenatal care. More educated women were less likely to smoke (Supplementary Table 1).

In Table 2 the association between childhood conditions and adult education, marital status and height is presented. Mothers with intermediate and high educated parents (vs. low educated parents) were, respectively, 2 and 4 times more likely to present high education. The association between childhood social class and maternal education was even stronger. When compared to women from low childhood social class, those in intermediate or high levels were, respectively, 1.6 and 2.0 times more likely to be taller. Family structure was not related with adult conditions or maternal height. No childhood social indicator was related with marital status.

Independently of maternal age and gravidity, SGA was less likely to be present in taller [vs. 10th–90th percentiles: OR = 0.62 (95% CI: 0.46–0.83)], more educated [vs. low: 0.77 (0.65–0.90)] and in married women [vs. single: 0.64 (0.47–0.86)]. The association with marital status did not change after the adjustment for education [OR = 0.67 (95% CI: 0.49–0.90)]. Childhood social conditions were not associated with SGA (Table 3).

In Table 4 the association between SGA and maternal education and height is presented, stratified by childhood social environment. Mothers that increased to the highest education (vs. low education), but not those that moved to intermediate levels, showed lower risk of SGA: 32% less if they were from low social class; 21% if considering low grandparents' education. A non-significant decreased risk was found if mothers were from intermediate or high social class. Shorter women

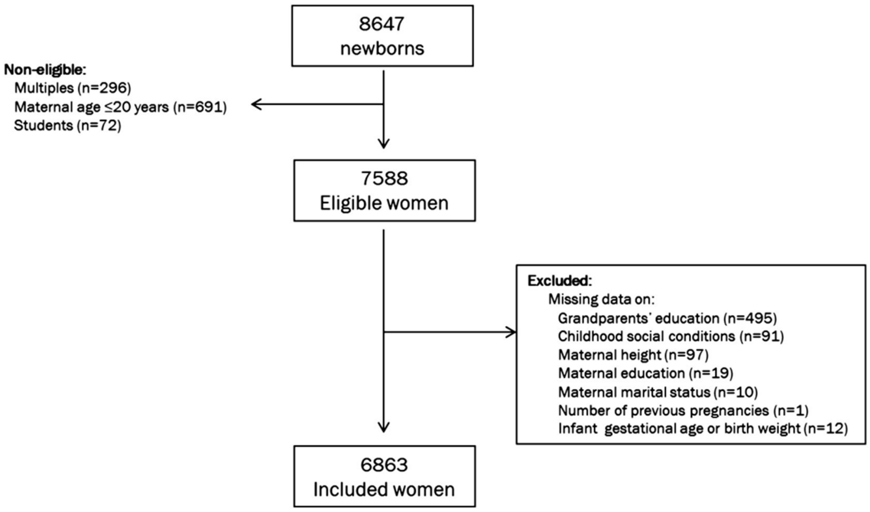

Fig. 1. Study participants.

were more likely to deliver SGA babies but the association was stronger among those from high childhood social class. Being taller decreased the odds of SGA among mothers from intermediate social class and low educated grandparents.

Table 1
Sample characteristics.

	n	%
Small-for-gestational age (SGA)	997	14.5
Maternal level of education		
Low (≤primary)	2124	31.0
Intermediate (lower secondary)	1525	22.2
High (≥upper secondary)	3214	46.8
Marital status		
Single	279	4.1
Cohabiting	1481	21.6
Married	5103	74.4
Maternal height		
<10th percentile (<153.0 cm)	674	8.8
10–90th percentiles (153.0–169.0 cm)	5547	80.8
>90th percentile (>169.0 cm)	642	9.4
Maternal age (years)		
21–25	1321	19.2
26–30	2461	35.9
31–35	2181	31.8
>35	900	13.1
Gravidity (previous pregnancies)		
None	3081	44.9
One	2453	35.8
Two or more	1326	19.3
Grandparents' level of education[a]		
Low (≤primary)	4443	68.3
Intermediate (secondary)	1146	17.6
High (>secondary)	912	14.0
Childhood social class (12 years)		
Low	1765	25.7
Intermediate	3415	49.8
High	1683	24.5
Childhood family structure (12 years)		
No parents	292	4.2
One parent	733	10.7
Both parents	5838	85.1

[a] Excluding 362 mothers with unknown grandparents education.

Discussion

In this study, maternal education and height were both negatively associated with growth restriction. Although childhood social environment was not found to be associated with SGA, a sufficient increase in education seemed to overcome disadvantage earlier in life. Other characteristics beyond social conditions may mediate the relation between maternal height and SGA.

Strengths and limitations

This study used data from a large population-based sample allowing the assessment of different social contexts. Women grew up in periods of major socio-cultural changes which make this group of particular interest for the research of social influences in health.

Our target population was defined according to the maternal adult area of residence. Thus, they may be different from the population of origin when they were 12 years of age. Due to the urban nature of our sample and to the observed association between grandparents and mothers' education, it is possible that we over-represent more educated grandparents. Included hospitals were responsible for 95% of all region deliveries and women were invited in the basis of "first come first served". Although not directly relatable with participation bias, the high participation proportion may decrease the impact of that potential limitation.

Although exposures and outcome were collected at the same time, temporal direction is clear and we do not expect our sample to be biased according to these characteristics. However, retrospective recall of childhood conditions may lead to information bias. It has been described that highly educated participants report their parents' occupation and education more accurately (Ward, 2011). We cannot exclude classification errors but several family assets were used to define social class and different socioeconomic indicators were tested, corroborating the robustness of the results. In addition, their use improves the ability to understand how different components of social environment influence pregnancy outcomes.

The period for childhood exposure was set to the age of 12. However, women might have been exposed to adversity in different periods of life which may influence health differently (Poulton et al., 2002; Sigle-Rushton et al., 2005). Also, the set of chosen indicators may not

Table 2
Association between childhood socioeconomic environment and adult height and socioeconomic indicators from the 2005/2006 Portuguese birth cohort.

	n	OR [95% CI]		
		Maternal height >90th percentile (n = 642)[a]	High maternal education (n = 3214)[b]	Single women (n = 279)[a]
Grandparents' level of education[c]				
Low (≤primary)	4443	Reference	Reference	Reference
Intermediate (secondary)	1146	1.31 [1.05, 1.62]	1.99 [1.52, 2.60]	1.31 [0.96, 1.78]
High (>secondary)	912	1.75 [1.41, 2.18]	4.24 [2.63, 6.86]	1.12 [0.76, 1.64]
Childhood social class (12 years)				
Low	1765	Reference	Reference	Reference
Intermediate	3415	1.64 [1.30, 2.06]	2.32 [1.71, 3.14]	0.81 [0.61, 1.10]
High	1683	2.02 [1.58, 2.58]	8.04 [4.79, 13.49]	0.75 [0.53, 1.08]
Childhood family structure (12 years)				
No parents	292	Reference	Reference	Reference
One parent	733	0.99 [0.66, 1.48]	1.35 [0.74, 2.46]	0.76 [0.45, 1.30]
Both parents	5838	0.95 [0.60, 1.51]	1.14 [0.76, 1.69]	1.01 [0.56, 1.85]

[a] Models adjusted for maternal age.
[b] Models adjusted for the interaction with maternal age.
[c] Excluding 362 mothers with unknown grandparents education.

be similarly distributed in time. Still, an effect modification by age was not observed (data not shown).

Data on gestational age and birthweight was retrieved from medical files, not influenced by maternal recall. We used the SGA cut-offs provided by Kramer et al. (2001) because no national reference curves exist. Using a Canadian reference population may explain the high prevalence of SGA (14%), since Portuguese babies are smaller (National Institute os Statistics (INE), 2005; Statistics Canada, 2005). Thus, part of the SGA babies may be healthy babies, the result of different exposures (Ananth and Vintzileos, 2009).

Table 3
Small-for-gestational-age babies (SGA) according to adult and childhood socioeconomic indicators from the 2005/2006 Portuguese birth cohort.

	n	SGA (n = 997)		
		n (%)	p-Value*	OR [95% CI] (adjusted for age and gravidity)
Maternal level of education			0.003	
Low (≤primary)	2124	324 (15.2)		Reference
Intermediate (lower secondary)	1525	253 (16.6)		1.01 [0.84, 1.21]
High (≥upper secondary)	3214	420 (13.1)		0.77 [0.65, 0.90]
Marital status			<0.001	
Single	279	60 (21.5)		Reference
Cohabiting	1481	246 (16.6)		0.77 [0.56, 1.06]
Married	5103	691 (13.5)		0.64 [0.47, 0.86]
Maternal height			<0.001	
<10th percentile (<153.0 cm)	674	151 (22.4)		1.56 [1.27, 1.91]
10–90th percentiles (153.0–169.0 cm)	5547	794 (14.3)		Reference[b]
>90th percentile (>169.0 cm)	642	52 (8.1)		0.62 [0.46, 0.83]
Grandparents' level of education[a]			0.972	
Low (≤primary)	4443	648 (14.6)		Reference
Intermediate (secondary)	1146	164 (14.3)		0.93 [0.78, 1.12]
High (>secondary)	132	132 (14.5)		0.98 [0.80, 1.20]
Childhood social class (12 years)			0.848	
Low	1765	259 (14.7)		Reference
Intermediate	3415	488 (14.3)		0.90 [0.76, 1.06]
High	1683	250 (14.8)		0.95 [0.78, 1.15]
Childhood family structure (12 years)			0.506	
No parents	292	42 (14.4)		Reference
One parent	733	117 (16.0)		1.10 [0.75, 1.62]
Both parents	5838	838 (14.4)		0.98 [0.70, 1.37]

* From chi-squared test.
[a] Excluding 362 mothers with unknown grandparents education.
[b] Also adjusted for maternal pre-pregnancy weight.

Interpretation

Adult socioeconomic conditions seem to be more important than previous childhood environment, at least among women that grew in more disadvantaged contexts. These results are not totally in accordance with the acknowledged independent effect of childhood background (Astone et al., 2007; Emanuel et al., 1992) and upward mobility (Colen et al., 2006). This might be explained by the fact that women grew up in periods of great economic and educational improvements, very different from the settings evaluated in the published literature. Women showed a marked increase in education in relation to their parents (while almost 70% of grandparents only achieved primary education corresponding to 4 schooling years, the proportion was 30% in the mothers (6 schooling years)). Women seem to benefit from an increase in education and part of the benefit appears to be related with the achieved level and part with the upward process: when compared to women with low adult education, an increase from low childhood class to the intermediate level did not reduce the risk of SGA. Small increases in socioeconomic position have not been reflected in better pregnancy outcomes, probably because the point of origin was particularly low. Together with an upward mobility protection, long-lasting effects of advantaged social environment were also found: in women from more affluent childhood backgrounds (highly educated grandparents or from high social class) – that were, a priori, at lower risk – SGA did not differ according to the achieved level. Those who fell in the social hierarchy did not present an increased risk of SGA. However, downgrading was a particularly rare phenomenon. Thus, wealthy childhood environment may, at least, shape adult social destinations, decreasing the probability of downgrading social conditions. The magnitude of the association between height and offspring growth restriction differed by childhood social strata. It is known that growth is influenced by nutritional and psychosocial factors acting during childhood and adolescence (Wadsworth et al., 2002). So, height may be a proxy of childhood social conditions. This relation has been extensively described (Hypponen et al., 2004; Lawlor et al., 2003; Kramer, 1987) but, to the best of our knowledge, this is the first study reporting that being shorter is more strongly associated with SGA in women with a least deprived childhood than in poorer ones. In average, those with a more deprived background were shorter than those from intermediate/high classes. Although we cannot control for grandparents' stature, it is plausible that they had shorter parents. Thus, low height distribution may somehow reflect familial short stature (although possibly resulting from long-lasting exposure to adversity). In more advantaged childhood backgrounds, being of short stature might represent exposure to pathological processes that resulted in an increased risk of SGA but were not related with the social background (Lawlor et al., 2003; Addo et al., 2013).

Table 4
Association between maternal education and height and the delivery of small-for-gestational-age babies (SGA), stratified by childhood social class and grandparents' level of education from the 2005/2006 Portuguese birth cohort.

		SGA (OR [95% CI])					
		Childhood social class			Grandparents' level of education[a]		
		Low (n = 1765)	Intermediate (n = 3415)	High (n = 1683)	Low (n = 4443)	Intermediate (n = 1146)	High (n = 912)
Adjusted for maternal age and gravidity	Maternal level of education						
	Low	Reference	Reference	Reference	Reference	Reference	Reference
	Intermediate	0.95 [0.66, 1.36]	1.02 [0.80, 1.31]	1.20 [0.60, 2.41]	1.00 [0.81, 1.24]	1.19 [0.69, 2.07]	0.34 [0.11, 1.06]
	High	0.66 [0.46, 0.97]	0.75 [0.59, 0.96]	0.86 [0.45, 1.64]	0.74 [0.61, 0.92]	0.75 [0.45, 1.26]	0.41 [0.15, 1.12]
	Maternal height[b]						
	<10th percentile	1.30 [0.91, 1.85]	1.59 [1.18, 2.15]	1.94 [1.21, 3.12]	1.51 [1.18, 1.92]	1.73 [1.00, 2.98]	1.38 [0.69, 2.75]
	10–90th percentiles	Reference	Reference	Reference	Reference	Reference	Reference
	>90th percentile	1.10 [0.60, 2.04]	0.46 [0.29, 0.74]	0.66 [0.40, 1.12]	0.61 [0.41, 0.92]	0.55 [0.27, 1.12]	0.66 [0.34, 1.28]
Mutually adjusted	Maternal level of education[c]						
	Low	Reference	Reference	Reference	Reference	Reference	Reference
	Intermediate	0.97 [0.68, 1.40]	1.06 [0.82, 1.36]	1.22 [0.60, 2.46]	1.03 [0.83, 1.28]	1.24 [0.71, 2.16]	0.33 [0.10, 1.02]
	High	0.68 [0.46, 0.99]	0.80 [0.63, 1.03]	0.90 [0.47, 1.73]	0.79 [0.64, 0.97]	0.80 [0.47, 1.35]	0.41 [0.15, 1.12]
	Maternal height[d]						
	<10th percentile	1.26 [0.89, 1.80]	1.55 [1.15, 2.10]	1.88 [1.17, 3.03]	1.46 [1.14, 1.87]	1.67 [0.96, 2.88]	1.37 [0.68, 2.76]
	10–90th percentiles	Reference	Reference	Reference	Reference	Reference	Reference
	>90th percentile	1.15 [0.62, 2.13]	0.48 [0.30, 0.76]	0.68 [0.40, 1.14]	0.64 [0.35, 0.96]	0.56 [0.28, 1.16]	0.66 [0.29, 1.29]

[a] Excluding 362 mothers with unknown grandparents education.
[b] Models are also adjusted for maternal pre-pregnancy weight.
[c] Models adjusted for maternal age, gravidity and height.
[d] Models adjusted for maternal age, gravidity, pre-pregnancy weight and maternal education.

Part of the association between height and SGA could be related with maternal weight. Taller women are more likely to be heavier, decreasing the risk of growth restriction (Kramer, 1987). However, estimates remained statistically significant after adjustment for maternal weight.

Marital status was associated with SGA independently of childhood social conditions: single and cohabiting mothers showed, respectively, 57% and 22% higher odds of SGA than married ones. Although cohabitation has become frequent and well accepted by the society, unmarried women remain more likely to be exposed to adverse health behaviours and to the lack of pregnancy planning and of social support (Shah et al., 2011; Raatikainen et al., 2005).

Conclusion

In a country that faced major social changes, childhood background still influenced educational achievement. However, a sufficient increase in education seems to overcome disadvantage earlier in life. Maternal growth was related with SGA not only reflecting social background but also by other mechanisms beyond economic conditions. Future research is needed to estimate other early exposures and to evaluate how social transmission changes in time and in countries with different cultural and economic characteristics.

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Sponsors were not involved in the study design; in the collection, analysis and interpretation data; in the writing of the report; and in the decision to submit the paper for publication.

Authors' contribution

Sofia Correia was responsible for the study concept, collection, analysis and interpretation of data and first draft of the manuscript; and Henrique Barros was responsible for the cohort study design, study concept and interpretation of data and revised the manuscript critically for important intellectual content. Both authors approved the final version of the manuscript.

Conflict of interest statement

The authors report no conflict of interest.

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Supplementary Table 1 – Maternal characteristics according women's education and height from the 2005/2006 Portuguese birth cohort

	All sample (%)	Maternal education (%)			Maternal height (%)		
	n=6864	Low n=2124	Intermediate n=1525	High n=3214	$<10^{th}$ p n=674	10^{th}-90^{th}p n=5547	$>90^{th}$p n=642
Maternal height							
$<10^{th}$ percentile (<153.0cm)	9.8	14.8	8.8	7.0			
10-90^{th} percentile (153.0-169.0cm)	80.2	78.5	83.0	81.3			
$>90^{th}$ percentile (>169.0cm)	9.4	6.6	8.2	11.7	---	---	---
			p<0.001				
Marital status							
Married	74.4	70.1	67.1	80.6	72.0	74.4	76.3
Cohabitant	21.6	24.9	26.4	17.1	22.8	21.7	19.3
Single	4.1	5.0	6.5	2.3	5.2	3.9	4.4
			p<0.001			*p=0.234*	
Maternal age (years)							
21-25	19.2	20.1	35.1	11.2	15.4	19.6	20.1
26-30	35.9	30.0	35.1	40.1	30.1	36.4	37.4
31-35	31.8	31.4	21.6	36.8	33.1	31.5	33.2
>35	13.1	18.5	8.1	12.0	21.4	12.6	9.4
			p<0.001			*p<0.001*	
Gravidity (previous pregnancies)							
None	44.9	27.7	48.4	54.6	34.0	45.9	47.7
One	35.8	40.6	35.3	32.8	42.2	34.9	36.1
Two or more	19.3	31.7	16.3	12.6	23.8	19.2	16.2
			p<0.001			*p<0.001*	
Pre-pregnancy BMI (Kg/m^2) [a]							
<25	67.8	56.5	66.4	75.9	55.7	68.5	74.1
25-29	23.0	29.0	23.8	18.7	29.1	22.8	18.3
≥ 30	9.2	14.5	9.8	5.4	15.2	8.7	7.6
			p<0.001			*p<0.001*	
Pre-pregnancy smoking (3 months before) [b]	24.7	25.3	32.1	20.7	22.8	24.8	25.0
			p<0.001			*p=0.509*	

	All sample (%) n=6864	Maternal education (%) Low n=2124	Intermediate n=1525	High n=3214	Maternal height (%) $<10^{th}$ p n=674	10^{th}-90^{th}p n=5547	$>90^{th}$p n=642
Private prenatal care [c]	39.8	17.0	26.8	61.0	30.1	40.2	46.1
			p<0.001			*p<0.001*	
First antenatal visit >13 GW [c]	9.4	14.4	10.9	5.5	13.6	9.0	8.5
			p<0.001			*p=0.001*	
Smoking 3rd trimester [b]	13.4	16.7	18.5	8.7	12.4	13.5	12.8
			p<0.001			*p=0.669*	
Gestational weight gain [d]							
Reduced	25.3	29.0	23.1	24.0	29.2	25.4	20.5
Adequate	37.5	35.6	36.1	39.5	37.9	37.2	39.8
Excessive	37.1	35.4	40.9	36.5	32.9	37.4	39.7
			p<0.001			*p=0.005*	
Gestational diabetes [e]	7.2	10.3	5.7	5.8	11.2	6.8	5.8
			p<0.001			*p<0.001*	
Gestational hypertensive disorders [e]	3.5	4.2	3.3	3.0	4.3	3.4	2.8
			p=0.054			*p=0.322*	

[a] Body Mass index: pre-pregnancy weight (Kg) divided by squared height (m^2)
[b] Smoking consumption: self-reported for 3 months before conception and at each pregnancy trimester.
[c] Women reported if had used public or private prenatal care facilities and the number of gestational weeks (GW) at the first visit.
[d] Gestational weight gain: considering weight gain in relation to maternal pre-pregnancy body mass index and according the to the Institute of Medicine recommendations (2009).
[e] Gestational diabetes and hypertensive disorders were retrieved from medical records.

4.7. Socioeconomic variations in female fertility impairment: a study in a cohort of Portuguese mothers

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Socioeconomic variations in female fertility impairment: a study in a cohort of Portuguese mothers

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ABSTRACT

Objectives: This study aimed to assess the association of socioeconomic conditions with female fertility impairment among women who delivered a live birth.

Design: Cross-sectional analysis.

Setting: Population-based birth cohort (Generation XXI) assembled in 2005/2006 from five public maternity units in Porto Metropolitan Region, Northern Portugal.

Participants: 7472 women aged 18 or more with spontaneous conception and no male diagnosis of infertility were recruited and interviewed immediately after birth with structured questionnaires.

Exposures of interest: Maternal education, occupation and income were recorded as proxy indicators of social conditions.

Outcome: Impaired female fertility, defined as women who had unsuccessfully tried to conceive for over a year.

Data analysis: Multivariate logistic regression models were fitted to estimate the association between each socioeconomic indicator and impaired female fertility, stratified by previous pregnancy experience and adjusted for age, pregnancy planning and behavioural characteristics.

Results: Among primigravidae, 7.7% (95% CI 6.8% to 8.6%) presented impaired fertility and the prevalence was 9.6% (95% CI 8.7% to 10.6%) in multigravidae. In crude analysis, we found women with impaired fertility to be older, less educated, more likely to have planned the current pregnancy and to be overweight/obese; they had similar levels of income or occupation. In multivariate models, a significant independent association between educational level and female fertility impairment remained among primigravidae (OR (95% CI) vs ≤6 schooling years: 7–9: 0.85 (0.54 to 1.34); 10–12: 0.34 (0.21 to 0.54); >12: 0.24 (0.14 to 0.40), p_{trend}<0.001) but not in multigravidae.

Conclusions: This study shows that education might be important in understanding female fertility impairment, particularly among first-time pregnant women. It also points out that the association is not totally explained by other sociodemographic and lifestyle characteristics that have been previously found to be important to disclose this relation.

Strengths and limitations of this study

- This study used a large sample of truly fertile women allowing the understanding of the different social realities.
- Not restricting the sample to planned pregnancies or to women attending fertility clinics, strengthened its external validity.
- Data on fertility impairment were collected retrospectively after birth and misclassification may have occurred.

INTRODUCTION

International reviews of the prevalence of fertility impairment, defined as women unable to achieve a clinically recognised pregnancy after attempting for more than 1 year, found that ranges from 7% to 39%, depending on the reproductive outcome assessed (whether pregnancy or live birth) and the populations included—for example, all women trying to get pregnant for the first time or married women.[1–3]

Women's age, sexually transmitted diseases, polycystic ovary syndrome, endometriosis and pelvic inflammatory disease have been considered the proximal causes of female fertility impairment.[4–8]

Over the recent decades, several countries have shown a decrease in their total fertility rates (in a demographic perspective considering the total number of children per woman).[9] However, there is no consensus whether it may result from a decline in biological fertility. Some authors report an increase in the ability to conceive explained by better social conditions and less sexually transmitted infections,[10 11] others a fertility decrease related to women's postponement of childbearing age and adverse lifestyles[12 13] while yet others have found no differences in trends.[14]

Hence, in addition to the pathological factors related to the female reproductive system, socioeconomic circumstances could influence fertility through different pathways.

More highly educated women are more likely to postpone childbearing to an age when the probability of conception decreases and the probability of early pregnancy loss increases.[15 16] They are also more likely to plan pregnancy and to be aware of fertility problems, promoting the decision to seek for help.[17] However, less-educated women are more likely to be overweight, to smoke and to have more risky sexual behaviour which may negatively impact female fertility.[18–20] Despite the correlation between different dimensions of socioeconomic circumstances, their components may impact fertility by different mechanisms. Income allows easier or faster access to health services, namely infertility clinics and also to material resources as better food or service promoters of better health.[21] Occupation may also be related to infertility because of labour pressure, working schedules and psychosocial stress or because of the exposure to environmental pollutants known to decrease implantation rates and increase spontaneous abortion.[19]

Aiming at understanding how social circumstances might impact female fertility decline, we designed a cross-sectional analysis of the association between socioeconomic conditions (measured by different proxy indicators) and the occurrence of female fertility impairment in women who had subsequently delivered a live birth.

METHODS

This study was conducted within Generation XXI, a population-based cohort of 8647 babies and 8495 mothers assembled between April 2005 and August 2006 from five public maternity units in the Porto Metropolitan Area in the North of Portugal. All resident women delivering a live birth with more than 23 gestational weeks were eligible. In all, 70% of the eligible mothers were consecutively invited (not all eligible mothers were invited due to logistic constraints, namely availability of human resources; in these circumstances, women were invited on a basis of first come, first served) and 8% of those refused to participate. Participants were interviewed face to face between 24 h and 72 h after delivery. Data were collected using a standardised questionnaire on maternal sociodemographics, obstetric and gynaecological history, planning and occurrence of the current pregnancy, prenatal care and lifestyles.[22] A subgroup of women was recruited in pregnancy when pregnant women went to their first hospital antenatal appointment at two of the included units (up to the 13th gestational week). These interviews were conducted during each trimester and so, most data were collected at different stages compared to the rest of the cohort.[23] The study was approved by the ethics committee from the University of Porto Medical School/Hospital S. João and all women taking part were required to sign a consent form, designed according to the Declaration of Helsinki.

For the current analysis women aged 18 years or more (8334) were eligible. We excluded 105 women who reported a diagnosis of male infertility in their partner and a further 119 who had non-spontaneous conception, including pregnancies resulting from assisted reproductive technology or after ovulation induction medication. Because of different timings of data collection 280 women recruited during pregnancy and 358 with missing data for fertility status, parity or the exposure variables were also excluded (figure 1).

Socioeconomic measures

Maternal educational level, occupation and household monthly income were indicators of the socioeconomic circumstances. Educational level was recorded as the number of completed years of education and categorised as ≤6, 7–9, 10–12 and >12. Occupation was recorded using self-reported current job and daily tasks and classified using the National Occupation Classification (1994, revised in 2000), supplementary classified as ISCO-2008. Occupations were further grouped into higher level white-collar workers (managers, professionals, technicians and associate professionals), lower level white-collar workers (clerical support workers, services and sales workers), skilled blue-collar workers (skilled agricultural, forestry and fishery workers, craft and related trades workers, plant and machine operators) and unskilled blue-collar workers (elementary occupations).[24] Household monthly income was recorded in €500 categories and was grouped as ≤€1000; €1001–€2000; >€2000 and those who said they did not know or who did not want to reply.

Fertility status

Women were asked whether they had ever tried to conceive for more than a year without success. Those who said they had were classified as having female fertility impairment and were asked how long they had spent attempting to get pregnant. This was categorised as 13–23; 24–35 and >35 months. Women were asked if they had ever sought medical help (advice or treatment) because

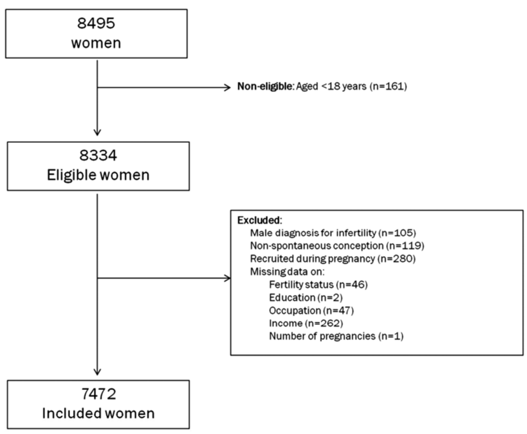

Figure 1 Participants selection.

they could not get pregnant. Those who had done so reported the medical diagnosis for their delay in conception.

Women were asked if they had planned the current pregnancy and those who answered yes were also asked how long it had taken them to become pregnant. This was grouped into under 6, 6–11, 12–24 and over 24 months.

Covariates

Women were asked about their age at the time of birth, their marital status, age at menarche, regularity of their menstrual cycle (considered as regular if occurring once a month for around 5 days) and age at first sexual intercourse.

Smoking 3 months before pregnancy was categorised as: never smokers (including occasional smokers), ex-smokers (former smokers who had not smoked during the 3 months before conception), smokers of 1–14 cigarettes/day and smokers of more than 14 cigarettes/day.

The self-reported pre-pregnancy weight was used to calculate maternal pre-pregnancy body mass index (BMI). Height was measured whenever possible, otherwise data were copied from their citizen identity card. BMI was calculated as 'weight (kg)/(height×height) (m)' and grouped as ≤24.9; 25–29.9; ≥30 kg/m^2.

Data on pregnancy screening tests for infections were retrieved from maternal pregnancy passports (booklet provided to all women; contains the record of check-ups, ultrasounds, tests and medical notes). Women were classified as having an infection if they were positive for syphilis (Venereal Disease Research Laboratory test—VDRL), hepatitis B (hepatitis B surface antigen—HBsAg), hepatitis C (antibodies against hepatitis C virus—Anti-HCV) or HIV.

Data analysis

Women's characteristics were analysed according to the fertility status and compared using χ^2 tests. Multivariate logistic regression models were used to calculate OR and their respective 95% CIs (95% CI) as measures of the association between each socioeconomic indicator (education, occupation and income) and female fertility impairment, independently of age, pregnancy planning, pre-pregnancy BMI, smoking, age at first sexual intercourse, infection status and age at menarche. The final model includes only the variables that changed the OR by more than 10%.

The number of previous pregnancies modified the effect of education on fertility impairment and so we stratified the analysis by the number of previous pregnancies: primigravidae (first pregnancy) and multigravidae (more than one pregnancy). The possible interaction between age and education was also tested. The analysis was repeated including only women who had not sought medical help or infertility problems. For multigravidae, sensitivity analyses were performed excluding women with no previous successful pregnancy (multigravidae but nulliparous) and those that reported current time-to-pregnancy over 12 months.

RESULTS

The final sample comprised 7472 women who were similar to the excluded participants in terms of socioeconomic indicators and BMI but were more likely to be younger (29 vs 30 years, p<0.001) and to be smokers (26% vs 20%, p<0.001; table 1).

Table 1 Characteristics of included and excluded women

	N	Mean age (SD)	Mean education (SD)	Living with partner, n (%)	Monthly income > €2000, n (%)	Blue-collar occupation, n (%)	Mean BMI (SD)	Smokers†, n (%)
Eligible								
Included	7472	29.1 (5.4)	10.5 (4.2)	7040 (94.5)	1062 (15.7)	682 (9.1)	23.9 (4.3)	1952 (26.4)
Excluded	862	30.0 (5.3)	10.6 (4.2)	787 (94.1)	63 (13.2)	62 (7.9)	23.8 (4.3)	156 (20.3)
p Values‡		p<0.001	p=0.670	p=0.691	p=0.146	p=0.253	p=0.636	p<0.001
Male infertility	105	30.9 (4.3)	11.3 (4.0)	99.0	20.2	6.7	23.9 (4.3)	20.0
Non-spontaneous conception	119	31.5 (4.1)	12.2 (4.3)	99.2	27.4	3.4	23.6 (3.8)	13.0
Recruited during pregnancy	280	29.5 (5.8)	9.2 (3.6)	89.9	4.9	13.1	24.7 (4.8)	30.0
Missing data*	358	29.7 (5.4)	10.9 (4.4)	94.4	10.3	5.2	23.3 (4.1)	15.2
Non-eligible								
Age <18	161	16.4 (0.9)	7.1 (2.1)	51.6	2.6	5.3	21.8 (3.0)	40.4

*Missing data on: fertility status, education, income, occupation, number of previous pregnancies.
†Smokers—smoking 1 or more cigarettes per day 3 months before conception.
‡p Values for the comparison between included and excluded participants.
BMI, body mass index.

Among primigravidae, 7.7% (95% CI 6.8 to 8.6) had taken more than 1 year to conceive. The prevalence was 9.6% (95% CI 8.7 to 10.6) in those with a previous pregnancy. Within fertility impaired women, 39% (86/219) of primigravidae and 35% (123/348) of multigravidae had taken 3 years or more to get pregnant. Although not statistically significant, less educated women were more likely to report more than 3 years of involuntary childlessness (≤6 vs >12 schooling years: 44.5% vs 31.9%). Seven per cent of women (517/7402) had sought medical help because they could not get pregnant and 71% reported a clinical diagnosis. Among impaired women, seeking for help was more frequent in the more educated (69.4% in women with ≥12 years of education vs 58.2% in women with ≤6 years), but no differences were found in fertile women. More detailed data on seeking behaviour and clinical diagnosis may be found in online supplementary table S1.

As described in table 2, women trying to conceive for more than 1 year were older (≥40 years: 5.6% vs 2.3%, p<0.001), less educated (>12 schooling years: 19% vs 25%, p=0.001) and less likely to be single (2.8% vs 5.8%, p<0.001) but similar in terms of household monthly income (>€2000: 14.9% vs 15.8%, p=0.748), occupation (blue-collar: 25% vs 22%, p=0.178) or employment status (employed: 74% vs 73%, p=0.070).

Women with fertility impairment were less likely to report having regular menstrual cycles, were more likely to have had the onset of menarche before 12 years or over 13 years of age and were more likely to have planned the current pregnancy. Among multigravidae, they reported more frequently to have had a previous adverse pregnancy outcome. Smoking habits were similar according to the fertility status. Overweight and obesity were found in 41% of women with fertility impairment (and in 29.8% of fertile women, p<0.001) but no statistically significant differences were found according to the self-perception of health status.

Low-educated women (<6 years) were more likely than more educated (>12 years) to be overweight or obese (45% vs 20%) and to report early age at sexual initiation (<16 years: 12% vs 2%).

From figure 2 it can be observed that, among primigravidae, higher education level was associated with a decrease in female fertility impairment, independently of other demographic and behavioural characteristics. Compared to those with six or less years of education, having 7–9, 10–12 and more than 12 years of formal education was associated with lower odds of having infertility (OR (95% CI) vs ≤6 years: 7–9 years: 0.85 (0.54 to 1.34); 10–12 years: 0.34 (0.21 to 0.54); >12 years: 0.24 (0.14 to 0.40), p_{trend}<0.001). The results were accentuated in the analysis restricted to women who did not seek medical help (7–9 years: 0.54 (0.27 to 1.09); 10–12 years: 0.18 (0.08 to 0.40); >12 years: 0.11 (0.04 to 0.29), p_{trend}<0.001). No significant association was found in the interaction between age and education.

Among multigravidae, no statistically significant differences were found. However, the association between education and female fertility impairment seems to assume a U shape (7–9 years: 1.26 (0.88 to 1.84); 10–12 years: 1.42 (0.99 to 2.05); >12 years: 1.00 (0.66 to 1.52); figure 2). Similar results were observed when considering only multigravidae with a previous live birth (7–9: 1.20 (0.79 to 1.82); 10–12: 1.45 (0.97 to 2.18); >12: 1.19 (0.75 to 1.90)) or within those for whom the current pregnancy was achieved in ≤12 months (7–9: 1.68 (0.83 to 3.41); 10–12: 1.26 (0.60 to 2.64); >12: 1.76 (0.87 to 3.56)).

Income and occupation were associated with infertility within primigravidae but no association was found for multigravidae (table 3). More affluent primigravidae and women in higher level white-collar occupations had significantly lower odds of infertility. The differences were attenuated and no longer significant after adjustment for years of education which remained significantly associated with fertility with similar point estimates.

DISCUSSION

Among primigravidae who had recently delivered a live birth we found that higher education was associated with a decrease in female fertility impairment independently of age and other behavioural factors, but no other socioeconomic indicator was related. In women who had already experienced a previous pregnancy, neither educational level nor other social indicators were associated with this condition.

The association between education and fertility impairment was previously described in other large population-based European studies among primiparous women,[11 18] and was explained by the effect of education on decreasing the exposure to adverse lifestyles, risky sexual behaviour and body weight. On the contrary, an increase in infertility with increasing education was also found in another study in the UK although the authors argue that it reflects the increasing recognition of the fertility problem among this group of women and does not result from a biological reduction in the ability to conceive.[25] Other studies in Denmark[26] and Scotland[14] found no relation between social class/education and infertility. These different results may reflect the huge geographical variations of socioinequalities in health[27] besides differences in the definitions and in the socioeconomic indicators used.

Our results were only partly explained by variations in women's behaviours. It is known, and was also previously found for this cohort, that smoking and obesity are more frequent in socially deprived women.[22] Yet, our results may reflect reverse causation because women with impaired fertility might have been advised to adopt healthier lifestyles. However, the proportion of women seeking medical help because of infertility problems was small (7%) and the results were even of greater magnitude when excluding these women.

Table 2 Women's characteristics by fertility impairment status

	Female fertility impairment		
	No (n=6820)	Yes (n=652)	p Value
Age (years)			
18–24	1490 (21.8)	87 (11.9)	
25–29	2101 (30.8)	189 (25.8)	
30–34	2173 (31.9)	265 (36.2)	
35–39	897 (13.2)	149 (20.4)	
≥40	159 (2.3)	41 (5.6)	<0.001
Education (years)			
≤6	1539 (22.6)	182 (27.9)	
7–9	1745 (25.6)	179 (27.4)	
10–12	1850 (27.1)	167 (25.6)	
>12	1686 (24.7)	124 (19.0)	0.001
Single women	394 (5.8)	18 (2.8)	0.001
Monthly income (€)			
≤1000	2456 (40.0)	253 (41.3)	
1001–2000	2711 (44.2)	268 (43.8)	
>2000	971 (15.8)	91 (14.9)	0.748
Not known/no answer	*10.0*	*6.1*	
Occupation			0.178
Higher level white-collar	1607 (23.6)	136 (20.9)	
Lower level white-collar	3281 (48.1)	310 (47.6)	
Skilled blue-collar	876 (12.8)	104 (16.0)	
Unskilled blue-collar	622 (9.1)	60 (9.2)	
No occupation	434 (6.4)	42 (6.4)	
Employment status			
Employed	4942 (72.6)	471 (74.2)	
Unemployed	1316 (19.3)	131 (20.1)	
Housewife	405 (6.0)	46 (7.1)	
Student	127 (1.9)	4 (0.6)	
Other	19 (0.3)	0 (0.0)	0.074
Planned pregnancy	4482 (65.8)	531 (81.4)	<0.001
Previous pregnancies			
None	3227 (47.3)	268 (41.1)	
One or more	3593 (52.7)	384 (58.9)	0.002
From the same father	2901 (81.8)	318 (84.6)	0.177
With live birth	2990 (84.7)	302 (80.1)	0.020
Age at menarche (years)			
≤11	1708 (25.3)	181 (28.0)	
12	2049 (30.4)	162 (25.1)	
13	1520 (22.5)	149 (23.1)	
>13	1468 (21.8)	154 (23.8)	0.038
Age at first sexual intercourse (years)			
≤15	344 (7.4)	36 (8.6)	
16–17	1239 (26.6)	115 (27.3)	
18–19	1630 (35.0)	129 (30.6)	
20–24	1152 (24.8)	117 (27.8)	
≥25	286 (6.2)	24 (5.7)	0.349
Regular menstrual cycles	5618 (83.4)	417 (64.6)	<0.001
Self-reported health status before pregnancy			
Poorer or fair	990 (14.6)	101 (15.6)	
Good	3666 (54.1)	362 (56.0)	
Very good	930 (13.7)	80 (12.4)	
Excellent	1194 (17.6)	104 (16.1)	0.496
Pre-pregnancy body mass index (kg/m^2)			
<180	267 (4.0)	16 (2.5)	
180–24.9	4391 (66.2)	361 (56.6)	
250–29.9	1405 (21.2)	175 (27.4)	
≥300	574 (8.6)	86 (13.5)	<0.001

Continued

Table 2 Continued

	Female fertility impairment		
	No (n=6820)	Yes (n=652)	p Value
Smoking status 3 months before pregnancy			
Never-smoker	4212 (62.3)	400 (61.7)	
Ex-smoker	768 (11.4)	72 (11.1)	
1–14 cigarettes/day	952 (14.1)	96 (14.8)	
≥15 cigarettes/day	824 (12.2)	80 (12.4)	0.960
	n=5280	n=507	
Infection*	83 (1.6)	9 (1.8)	0.727

*Positive result for syphilis (Venereal Disease Research Laboratory), hepatitis B (HBsAg), hepatitis C (Anti-HCV) or HIV.

The (non)-observed attenuation may be underestimated because the study recruitment strategy was on live born children. In fact, the socioeconomic circumstances may affect the different stages of conception. Obesity and smoking status could be associated with delays in conception and also with early pregnancy loss.[19 28 29]

It is known that early age at the first sexual intercourse may be associated with a higher risk of infertility because of the higher probability of sexually transmitted diseases.[30] Early age at the first sexual intercourse is also more frequent among least affluent women. In our study it did not entirely explain the association between education and fertility impairment, probably because this indicator may not have fully captured sexually transmitted infections. Similar was the situation when controlling for infection status although we do not have data for other infections such as *Chlamydia trachomatis* or *Neisseria gonorrhoeae* that are known to be associated with infertility.[7]

Therefore, we cannot exclude the possibility that years of education were associated with decreased ability to conceive by means of other biological mechanisms as well as through different social attitudes towards motherhood. Also, maternal age could modify the association between education and fertility impairment assuming that (1) fertility does not decline steadily with age and (2) other pathological conditions may contribute to female infertility distinctively across women's reproductive life.[13] We had not found a statistical significant interaction between age and education but the effect of education seemed to be attenuated with increasing age (data not shown). This may be a reason for the null effect found among multigravidae (mean age 31 years vs 27 in primigravidae). Besides that, if education and the pressure of the labour market lead to the postponement of childbearing, it is also possible that better social conditions may increase the likelihood of having more than one child.[9] We could not know if fertility impairment had occurred in more than one pregnancy. Joffe and colleagues, in a multicentre analysis found that couples experiencing a previous history of infertility may be more likely to experience it in a subsequent pregnancy. However, other behaviours might also influence the reproductive history in the sense of not having another child.[31] These unmeasured characteristics hold back a clear understanding of which factors may have more impact on fertility impairment in women with a previous child.

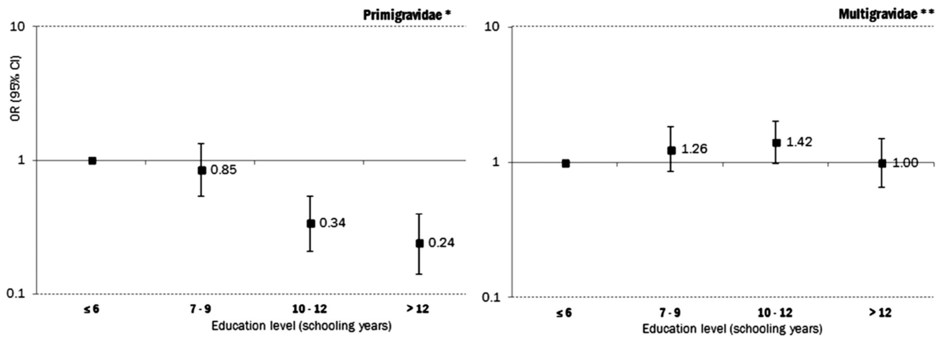

Figure 2 Association between educational level and female fertility impairment, stratified by the occurrence of a previous pregnancy. * Primigravidae: OR adjusted for maternal age, pregnancy planning and age at first sexual intercourse; ** Multigravidae: OR adjusted for maternal age, pregnancy planning, age at first sexual intercourse and body mass index.

Table 3 Association between each socioeconomic indicator and female fertility impairment, stratified by the number of previous pregnancies

	Female fertility impairment	
	OR (95% CI)	
	Model 1*	**Model 1+maternal education**
Primigravidae (n=2375)		
Monthly income (€)		
≤1000	1	1
1001–2000	0.62 (0.43 to 0.89)	0.93 (0.64 to 1.37)
>2000	0.47 (0.27 to 0.81)	1.02 (0.54 to 1.91)
Not known/no answer	0.60 (0.31 to 1.18)	0.70 (0.36 to 1.38)
Occupation		
Unskilled blue-collar	1	1
Skilled blue-collar	0.93 (0.52 to 1.68)	0.81 (0.44 to 1.47)
Lower level white-collar	0.49 (0.30 to 0.80)	0.69 (0.41 to 1.15)
Higher level white-collar	0.32 (0.18 to 0.57)	0.86 (0.41 to 1.79)
	Model 2†	**Model 2+maternal education**
Multigravidae (n=2582)		
Monthly income (€)		
≤1000	1	1
1001–2000	1.11 (0.81 to 1.51)	1.05 (0.75 to 1.46)
>2000	0.94 (0.61 to 1.44)	0.97 (0.59 to 1.60)
Not known/no answer	0.61 (0.33 to 1.12)	0.59 (0.32 to 1.10)
Occupation		
Unskilled blue-collar	1	1
Skilled blue-collar	0.94 (0.58 to 1.53)	0.94 (0.58 to 1.52)
Lower level white-collar	1.08 (0.73 to 1.62)	0.98 (0.64 to 1.49)
Higher level white-collar	1.00 (0.63 to 1.61)	1.08 (0.59 to 2.00)

*Model 1, adjusted for maternal age, pregnancy planning, age at first sexual intercourse.
†Model 2, adjusted for maternal age, pregnancy planning, age at first sexual intercourse, body mass index.

Educational level was the only socioeconomic indicator found to be significantly associated with female fertility impairment. Depending on the setting, each indicator embodies distinct dimensions of social status and these may differ in their effects on individuals' health. In young adulthood, education seems to be the factor most strongly associated with health[21] as it happened in our sample. Although occupation and income were also associated with impaired female fertility, the estimates were no longer significant when controlling for education. However, these social dimensions seem to be highly correlated and the models may be overadjusted.[32] Also, some occupations may be associated with environmental exposures related to fertility impairment but we were unable to identify these.[33]

This study used a large population-based sample of mothers who delivered a live birth. Sampling only truly fertile women reduced bias as it excluded sterile women who will never be able to conceive and for whom factors leading to female fertility impairment may be different.[7] It should be borne in mind that male reproductive impairments are among the possible causes of the current trends in fertility.[34] We have excluded participants whose partners had a clinically recognised male cause of infertility but we cannot completely rule out male factors for infertility. Only 63% of women with impaired fertility sought medical help and among these, a clinical diagnosis for infertility was provided for 71% of women. Therefore, we acknowledge that we might not have totally dissociated the women causes from male or even the couples' causes along with the effects of shared risk factors. Studies show that the risk of infertility is higher if both partners present obesity[35] and if both are older.[36] For a subgroup of primigravidae (n=813) for whom we have data from the father at the moment of birth (self-administered questionnaires) we conducted the same analysis adjusting for the shared overweight/obesity and age over 35 years: the relation between education and infertility did not significantly change (data not shown). We asked women about delay in conception ever in their life. Because of that, it is possible that apparent fertility impairment was related with previous partners' male infertility. But the proportion of previous pregnancies from the same father did not differ between the groups and is less likely to have influenced our results.

This study was not restricted to planned pregnancies or to women attending fertility clinics, strengthening its external validity. Inequalities in seeking help for infertility treatment have been observed elsewhere but are not universal.[25 37] More educated women tend to look for infertility treatment sooner, achieving earlier pregnancies and with higher probability of success, possibly resulting in a misclassification of their fertility status. Although we have found this educational pattern among women with fertility impairment, it was not observed in fertile women. Consequently, misclassification is unlikely to have occurred. On the contrary, less educated impaired women might have not sought for treatment and, if they had not achieved a successful pregnancy, they would not have been included in this study. If they had, this would have increased the differences that we found.

Because of different timings of data collection, we have excluded a subgroup of women recruited during pregnancy. We found these women to be less educated than those included in the current analysis. However, assuming that we have correctly estimated the association between education and fertility impairment, the exclusion of this group decreased the power of the current study to detect real differences and did not bias the results.

Female fertility impairment was collected after birth and misclassification may have occurred. However, if misclassification occurred and if it was differential we expect less educated women to be more likely to ignore/under-report their fertility status.[38] If so, even greater socioeconomic gaps would be observed.

This study shows that social circumstances, particularly education, might be important in understanding patterns of fertility impairment. Their impact seems to depend on the previous reproductive experience. Among first-time pregnant women, infertility decreased with increasing education. This relation was not totally explained by other sociodemographic and lifestyle characteristics that have been previously found to be important to disclose this relation.

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Contributors SC was responsible for the collection, analysis and interpretation of data and for the first draft of the manuscript. TR revised the manuscript critically for important intellectual content; HB was responsible for the cohort study design, study concept and interpretation of data and revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

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Supplementary Table 1 – Sought for medical advice for self-perceived conceiving problems according fertility status

		Female fertility impairment		
	Total (n=7402)	No (n=6751)	Yes (n=651)	p
Sought for medical help	517 (7.0)	110 (1.6)	407 (62.5)	<0.001
Clinical diagnosis for problems conceiving	364 (71.1)	77 (72.0)	287 (70.9)	0.824
Stress or anxiety	138 (38.3)	29 (38.2)	109 (38.4)	0.972
Female causes				
Hormonal disturbances	80 (22.2)	17 (23.7)	62 (21.8)	0.730
Polycystic ovary syndrome	51 (14.2)	9 (11.8)	42 (14.8)	0.513
Tubal obstruction	19 (5.3)	1 (1.3)	18 (6.3)	0.082
Endometriosis	9 (2.5)	0 (0.0)	9 (3.2)	0.116
Medication use	185 (44.9)	40 (50.6)	145 (43.5)	0.255

5. Overall discussion

In the present thesis we aimed at assessing the relation between different spheres of social circumstances and reproductive health. By using different approaches to appraise social determinants it was possible to analyse their evolution in time, how they are transmitted in subsequent generations and if health care services had a role on the attenuation of social differences.

We found that less privileged Portuguese women are still the ones presenting worst reproductive and pregnancy outcomes. The social influence was reflected in individual educational differences in those outcomes (papers III-VII), partly attenuated by prenatal care provider (paper V). Although social destiny remains strongly related with parent's social conditions, in the past few decades when a societal effort to improve education in the country was observed, a sufficient increase in the educational hierarchy seems to overcome disadvantage earlier in life (paper VI). Individual disparities remained relatively constant in the last twenty years, although in periods of major economic growth educational inequalities in adverse birth outcomes seem to decrease (paper III). The recent economic contraction seems to limit the intention or ability of families to have children but is also associated with an increase in low birthweight (paper II).

This work relied on the need to understand the magnitude of social inequalities in perinatal outcomes in the Portuguese setting and how much of these inequalities are driven from contextual factors beyond maternal adult socioeconomic position. It assumed individual social background and contextual effects to interconnect, promoting or attenuating socioeconomic inequalities in perinatal outcomes and, consequently, in health later in life (Figure 15). We consider that the individuals' autonomy and capacity to make choices is not an isolated feature and public health interventions focus on changing physical, social and or economic factors in the environment are likely to promote the health of the population.

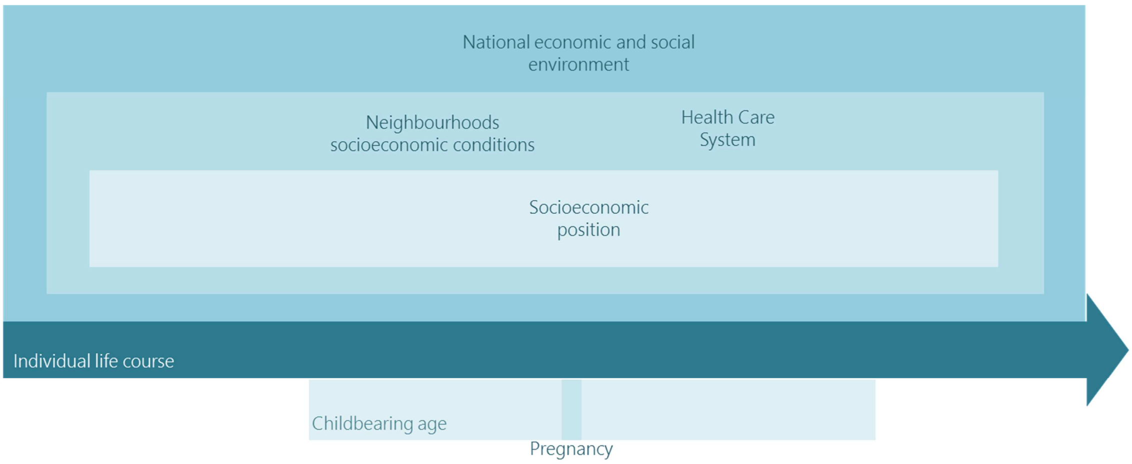

Figure 15 - Simplified diagram of the theoretical assumptions considered in the current work

At the macro-level, societal impact on reproductive and perinatal outcomes in Portugal was clear. First, for the very recent years of economic constraints, a steepest decline of 5% per year in the number of live births was observed after 2008, when compared to the average 2% of annual decline observed previously to that date (paper II). The fall in the number of live births was above the average decline in Europe. Between 2008 and 2011 the number of live births fell by 3.5% in

Europe [222] while, for the same time period, Portugal faced a fall of 7.4%. The persistence of the economic recession led to a decline of 21% in the number of live births in the country until 2013 (when compared to 2008), the highest decline in Europe but similar to the trend observed in some Southern European countries, as Greece (20%) or Spain (18%) [208]. Although part of this change is likely to be related with migration of women in childbearing ages (particularly those between 25 and 34 years), changes in the reproductive behaviour seemed to explain most of the decline. Main changes were related with a decrease in the number of children among youngest women (below 30 years). A major decline was found in those below 25 years (for whom the number of live births in 2013 has halved the number observed in 2008), which reflects a possible differential selection into pregnancy of older women. However, due to the lower impact of changes in the number of live births among women below 25 years (prevalence less than 15%) when compared to those between 25 and 34, and considering that we expect to continuously decrease teenage pregnancies and those between 20 and 24 years because of the increasing number of schooling years, women between 25 and 34 years seem to be the ones more affected by the recent recession in terms of parenting practices. The observed changes among these women may be the result of unemployment and financial insecurity and a more pronounced probability of childbearing postponement until older ages due to economic context. The most recent National fertility survey showed that parents, detached from any constraints, desired an average of 2.31 children [223], while the observed number of children per woman reached 1.21 in 2013 [11]. Based on these figures and the obstacles reported for parenthood, several proposals are being discussed to increment birth rate in Portugal, including financial and fiscal incentives, extension of parental leaves, flexibility in employment conditions and structural conditions to support childcare.

By itself, low fertility rates influence population growth with important consequences in the country sustainability in the future years. In addition, these fertility trends raise the question of impaired fecundability over time. Fertility impairments are shown to be increasing due to childbearing postponement and lifestyle factors as obesity and smoking habits [20] but the ability to conceive is likely to have improved as a result of ameliorated social conditions [21]. In paper VII we found that, among first time mothers, fertility impairments were less likely to have occurred in more educated women. Contrarily to what has been describe, the association was not fully explained by maternal age, body composition, smoking behaviours, age at the first sexual intercourse or pregnancy planning. Even among planned and younger (bellow 35 years) primiparous women, similar associations were found (data not shown), suggesting that other characteristics may be implied in fertility impairment among less educated women that should be addressed in future studies.

In addition, it seems that we are observing an unfavourable combination of fewer births accompanied by a higher proportion of babies at increased risk, as the frequency of low birthweight increased among singletons, after some years of stable estimates (paper II). The increased low birthweight was not fully explained by increasing maternal age since low birthweight prevalence increased mostly among women below 35 years of age. Also, this trend may be the result of differential selection to pregnancy of less educated women. In fact, between 1998 and 2008, the increase in more educated women was more frequent among pregnant women than in the general female population (more 64% vs. more 54%) but the inverse was observed in recent years (2008-2013: more 22% vs. more 39%), while the proportional decrease of less educated was similar in both periods. Smoking habits in pregnancy and inadequate nutritional uptake may be possible mediators of the effect of economic context and growth restriction. Also, unemployment and financial instability, mostly related with preterm, can be possible reasons for this pattern. It would be useful to consider the overall preterm trends to disentangle the different etiologic pathways that lead to low birthweight. However, we found that national preterm estimates may be overestimated for the years 2006 to 2009 which limits our ability for comparisons (paper I).

In paper III, educational inequalities in low birthweight and preterm birth did not significantly increase with recession (although inequalities increased 6% and 5%, respectively). This argues in favour of an effect of the economic crisis not only in those less privilege but in the overall population. However, when analysing socioeconomic inequalities in perinatal health, as in other outcomes, one must take into account what the gap between individuals at the top and at the bottom of the social hierarchy represents. Shortening social inequalities in health aim the reduction of social differences by proportionally greater improvements at the bottom of the hierarchy, which are likely to result in gains in the overall population health [224]. Particularly for the recent years, the observed greater increase in preterm and low birthweight within more educated women may disguise worse results among less educated, resulting in the observed stable inequalities. Even so, an increase of adverse pregnancy outcomes in more privileged women should also be a focus of attention. The increase in the overall women's education, although carrying out an improved ability to individual healthier choices and a decreased risk to adverse exposures, may pose some challenges regarding reproductive health and fertility practices. The integration of women in the labour market, particularly in high standard positions, as mentioned above, is associated with childbearing postponement carrying additional risk to pregnancy complications and adverse birth outcomes. The fast progression of the overall maternal education in the country may have not been followed by structural changes to meet individual expectations between professional and family life.

In a country that faced such fast and great increase in education, childhood social environment seem to have smaller contribution to future perinatal outcomes, contrarily to settings with relatively stable literacy and social conditions. In paper VI we tested if childhood social environment was associated with offspring's growth restriction and if the association between this outcome and adult social conditions and adult height was reflecting earlier social circumstances. We found no association between childhood social environment and the delivery of small-for-gestational age babies, contrarily to what has been previously reported. In fact, despite the strong intergenerational transmission of social conditions (high education was 4 and 8 times more likely in women with, respectively, high educated parents or high childhood social class), society-related changes in access to institutional education seem to have offset part of this dependency in terms of birth outcomes. However, we found that the growth restriction protection conferred by the rise in socioeconomic position was only observed for those that achieved high levels of education indicating that small increases may had not be sufficient. This may represent that in particularly deprived settings, a population approach to increase overall social conditions may buffer the protection conferred by the individual processes of upward mobility. Fall in the social hierarchy did not increase the risk of SGA which might indicate some protection in adult life of a more privileged childhood. However, in this setting, downgrading was a rare event. Adult height, a proxy indicator of growth, is also used as a surrogate of childhood social environment as a result of nutritional, health and psychological stress throughout the growing years [225]. We found that, although women with a more privileged childhood were two times more likely to be taller (height above the 90^{th} percentile of the sample distribution), insults to growth were beyond social adversity: the association between maternal height and off-spring growth restriction was stronger among women from high childhood social class than among more deprived women. It seems that growth disturbances in more privileged children might have had a more deleterious effect in off-spring health, possibly due to unmeasured exposures affecting both maternal growth and fetal growth restriction (e.g. maternal birthweight, genetics or chronic conditions).

In the last 40 years, together with the improvement of social conditions, the National Health Service was launched, guaranteeing universal access to health care. In this framework, and contrary to the user charges required for the general population, pregnant women and children are entitled free care. That and the high prevalence of women with attempted care (almost 90% begun care before 13 gestational weeks) allow us to expect prenatal care to be reasonably equitable in Portugal. Even so, social inequalities in the access remain and should be addressed carefully. In the context of social inequalities in birth outcomes, one cannot disregard the potential buffering effect of prenatal, birth and neonatal health care services. Specifically, we have tested differences in outcomes according public and private prenatal care providers (paper V) but the effect of health care may also explain other results that we have found. Contrary to low birthweight that increased in the recent years of economic recession, fetal, neonatal and infant mortality may have been safeguarded and remained stable (paper II), possibly as a result of effective management of high risk babies in the national health care service. The increasing access to care and the pervasive use of ultrasonography may also explain the larger decrease in preterm birth among less educated women in the late nineties (paper III), though it might reflect not only effective prenatal care but improvements in pregnancy duration assessment.

Portugal is now a country where an excessive medicalization of pregnancy and birth has been reported, namely the high frequency of obstetric interventions as induction of labour, episiotomies or caesarean deliveries [30]. The widespread use of such interventions in the country (which seems to be increasing [30]) may also be partly related with the increase in preterm (and consequently low birthweight) babies because of the lowered threshold for indicated preterm labour (paper III). We have previously found that caesareans were socially patterned with more educated women presenting higher rates, despite their allegedly lower risk of adverse birth outcomes [205]. We also found, for women delivering in public facilities, that low risk women using public prenatal care presented lower rates of this intervention (paper V). Although these differences are more likely to be reflected in the delivery of babies at term, it is plausible that an increase in near term deliveries among more educated women is in course, narrowing inequalities. As mentioned above, this pattern suggests that inequalities in birth outcomes could be even greater. In paper V we also observed that a large amount of prenatal care is provided, particularly in private settings. Interestingly, the amount of care and the differences between providers were not related with pre-pregnancy risk of adverse birth outcomes, which alerts for a possible excessive use of resources. Among high-risk women, provision of care seems to be more standardised, leading to similar outcomes between public and private users. Low-risk public care users, independently of a less favourable social profile, experienced some birth outcomes as good as those who received private care. However, the higher likelihood of outcomes related with behavioural characteristics, such as excessive weight gain, gestational diabetes and the delivery of small-for-gestational age babies, suggest that more attention is still needed. In addition to addressing barriers to care, action should focus on components and quality of care. It seemed clear that, besides high-risk prenatal care approaches, those focused on apparently low-risk women should be emphasised. Such purpose is likely to be a cost-effective benefit to more equitable access to high quality care, promoting population health improvements.

Finally, effective, attempted and of good quality prenatal care might have contributed to attenuate and disguise a potential effect of the neighbourhood characteristics on the delivery of preterm and small-for-gestational-age babies (paper IV). Although methodological and operational limitations might explain the observed non-association between place of residence and birth outcomes in Porto Metropolitan Region, the relation was observed in Pelotas, Brazil. Lower level of neighbourhood clustering is likely to be observed in Porto Region than in Pelotas, which may explain the observed differences. Also, beyond social features measured by age, education, occupation and housing, other aspects of neighbourhood physical characteristics, social cohesion, crime and self-perception of the social environment are probably important to understand how the context of living affect women's behaviours and pregnancy outcomes. Although in Pelotas we had not found an effect of area social circumstances, different neighbour-to-neighbour variations were observed by ethnic group and for different outcomes: preterm births were contextual clustered among white women while neighbourhood heterogeneity in SGA was observed in black mothers. This argues in favour of different pathways by which setting-specific characteristics affect specific ethnic groups.

Some controversy on the ability of epidemiology to evaluate upstream determinants of health has arisen with Rothman arguing that the "further upstream we move from the occurrence of disease towards root causes, the less secure our inferences about the causal path to disease become" [226]. However, the non-recognition of the entire net of socioeconomic factors when exploring the causal mechanisms that affect population health engenders insufficient knowledge on disease causation. Together with research on more proximal causes of disease, understanding the social, community and policy determinants of health increases the opportunity for public health interventions to reduce socioeconomic inequalities in health [227]. Throughout this work we identified several characteristics (such as economic growth, population unemployment rates, prenatal care provision and individual education and respective trajectory) that, at different levels, are likely to influence the occurrence of adverse reproductive and pregnancy outcomes. But much more remains unknown and deserves further attention.

Currently, women have become more educated and greater improvements are still expected to be observed in the following years. Targeting education is unlikely to provide the same improvements in health as in previous years, since most population is now educated. More research is needed to understand potential changes in the benefit of higher education in this and other settings. Policies to increase a population educational distribution are likely to ameliorate population health, possibly contributing to the reduction of social inequalities in health. However, for the effectiveness of implemented policies is important to understand which groups of the population benefit the most with education improvement in the following years.

Future research to understand the combined effect of different levels of social, institutional and economic environment and of behavioural, psychological and genetic characteristics, including father and couples'-related features is fundamental. Innovative methodological approaches and the use of other socioeconomic domains are likely to contribute to effective strategies to reduce inequalities in perinatal health. Which macro, mezzo and micro characteristics are important, why they are important, how women embody and biologically express exposure to the social environment are still unanswered questions. The life course approach to social inequalities, using longitudinal data collected at early ages, namely by the use of birth cohorts, is likely to improve our knowledge on the origins of such inequalities. Together with the conceptual and analytical complexities of life course approach, integration with psychological and socioeconomic data at different levels is challenging but fundamental.

Research of social inequalities in reproductive and perinatal health should continue to focus on the role and performance of health care. Current social and economic context impose the understanding of new potential barriers to care. As mentioned above, an excessive medicalization of pregnancy and birth is evident in the Portuguese context. Well-designed effectiveness interventions and the research of quality components of care are of extremely relevance in our context to guarantee and guide cost-effective strategies.

6. Conclusions

Throughout this work, a consistent association between socioeconomic conditions and reproductive and perinatal outcomes was observed. National socioeconomic development seems to be reflected in the overall distribution of these outcomes, as in their social inequalities, reinforcing the need for universal and targeted policies.

In the Portuguese context, but not in the Brazilian setting, neighbourhood variation on birth outcomes was not observed. Other contextual characteristics should be addressed in the future, as their interaction with prenatal care. In Portugal, women using prenatal care provided by the National Health Service, particularly those at high risk of adverse conditions, appear to have pregnancy outcomes as good as those using private settings. As some behavioural-related consequences were still more prevalent among low risk women, a population approach to care should be more carefully addressed, not disregarding potential improvements when high risk approaches apply.

Despite the observed overall mobility towards higher education, childhood background in the Portuguese setting remained strongly associated with academic achievements. However, a sufficient rise in education seems to have overcome early social disadvantage in the risk of adverse birth outcomes. Childhood insults to women's anthropometric development seem to be important to the risk of adverse birth outcomes, particularly among those that grow in environments where social disadvantage is no longer a problem.

These results, together the observation that socioeconomic inequalities were observed even previously to conception, showed the interdependency of social contextual effects on perinatal outcomes. Eliminate poverty is probably an utopia, but improving women's daily living conditions and the equal allocation of resources is likely to be effective aiming better perinatal outcomes. This work did not intend to provide 'the' solution to reduce inequalities in early life but provides a picture of possible targets for intervention. To implement preventive strategies based on the high quality data we also argue for the need of a more robust perinatal surveillance system.

7. References

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