Maternal health indicators during pregnancy and birth outcomes during times of great macroeconomic instability: the case of Iceland

Védís Helga Eiríksdóttir

Thesis for the Degree of Philosophiae Doctor

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Heilsa barnshafandi kvenna og fæðingaútkomur á tímum mikilla efnahagsþrenginga á Íslandi

Védís Helga Eiríksdóttir

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Ágrip

Inngangur: Sýnt hefur verið fram á að sveiflur á efnahagsástandi þjóða geta haft áhrif á lýðheilsu. Hinsvegar er ekki mikið vitað um áhrif slíkra sveiflna á heilsu mæðra og fæðingarútkomur. Niðurstöður þeirra rannsókna sem gerðar hafa verið hafa verið misvísandi. Meginmarkmið þessa doktorsverkefnis var að rannsaka möguleg áhrif íslenska efnahagshrunsins, haustið 2008, á heilsu barnshafandi kvenna og fæðingarútkomur. Ennfremur að kanna að hversu miklu leyti efnahagsástandið á Íslandi skýrði mögulegar heilsufarsbreytingar hjá ofangreindum konum og afkvæmum þeirra.

Efni og aðferðir: Í rannsókn I var notað slembiúrtak úr Fæðingaskrá Íslands sem samanstóð af 1329 konum sem eignuðust börn á tímabilinu 2001 til 2010. Upplýsingum um *reykingavenjur* á meðgöngu, *líkamsþyngdarstuðul* og lýðfræðilegar upplýsingar um móður voru fengnar úr Fæðingaskrá og úr mæðraskrám. Notuð var lógistísk og línuleg aðhvarfsgreining til að reikna breytingar á reykingum á meðgöngu, líkamsþyngdarstuðli og offitu eftir árum og eftir lýðfræðilegum bakgrunnsþáttum móður.

Í rannsóknum II-IV var Fæðingaskráin notuð til að bera kennsl á allar konur sem fæddu lifandi einbura á árunum 2002 til 2012 (2006-2009 fyrir rannsókn III). Upplýsingum um meðgöngutengda háþrýstingssjúkdóma (*meðgönguháþrýstingur, meðgöngueitrun*) og óhagstæðar fæðingarútkomur (*léttburafæðingar, fyrirburafæðingar, vaxtarskerðing í móðurkviði*), auk lýðfræðilegra upplýsinga um móður og föður voru fengnar úr Fæðingaskrá en upplýsingar um notkun háþrýstingslækkandi lyfja (*β-blokkar, kalsíumgangalokar*) fengust úr Lyfjagagnagrunni. Efnahagsvísar Íslands voru fengnir frá Hagstofu Íslands. Lógistísk aðhvarfsgreining var notuð til að meta breytingar á meðgöngutengdum háþrýstingssjúkdómum og notkun á háþrýstingslækkandi lyfjum, auk breytinga á óhagstæðum fæðingarútkomum á árunum eftir efnahagshrunið, samanborið við árin fyrir hrun.

Niðurstöður: Niðurstöðurnar gefa til kynna að árlega hafi dregið úr reykingum (gagnlíkindahlutfall (GLH) 0.94, 95% öryggismörk (ÖM) 0.88-1.00) á meðal ófrískra kvenna á Íslandi á fyrsta áratug aldarinnar. Á sama tíma virðist ekki hafa orðið marktæk breyting á tíðni offitu hjá ófrískum konum (GLH 1.02, 95% ÖM 0.96-1.07). Hæsta tíðni reykinga á meðgöngu og offitu virðist hafa verið í aðdraganda efnahagshrunsins, eða á árunum 2005 til 2006.

Niðurstöður er varða heilsu barnhafandi kvenna gefa til kynna að konur sem voru ófrískar á fyrsta árinu eftir hrun voru í aukinni áhættu fyrir

meðgönguháþrýstingi (GLH 1.47, 95% ÖM 1.13-1.91) samanborið við konur sem voru ófrískar fyrir hrun, með samsvarandi aukningu í notkun β-blokka á þessu sama tímabili (GLH 1.43, 95% ÖM 1.07-1.90). Þessi aukning virðist hafa verið bundin við fyrsta árið eftir hrun og sást ekki þegar lengra dró frá hruni. Ennfremur, þegar leiðrétt var fyrir atvinnuleysisstigi þá hvarf þessi aukning sem gefur til kynna að dýpt kreppunnar, mæld með atvinnuleysisstigi í landinu, sé skýringin á þeim tengslum sem fundust. Engin breyting varð á tíðni meðgöngueitrunar eftir efnahagshrunið, samanborið við árin fyrir hrun.

Niðurstöður er varða fæðingaútkomur gefa til kynna aukna áhættu á fæðingum léttbura á fyrsta árinu eftir efnahagshrunið (GLH 1.35, 95% ÖM 1.12-1.63), samanborið við árin fyrir hrun. Þessi aukning virtist vera bundin við fyrsta árið eftir hrun og sást ekki þegar lengra dró frá hruni. Sú aukning sem varð á léttburum eftir hrun virðist að einhverju leyti vera tilkomin vegna vaxtarskerðingar í móðurkviði. Á fyrsta ári eftir hrun varð aukning á vaxtarskertum nýburum (GLH 1.11, 95% ÖM 1.00-1.23) sem virtist vera viðvarandi út rannsóknartímabilið (GLH 1.08, 95% ÖM 1.01-1.16). Þegar leiðrétt var fyrir efnahagsvísum þá hvarf þessi aukning á fæðingum léttbura og vaxtarskertra barna, sem gefur til kynna miðlunaráhrif af efnahagsástandi í landinu. Ennfremur gefa niðurstöðurnar til kynna að börn ungra kvenna, þeirra sem ekki voru í sambúð og foreldra þar sem báðir voru án launaðrar atvinnu, voru í aukinni áhættu á að fæðast of létt eða vaxtarskert í kjölfar efnahagshrunsins samanborið við sömu hópa fyrir hrun. Engar marktækar breytingar urðu á tíðni fyrirburafæðinga eftir hrun, samanborið við fyrir hrun.

Ályktun: Niðurstöðurnar gefa til kynna að efnahagshrunið á Íslandi haustið 2008 hafi haft neikvæð áhrif á heilsu barnshafandi kvenna og á fæðingaútkomur þeirra. Nánar tiltekið þá virðist efnahagshrunið hafa valdið aukningu á meðgönguháþrýstingi og notkun háþrýstingslækkandi lyfja á fyrsta og alvarlegasta ári efnahagsþrenginganna, auk þess að hafa haft neikvæð áhrif á vöxt barna í móðurkviði. Neikvæð áhrif efnahagshrunsins á fósturvöxt virðist hafa verið mest hjá viðkvæmustu hópum þjóðfélagsins sem ýtir undir ójöfnuð í fæðingaútkomum eftir þjóðfélagshópum á tímum efnahagsþrenginga. Ólíklegt verður að teljast að neikvæð áhrif efnahagshrunsins á heilsu barnshafandi kvenna og fæðingaútkomur hafi verið miðlað í gegnum verri heilsuhegðun hjá barnshafandi konum.

Lykilorð:

Efnahagskreppur, heilsuhegðun, háþrýstingssjúkdómar á meðgöngu, óhagstæðar fæðingaútkomur, þjóðhagfræðileg staða

Abstract

Background and aims: Macroeconomic fluctuations have shown various effects on population health, but the evidence base for their influence on maternal health and birth outcomes is scarce and inconclusive. The overall aim of this thesis was to examine the potential effect of the 2008 economic collapse in Iceland on maternal diseases and health behaviors during pregnancy as well as on adverse birth outcomes. Furthermore, we aimed to explore the effect of the surrounding economic climate in Iceland on potential changes in the health of the pregnant women and birth outcomes.

Material and methods: In *study I* we used a random sample of 1329 births occurring between 2001, and 2010. Information on maternal smoking status, body mass index and demographic characteristics were retrieved from the Icelandic Medical Birth Registry and maternity records. Trends in continued smoking into the second trimester of pregnancy, obesity, and body mass index were assessed using logistic and linear regression analyses. Logistic regression analysis was used to calculate the annual odds of smoking and obesity, both overall and by maternal demographic characteristics. In *studies II-IV*, the Icelandic Medical Birth Registry was used to identify all women giving birth to live-born singletons between the years 2002 and 2012 (2006-2009 for study III). Information on pregnancy-induced hypertensive disorders, birth outcomes, and parental demographic characteristics were retrieved from the Birth Registry and use of antihypertensive drugs during pregnancy, including β-blockers and calcium channel blockers, from the Icelandic Medicines Registry. Information on the aggregate economic climate was retrieved from Statistics Iceland. With the pre-recession period as a reference, we used logistic regression analyses to assess changes in pregnancy-induced hypertensive disorders, prescription fills for antihypertensive drugs and adverse birth outcomes during the recession years.

Results: There was an annual decrease in continued smoking (odds ratio (OR) 0.94, 95% confidence interval (CI) 0.88-1.00) among pregnant women in Iceland giving birth during the first decade of the 21st century, whereas no significant changes in obesity were observed (OR 1.02, 95% CI 0.96-1.07). The highest prevalence of maternal smoking and obesity was observed in the years leading up to the economic collapse or in 2005 to 2006.

With regard to maternal diseases and using the pre-recession period as a reference, we observed an increase in gestational hypertension during the first recession year (OR 1.47, 95% CI 1.13-1.91) with a concurring increase in prescription fills for β-blockers during the same year (OR 1.43, 95% CI 1.07-1.90). The increase was confined to the first recession year and was not observed in the subsequent recession years. Furthermore, the increase disappeared when adjusting for aggregate unemployment rate, indicating that the economic conditions, as proxied by aggregate unemplyment, is the reason for the observed effects. No changes were observed for preeclampsia or in prescription fills for calcium channel blockers between the pre-recession and recession periods.

With regard to adverse birth outcomes and using the pre-recession period as a reference, we observed an increase in low birth weight during the first recession year (OR 1.35, 95% CI 1.12-1.63) but not during the subsequent recession years. Furthermore, we noted an increase in small for gestational age births, both during the first recession year (OR 1.11, 95% CI 1.00-1.23) and the subsequent three recession years (OR 1.08, 95% CI 1.01-1.16). The observed increase of low birth weight and small for gestational age births were attenuated when adjusting for aggregate economic indicators. Moreover, the findings indicated infants born to young women, those not cohabitating and parents not working paid labor-market jobs, were at higher risk for these adverse birth outcomes during the recession years compared with their peers during the pre-recession years. No significant change was observed for preterm births between pre-recession and recession periods.

Conclusions: The findings of this thesis lend support to the notion that the 2008 economic collapse in Iceland had adverse effects on the health of pregnant women and their offspring in Iceland during the first four years of the economic recession. More specifically, the findings indicate a transient increase in gestational hypertension and in the use of β-blockers during the first and most severe year of the economic recession, as well as a negative influence on fetal growth, which was particularly observed among the most vulnerable groups of the society, resulting in widening disparities in birth outcomes in Iceland during the recession.

Keywords:

Economic recession, health behaviors, pregnancy-induced hypertensive disorders, adverse birth outcomes, macroeconomic conditions

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I can still remember the exact time when I came across the concept of epidemiology. I instantly knew that it was it – I wanted to study epidemiology. The opportunity to systematically use large amount of health data to create new knowledge both intrigued and inspired me to start this journey which now is near its destination. During this journey I have been immensely fortunate to have the greatest mentors, colleagues and friends who have, with their support and positivity, encouraged me during the difficult times and felicitated with me during the high points of the journey. First and foremost, I would like to start by thanking my main advisors, Unnur Valdimarsdóttir and Helga Zoëga. Unnur, you're one of a kind. You have such a strong and positive presence, always ready to listen and give your advices, even when you have tons of deadlines ahead of you. Thank you so much for believing in me and for your great mentoring through the years, it has been invaluable. Helga, I'm extremely lucky that you decided to move back to Iceland as it resulted in you taking place in my PhD committee. Your enthusiasm, energy and positivity is contagious and I always felt motivated after our meetings and discussions. Thank you so much for your help with all the obstacles during the journey – you're a true role model. I would also like to thank the other members of the PhD committee for their valuable input in the work. Tinna Laufey, I'm grateful to you for lending your expertise in the field of health economy. Although, at times challenging, it definitely brought a different perspective to the project. Arna, thank you for your moral support, encouraging words and all the tips regarding the stress and crisis literature. I thank Sven Cnattingius and Ragnheiður Bjarnadóttir for lending their expertise in the field of obstetrics and gynecology. Sigrún Helga Lund gets thanks for her help with biostatistic challenges and her ever bright humor. My sincere gratitude to Dóra, who is the rock at the Centre of Public Health. There is nothing Dóra can't solve with easiness. Thank you for all your help and many enjoyable conversations during the past years. My dear roommate Hildur, whom I have shared so much with - not only are you a great and reliable friend – you have also taught me the invaluable trait of patience and tolerance. Thank you for being who you are and standing with me when things got tough. And to my caring friend, Jóhanna, I thank you for all the talks, jogging, swimming and crossfitting – you are the best. I also wish to thank all my coworkers in Stapi who have not only made the past years surmountable, but also joyful and rewarding. Thanks to you all, Maríanna, Ragna, Agnes, Edda, Emma, Elsa,

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Contents

List of abbreviations

ATC	Anatomical therapeutic chemical
BMI	Body mass index
CI	Confidence interval
GDP	Gross domestic product
CRH	Corticotrophin-releasing hormone
HPA	Hypothalamic-pituitary-adrenal axis
ICD	International Classification of Diseases
IUGR	Intrauterine growth restriction
LBW	Low birth weight
OR	Odds ratio
PB	Preterm birth
SD	Standard deviation
SE	Standard error
SES	Socioeconomic status
SGA 2SD	Small for gestational age (<2 standard deviations)
SGA 10^{th} pct.	Small for gestational age (<10^{th} percentile)
TFR	Total fertility rate
US	United States

List of figures

List of tables

List of original papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals (I-IV):

I. **Smoking and obesity among pregnant women in Iceland 2001-2010.** Eiríksdóttir VH, Valdimarsdóttir UA, Ásgeirsdóttir TL, Gísladóttir A, Lund SH, Hauksdóttir A, Zoëga H (2015). Eur J Public Health 25(4):638-43.

II. **Pregnancy-induced hypertensive disorders before and after a national economic collapse: a population based study.** Eiríksdóttir VH, Valdimarsdóttir UA, Ásgeirsdóttir TL, Hauksdóttir A, Lund SH, Bjarnadóttir RI, Cnattingius S, Zoëga H (2015). PLoS ONE doi: 10.1371/journal.pone.0138534

III. **Low birth weight, small for gestational age and preterm births before and after the economic collapse in Iceland: a population based cohort study.** Eiríksdóttir VH, Ásgeirsdóttir TL, Bjarnadóttir RI, Kaestner R, Cnattingius S, Valdimarsdóttir UA (2013). PLoS ONE 8(12): e80499.

IV. **Increase in small-for-gestational age births during an economic recession: a nationwide cohort study in Iceland.** Eiriksdottir VH, Zoëga H, Lund SH, Ásgeirsdóttir TL, Hauksdóttir A, Cnattingius S, Valdimarsdóttir UA. *Submitted manuscript.*

In addition, some unpublished data is presented:

Paper I is reprinted by kind permission of the publisher.

Declaration of contribution

The doctoral student, Védís Helga Eiríksdóttir, planned the research work for Papers I-IV of which she is the first author. She applied for the appropriate ethical and research approvals and obtained the relevant data. Statistical analyses were run in cooperation with her supervisor, advisor and a statistician. The doctoral student drafted the papers and responded to the reviewers' comments in collaboration with her co-authors. She wrote this thesis with the solid guidance of her supervisor, advisor and the doctoral committee.

1 Introduction

The 2008 global financial crisis (hereafter referred to as the Great Recession) has resulted in the most widespread economic downturn since the Great Depression of the 1930s. It adversely affected the world economy, even in countries with stable macroeconomic fundamentals. The Great Recession was characterized by synchronous crises in the global financial system, employment and in housing markets. In the United States (US), the unemployment rate rose from 4.6% in 2007 to a peak of 10.1% in October 2009, resulting in an additional 7.9 million unemployed individuals. In Europe, the unemployment rate rose from 7.3% in December 2009 to 10.1% in April 2009, with significantly larger rises in Spain and Ireland (1).

Those rapid changes caused concern regarding consequences for population health - concerns that are supported by a long line of research indicating a detrimental effect of low income and unemployment on health at the individual level (2, 3). In a recent meta-analysis including 42 studies, Roelfs and colleagues (3) reported a 63% higher risk of all-cause mortality among individuals who had experienced unemployment compared with those who had not experienced unemployment. This increase persisted even after adjusting for potential confounders, affecting the association between unemployment and mortality (i.e. health status prior to unemployment and health behaviors following an employment change). With respect to psychological health, a recent meta-analysis found unemployed individuals to be considerably more likely to suffer from a wide range of psychological morbidity, including distress, depression, anxiety, psychosomatic symptoms, as well as decreased well-being and self-esteem, compared with employed people (2).

While the link between socioeconomic status (SES) and health is quite well established at the individual level, the link between economic changes at the aggregate level and health is less clear cut. Early studies in this field suggested an increased mortality and morbidity during times of economic downturns (4-6), which harmonized well with findings from individual level studies linking financial stress to ill health (2, 3). However, in 2000, Ruhm (7) published an influential study, contradicting the previous findings by demonstrating strong evidence for decreased mortality during short-term macroeconomic recessions in 50 US states between 1972 and 1991. Several subsequent studies using data from other countries have substantiated

Ruhm's findings (8-12), although some variation in findings exists across settings (i.e. in terms of time, countries, welfare systems etc.). However, not all later studies have observed improved population health during macroeconomic downturns. Some report null findings (13, 14), while other report declining indicators of health (15, 16). Indeed, using techniques similar to Ruhm's, although with additional adjustments for demographic and lifestyle factors, Economou and colleagues (16) analyzed data from 13 European Union countries during a twenty-year time period, 1977-1996, and found that when unemployment rate increased by one percentage point, the mortality rate increased by 1.54 per 100,000 inhabitants.

While mortality is the most commonly used health indicator in studies examining the association between macroeconomic conditions and health, other indicators of health have also been investigated, such as psychological health. Indeed, findings of studies examining the effect of macroeconomic conditions on psychological health have very much been in concordance, indicating worsened psychological health (17, 18) and increased suicides rates (7, 13, 19-21) during times of economic recessions. A recent systematic literature review indicates that economic recessions are significantly associated with increased rates of common psychological morbidity, substance related disorders and suicidal behaviors. The authors conclude that the increase in these disorders is most likely mediated by increases in unemployment, income decline, and unmanageable debts among affected individuals (17).

Thus, it is clear that there is a discrepancy between findings from individual vs. aggregate-level studies that is hard to reconcile. However, most of the aggregate-level research conducted prior to the year 2008 is based on normal oscillations in the macroeconomy. The Great Recession represented considerably more severe economic conditions, potentially affecting individuals differently than normal economic fluctuations. This hypothesis is supported by a recent review of 85 studies which found that the literature from aggregate and individual level studies on the Great Recession is in more correspondence compared to the pre-Recession literature. The main conclusion of this review is that the Great Recession had an overall detrimental impact on health. Job loss and financial strain led to increased risk of psychological distress as well as adverse physical symptoms and suicides, where both vulnerable (i.e. those who suffered from job-, income-, or housing loss) as well as less vulnerable groups seemed to have been negatively affected by the Great Recession (22). Furthermore, there is evidence for a greater health impact of economic recessions in sensitive

populations, e.g. with lower societal protection while countries investing in active labor market programs and general societal protection seem to be less affected (13, 22).

1.1 The effect of the Icelandic economic collapse on inhabitants' health

Iceland was one of the countries particularly hard hit by the Great Recession, starting with a collapse of the country's banking system in the beginning of October 2008, subsequent emergency laws and currency restrictions in order to hinder the flow of capital out of the country (23). The economic collapse in Iceland did not only affect the financial market but also the political landscape of the country. As a response to what Icelanders experienced as negligence and corruption, mass protests took place outside the Parliament with demands for a resignation of the sitting government, resulting in a cabinet change in April 2009. The economic collapse in Iceland had a considerable effect on the country's macroeconomic environment. During the four years preceding the collapse, Iceland had been experiencing an economic boom with a 6% average annual growth in gross domestic product (GDP) (Figure 1) and an extremely low unemployment rate, i.e. an annual rate around or below 3% (Figure 2). During the first year following the economic collapse in Iceland the GDP declined by 6.5 percentage points and the unemployment rate more than doubled.

The decline in GDP in Iceland was larger than declines experienced by other hard-hit countries, such as Spain and Ireland (24). With a sharp devaluation of the Icelandic krona and 80 percent of the household debt indexed to inflation (23), up to 50% of Icelandic households had difficulties covering expenses through the pay period in 2010 and 2011 (25). However, despite the sharp bust, the recovery of the Icelandic economy was unusually quick (24), with economic growth realized already in 2011 (Figure 1). Furthermore, the unemployment rate has dropped since its peak in 2010 and was 4% by the end of 2015.

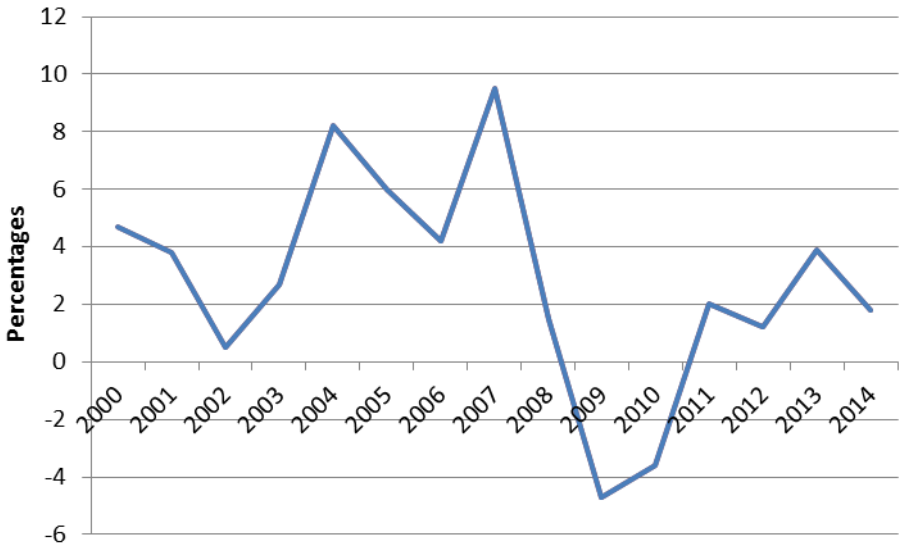

Figure 1. Annual Gross Domestic Product volume growth in Iceland 2000-2014. Source: Statistics Iceland

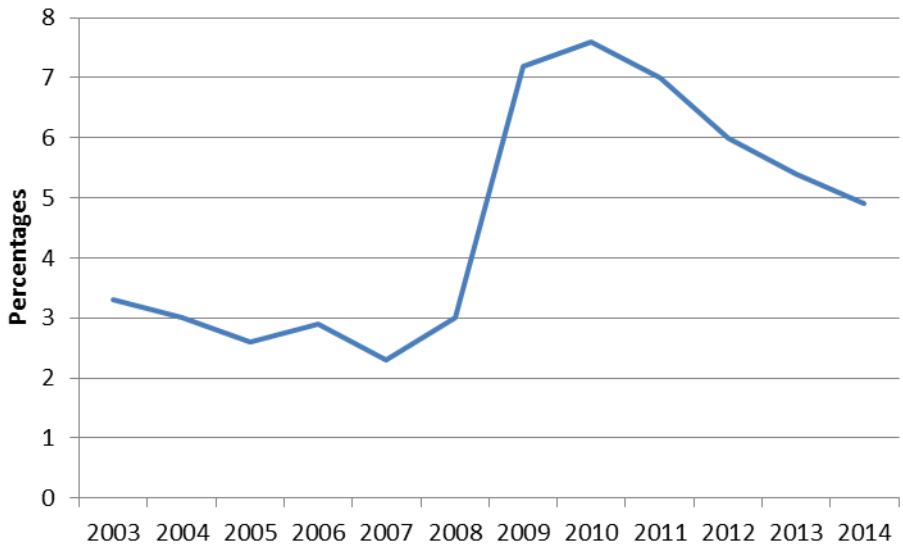

Figure 2. Unemployment rate in Iceland, 2003-2014. Source: Statistics Iceland

The largely unforeseen collapse of the nation's economy came as a shock for the majority of Icelanders and undoubtedly represented a great stressor that affected the majority of the nation's inhabitants in some way or another. Studies examining the health consequences of the Icelandic economic collapse have indicated an increase in sickness and sickness absence among employed individuals (26), as well as an immediate increase in self-reported stress (27) and depression symptoms (28), where the increase in stress was found to be mostly confined to unemployed women and women holding non-skilled positions (27), while no gender differences were observed with respect to depressive symptoms (28). However, no overall increase in attendance rates due to suicide attempts or self-harm was observed following the economic collapse (29). Furthermore, a short term increase in attendance to the cardiac emergency department was observed, where women seemed to have been particularly affected (30). On the contrary, Asgeirsdottir and colleagues (31) did find evidence of increased risk of hypertension, although only among men, following the collapse. Moreover, the adverse effects of the economic collapse on health were more apparent among individuals with low income, with increased male health-income inequalities after the collapse while health disparities remained stable among women (32). Asgeirsdottir and colleagues (24) used individual-level data to examine the effect of the Icelandic economic collapse on health behaviors from a pre-crisis boom 2007, to a deep crisis in 2009, to recovery in 2012. They reported a decline in health-compromising behaviors (e.g. smoking, heavy drinking, intake of sugar-sweetened drinks, sweets and fast food) immediately following the economic collapse in 2009 as compared to the pre-collapse rates; all of which continued to decline throughout 2012 (except sweets). Furthermore, an improvement in some health-promoting behaviors following the economic collapse was observed across the three waves of assessment, although the pattern varied by behavior. Fruit consumption declined first after the economic collapse but had reached its pre-collapse level in 2012. Fish oil consumption increased during the crisis and continued to increase in the recovery, while vitamin supplementation remained unchanged during the crisis but increased in the recovery. Similar findings of reduction in smoking (33, 34) and improved nutrition (35) following the economic collapse have been reported in other studies. Lastly, McClure and colleagues (36) did not find indications of worse dental health behaviors during the crisis, despite the fact that dental cost is not reimbursed by the Icelandic health insurance system.

1.2 Financial strain, maternal health and health behaviors

Considering the plausible link between economic recessions and declining health in the general population, the potential effect of the Great Recession on women of reproductive age and pregnant women has been a matter of concern. Unemployment and decreased income as a result of the recession could potentially push a larger proportion of women into economically disadvantaged groups of the society, which again could affect their health status, the course of their pregnancies, and birth outcomes. Ensor and colleagues (37) recently reported a modest increase in maternal mortality during times of economic recessions in 14 high and middle income countries during the 20th century. This increase was observed early during the last century among the high income countries and later in middle income countries, suggesting that countries at early stage of development are more vulnerable to macroeconomic fluctuations than the more developed countries.

Below, the literature on economic conditions and maternal health and health behavior during pregnancy as well as birth outcomes will be summarized. First, general background information on these topics is provided, followed by a discussion on how individual financial status, on one hand, and macroeconomic conditions, on the other, can affect the process of pregnancy and birth outcomes. Findings from individual-level and aggregate-level studies will be discussed separately throughout this chapter. This is followed by a discussion on the potential mechanisms linking economic contractions to changes in maternal health and birth outcomes.

1.2.1 Individual financial status, maternal health and health behaviors

It is well established that SES is a strong indicator for general health, including maternal health, with worse health conditions being more prevalent among people in the lowest SES groups of the society (38). The suggested contributing factors to this socioeconomic gradient in health are numerous, including destructive coping behavior, suboptimal health behavior or even risk taking behavior, as well as psychological stress due to financial strain associated with unemployment or low-wage employment (38). Studies exploring the socioeconomic health disparities among the pregnant population have shown that compared with women with high SES, those with the lowest SES are more likely to suffer from various medical conditions, such as pre-pregnancy (39) and gestational diabetes (40), pre-existing (39) and pregnancy-induced hypertension (41, 42), as well as obesity (39).

Furthermore, maternal smoking is more common among women with low SES. In a US study, the prevalence of smoking during pregnancy was 18% among women with low SES compared to 1% among women with high SES (39). A similar socioeconomic gradient in smoking was found among pregnant women in the Nordic countries where women with low SES were 6-7 times more likely to smoke compared to women with high SES (43). Other suggested explanations for this socioeconomic gradient in maternal health are increased susceptibility among women with low SES to contagious infections such as influenza (44) and bacterial vaginosis (45), increased risk of being nutritionally deprived (46), and higher exposure to psychosocial stress and general hardship (47) compared with women with high SES.

1.2.2 Macroeconomic conditions and maternal health behaviors

Prior studies on the association between macroeconomic contractions and health behaviors have yielded mixed results. Some studies report improved health behaviors in the general population (7, 48, 49), while other report more suboptimal health behavior during times of recessions (50). Two studies have explored this association among the pregnant population (51, 52). Firstly, in a study of US births between 1979 and 1999, Dehejia and Lleras-Muney (51) found that increases in unemployment rates in the year of conception was associated with an overall decrease in maternal smoking and alcohol intake during pregnancy. Contrary to these results, the second study did not find economic contractions (as proxied with unemployment rate higher than expected) to be associated with maternal smoking or (inadequate/excessive) gestational weight gain. Furthermore, the authors found economic contractions to be associated with a 15% increase in the risk of alcohol intake during pregnancy (52). Thus, the findings on the effects of macroeconomic contractions on maternal health behaviors are mixed and more studies are needed in order to draw sound conclusions on this matter.

1.3 Financial strain and pregnancy-induced hypertensive disorders

Pregnancy-induced hypertensive disorders are among the most common health complications during pregnancy, with a prevalence ranging from 4% to 10% (53, 54). These disorders carry substantial risks for both pregnant women and their fetuses/babies and are the leading cause of maternal and perinatal mortality throughout the world (54). The disorder is defined as hypertension with new-onset after 20th completed week of gestation and ranges from hypertension alone (gestational hypertension) through

proteinurea, multiorgan dysfunction (preeclampsia), seizures, and coma (eclampsia) (53). The pathophysiology of pregnancy-induced hypertensive disorders is still relatively unknown. Gestational hypertension and preeclampsia share several known risk factors, including high maternal age, twin pregnancies, preexisting medical conditions such as renal or cardiac disease, diabetes, and obesity (55). Furthermore, nulliparity, family history of preeclampsia or preeclampsia in previous pregnancies are associated with increased risks of preeclampsia while smoking during pregnancy is associated with reduced rate of preeclampsia (56) and, to somewhat lesser degree, reduced rate of gestational hypertension (57).

1.3.1 Individual economic conditions and pregnancy-induced hypertensive disorders

Low SES is a known risk factor for hypertension (58), cardiovascular disease (59), and metabolic syndrome (60). Furthermore, psychological distress, employment insecurity and unemployment have been found to increase the likelihood of developing hypertension (61, 62). Thus, these factors have also been suggested to increase the risk of pregnancy-induced hypertension as these disease entities (i.e. cardiovascular diseases and pregnancy-induced hypertension) share some common antecedents (63). However, there are relatively few studies that have examined the effect of SES or employment status on pregnancy-induced hypertensive disorders. Earlier studies have focused primarily on preeclampsia and most, but not all (64, 65), report an increased risk of preeclampsia among unemployed (66) and more socioeconomically deprived women (41, 67, 68). Studies focusing on gestational hypertension show more mixed findings. Of the three identified studies that evaluated SES in relation to gestational hypertension, two reported null findings (64, 68), while one found a modest increased risk of gestational hypertension among women with low SES (42). To conclude, findings of existing studies suggest low SES to be a risk factor for preeclampsia while the evidence for an association between SES and gestational hypertension is inconclusive. Whether this association is mediated by psychosocial stress or other maternal characteristics (e.g. obesity), which are generally higher among low SES women (39), remains to be studied.

1.3.2 Macroeconomic conditions and pregnancy-induced hypertensive disorders

The literature on the effect of macroeconomic conditions on maternal health during pregnancy is very scarce with no study, to the best of my knowledge,

examining the effect on pregnancy-induced hypertensive disorders. However, as pregnancy-induced hypertensive disorders and cardiovascular diseases share many common risk factors (63), an overview of studies examining the association between macroeconomic conditions and cardiovascular diseases will be provided. Most aggregate level studies in this field have focused on mortality due to cardiovascular diseases while very few studies have focused on cardiovascular morbidity or its main risk factor, hypertension. Findings on the effect of macroeconomic conditions on cardiovascular mortality are mixed. Some studies have reported a decrease in cardiovascular mortality during economic recessions (7, 8, 10, 69, 70), while others have found an increase in mortality (14-16, 71). Stuckler and colleagues (71) reported a 6.4% increase in male cardiovascular mortality rates during the first year following banking crises in 19 high income countries. Furthermore, Asgeirsdottir and colleagues (31) found an increase in hypertension among males following the economic collapse in Iceland, as compared to the year before the collapse.

1.4 Financial strain and birth outcomes

Infants born preterm, or before completed gestational week 37 are often born with low birth weight (LBW), which is defined as birth weight below 2,500 grams. However, birth weight is also determined by the fetal growth rate. In cases where a fetus is growth restricted in utero, it can be born with LBW despite being carried full-term. It is then considered to be small for gestational age (SGA), i.e. to have a low birth weight for gestational age. Although SGA is a statistical definition and intrauterine growth restriction is a dynamic condition, SGA is a common proxy for intrauterine growth restriction (IUGR). The most commonly used definition of SGA is birth weight in the lowest 10^{th} percentile of a fetal (or neonatal) growth curve, which is usually sex-specific and customized depending on the population being examined. However, as constitutionally small infants can inappropriately be categorized as SGA, a stricter approach is to use two standard deviations below the mean weight as a cut-off for SGA infants, who are then typically more growth restricted. Birth weight and gestational length both serve as markers of the intrauterine environment, with LBW and short gestational length indicating adverse conditions in utero. Infants born small for their gestational age or preterm are at increased risk of infant mortality (72) and short- and long-term morbidity, including respiratory health, cerebral palsy, as well as range of neurobehavioral abnormalities that are strongly correlated with immaturity at birth (73). As birth outcomes are highly associated with subsequent health,

they are commonly used as proxies for the health status of a nation. National numbers on LBW and preterm birth (PB) are objectively measured and routinely published both nationally and internationally. The worldwide prevalence of PB and LBW is estimated to be 11.1% and 15.0%, respectively, with the highest rates in some African and Asian countries while European countries generally have low rates (74, 75).

There are many factors that influence fetal growth and gestational length, both at the individual level and community level (76). Further, it is known that the factors influencing gestational length may differ from the factors influencing fetal growth, indicating the importance of separating these two birth outcomes when reviewing the literature (77). Table 1 gives an overview of well-established direct risk factors for IUGR and PB (77, 78). Smoking during pregnancy has consistently been found to be a robust predictor of PB and LBW (79). Infants, whose mothers smoke during pregnancy, are 2.5 times more likely to be born with LBW and 1.3 times more likely to be born preterm, compared to infants of non-smoking mothers (77). Low pre-pregnancy body mass index has also been linked with PB and LBW. In addition, low energy intake during pregnancy has been shown to predict slower fetal growth (79).

Table 1. Risk factors of in utero growth restriction (IUGR) and preterm birth (PB)

Risk factors	IUGR	PB
Cigarette smoking	x	x
Low weight gain during pregnancy	x	
Low body mass index	x	x
Primiparity	x	
Short stature	x	
Pregnancy-induced hypertensive disorders	x	x
Non-white race	x	
Congenital malformation	x	
Alcohol and drugs	x	
Multiple birth		x
Incompetent cervix		x
Prior preterm birth		x
Abruptio placentae		x
Heavy work		x
Genitourinary tract infection and inflammation		x
Adverse psychological factors	x	x
Air pollution	x	
Stress	x	x

1.4.1 Individual financial conditions and birth outcomes

A socioeconomic gradient in birth outcomes has been repeatedly established in previous studies, with higher rates of intrauterine growth restriction and preterm births associated with increasing socioeconomic disadvantages (39, 77, 78, 80-87). In 2011 in the US, the prevalence of LBW was approximately 13% among the most disadvantaged group while it was just below 4% among the most advantaged mothers (39). Such disparities in birth outcomes, although to a lesser degree, have also been documented in countries with a smaller gap between the rich and poor (77). For example, in the Nordic countries, with their universal health care systems and general equity, women with less than 10 years of education had between 1.4 to 2 fold increased risk of PB compared with women with >12 years of education (88).

Similar socioeconomic gradient in fetal growth by education is also apparent in the Nordic countries (89). However, SES per se is most likely not a direct risk factor for adverse birth outcomes, but rather works through multiple and interrelated behavioral and psychological risk factors as well as medical conditions, which are accumulated among women with low SES. In Western societies, smoking during pregnancy is the most important mediator between socioeconomic status and adverse birth outcomes (39, 77, 90). Other mechanisms include unhealthy behavior, such as inactivity and poor diet (46), psychological- and financial stress and chronic health conditions, such as hypertensive disorders (39, 41, 42), diabetes (39, 40) or obesity (39), which are more prevalent among women in the lower socioeconomic groups of the society as discussed above.

Although an abundance of studies exists focusing on the socioeconomic gradient in birth outcomes, only three individual level studies were identified examining the isolated effect of economic changes, as proxied by change in parental employment status, on birth outcomes. Job loss shortly before or during pregnancy could represent a stressor potentially contributing to LBW and PB. This hypothesis was tested by Dooley and Prause (91) where they examined the association between maternal shift from adequate employment to involuntary part-time employment, unemployment, or poverty wage employment during pregnancy and subsequent birth outcomes. The results indicate that infants born to women, who shifted from adequate employment to involuntary part-time employment or unemployment during pregnancy, were significantly lighter compared with infants of women who remained adequately employed during pregnancy. Interestingly the effect size was larger among involuntary part-time employed women [β standard error (SE) = -418.0 (165.2)] than among the unemployed women [β (SE) = -185.4 (77.2)], suggesting that this type of unemployment is particularly detrimental for birth outcomes (91). Similarly, using individual level data Lindo (92) explored the extent to which health effects of displaced male workers extend to the birthweight of their subsequent children. The findings indicate that a husbands' job displacement decreased the birth weight of subsequent children by 4.7% (approximately 140 g) compared with siblings born before the displacement; a decrease which was not ameliorated by re-employment of the father. The last study identified is a Danish study, examining the effect of work per se on birth weight. The authors report no significant association between any of the work categories, including a category of women working during the first trimester while unemployed during late pregnancy, and birth weight. However, it is not clearly explained whether the unemployment during

late pregnancy was due to involuntary job loss or due to other causes (i.e. inability to work or choosing not to work during pregnancy) which is likely to affect women's perception of the unemployment status (93). To conclude, the existing individual level studies seem to indicate an adverse effect of involuntary parental employment change on their subsequent children's birth weight, although more studies are needed to support that claim.

1.4.2 Macroeconomic conditions and birth outcomes

The findings of aggregate level studies that have examined the association between economic contractions and birth outcomes differ by population and methodology. Of studies reporting higher prevalence of adverse birth outcomes during times of economic contraction (94-102), a few are especially noteworthy. Firstly, Bozzoli and Quintana-Domeque (101) investigated the effect of the Argentina macroeconomic recession in 2001-2002 on birth weight and found that the average birth weight decreased by approximately 35 grams during the recession and there was also an increase in the incidence of low birth weight. Moreover, the recession affected birth weight differently by the pregnant women's SES, with larger effects in the lower socioeconomic strata. Secondly, two studies have examined the effects of anticipating an adverse change in economic conditions on birth weight. Carlson (98) found that birth weight deteriorated by 15-20 grams in anticipation of job loss events that were announced with substantial forewarning in four states in the US. By separating the anticipatory effects from the actual job loss, it was demonstrated that direct consequences of job loss on birth weight were ruled out. The findings from this study suggest that the arrival of bad news about the local economy can indeed generate a wave of stress or unhealthy coping mechanism that lead to a decrease in birth weight. Similar anticipatory effects were observed by Catalano and Serxner (94), who report an increase in low birth weight following an ambient threat to employment security in Sacramento, California 1979. Lastly, Catalano and colleagues (95) and Margerison-Zilko and colleagues (97) reported an increased risk of very LBW and SGA, respectively, among infants born to mothers who had been exposed to high unemployment rate during pregnancy. On the contrary, unemployment rate was not found to be associated with LBW in New York between 1970 and 1986 (103), and Tennessee between 1970 and 1989 (104). Also, no changes in LBW were observed during the recession in Sweden during the 1990's (105). In contrast, one study reported birth weight to be higher during times of economic contraction (51). In a comprehensive analysis, Dehejia and Lleras-Muney (51) matched the yearly average unemployment rate in the US with

birth certificates from 1975-1999. The authors reported that babies that were conceived during times when the unemployment rate was high had a reduced incidence of low and very low birth weight. The authors suggest that selection of pregnancies (reduced fertility among poorer families) and improved health behavior (less smoking and drinking) of the pregnant women may be likely explanations for the observed improvement in infant health (51). To summarize, the findings from the aggregate level studies are somewhat inconclusive, although the majority of the identified studies seem to be in line with the findings of individual level studies, i.e. indicating shorter gestations and lighter newborns during economic downturns.

1.5 Biopsychosocial model associating recessions to hypertensive disorders and adverse birth outcomes

There are a number of routes through which recession may impact the process of pregnancy and birth outcomes. A hypothetical model of possible pathways linking economic recessions to the process of gestation and birth outcomes is presented in figure 3.

On a macro-level, recessions typically lead to a general contraction of economic activity in communities (d) and elevated in unemployment rates (b). A subsequent decrease in governmental resources typically results in cuts in public services such as health care and educational and social systems (d) (106, 107). At the individual level, economic contractions can have heterogeneous effects. Lay-offs at work places (a) are one appearance that leads to loss of income for those affected (e), both at the individual (e) and family level (c) (108). Those who remain employed may accept cuts in wages (e) or an increase in work load in order to maintain their jobs (b). Job insecurity and unemployment are associated with worse psychosocial health, including stress (f) (109-111). Psychosocial stress and/or loss of resources, at the individual level, may lead to changed nutritional habits (better or worse) (i) (24, 112), changed sleep pattern (both in terms of increased and decreased sleep) (112, 113, 114), changes in personal care (i) or to negative coping behavior, i.e. smoking (j) (115, 116). Evidence links these multiple pathways with physiological changes to the endocrine-, immune- and cardiovascular systems (l) of pregnant women (117-119), which in turn may affect the length of gestation and/or fetal growth (120-122).

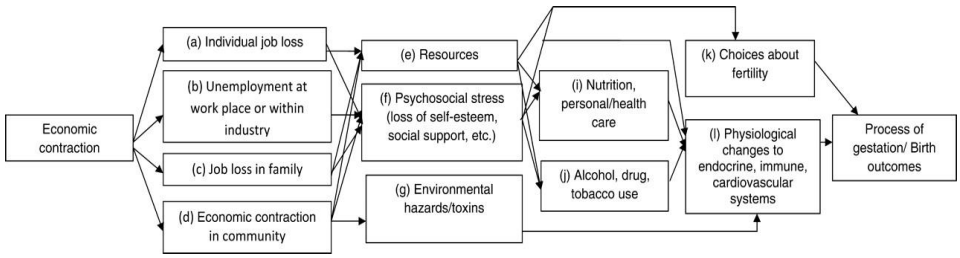

Figure 3. Plausible mechanisms connecting economic contraction to gestational outcomes - a hypothetical model. Adapted from *Economic contraction and birth outcomes: an integrative review* with the curtesy of Margerison-Zilko (123).

1.5.1 The biological channel linking stress to maternal health and adverse birth outcomes

The study of the influence of stress on the process of pregnancy and birth outcomes became of interest in the early 1990‘s due to the fact that even a complete analysis of known risk factors did not adequately account for the variation in the rates of adverse birth outcomes (76, 124). The biological channel linking stress to adverse birth outcomes involves the hypothalamic-pituitary adrenal (HPA) axis. When individuals are faced with stressful stimuli, either due to psychosocial or acute stress, the HPA axis is activated to prepare for the appropriate responses (fight or flight response). Upon activation, the HPA axis secretes corticotrophin-releasing hormone (CRH) which acts upon the adrenal glands to produce the stress hormone cortisol (125). In general, the stress response is designed to be of limited time and the resulting changes in hormonal- and neurotransmitter activity are restored to equilibrium within minutes or hours. However, when stress is chronic or excessive, these adaptive mechanisms may fail, resulting in a prolonged activation of the HPA axis which can ultimately cause disease (121, 126). CRH plays an important role in fetal maturation and in the process of parturition. Studies have found a strong correlation between maternal psychological stress, high levels of circulating CRH in early to middle pregnancy and preterm birth as well as pregnancy-induced hypertension (127-130). Increased levels of stress hormones (i.e. cortisol and catecholamines) may also impair fetal growth by restricting the uteroplacental perfusion, leading to a decrease in the availability of oxygen and nutrition to the fetus (125, 126, 131). Further, abnormal activity of the HPA-axis during pregnancy (e.g. due to maternal stress) may have a lasting ‘programming’ effects on the physiological and behavioral development of the offspring, resulting in increased risk of cardiovascular disease, metabolic syndrome and psychopathology later in life (125, 132).

There are several epidemiological findings indicating that psychosocial stress is involved in the etiology of pregnancy-induced hypertensive disorders. Studies have found an increased risk of both gestational hypertension and preeclampsia among women who report high work-related stress (133-136), although this effect seems to be more potent for the development of preeclampsia than for gestational hypertension. Furthermore, general and acute stressful life-events, depression, and anxiety have also been linked with pregnancy-induced hypertensive disorders (137-141).

To date, an abundance of studies examining the association between stress and adverse birth outcomes has been published. In a recent review, Dunkel Schetter and Glynn (142) summarized the findings of recent studies on the association between stress and gestational length or PB. In this review, the types of stressors were organized by stress concepts, assessing separately studies focusing on episodic stressors, catastrophic/traumatic events, chronic stress, emotional states or pregnancy-related anxiety. Based on this review, the authors conclude that there is quite clear evidence that stress contributes to the etiology of PB. Notably, they found that some types of stress seem to be more important for the etiology of PB than others. The most consistent findings were observed for pregnancy-related anxiety and major life events. Further, catastrophes, community stressors and chronic stress were found to be of importance although the findings were somewhat more mixed for these types of stressors (142). A similar review was conducted by Dunkel Schetter and Lobel (76) where the focus was on the association between stress and birth weight (and IUGR and LBW); an association that has received much less attention than PB. Also in this review, the types of stressors were organized by stress concepts which included measures of life events, anxiety, depression, perceived stress, daily hassles and general distress, as well as community stressors. The vast majority of studies reviewed, indicate a positive association between stress measures and birth weight, i.e. increased level of stress predicted lower birth weight. Interestingly, the authors found that chronic stress and depressed mood seemed to be stronger risk factor for LBW compared to other stress measures while studies on life events are more inconclusive.

To conclude, stress, in various forms, seems to predict both PB and LBW although the most potent form of stress differs for these two birth outcomes. Depression and chronic stress appears to be strongest related to LBW whereas anxiety and life events are more linked to PB. It is plausible that the inevitable financial and psychological strain experienced by most people during times of economic contractions, could affect the homeostasis of the

bodily stress system among the general as well as the pregnant population. This disrupted equilibrium may lead to over-activity of the HPA-axis, resulting in increased level of circulating stress hormones which can have detrimental effects on maternal health and birth outcomes.

1.5.2 Behavioral changes as a response to financial strain and recessions

Within the socioeconomic literature, there is a line of research focusing on the isolated effect of job loss or employment insecurity on health. There are numerous reasons to anticipate that job loss or employment insecurity is hazardous to health, with several postulated mechanisms through which the job loss may affect health. These include, for example, increased stress, destructive coping behavior such as smoking (143-145) and alcohol intake (146), decreased control over owns life, and potential social stigma (147). Furthermore, job loss is usually followed with an extended period of unemployment leading to income loss and increased financial strain (148, 149). Some studies indicate that the consequences of job loss can have lasting effects on long-term earning potential and therefore reduce the ability of individuals to purchase health promoting goods.

Unfortunately, no individual level studies were identified, examining the direct effect of job loss on maternal health behavior during pregnancy. However, there are several individual level studies linking increased stress to worse maternal health behavior (150-153). Pregnant women with high perceived stress have been found to be more likely to smoke during pregnancy (151-153), to drink coffee, and eat unhealthy food (151). Moreover, reporting high stress during pregnancy has been linked with less exercise (151, 152), and less vitamin use (151). With only two identified studies (51, 52) at the aggregate level, no firm assumptions can be drawn on whether economic recessions lead to changes in health behaviors during pregnancy.

1.5.3 Demographic changes as a response to financial strain and recessions

It has been speculated that the consequents of an economic downturn, e.g. unemployment, employment instability and uncertainty about the future, may indeed change the demography of the pregnant population as many people may revise their fertility plans during economic difficulties. Studies exploring the association between economic recessions and fertility were recently reviewed by Sobotka and colleagues (154). Most of the studies included in

the review found a decreased fertility during times of economic contractions. This decrease was particularly observed among the higher educated women and among younger parents, suggesting a postponement of fertility rather than an overall reduction. Thus, economic contractions could lead to increases in maternal age as well as an increased proportion of lower educated women becoming pregnant. These demographic changes could lead to increases in various medical conditions during pregnancy, such as pregnancy-induced hypertensive disorders and diabetes, congenital malformations, and labor complications; all of which are associated with PB and/or LBW. On the contrary, Dehejia and Lleras-Muney (51) observed a race specific selection into pregnancies during times of economic downturns, i.e. low educated black women chose against becoming pregnant while low educated white women chose to become pregnant when the economic was bad, resulting in an overall improvement in infant health. To sum, the potential effect of economic recessions on the demography of the pregnant population is likely to differ between countries and to be dependent upon many factors, such as race, age, education, work status as well as the welfare state context.

2 Aims

With this background, the overarching aim of this PhD project was to explore potential change in the prevalence of maternal diseases, health indicators during pregnancy as well as adverse birth outcomes following the economic collapse in Iceland, and whether or not these changes were long lasting. Moreover, by including information on aggregate economic indicators in our analyses, we aimed to explore whether the surrounding economic climate in Iceland affected the health of pregnant women and birth outcomes. The research was divided into four parts, each resulting in one scientific paper. Specific aims for each paper were as follows:

I. To examine the secular trend and patterns of smoking prevalence and body weight among pregnant women in Iceland between 2001 and 2010.

II. To examine whether the prevalence of pregnancy-induced hypertensive disorders and use of antihypertensive drugs during pregnancy changed following the 2008 economic collapse in Iceland. Further, to examine whether the potential changes in hypertensive disorders and drug use during pregnancy were due to the surrounding economic climate.

III. To examine the short-term effect of the Icelandic economic collapse on infant health, as measured by low birth weight, preterm birth and small-for-gestational age during the first 15 months following the economic collapse.

IV. To examine whether the incidence of adverse birth outcomes increased during the first four years following the economic collapse compared to the previous years and if so, whether such changes were mediated by the maternal individual level factors and/or by the surrounding economic climate.

3 Materials and methods

3.1 Data sources

All the studies in this project are register based cohort studies, based on individual-level data from maternity records (paper I), the Icelandic Medical Birth Registry (papers I-IV) and the Icelandic Medicines Registry (paper II). The Icelandic Medical Birth Registry and maternity records used in paper I were linked by a unique personal identification number, held by all Icelandic citizens. Similar linkage of Icelandic Medical Birth Registry and Icelandic Medicines Registry was performed for paper II. Further, we used aggregate-level data on Iceland's economic indicators from Statistics Iceland (papers II, IV).

3.1.1 The Medical Birth Registry

All the papers in this thesis were based on data from the Icelandic Medical Birth Registry, which is a population based register with a compulsory notification of all live births as well as stillbirths, from completed gestational week 28, in Iceland since 1972. In 1994, the World Health Organization changed the definition of birth to include also those infants born after completed gestational week 22. Prior to that, infants born between weeks 22w0d and 27w6d were considered miscarriages. The Icelandic Medical Birth Registry has been in electronic form since 1981. The register is a rich source for information on all parental-, pregnancy- and delivery characteristics, as well as on birth- and neonatal outcomes, at the individual level. The parental information included in the Icelandic Medical Birth Registry is registered in a uniform way with the exception of the parents' employment status, which is written out in free text. All diagnoses regarding maternal and infant health are registered according to the International Classification of Diseases codes updated to the 10th version (ICD-10), allowing for cross-country research and comparison. The Directorate of Health is responsible for the Icelandic Medical Birth Registry but has assigned the operational responsibility to the Department of Obstetrics and Gynecology at Landspitali - The National University Hospital. The Icelandic Medical Birth Registry publishes an annual report including a number of quality indicators on pregnancy-, delivery, and birth outcomes. The quality of the Icelandic Medical Birth Registry in has not been systematically validated.

3.1.2 Maternity records

All pregnant women (99.5%) in Iceland attend to publicly funded antenatal care at local clinics every two to four weeks of pregnancy (155, 156). Maternal and obstetric information are recorded by midwives and physicians providing antenatal care over the course of pregnancy. These maternity records are in paper form while the Icelandic Medical Birth Registry is in electronic form, thus limiting the use of the maternity records for research. Despite the richness of data in the Icelandic Medical Birth Registry, information regarding the pregnant women's smoking habits and maternal weight is not registered. This information is, however, registered in their maternity records. We, therefore, used data from maternity records in paper I where the aim was to examine the changes in maternal behavioral factors, i.e. maternal smoking during pregnancy and maternal weight over time.

3.1.3 The Icelandic Medicines Registry

The Icelandic Medicines Registry is a centralized database containing individual level information on nearly all dispensed drugs to the outpatient population in Iceland since January 1st, 2003. However, it does not include information regarding over the counter drugs or drugs dispensed in hospitals. All reimbursed and non-reimbursed prescription drugs in the Icelandic Medicines Registry are registered according to the Anatomical Therapeutic Chemical (ATC) classification system with data on dispensed drug substance, brand name, and quantity as Defined Daily Doses (DDD's) together with the date of dispensation (157). The Directorate of Health is responsible for and operates the Icelandic Medicines Registry, which main purpose is to monitor prescription practices as well as to ensure the safety of users and quality in health services. Icelandic law and regulations require pharmacies to collect and send data of individual's pharmacy records electronically to the Social Insurance Administration for reimbursement and to the Icelandic Medicines Registry. A comparison of dispensed drugs sold in pharmacies (as registered in the Icelandic Medicines Registry) with sales figures from the Medicine Agency (responsible for the supervision of imported drugs as well as domestic production) reveal a 97-98% consistency between these two registers for the years 2013-2014 while this number was 91-97% for the years 2007-2008 (158). Thus, the internal validity of the Icelandic Medicines Registry is high. Data from the Icelandic Medicines Registry was used in paper III.

3.1.4 Statistics Iceland

Statistics Iceland is the center for official statistics in Iceland and collects, processes and publishes data on the country's economy and population. It was founded in 1914 as the National Statistical Institute of Iceland and has been a professionally-independent institution under the auspices of the Minister of Finance and Economic Affairs, since 2008 (159). Data from Statistics Iceland was used in papers III and IV.

3.2 Setting and population

Iceland is an island in the Atlantic Ocean with a population of approximately 332 thousand at the end of 2015. The country is considered to be a high-income country, following the Nordic Model of economic and social structure. The Icelandic welfare system is of universal nature and is funded through taxation (159). All individuals who have been legally resident in Iceland for over 6 months automatically become members of the Icelandic social insurance system, providing health insurance when medical assistance is needed (160). During the study period there were on average 4,400 births annually. The majority of the births (73% in 2012) occur at Landspitali – The National University Hospital of Iceland in the capital Reykjavik, which is the only tertiary referral hospital in the country (161).

3.2.1 Maternal health behavior (paper I)

Maternal smoking and body weight is only recorded in maternity records at the first antenatal visit around completed week 12 of pregnancy. Unfortunately, these records are not available in electronic form and any data used for research has to be retrieved manually. Therefore, in paper I we used data from an ongoing study where the information on smoking and body weight during pregnancy had already been collected and digitized. The aim of this ongoing study is to examine the risk of adverse maternal- and obstetric health and adverse birth outcomes among women who, at some previous time-point, had sought help in the Rape-Trauma Service following an exposure to sexual violence. The study population consists of 915 exposed women and 1,641 unexposed women, matched on month of delivery, who gave birth to live-born infants between 1993 and 2011. As the findings of this study indicate that sexually assaulted women are almost 3 times as likely to smoke (162), we only included the group of pregnant women who represented the unexposed population in our study population. Our study population consisted of 1,312 women with a total of 1,329 pregnancies occurring in Iceland between January 1st, 2001, and December 31st, 2010.

3.2.2 Pregnancy-induced hypertensive disorder and antihypertensive drugs (paper II)

Eligible in study II were all expecting women in Iceland who were at least 20 weeks 0 days pregnant on September 27th, 2004, and all pregnancies from that time-point, subsequently giving birth to live-born singletons throughout December 31st, 2012 (N=35,231). Information on gestational length was missing for 20 pregnancies which were excluded from the study, leaving a total of 35,211 women in the study.

3.2.3 Birth outcomes – one-year follow-up (paper III)

All Icelandic women, registered in the Icelandic Medical Birth Registry between January 1st, 2006, and December 31st, 2009, were considered for the study described in paper III. We excluded women with multiple gestation (n=298) and perinatal death (n=47). The study population, therefore, consisted of 16,271 women.

3.2.4 Birth outcomes – four-year follow-up (paper IV)

The study population consisted of all singleton pregnancies resulting in live births after completed gestational week 22 in Iceland between September 30th, 2002, and September 30th, 2012 (N=43,693).

3.3 Outcome measures

3.3.1 Maternal health behavior (paper I)

The main outcomes in paper I were self-reported smoking and maternal weight at first antenatal visit. Of the 1,329 pregnancies, information about smoking and maternal weight was available for 1,325 (99.7%) and 1,281 (96.4%) pregnancies, respectively. With regard to smoking status, the women were either categorized as non-smokers, discontinued smokers including women who quit smoking (i.e. before the end of first trimester) early in pregnancy, or continued smokers including women who smoked at the time of the first antenatal visit. Maternal physique was assessed using body mass index (BMI), calculated according to measured height and weight (kg/m^2) at the first antenatal visit, occurring on average at completed gestational week 13, both on a continuous scale as well as categorical. Women were considered overweight if they had a BMI value ≥25 and <30, and obese if their BMI was ≥30, according to the international BMI classification for adults (163).

3.3.2 Pregnancy-induced hypertensive disorders and antihypertensive drugs (paper II)

The main outcome measures for study II were pregnancy-induced hypertensive disorders. Pregnancy-induced hypertensive disorders are registered in the Icelandic Medical Birth Registry according to ICD-10 codes and include gestational hypertension, preeclampsia, and eclampsia. Gestational hypertension (ICD-10 code O13) is defined as diagnosed hypertension after completed gestational week 20 (systolic blood pressure ≥140 and diastolic blood pressure ≥90). Preeclampsia was a combination of three ICD-10 diagnoses consisting of preeclampsia superimposed on chronic hypertension (ICD-10 code O11), preeclampsia (ICD-10 code O14), and eclampsia (ICD-10 code O15). To meet the diagnostic criteria for preeclampsia, a significant proteinuria (>300 mg protein in 24 hour sample) has to be present concurring with pre-existing or gestational hypertension. Hypertensive women could only be assigned as either preeclamptic or with gestational hypertension. In the cases were women were registered with both diagnoses, preeclampsia overruled gestational hypertension as it is the more severe form of the pregnancy-induced hypertensive disorders.

A secondary outcome in study II was prescription fills for antihypertensive drugs. For the women in the study population, we extracted all prescriptions for β-blockers (ATC code C07) and calcium channel blockers (ATC code C08) filled after gestational length 20 weeks 0 days onward. The reason for the choice of these therapeutic agents is that the β-blocking agent labetalol is the first line of treatment of pregnancy-induced hypertensive disorders in Iceland. If treatment with labetalol proves insufficient the calcium channel blocker, nifedipine, is prescribed (Bjarnadóttir, R., oral communication).

3.3.3 Birth outcomes (papers III and IV)

The main birth outcomes examined in papers III and IV were LBW, PB and SGA. LBW was defined as birth weight less than 2,500 g and PB as delivery before completed gestational week 37. Gestational length was missing for 8 and 33 of the pregnancies in paper III and IV, respectively, which were excluded in analyses involving PB as an outcome variable. We utilized two different definitions of SGA which is a proxy for intrauterine growth restriction. In paper III, SGA was defined as infants with birth weight more than 2 standard deviations (SD) below the mean for gestational length, according to the sex-specific Swedish growth curve (164) (hereafter referred to as SGA 2SD). As the mean birth weight of Icelandic infants is higher than that of Swedish infants (165, 166), the number of infants classified as SGA in our

study population was low and infants fulfilling criteria were severely growth restricted. Thus in study IV, we decided to use a more appropriate definition of SGA, including infants with fetal growth rate index in the lowest 10th percentile according to sex-specific z-scores (164) (hereafter referred to as SGA 10th pct.). In study IV, information on gestational length and infant sex was missing for 44 births, which were excluded from analyses of SGA.

3.4 Explanatory measures

In papers II-IV, we used calendar time as the main exposure variable to model the Icelandic economic collapse and the subsequent economic recession. As the nature of the economic collapse allowed us to pin down the beginning of the crisis to a distinct time point, we categorized the time into a pre-recession period (unexposed to the economic recession) and a recession period (exposed to the economic recession to a varying degree). An overview of the timeline of each study in the thesis can be seen in Figure 4. Furthermore, we used aggregate economic indicators obtained from Statistics Iceland to explore the association between the macroeconomic conditions and the outcomes of interest in papers II and IV. The economic indicators tested were unemployment rate and GDP (paper II, IV), as traditional measures of economic conditions. As the Icelandic collapse mainly resulted in debt crisis at the individual and national levels, we also tested the balance of accounts and rates of homes that had defaults on loans or rent or had difficulties in covering the expenses through the pay period (paper II). The unemployment rate and GDP were on a quarterly basis while the other economic indicators were on a yearly basis.

In subsections 3.4.1-3.4.4 below, the definition of each main exposure variable (i.e. pre-recession vs. recession periods) in each paper will be described separately in more detail, as it differed slightly between papers II, III and IV due to two reasons. Firstly, the aim of paper III was based on different dataset than used in papers II and IV, and contained more detailed information regarding the timing of births, down to actual date of birth, while the dataset used in papers II and IV had this information on weekly basis. Secondly, in papers III and IV we used time of birth as the main indicator of how to locate each mother-infant dyad with respect to the economic collapse although in paper III, we further explored the association between the economic collapse and birth outcomes by using date of conception as this indicator instead of date of birth. In paper II, gestational length ≥20 week 0 day served as an indicator of where to locate each pregnancy with respect to

the collapse, as pregnancy-induced hypertensive disorders do not occur before completed 20 weeks of gestation.

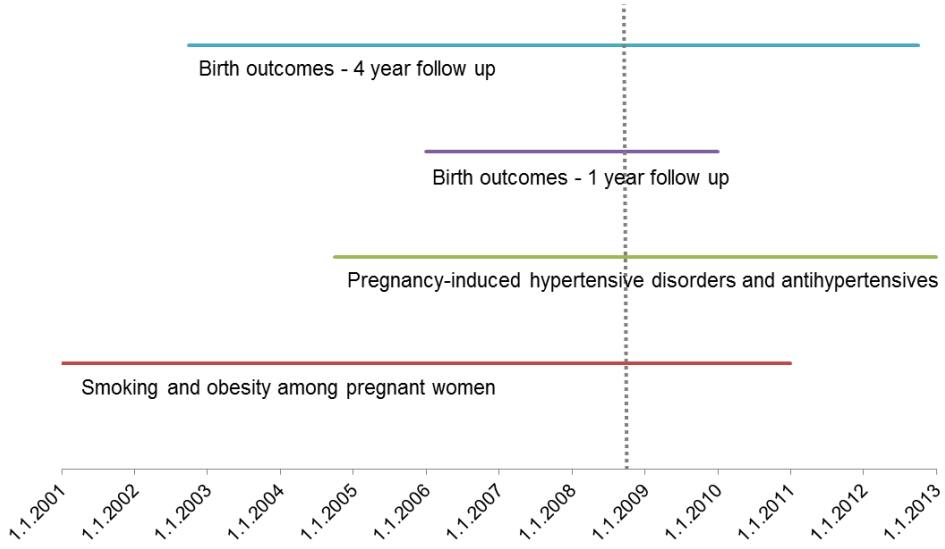

Figure 4. The time-line of each study in the thesis. The grey vertical dotted line represents the timing of the October 6, 2008.

3.4.1 Maternal health behavior (paper I)

Paper I was a descriptive paper where the aim was to explore the trend in maternal health behavior over a 10-year period. The unit of analysis was calendar time, although we did not model time to explore the effect of the economic collapse as in the subsequent papers.

3.4.2 Pregnancy-induced hypertensive disorders and antihypertensive drugs (paper II)

During the first week of October 2008, three of the largest banks in Iceland collapsed and data on the economic climate showed dramatic changes between the third and fourth quarter of 2008. As mentioned above, the dataset used for this study only had information on the timing of birth on a weekly basis. Thus, we used the first week of October 2008 as a marker for the beginning of the economic collapse in study II which coincided with the beginning of the fourth quarter of 2008. Calendar time was categorized into a pre-collapse period and four separate post-collapse years. The pre-collapse category included women who were 20 weeks 0 day pregnant or more between September 27th, 2004, and September 28th, 2008, and subsequently

gave birth to live-born singletons. Each of the four post-collapse categories included women who were 20 weeks 0 day pregnant or more between i) September 29th, 2009, and September 27th, 2009, (post-collapse year 1), ii) September 28th 2009 and October 3rd 2010 (post-collapse year 2), iii) October 4th, 2010, and October 2nd, 2011, (post-collapse year 3), and iv) October 3rd, 2011, and September 30th, 2012, (post-collapse year 4) and subsequently gave birth to live singletons.

In order to further explore the short time effect of the timing of the economic collapse on the main outcomes of interest, we divided the first post-collapse year into two 6-month periods, each including pregnancies with gestational length of 20 weeks 0 day or more during I) September 29th, 2008, – March 29th, 2009, and II) March 30th, 2009 – September 28th, 2009.

3.4.3 Birth outcomes (paper III)

In this paper, we used October 6th, 2008, as a marker of the beginning of the Icelandic economic recession (the day of the collapse). On this day, the Icelandic Prime Minister, Mr. Geir Haarde, appeared on a national television broadcast, interrupting the scheduled program, where he informed the Icelandic nation of an unusually swift and severe economic downturn facing the country as a whole. Thus, the study period was dichotomized into an unexposed pre-collapse period, spanning from January 1st, 2006, to October 5th, 2008, and an exposed post-collapse period, spanning from October 6th to December 31st, 2009.

3.4.4 Birth outcomes (paper IV)

The aim of paper IV was to explore whether the economic recession in Iceland affected birth outcomes beyond the first post-collapse year. As in paper II, the timing of birth was recorded on a weekly basis and with the same arguments regarding dramatic changes in the economic climate between the third and fourth quarter 2008, we categorized time into a pre-recession period, including all live singleton births occurring between September 30th 2002 and September 28th 2008 and a recession period which was further divided into two separate groups. The two separate recession groups included all live singleton births occurring between i) September 29th 2008 and September 27th 2009 (recession year 1), and ii) September 28th 2009 and September 30th 2012 (recession years 2-4).

3.5 Covariates

Individual-level information on the study participants' characteristics was obtained from the Icelandic Medical Birth Registry. Parental characteristics included maternal age, parity, gravidity, relationship status, place of residence, citizenship and maternal and paternal employment status. Place of residence was dichotomized into rural and capital area based on postal codes. The capital area included postal codes from 101-172, 200-225, and 270-276. All other postal codes were classified as rural area. Parental employment status was written out in text in the Icelandic Medical Birth Registry. Based on this text, an employment variable was created containing five categories (paid labor-work, unemployed, on disability, homeworkers, and student).

Pregnancy-related diseases, known to influence fetal growth and gestational length, included diabetes mellitus and hypertensive disorders of pregnancy. Obstetric characteristics included time of birth, gestational length, infant sex, mode of delivery, five minute Apgar scores, and congenital malformation. Information regarding the gestational date of first maternal weight measurement was retrieved from maternity records. The variables were not categorized uniformly across the four separate studies nor were they all included in each study. More detailed information regarding the categorization and use of each parental, pregnancy-related and obstetric characteristic can be found in Table 2.

In paper II and IV we further explored the mediational effect of the aggregate economic indicators on the association between the main exposure variables (pre-recession vs. recession periods) and the outcomes of interests in order to capture whether the potential influence of time on the main outcomes was due to changes in the surrounding economic climate.

In paper III the exposure categories were not equally balanced with respect to time. In order to account for potential seasonal variation in this paper, we divided each calendar year into four 3-month time-intervals (December-February; March-May; June-August; September-November), which we grouped together. In papers II and IV the exposure categories are equally balanced with respect to time and thus, we did not adjust for seasonality in the main analyses. We did, however, test whether seasonality affected the observed associations in paper II in supplementary analyses, by grouping together each quarter of a calendar year.

Table 2. The categorization of the parental characteristics used in papers I-IV

Parental characteristics	**Papers**			
	I	**II**	**III**	**IV**
Maternal age *(continuous; <25, 25-34, ≥35)*	X	X	X	X
Parity *(nulliparous, multipara)*	X			
Parity *(nulliparous, primiparous, multipara)*			X	
Gravidity *(primigravida, multigravida)*		X		X
Relationship status *(cohabitating, not cohabitating)*	X	X	X	X
Place of residence *(capital area, rural area)*	X	X	X	X
Citizenship *(Icelandic, foreign)*		X	X	X
Maternal employment status *(working, not working)*			X	
Maternal employment status *(employed, students,unemployed/on disability/homemakers)*	X	X		
Parental employment status (*both in payed work, one in payed work, neither in payed work)*				X
Gestational date of first weight measurement	X			

Table 3. The categorization of the pregnancy related characteristics in papers I-IV

Pregnancy related diseases	**Papers**			
	I	**II**	**III**	**IV**
Pre-existing diabetes (ICD-10 codes O24.0-24.3)		x	x	x
Gestational diabetes (ICD-10 codes O24.4-24.9)		x	x	x
Pre-existing hypertension (ICD-10 codes O10)		x	x	x
Pregnancy induced hypertension (ICD-10 codes O11-15)			x	
Gestational hypertension (ICD-10 codes O13, O16)		x		x
Preeclampsia (ICD-10 codes O11, O14-15)		x		x
Pregnancy induced hypertension (ICD-10 codes O11, O13-15)				x

Table 4. The categorization of the obstetric characteristics in papers I-IV

Obstetric characteristics	**Papers**			
	I	**II**	**III**	**IV**
Time of birth (days)			x	
Time of birth (weeks)		x		x
Gestational length (days)		x	x	x
Infant sex		x	x	x
Apgar score at 5 minutes (<7, ≥7)			x	x
Congenital malformation (ICD-10 codes Q00-99)			x	x
Mode of delivery (vaginal, elective cesarean (ICD-10 codes O82.0), emergency cesarean (ICD-10 codes O82.1,82.2))				x

3.6 Data analysis

Data analyses in paper I-IV were performed using IBM SPSS Statistic version 20/22 (167, 168). The trend analyses in paper IV were performed using R statistical package, version 3.2.2 (169).

3.6.1 Maternal health behavior (paper I)

Data are presented as proportion of continued and discontinued smoking as well as of overweight and obesity, among the pregnant women over the 10-year study period, in 2-year intervals. Differences in the proportions between the time-intervals of these categorical variables were assessed with Pearson χ^2 test with Bonferroni correction. Linear regression analysis was used to assess the annual change in women's BMI. In order to explore the secular trend of the main outcomes, we used logistic regression analysis to assess the annual change of continued smoking and obesity, overall and stratified by maternal characteristics. All analyses, involving maternal physique (BMI, overweight, obesity) as an outcome variable, are adjusted for gestational date of first weight measurements.

Supplementary analysis

A supplementary analysis (unpublished data) was conducted in order to examine the pattern of continued smoking and obesity among subgroups of women. We used multivariate logistic regression analysis to calculate the mutually adjusted odds ratios (OR's) and their 95% confidence intervals (95% CI) of continued smoking and obesity by bi-annual time intervals and stratified by maternal socio-demographic characteristics.

3.6.2 Pregnancy-induced hypertensive disorders and antihypertensive drugs (paper II)

Data are presented as frequencies of maternal and obstetric characteristics across exposure categories and differences assessed with Pearson χ^2 tests (categorical variables) and one-way ANOVA (continuous variables). Logistic regression analyses were used to calculate the crude and adjusted OR's and their 95% CI of pregnancy-induced hypertensive disorders as well as of prescription fills for antihypertensive drugs, contrasting each post-collapse year with the pre-collapse period. The total number of calendar weeks in the study was used, starting from September 27th 2004, as a continuous variable, to address potential changes in the diagnoses of hypertensive disorders and prescription habits over time (time-trend). In addition to crude regression models, we created three separate models, adjusting for maternal and infant

characteristics. Model I was adjusted for maternal age, gravidity, time-trend. Model II for maternal age, gravidity, time-trend, infant sex, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship. In order to assess whether possible influence of time on the main outcomes was mediated by changes in the aggregate economic environment in Iceland, we adjusted for those aggregate economic indicators associated with the outcomes of interest in the primary supplementary analysis. Thus, in model III we adjusted for maternal age, gravidity, time-trend, and unemployment rate. We used a similar approach when calculating the adjusted odds ratios in months 1-6 and months 7-12 following the economic collapse, in order to examine the short-term effect of the economic collapse.

In the primary supplementary analysis, the association between each aggregate economic indicator and the outcomes of interest was assessed with logistic regression analysis, with the economic indicators modelled as continuous variables. The unemployment rate and GDP were on a quarterly basis and balance of accounts and rates of homes that find it difficult to make ends meet (cover expenses through the pay period) or had defaults on loans and rent were on a yearly basis. We constructed three different regression models in the supplementary analysis, adjusting for i) time-trend, ii) time-trend, maternal age, and gravidity and, iii) time-trend, maternal age, gravidity, relationship status, place of residence, employment status, citizenship, diabetes, pre-existing gestational hypertension (ICD-code O10), and infant sex. We tested the effect of seasonality on the observed association between the economic collapse and the outcomes of interest in a secondary supplementary analysis by adjusting for quarters of the calendar year.

3.6.3 Birth outcomes (paper III)

Descriptive statistics were calculated for all maternal and obstetric characteristics as well as for outcome variables, contrasting frequencies before and after the economic collapse. Frequencies' differences between the exposure categories (i.e. pre- and post-collapse periods) were assessed with Pearson's χ^2 tests for categorical variables and independent sample t-tests for maternal age. Linear regression analysis was used to assess the change in gestational length, where we adjusted for maternal age, parity and seasonality. One-way ANOVA with Tukey's honestly significant difference (HSD) post hoc tests were used to assess the homogeneity of birth weight and gestational length between seasons.

Logistic regression analyses were used to calculate the OR's and their 95% CI for LBW, PB, and SGA 2SD in the post-collapse period using the pre-collapse period as a reference. We adjusted for each covariate separately and combined, creating three separate regression models. Model I was adjusted for maternal age, parity and seasonality. Model II was further adjusted for hypertension and diabetes. Model III was the fully adjusted model, where we adjusted for relationship status, residence and employment status, in addition to the variables in model I and II. Analyses involving LBW and PB were also adjusted for infant sex.

In paper III we also explored whether the risk of LBW, PB, and SGA 2SD differed by subgroups of women. We performed a logistic regression analysis to calculate the OR (95% CI) of the outcomes of interest in the post-collapse period compared to the pre-collapse period, stratified by maternal age, parity, relationship status, place of residence and employment status. The stratified analysis was adjusted for maternal age (continuous), parity (except where we stratified by parity), and seasonality.

To further explore whether the effects of the economic collapse on the outcomes of interest differed depending on when during gestation the collapse hit, we divided the study period into intervals of three months and used logistic regression analysis to calculate the odds ratios of LBW, PB and SGA 2SD in each interval in 2008 and 2009, using the corresponding combined intervals in 2006 and 2007 as a reference.

Sensitivity analysis

In order to test whether the observed findings were robust to changes in the definition of the exposure category, we repeated the main logistic regression analyses where we used date of conception instead of date of birth as an indicator of where to place each birth with respect to the economic collapse. We further explored the shock effects of the collapse on LBW, PB and SGA 2SD by including the women who were pregnant on October 6th 2008 in the exposed group with the reference group consisting of all women who were pregnant on October 6th in the years 2006 and 2007 (combined). Lastly, we explored the selection effects of the collapse by contrasting women who became pregnant after the October 6th 2008 and gave birth in the latter half of 2009.

3.6.4 Birth outcomes (paper IV)

Descriptive statistics were calculated for all parental- and pregnancy related characteristics, contrasting frequencies across the pre-recession and recession categories. Differences between the exposure categories were assessed with χ^2 tests for the categorical variables and one-way ANOVA for mean maternal age. Time-trend was visually inspected by plotting the quarterly average prevalence of LBW, PB, and SGA 10th pct. and fit a loess curve, with a 95% CI, through the data points. Further, the potential time-trend in LBW, PB, and SGA 10th pct. was assessed in a supplementary analysis by using a Poisson regression analyses to calculate the change per year (relative risks, 95% CI's), separately for the pre-recession and recession periods. Further, likelihood ratio tests were used to assess differences in average prevalence before and after the economic collapse.

Logistic regression analyses were used to calculate the adjusted odds ratio (aOR) and the 95% CIs for LBW, PB, and SGA in each of the two recession periods with the pre-recession period as a reference. In model 1, adjustments were made for maternal age (continuous) and gravidity. In model 2, we adjusted for relationship status, maternal residence, maternal citizenship, parental employment status, hypertensive disorders of pregnancy, congenital malformation and gestational and pre-existing diabetes, in addition to maternal age and gravidity. A supplementary logistic regression analysis was performed to examine the association between the aggregate economic indicators (GDP and unemployment rate) and birth outcomes. Aggregate indicators, which were significantly associated with the index outcome at a significance level of 0.10 in this supplementary analysis, were introduced separately into model 1 (model 3: GDP; model 4: unemployment rate). This was done to assess the role of these surrounding economic indicators on the observed associations between the timing of the economic collapse and birth outcomes. Finally, we conducted stratified logistic regression analyses by parental demographic characteristics and maternal medical conditions during pregnancy.

Supplementary analysis

A supplementary analysis (unpublished data) was conducted in order to examine the fertility rate (TFR = number of births / total female population, in particular 5 year age groups) of the study population. The fertility rate was calculated for all live-singleton births among women who were 15-49 years old and plotted against time (in years).

3.7 Data protection and ethical approvals

The registers used in studies I-IV have various purposes stated in the law (170), including surveillance and research, provided the necessary ethical and data protection requirements are met. During the study process, all appropriate ethical requirements were fulfilled. All the studies were register based and did not involve direct contact with study participants. Informed consent from study participants was therefore not obtained as all personal information was anonymized and de-identified before we obtained the data for analyses.

Study I was approved by the Icelandic National Bioethic committee (VSNb2010050014/03.7), the Data Protection Authority (2010050499LSL/--) and the Directorate of Health (2010050296/5.6.1/HBS/hbs).

Study II was approved by the National Bioethic committee (VSNb2010050009/03.7) and the Data Protection Authority (2010060504AT/--), with additional acceptance from the Landspitali-University Hospital authority and the Directorate of Health.

Studies III and VI were approved by the Icelandic National Bioethic committee (VSNb2013010002/03.07), the Data Protection Authority (2012121499HGJ/--) and the Directorate of Health (1301064/5.6.1/gkg).

4 Results

4.1 Maternal health behavior (paper I)

4.1.1 Smoking

In 21.1% of the pregnancies included in the study, women reported smoking at some point during early pregnancy, while 10.9% continued smoking into the second trimester of pregnancy, during the 10-year study period (2001-2010). The prevalence of continued smoking was highest in 2005-2006 (16.1%), which was significantly higher than in the years 2007-08 (8.5%) and 2009-10 (8.7%). Although the trend in smoking was not entirely linear (Figure 1a, paper I), we found a statistically significant annual decrease in continued smoking over the study period (OR 0.94, 95% CI 0.88-1.00), i.e. a decrease by 0.06 for each year of the study. The decrease was confined to women with Icelandic citizenship (OR 0.92, 95% CI 0.86-0.98), and was most apparent among women not cohabitating (0.88, 95%CI 0.77-0.99) and women older than 35 years (OR 0.87, 95% CI 0.74-1.02) (Table 2, paper I).

4.1.2 Maternal body mass index (BMI)

Of the 1,281 pregnancies included in the study with available data on weight and height, 45.5% had BMI ≥ 25 and the mean BMI was 25.7 as measured at women‘s first antenatal visit. The prevalence of overweight was 27.5% whereas the prevalence of obesity was 18.1%. Although visual inspection of the prevalence of maternal BMI implies an upward trend, no statistically significant changes were observed in the mean BMI over the study period (p=0.09). During the study period, the prevalence of overweight and obesity, respectively, increased from 25.9% and 13.0% in 2001-2002 to 27.7% and 16.2% in 2009-2010. The highest prevalence of overweight and obesity was observed in 2005-2006 where 27.9% were overweight and 20.7% were obese although this was not significantly different from other time periods (Figure 1b, paper I). No significant changes were observed for secular trends of overweight and obesity, over the study period (aOR 1.02, 95% CI 0.97-1.06; 1.02, 95% CI 0.97-1.02, respectively).

Supplementary results

Age, relationship status, occupational status, residence, and citizenship were associated with continued smoking during pregnancy among pregnant women in Iceland during the study period. Women were more likely to

continue smoking during pregnancy if they were younger than 25 years (aOR 2.34, 95% CI 1.17-4.66), if they had one or more child (aOR 1.82, 95% CI 1.13-2.93), if they were of non-Icelandic citizenship (aOR 2.29, 95% CI 1.19-4.42), if they were not cohabitating with the other parent (aOR 3.58, 95% CI 2.28-5.62), and if they were unemployed/on disability/homemakers (aOR 3.48, 95% CI 2.16-5.61), compared with each relevant category of comparison (Table 5).

Obesity was not as strongly associated with women's socio-demographic characteristics as continued smoking during pregnancy. Still, women of non-Icelandic citizenship and women who were younger than 25 years were less likely to be obese compared with Icelandic women and women older than 35 years (aOR 0.18, 95% CI 0.07-0.51; aOR 0.35, 95% CI 0.19-0.63, respectively), while women living in rural areas of Iceland were more likely to be obese compared with those living in the capital area (aOR 1.81, 95% CI 1.30-2.52) (Table 5).

Table 5. Multivariate logistic regression analysis of continued smoking and obesity (BMI≥30 kg/m^2) at first antenatal visit in Iceland in 2001-2010, by biannual time-intervals and socio-demographic characteristics.

Socio-demographic characteristics	***Model 1*[α]*: S*moking**		***Model 2*[β]*:* Obesity**	
	OR	95% CI	OR	95% CI
Year of delivery				
2001-2002	1.00	ref.	1.00	ref.
2003-2004	0.66	0.32 – 1.35	1.48	0.80 – 2.73
2005-2006	1.13	0.60 – 2.11	1.76	0.98 – 3.14
2007-2008	0.53	0.27 – 1.04	1.64	0.92 – 2.94
2009-2010	0.54	0.28 – 1.04	1.64	0.92 – 2.92
Age				
<25	2.32	1.16 – 4.62	0.35	0.19 – 0.63
25-34	1.39	0.80 – 2.44	0.90	0.62 – 1.30
≥35	1.00	ref.	1.00	ref.
Parity				

Nulliparous	1.00	ref.	1.00	ref.
Multipara	1.83	1.13 – 2.94	1.23	0.85 – 1.77
Citizenship				
Icelandic	1.00	ref.	1.00	ref.
Foreign	2.29	1.19 – 4.42	0.18	0.07 – 0.51
Relationship status				
Cohabitating	1.00	ref.	1.00	ref.
Not cohabitating	3.55	2.25 – 5.59	1.19	0.76 – 1.87
Employment status				
Employed	1.00	ref.	1.00	ref.
Student	0.68	0.38 – 1.24	0.70	0.43 – 1.14
Unemployed/on disability	3.78	1.80 – 7.90	1.16	0.51 – 2.64
Homemakers	3.33	1.88 – 5.89	1.00	0.57 – 1.77
Place of residence				
Urban	1.00	ref.	1.00	ref.
Rural	1.37	0.90 – 2.07	1.81	1.30 – 2.52
Body mass index				
Not obese (BMI <30)	1.00	ref.	-	-
Obese (BMI ≥30)	1.45	0.91-2.33	-	-
Smoking				
No	-	-	1.00	ref.
Yes	-	-	1.39	0.87-2.23

[α]Mutually adjusted for age (continuous), parity, citizenship, relationship status, employment status, place of residence and year of delivery (continuous) and obesity. Age and year of delivery are used as categorical variables when calculating OR within each particular strata.
[β] Mutually adjusted for age (continuous), parity, citizenship, relationship status, employment status, place of residence and year of delivery (continuous), smoking and gestational date of first weight measurement. Age and year of delivery are used as categorical variables when calculating OR within each particular strata.

4.2 Pregnancy-induced hypertensive disorders and antihypertensive drugs (paper II)

In paper II, we explored the changes in the prevalence of pregnancy-induced hypertensive disorders (gestational hypertension and preeclampsia) and prescription fills for antihypertensive drugs (β-blockers and calcium channel blockers) among pregnant women in Iceland during the first four years following the economic collapse, compared with the pre-collapse years.

4.2.1 Pregnancy-induced hypertensive disorders

The prevalence of gestational hypertension increased from 2.4% in the pre-collapse period to 3.1% in post-collapse year 4, peaking in 3.9% during the first post-collapse year (Table 1, paper II). Adjusting for time-trend, maternal age and gravidity, we observed a statistically significant increase in gestational hypertension during the first year following the economic collapse (aOR 1.47, 95% CI 1.13-1.91), as compared to the pre-collapse period. Further adjustments for other maternal- and pregnancy related covariates did not affect the observed association. However, when adding unemployment rate to the model, the association between time and gestational hypertension disappeared (aOR 1.04, 95% CI 0.74-1.47). There was no association between the economic collapse and gestational hypertension in the subsequent three post-collapse years (Table 2, paper II).

On the contrary, there was a decrease in preeclampsia over the study period, from 3.6% in the pre-collapse period to 3.3% in post-collapse year 4 (Table 1, paper II). No statistically significant changes were observed for preeclampsia between the pre- and post-collapse years (Table 2, paper II). When further exploring the short-term effect of the economic collapse, we did not observe any indications of larger effect sizes in the first half year of the economic recession than in the second half year (Supplementary table 4, paper II).

4.2.2 Antihypertensive drugs

The pattern of prescription fills of β-blockers across exposure categories was similar to what was observed for gestational hypertension. The prevalence increased from 1.9% in the pre-collapse period to 2.8% in post-collapse year 4, peaking in 3.1% during the first post-collapse year (Table 1, paper II). Compared to the pre-collapse period, there was a statistically significant increase in the prescription fills of β-blockers (aOR 1.43, 95% CI 1.07-1.90) during the first post-collapse year; an increase which disappeared when adding the unemployment rate to the regression model (aOR 1.05, 95% CI 0.72-1.54) (Table 3, paper II).

There was a linear increase in the prescription fills of calcium channel blockers across the exposure categories, from 0.4% in the pre-collapse period to 1.6% in post-collapse year 4 (Table 1, paper II). After adjusting for time-trend, the observed increase in the prescription fills of calcium channel blockers disappeared (Table 3, paper II).

4.3 Birth outcomes (paper III)

In paper III, we explored the immediate effect of the economic collapse on birth outcomes and found that Icelandic women who gave birth to live-born singletons in the first 15 months following the economic collapse had lower mean birth weight (~30 g) and increased odds of LBW compared with women giving birth before the collapse (aOR_{LBW} 1.25, 95% CI 1.02-1.53) (Table 3, paper III). The increase in LBW was most distinct 6-9 months after the collapse (aOR 1.70, 95% CI 1.11-2.59) (Figure 1, paper III), indicating that women who were in their first trimester of their pregnancies when the collapse hit, were particularly affected. A similar tendency of increased odds in SGA (2SD) following the economic collapse was observed, although the increase was not statistically significant. No statistically significant changes were observed for PB between the pre- and post-collapse periods (Table 3, paper III).

Furthermore, certain subgroups of women giving birth during the post-collapse period were disproportionally affected by the economic collapse. In particular, young women (<25 years) and women not in a paid labor-job had increased odds of LBW (aOR 1.85, 95% CI 1.25-2.72; aOR 1.61 95% CI 1.10-2.35, respectively) and SGA (2SD) (aOR 1.87, 95% CI 1.09-3.23; aOR 1.86 95% CI 1.09-3.17), compared to the the same subgroups of women giving birth in the pre-collapse period (Table 4, paper III).

4.4 Birth outcomes – 4 year follow-up (paper IV)

In paper IV, we assessed the long term effects of the economic recession on infant health, measured as LBW, PB and SGA 10th pct., and whether potential changes in these birth outcomes were due to changes in the surrounding economic climate in Iceland.

Adjusting for maternal- and pregnancy related covariates, we observed a statistically significant increase in LBW during the first recession year (aOR_{year1} 1.35, 95% CI 1.12-1.63), compared with the pre-recession period, but not in the three subsequent recession years. Adjusting for the same covariates, a significant increase was observed for SGA 10th pct. in the first

year of the recession (aOR_{year1} 1.11, 95% CI 1.00-1.23) as well as in the second to fourth recession years ($aOR_{years2-4}$ 1.08, 95% CI 1.01-1.16). Albeit not statistically significant, a tendency towards increase in PB was observed only for the first recession year (model 2: aOR 1.12, 95% CI 0.97-1.31). When assessing the mediating effects of the aggregate economic indicators on the index outcomes, we found that the observed increase in LBW and SGA 10th pct. diminished and became insignificant after adjustment for GDP or unemployment rate (Table 2, paper IV).

When examining the association between the pre-recession and recession periods, and birth outcomes stratified by subgroups, we found employment status of the parents to be considerably related to LBW and SGA births. Compared with the pre-recession period, infants of parents, where only one parent was working a labor-market job, had increased odds of LBW during the first year of the recession (aOR_{year1} 1.66, 95% CI 1.19-2.31). This increase was even greater when neither parent was working and lasted beyond the first recession year ($aOR_{post-year1}$ 2.36, 95% CI 1.00-5.55; $aOR_{post-year2-4}$ 2.88, 95% CI 1.61-5.14). A similar pattern was observed for the odds of SGA by employment status of the parents although the point estimates were lower (Table 3, paper IV).

Supplementary results

During the recession years, pregnant women were older, more likely to be of foreign citizenship, and less likely to be in paid labor work. Furthermore, they were more likely to suffer from gestational diabetes (Table 1, paper IV). The fertility rate among 15-49 year old women giving birth to live singletons in Iceland increased steadily during study period, reaching 2.17 during the second recession year. During the last two years of the study period, a steep decline was observed in the fertility rate, resulting in a rate of 1.92 which is similar to what was observed in the beginning of the study period (Figure 5).

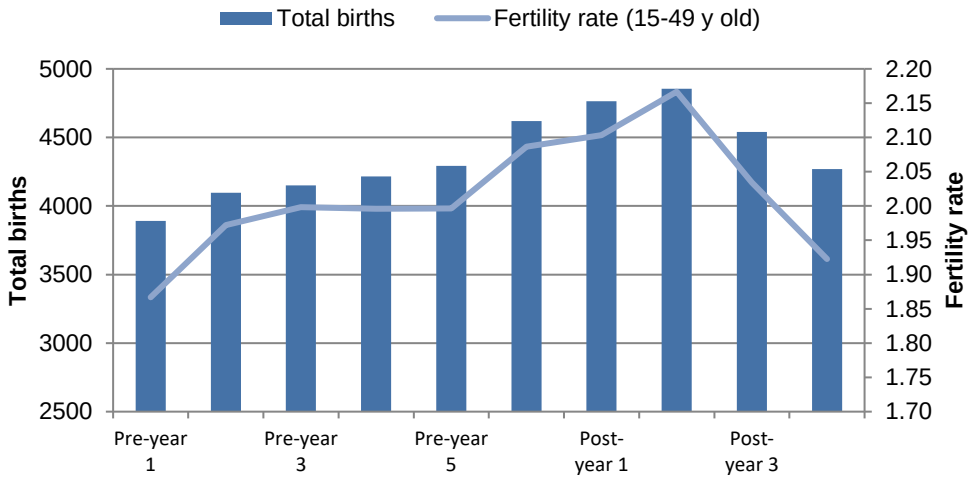

Figure 5. The number of live singleton births (right vertical axis) and the fertility rate among 15-49 year old women (left vertical axis) in Iceland during pre-recession and recession years, October 2002 to September 2012. Pre-year stands for pre-recession year (ranging from Oct-Sep). Post-year stands for recession year (ranging from Oct-Sep).

5 Discussion

5.1 Main findings

The main findings from our research on maternal diseases and health indicators during pregnancy and at birth during times of great macroeconomic instability in Iceland indicate an increase in gestational hypertension and a corresponding increase in prescription fills for β-blockers during the first year of the economic recession, which seemingly was mediated by the macroeconomic conditions in Iceland during that time. Furthermore, parallel with the declining economic conditions in Iceland in the years leading up to the crisis, there was an upward trend in LBW and SGA births. These rates peaked during the first and most severe year of the recession, with lingering increase in SGA births throughout the study period. Women who were in their first trimester when the economic collapse hit were particularly at increased risk of LBW. Further, infants of parents not working a paid labor-market job, young women and women living outside the capital area were particularly at increased risk of LBW and SGA during the economic recession, compared to their peers during the pre-recession years. The findings suggest that the economic collapse had a negative impact on fetal growth, which was, at least to some degree, explained by the macroeconomic environment. Our findings indicate a decrease in maternal smoking during pregnancy and stability in the prevalence of obesity during this time period. Thus, deterioration in maternal health behaviors must be considered an unlikely explanation for the observed increase in gestational hypertension and slower fetal growth following the economic collapse in Iceland.

5.2 General discussion

5.2.1 Maternal health behavior during the Icelandic recession

Our findings in paper I suggest an overall decrease in the prevalence of continued smoking into the second trimester of pregnancy among Icelandic women during the first decade of this century, a time period characterized by dramatic changes in Iceland‘s economy. This decrease is in line with findings from the other Nordic countries (43). Moreover, our findings reflect the smoking trend among the general population in Iceland, which is reported to have decreased from 26.8% to 18.5% during the study period (171).

Contrary to findings of previous studies reporting substantial increases in the body mass index of the general population in Iceland between 1990-2010 (35, 172-174), we did not observe any significant overall changes in maternal mean body mass index, overweight, or obesity (a proxy for general health behavior) during the study period, i.e. 2001-2010. The initial increase in obesity observed until the years 2005-2006, seemed to level off in the latter half of the study period. A similar pattern of a stagnation in the growing prevalence of obesity has been observed in non-pregnant populations in other countries (175-177) as well as in some (178), but not all (179, 180), pregnant populations.

It has been hypothesized that economic recessions, with the associated rises in unemployment, job insecurity, and financial stress, may lead to an increase in risky health behaviors, such as smoking and intake of less nutritious food (i.e. fruits and vegetables), for example due to crisis-induced changes in prices of healthy goods (114). This hypothesis is supported by studies, indicating that women who have high levels of stress are more likely to continue smoking while pregnant (151-153) as well as by studies indicating less intake of fruits and vegetables during economic downturns (24, 50). However, our findings of decreased maternal smoking in Iceland during the whole study period (also during the two years following the economic collapse) do not lend support to this hypothesis. Instead, our findings bear some similarities to the findings of Dehejia and Lleras-Muney (51), who reported a reduced maternal smoking during times of economic downturns. In fact, we observed the highest prevalence of continued smoking and obesity among pregnant women in Iceland in the years 2005-2006, which coincided with the most prosperous years of the nation‘s economy. Indeed, our findings concur with findings of studies that indicate better health behaviors during times of economic contractions. Both Ruhm (48) and Xu (181) found smoking prevalence to be highest during economic booms when the unemployment rate was low. Furthermore, our findings concur with findings of recent studies indicating improved health behaviors of the Icelandic population during the recession (24, 33-35). In a recent study, Asgeirsdottir and colleagues (24) used longitudinal data (the Health and Wellbeing Study in Iceland) to examine changes in health behaviors of Icelanders between the years 2007, 2009 and 2012. They report a continual decrease in all health-compromising behaviors (except for daily intake of sweets), including smoking and intake of sugared soft drinks and fast food between the three waves of assessments. Similar findings were obtained in a survey of the dietary habits of Icelanders in 2010-2011 where 33.6% of women reported a

change in their dietary habits following the economic collapse in 2008. More specifically, there was a 51.3%, 46.9% and 63.2% decrease in the consumption of sweets, beverages and fast food, respectively (35). Furthermore, a slowed down weight gain following a job loss after the economic collapse has been reported, particularly for females. This finding lends further support to a levelling off in maternal weight of pregnant women in Iceland (182). The observed improvement in the smoking habits of Icelanders following the economic collapse was found to be explained by crisis-induced price increases of imported goods following the economic collapse in Iceland due to devaluation of the Icelandic currency (34). It is likely that these price increases also caused a reduction in other health-deteriorating behaviors, such as intake of fast food and soft drinks.

The socio-demographic gradient in the prevalence of smoking (183, 184), as well as overweight and obesity (39, 185) among the pregnant population is well acknowledged in the literature, with higher prevalence of these behavioral risk factors further down the social hierarchy. Our findings from the supplementary analysis concur with these previous studies and indicate that, among pregnant women in Iceland, young women, multiparas, women not cohabitating, women of foreign citizenship and women inactive on the labor market (unemployed/on disability/homemakers) were two to four times as likely to continue to smoke into the second trimester of pregnancy compared with their counterparties. Furthermore, in our data, obesity among pregnant women was positively associated with rural area of residence and foreign citizenship.

5.2.2 Maternal health and birth outcomes during the Icelandic recession

5.2.2.1 Pregnancy-induced hypertensive disorders

Our findings in paper II indicate a rapid and transient increased risk of gestational hypertension during the first and most severe year of the economic recession in Iceland, which levelled off parallel to the recovery of the macroeconomic conditions. Furthermore, we observed a corresponding increase in prescription fills for β-blockers, which are the first line of treatment of pregnancy-induced hypertensive disorders in Iceland (Ragnheiður Bjarnadóttir, personal communication). There were, however, no changes in the risk of preeclampsia or calcium channel blocker use between the pre-recession and recession periods.

Our findings suggest that the observed increase in gestational hypertension and the corresponding increase in prescription fills for β-blockers during the first recession year may be explained by the macroeconomic conditions in the country at that time. This is reflected in our findings indicating a strong mediating effect of the national unemployment rate on the association between the economic collapse and gestational hypertension and prescription fills for β-blockers. It is likely that the sharp rise of unemployment following the economic collapse caused an increase in socioeconomic difficulties, with up to 50% of the Icelandic population reporting difficulties covering expenses through the pay period during that time (186). Indeed, there are several studies linking socioeconomic status with pregnancy-induced hypertensive disorders (41, 42, 66-68) with increased risk of these disorders among the more disadvantaged groups of women.

To my knowledge, this is the first study to explore the effect of an economic recession on pregnancy-induced hypertensive disorders. There are, however, several studies (14-16, 71) that have found increased cardiovascular morbidity and mortality during economic downturns. Asgeirsdottir and colleagues (24) examined the association between the Icelandic economic collapse and cardiovascular morbidity and hypertension using data from the Icelandic Health and Well-being study from 2007 and 2009. They found an increase in hypertension for males following the economic collapse, but not for females, which was mediated through changes in working hours and stress level, rather than income changes. Furthermore, Gudjonsdottir and collegues (30) reported a short term increase in female attendance rate to the cardiac emergency department in the first weeks after the economic collapse in Iceland; an increase which could reflect the cardiovascular health of the Icelandic population during that time. However, it could be that the pregnant population represents a group of women who are particularly vulnerable to socioeconomic difficulties brought about by national recessions.

5.2.2.2 Birth outcomes

The findings of studies III and IV examining birth outcomes following the economic collapse in 2008 indicate an upward trend in LBW and SGA births, starting in the year before the collapse, in parallel with the declining economic conditions in Iceland during that time. This rise resulted in a statistically significant increase in LBW and SGA during the first and most severe year of the economic recession, with seemingly lasting increase in SGA births

throughout the four studied years of the recession. The findings indicate that economic recession in Iceland negatively affected fetal growth, and that the macroeconomic conditions in Iceland during the recession, i.e. the increase in unemployment rate, may largely serve as an explanation for the observed findings. The findings are in correspondence with some of the previous studies indicating a reduced birth weight during times of economic uncertainties (91, 92, 94-102). The increase in LBW was most distinct among women who were in their first trimester of pregnancy during the beginning of the recession, i.e. on October 6, 2008, which is in accordance with previous studies (97, 187-189).

Previous studies have found widening health inequalities by SES status during recessions, which size seem to be dependent on countries' welfare systems, with narrower gaps in societies with strong welfare systems, e.g. in the Nordic countries (190, 191). Despite a publicly funded antenatal care program in Iceland and a strong welfare system, the increase in LBW and SGA during the first recession year was mostly confined to socially and economically vulnerable groups of women (i.e. young women and women who were not in a paid labor-work), suggesting widening inequalities in birth outcomes following the economic collapse in Iceland. Similar findings have been reported in Spain following the 2008 economic recession, where a maternal educational gradient in perinatal outcomes was observed, with the highest risk of PB and LBW among women with primary education (192). Furthermore, a dose-response association was observed between the parental employment status and LBW throughout the studied four years of the economic recession, where the risk increment was largest when neither of the parent were in paid work. Thus, although there was not an overall increase in LBW beyond the first recession year, the effect of the recession was lasting among parents in the lowest SES groups (as proxied by employment status)

5.2.2.3 Potential pathways

As previously discussed, there are number of pathways by which recessions can affect the process of pregnancy and birth outcomes. Below, the findings of studies II-IV will be discussed in the context of the stress-, behavioral-, and demographic mechanisms, respectively.

<u>The stress mechanism</u>

In studies II-IV we were unable to disentangle potential underlying mechanisms for the observed increase in gestational hypertension, LBW and

SGA. As previously discussed, extreme or chronic stress can result in an over-activation of the HPA-axis (121, 125, 126) resulting in increased level of circulating stress hormones which may cause pathophysiological changes, including pregnancy-induced hypertensive disorders or restricted fetal growth (127-130). A wide array of research based on different methodological approaches has shown that women experiencing high stress levels, anxiety or depression before or during pregnancy are at increased risk of developing pregnancy-induced hypertensive disorders (133-141), as well as giving birth to smaller infants (76) or preterm (142). Indeed, recent studies of the health consequences of the Icelandic economic collapse indicate an increase in high stress levels (27) and depressive symptoms (28) among Icelandic women during the first year of the recession, where socially and economically vulnerable groups of women were particularly found to be at increased risk (27). Thus, it is possible that the increase in psychological morbidity among Icelandic women following the economic collapse may serve as an explanation for the increase in gestational hypertension, LBW and SGA observed in our studies. Furthermore, there is a line of studies indicating differences in stress responses, where individuals who have been exposed to chronic stress or traumatic life events are found to be more susceptible to stress compared to those who have not experienced such an exposure (76, 142). These differences suggest that stress exposure during pregnancy is more likely to have adverse effects on birth outcomes in women who are more vulnerable before pregnancy. Indeed, this literature harmonizes well with our findings of higher risks of adverse birth outcomes among the more disadvantaged groups of women in our study population (i.e. young women, women/parents not in paid work).

The numerous studies examining the role of various forms of stress in the process of pregnancy and birth outcomes indicate that chronic stress seems to be a stronger risk factor for LBW while acute stress and anxiety is more strongly related to PB (76, 142). This different effect by types of stress may explain the non-significant indication of increase of PB observed only during the first recession year in paper IV (acute stress effect) while the increased risk of SGA lasted throughout the four studied year of the recession (chronic stress).

The lack of association between the economic collapse and preeclampsia came somewhat as a surprise, when keeping in mind that several previous studies have linked both psychological morbidity, including stress (134-137, 139-141), and low SES (41, 67) to preeclampsia. We hypothesize two plausible explanations for the observed increase in gestational hypertension

but not preeclampsia. Firstly, if gestational hypertension is viewed as a precursor or a milder form of preeclampsia it could be that the national economic collapse was not a stressor of sufficient magnitude to cause the disease with refer to as preeclampsia. Secondly, if these two disorders are viewed as separate diseases with different etiologies, it could be that the mechanisms underlying gestational hypertension are more sensitive to stress than those of preeclampsia.

Behavioral changes

Other possible mechanism by which the economic recession could affect maternal health and birth outcomes is through behavioral changes (52, 193) as a response to reduced income, limiting the ability to purchase healthy goods or as a response to stress. Women experiencing stress or depression during pregnancy have been found to be more likely to exhibit poor health behaviors (150-153), for example smoking, less exercise and unhealthy eating. Many of these risk factors are associated with pregnancy-induced hypertensive disorders and adverse birth outcomes, with the counterintuitively exception of reduced risk of pregnancy-induced hypertensive disorders among women who smoke during pregnancy. As the data used in papers II-IV did not include information regarding these health behaviors among the study population, we were unable to adjust for them in the data analyses. The findings of paper I show evidence of reduced prevalence of smoking and a levelling off in maternal overweight and obesity between the years 2001-2010; findings which have since been corroborated by previously mentioned studies indicating an overall improvement in the health behaviors of the Icelandic population after the economic collapse in 2008 (24, 34, 35). It is theoretically possible that the decrease in maternal smoking contributed to the observed increase in gestational hypertension while it may have had positive effect on birth outcomes. It should, however, be noted that the alleged protective effect of smoking on pregnancy-induced hypertensive disorders reported by several studies (56) is most likely caused by selection bias, as reported by Luque-Fernandez and collegues (194). The levelling off in maternal body weight is likely to reduce both the risk of pregnancy-induced hypertensive disorders as well as birth outcomes. However, we cannot rule out that the observed increases in gestational hypertension, LBW and SGA are caused by an alteration in the health behaviors of pregnant women in Iceland after the economic collapse.

Demographic changes

Previous studies have indicated that economic recessions can affect the

demography of the pregnant population where young people and higher educated women have been found to postpone or revise their fertility decisions during times of economic hardship (154). In Iceland, we did find some changes in the demography of the pregnant women as well as in the medical risk factor profiles during the recession years (i.e. age, citizenship and employment status). However, adjusting for these changes did not seem to have a great impact on the overall increased risk of gestational hypertension, LBW and SGA after the economic collapse. The sharp drop in the fertility rate observed in the last two years of the study period is in accordance with previous studies (154) although this drop, per se, cannot explain the observed findings.

5.3 Strengths and limitations

5.3.1 Maternal health behavior

The main strength of this study is the prospective and objective measurements of maternal physique (i.e. height and weight), performed by midwives at the first antenatal visits. Indeed, studies have indicated that self-reports tend to overestimate height and underestimate weight (195) while objective measurements undertaken by health care professionals are found to be more dependable than self-reported data (196).

As previously mentioned, information regarding maternal smoking, body weight and height are not recorded in the Icelandic Medical Birth Registry, limiting the study to a rather small sample, resulting in relatively low statistical power. The study population consists of women representing the unexposed group of pregnant women in a study on maternal health and birth outcomes of all women previously exposed to sexual violence and subsequently seeking help in the Rape and Trauma Service in Iceland (162). Hence, none of the women in our study population had attended the Rape and Trauma Service which might have resulted in an underestimation of the prevalence of smoking in our study, as the exposed women were more likely to smoke during pregnancy compared to the unexposed women (162). This underestimation is, however, unlikely to have great influence as the women in the exposed group of the abovementioned study gave birth to 1.7% of all births occurring between 2001 and 2010 in Iceland. Another source for potential misclassification in the prevalence of smoking during pregnancy could arise from the reluctance to reveal smoking status while pregnant. Indeed, studies have shown that pregnant women find it hard to disclose their smoking habits to a health care professional due to fear of stigma or societal

pressure (195) which leads to an underestimation of the true smoking prevalence and a potentially false decreasing trend in smoking during pregnancy. It is, however, unlikely that this misclassification should be differential between the recession- and non-recession time intervals.

5.3.2 Maternal health and birth outcomes

The main strength of studies II-IV is the completeness of the Icelandic Medical Birth Registry, allowing a prospective collection of detailed pregnancy-related and demographic information of all pregnant women in Iceland and their newborns during the study periods, independent of the economic collapse. The study population was further limited to singleton live births in order to enhance the internal validity. This was done as multiple gestations have been associated with increased risk of both pregnancy-induced hypertensive disorders and adverse birth outcomes.

There are two main limitations which only apply to paper II. The first involves a potential misclassification of pregnancy-induced hypertensive disorders. We cannot rule out that diagnoses of preeclampsia were temporarily misclassified as gestational hypertension, resulting in an increased risk of gestational hypertension during the first year of the recession. However, it is unlikely that such a misclassification would be restricted only to the first recession year. Also, the corresponding increase in the prescription fills for β-blockers further underpins the validity of the diagnoses of pregnancy-induced hypertensive disorders. Secondly, as our study population was restricted to pregnancies resulting in live births, it is possible that the increase in gestational hypertension during the first recession year led to an increase in stillbirths, resulting in an underestimation of the observed effect. However, the stillbirth rate during the first recession year was not found to deviate from the observed average stillbirth rate of 3.5 per 1000 births during the study period. Furthermore, a stillbirth rate of this magnitude is unlikely to significantly affect the observed findings.

The main limitation of papers II-IV is the ecological nature of our exposure measure. In general, ecological studies rely on rough exposure information for large groups or populations rather than individual-level exposure, thus making them subject to an ecological fallacy. The term ‘ecological fallacy’ refers to an error in the interpretation of data, i.e. an inference of an association at the individual level from findings observed at the group level (197). We use calendar time to approximate the economic recession, assuming that the pregnant population was affected equally. Indeed, it would have been ideal to obtain more accurate information on the financial status,

e.g. income tax, for each woman in the study population, in order to explore in more detail whether the observed findings were due to loss of income following the economic collapse. We did perform stratified analyses on maternal age and parental occupational status (obtained from the Birth Registry) generally revealing, as hypothesized, the strongest associations in economically vulnerable groups. Nevertheless, it is possible that some other unknown factors (i.e. increased pollution, natural disasters) occurred parallel to the course of the economic recession which might have affected the outcomes of interest. However, the economic collapse was by far the most extraordinary event at that time and other parallel factors were most likely a consequence of the collapse. Thus, we find that the risk of residual confounding due to unknown environmental changes to be minimal. A second limitation is the previously mentioned lack of information on maternal pre-pregnancy body weight and health behaviors of the pregnant women, restricting our possibility in determining the underlying mechanisms for the observed increases in gestational hypertension, LBW and SGA during the recession. Third, as the Icelandic population is small (each birth cohort around 4000 births), we were limited by small numbers to detect modest or weak associations. Lastly, it should be noted that all economic recessions have their own distinguished features and therefore the findings of studies II-IV may not be generalized to other populations of pregnant women undergoing economic recessions.

6 Conclusions

This work adds an important knowledge on how maternal and infant health may be affected by a severe economic recession occurring in a high income country. Our data suggest that the Icelandic economic collapse in 2008 was an important stressor resulting in an increased risk of gestational hypertension and a corresponding increase in prescription fills of β-blockers among pregnant women during the first and most severe year of the 2008 economic recession in Iceland. Furthermore, we found an increase in the prevalence of LBW and SGA deliveries during the first recession year with seemingly lingering increase in the rate of SGA deliveries throughout the first four years of the recession.

Although it cannot be ruled out, our findings of reduced prevalence of maternal smoking together with a levelling off in the prevalence of overweight and obesity during the first decade of the 21st century, indicate that the observed increases in gestational hypertension, LBW and SGA during the recession years cannot be explained by alterations in health behaviors of the pregnant population. On the other hand, it seems plausible that the transient rise in gestational hypertension and the compromised fetal growth may have been driven by the negative changes in the macroeconomic conditions in Iceland during the recession. The findings further indicate that the economic collapse predominantly seemed to affect the most vulnerable groups of pregnant women, such as young women and those who are not in paid labor-work, resulting in widening disparities in birth outcomes in Iceland during the recession.

Despite our reservations regarding the generalizability of the findings to other populations undergoing recessions, they still demonstrate the importance of surveillance of the pregnant population during times of severe economic downturns. In particular, special focus should be on vulnerable groups of the society in order to reduce the impact of economic recessions on widening inequalities in birth outcomes.

7 Future studies

The findings of studies II-IV need to be substantiated by obtaining more detailed information regarding the pregnant women's financial status over time. Future studies should involve gathering this financial information, available from Statistics Iceland, and merge it with the information obtained from Icelandic Medical Birth Registry and Icelandic Medicines Registry. In a perfect world, this study should be replicated with a larger study population in order to increase its power, including measurements of maternal health behaviours and potentially other measurements of chronic stress exposures.Furthermore, in light of studies indicating worsening of mental health following the economic collapse, a logical next step would be to explore the use of psychotropic drugs during pregnancy in relation to the economic collapse. Lastly, implementing data on maternal smoking as well as maternal height and pre-pregnancy weight into the Icelandic Medical Birth Registry cannot be stressed enough.

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Smoking and obesity among pregnant women in Iceland 2001–2010

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Background: The prevalence of smoking during pregnancy in Western societies has decreased in the last decades, whereas prevalence of overweight and obesity has increased. Our objective was to study secular trends and patterns of smoking and body weight among pregnant women in Iceland, during a period of dramatic changes in the nation's economy. **Methods**: On the basis of the Medical Birth Registry, we used a random sample of 1329 births between 1 January 2001 and 31 December 2010. Information on smoking, body mass index and background factors during pregnancy was retrieved from the Medical Birth Register and maternity records. Trends in smoking, overweight, obesity and body mass index were assessed using logistic and linear regression analyses. Logistic regression analysis was used to examine the annual odds of smoking and obesity and by socio-demographic characteristics. **Results**: We found a decrease in the prevalence of continued smoking during pregnancy from 12.4% in 2001 to 7.9% in 2010 [odds ratio (OR) = 0.94, 95% confidence interval (CI) (0.88–1.00)], particularly among women with Icelandic citizenship [OR = 0.92, 95% CI (0.86–0.98)], whereas no changes in obesity [OR = 1.02, 95% CI (0.96–1.07)] were observed. The highest prevalence of maternal smoking and obesity was observed in 2005–06. **Conclusion**: Our results indicate that smoking during pregnancy decreased among Icelandic women in 2001–10, whereas an initial increase in obesity prevalence seemed to level off towards the end of the observation period. Interestingly, we found that both of these maternal risk factors reached their highest prevalence in 2005–06, which coincides with a flourishing period in the nation's economy.

Introduction

The harmful effects of smoking and obesity on pregnancy and birth outcomes are well documented.[1–5] Smoking during pregnancy has been shown to increase the risk of stillbirths, preterm birth[1,5] and low birth weight,[5] with potential long-term health consequences for the unborn child.[6,7] Similarly, studies have shown that high maternal body mass index (BMI) and, in particular, obesity are associated with a range of pregnancy and delivery complications, such as gestational diabetes,[1,3] gestational-induced hypertension and preeclampsia,[1] foetal macrosomia, as well as with adverse birth outcomes such as dystocia, induction of labour,[2] preterm birth, caesarean section[2,4] and stillbirths.[1,4]

Because of their high prevalence, overweight and obesity are now considered to have replaced smoking as the most preventable factors for pregnancy complications and adverse birth outcomes.[4] Smoking during pregnancy—as in general—has declined over the past 20 years in most Nordic countries; from 20.6 to 16.5% in Norway, 30.6 to 12.5% in Denmark and 31.4 to 6.9% in Sweden, whereas being stable around 15% in Finland.[8] The prevalence of overweight and obesity has increased worldwide in the last decade.[9] This also applies for pregnant women in the Nordic countries. In 2012, 38% of Swedish women were overweight or obese at the time of registration in antenatal care, which corresponds to a 51% increase over 20 years.[10] In Denmark, the prevalence of overweight and obesity among pregnant women rose from 31.9% in 2004 to 36.0% in 2010.[11,12] Until now, published data regarding maternal smoking and BMI from Iceland have been largely lacking, partly due to the fact that the Icelandic Medical Birth Register (MBR) does not include information on these behavioural risk factors. However, 5% of the 1111 pregnant women participating in the Icelandic Childbirth and Health Study in 2009–10 reported smoking during early pregnancy.[13] Furthermore, recent studies on body weight in the general population indicate a substantial increase in BMI over the last two decades.[14–16]

During 2000–10, the Icelandic population experienced profound economic changes. In this decade, Iceland was considered to be one of the richest nations in the world, but in the autumn of 2008, the country suffered a major economic breakdown when three of the largest banks were nationalized resulting in increased unemployment, bankruptcy of hundreds of firms and an increase in private and public debt.[17] A growing body of literature indicates that macro-economic conditions influence population health and health behaviours,[18,19] and recent studies on the health effect of the Icelandic economic crisis indicate an overall reduction in health compromising behaviour,[19] whereas early signs of mental- and cardiovascular health seemed negative, particularly among women.[20,21] Furthermore, in our recent study, we observed an increase in low-birth-weight deliveries in the year following the economic collapse.[22] Yet, data are scarce on the influence of such massive societal changes on health behaviours among pregnant women.

Using data from an existing cohort study, the aim of this study was therefore to examine the secular trend and patterns of smoking prevalence and body weight among pregnant women in Iceland between 2001 and 2010, a period during which dramatic changes in the nation's economy occurred.

Methods

Study design

We used data from an ongoing study on the risk of adverse maternal health, obstetric and birth outcomes among women previously exposed to sexual violence.[23] Our study population consisted of the unexposed group from that study, which was extracted from the MBR. It is thus a random sample of pregnancies among

Table 1 Maternal socio-demographic characteristics among 1329 pregnancies in Iceland in 2001–10

Socio-demographic characteristics	2001–02 (*N* = 162)		2003–04 (*N* = 224)		2005–06 (*N* = 280)		2007–08 (*N* = 306)		2009–10 (*N* = 357)		*P**
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	
Age (years)											
<25	45	27.8	48	21.4	50	17.9	60	19.6	75	21.0	0.364
25–34	83	51.2	133	59.4	180	64.3	187	61.1	215	60.2	
≥35	34	21.0	43	19.2	50	17.9	59	19.3	67	18.8	
Parity											
Nulliparous	67	41.4	93	41.5	103	36.8	129	42.2	149	41.7	0.681
Multipara	95	58.6	131	58.5	177	63.2	177	57.8	208	58.3	
Citizenship											
Icelandic	156	96.3	218	97.3	265	94.6	279	91.2	304	85.2	<0.001
Foreign	6	3.7	6	2.7	15	5.4	27	8.8	53	14.8	
Relationship status											
Cohabitating	144	88.9	193	86.2	242	86.4	256	83.7	302	84.6	0.662
Not cohabitating	18	11.1	31	13.8	37	13.2	49	16.0	47	13.2	
Missing					1	0.4	1	0.3	8	2.2	
Occupational status											
Employed	113	69.8	160	71.4	202	72.1	223	72.9	260	72.8	0.655
Student	22	13.6	41	18.3	43	15.4	55	18.0	56	15.7	
Unemployed/on disability/homemaker	19	11.7	18	8.0	31	11.1	23	7.5	39	10.9	
Missing	8	4.9	5	2.2	4	1.4	5	1.6	2	0.6	
Place of residence											
Urban	102	63.0	152	67.9	206	73.6	231	75.5	285	79.8	0.039
Rural	48	29.6	60	26.8	62	22.1	75	24.5	72	20.2	
Missing	12	7.4	12	5.4	12	4.3	0		0		
Gestational date of first weight measurement, mean (SD)	99.0	(27.4)	99.1	(25.9)	98.0	(28.4)	97.6	(31.0)	93.2	(31.2)	0.10

SD, standard deviation.
**P* value is based on Pearson χ^2 test for differences of characteristics between bi-annual time intervals except for gestational date of first weight measurement where one-way analysis of variance was used.

women who gave birth in the same month as exposed women, i.e. who had previously attended emergency services due to sexual assault and subsequently given birth any time during a 10-year period. This resulted in a population of 1312 women with a total of 1329 pregnancies from 1 January 2001 through 31 December 2010.

The MBR is a population-based register containing information on all pregnancies and deliveries in Iceland since 1982. Registered data include parental-, pregnancy-, labour- and delivery characteristics as well as birth and neonatal outcomes. Despite the richness of the data, information on maternal weight and smoking is not registered in the MBR. This information is, however, registered in maternity records at women's first antenatal visit. All pregnant women attend publicly funded antenatal care in a uniform manner at local clinics every 2–4 weeks of pregnancy. The attendance rate is high (99.5%), with the first antenatal visit occurring between gestational weeks 10 and 12 for the majority of women.[24,25]

Study variables

Smoking and BMI

Information on self-reported smoking behaviour and maternal weight was manually retrieved from maternity records. Women were categorized according to smoking status as non-smokers and ever-smokers; the latter were then further divided into (i) discontinued smokers, including women who discontinued smoking during early pregnancy before their first antenatal visit and (ii) continued smokers, including women who still smoked at the time of the first antenatal visit but may have quit thereafter or smoked throughout pregnancy. We did not have the exact date of when women reported discontinued smoking, although this is generally registered at the first antenatal visit at around gestational week 12.

Women's BMI was calculated according to measured height and weight at the first antenatal weight measurement, which on average occurred on the 97th day of gestation [standard deviation 29.3 days, median = 90 days]. Women were considered overweight if they had BMI ≥ 25.0 kg/m^2 and <30.0 kg/m^2 and obese if their BMI was ≥30 kg/m^2, according to the international BMI classification for adults.[26] Information about smoking and BMI was available for 1325 (99.7%) and 1281 (96.4%), respectively, of the 1329 pregnancies.

Other measures

Information on maternal socio-demographic characteristics retrieved from the MBR included age at delivery (<25, 25–34, ≥35 years), maternal citizenship (Icelandic, foreign), parity (nulliparous, multipara), relationship status (cohabitating, not cohabitating with other parent), occupational status (employed, student, unemployed/on disability/homemaker) and place of residence (urban, rural). To describe the macroeconomic conditions in Iceland during the study period, information on the national unemployment rate and the real wage index was obtained from Statistic Iceland.[27]

Data analysis

We used year of delivery as an explanatory variable, both on yearly basis and in 2-year intervals (hereafter referred to as bi-annual time intervals).

First, we calculated the proportion of smokers during pregnancy (ever-smokers, discontinued or continued smokers) as well as the mean BMI and proportion of overweight and obesity at first antenatal weight measurement among the study population. The bi-annual proportion of continued smoking and obesity was

stratified by maternal socio-demographic characteristics. We used Pearson χ^2 test to assess the differences in the distribution of women's socio-demographic characteristics between bi-annual time intervals.

Linear regression analysis was conducted to assess the time trend in mean BMI among pregnant women at first antenatal weight measurement. This model was adjusted for the gestational date of first weight measurement.

To examine secular time trends of smoking, overweight and obesity among pregnant women during the study period, logistic regression analysis was used to calculate the odds ratios (ORs) and their 95% confidence interval (CI) for each outcome with calendar time in years (continuous) as the independent variable. When examining the time trend of overweight and obesity, the models were adjusted for the gestational date of first weight measurement. Similar analyses were performed to explore the trends of smoking and obesity among subgroups, where we stratified for age, parity, citizenship, relationship status, occupational status and place of residence. Differences in the proportions of smoking, overweight and obesity between bi-annual time intervals were assessed by Pearson χ^2 test with a Bonferroni correction to further locate the potential differences between the bi-annual time intervals. Statistical analysis was performed using IBM SPSS Statistics 20.

The study was approved by the Icelandic National Bioethics Committee (VSNb2010050009/03.7) and the Data Protection Authority (2010060504AT/–).

Results

Socio-demographic characteristics of pregnant women in the study were somewhat equally distributed across bi-annual time intervals, with the exception of citizenship and place of residence (table 1). The proportion of pregnancies with foreign citizenship increased considerably during the study period, as did the proportion of pregnancies occurring in the capital area.

In 21.1% (279/1325) of pregnancies, women reported smoking at some point during early pregnancy and 10.9% (145/1325) continued smoking into the second trimester during the 10-year observation period.

Figure 1a shows the prevalence of continued and discontinued smoking into second trimester by bi-annual time intervals. The prevalence of continued smoking was highest in 2005–06 (16.1%), which was higher than the prevalence of continued smoking in 2007–08 (8.5%; $P = 0.005$) and 2009–10 (8.7%; $P = 0.004$) (figure 1a). We found an annual decrease in maternal continued smoking over the entire study period [OR = 0.94, 95% CI (0.88–1.00)], a decrease evident among women with Icelandic citizenship but not among women of foreign citizenship. Further, the decrease was most apparent among women older than 35 years nulliparous women and those not cohabitating with partner (table 2).

In 27.5% (352/1281) of pregnancies, women were categorized as overweight and 18.1% (232/1281) as obese during the observation period. The mean maternal BMI was 25.7. There was no increase in mean maternal BMI during the study period ($P = 0.09$). We observed the highest prevalence in mean maternal BMI in 2005–06, which then declined towards the end of the study period (figure 1b). However, there was no difference in the prevalence of mean BMI between bi-annual time intervals. During the study period, the prevalence of overweight and obesity, respectively, increased from 25.9% and 13.0% (2001–02) to 27.7% and 16.2% (2009–10) (figure 1b). The highest prevalence of obesity occurred in 2005–06, but this was not significantly different from other time intervals. No change was observed for secular trends of overweight and obesity over the entire study period [$OR_{overweight}$: 1.02, 95% CI (0.97–1.06); $OR_{obesity}$: 1.02, 95% CI (0.97–1.07)]. However, when analysing the time trend by socio-demographic subgroups, we observed a marginal increase in obesity only among women who were either nulliparous or students (table 3).

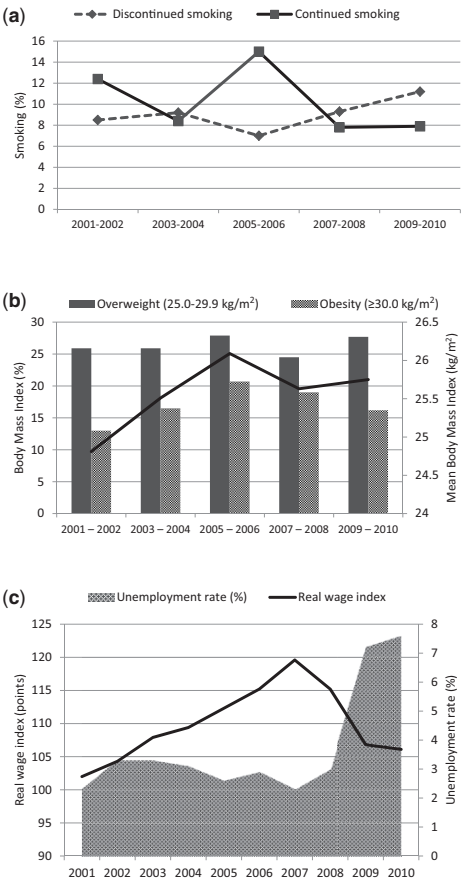

Figure 1 (a) Proportion of continued smoking and discontinued smoking at the beginning of second trimester among 1325 pregnancies in Iceland in 2001–10. (b) Overweight (BMI: 25.0–29.9 kg/m^2), obesity (BMI $\geq$ 30 kg/m^2) (left vertical axis) and mean BMI (right vertical axis) among 1281 pregnancies in Iceland in 2001–10. (c) The real wage index (left vertical axis) and unemployment rate (right vertical axis) in Iceland in 2001–10

Figure 1c, demonstrating the contextual economic conditions in Iceland over the study period, shows how the real wage index peaked in 2007 and the unemployment rate remained low until 2007, when it took a drastic turn for the worse.

Discussion

This is the first study that systematically examines the secular trends of behavioural risk factors, namely maternal weight and smoking during pregnancy in Iceland. We found an overall significant decrease in the prevalence of continued smoking into the second trimester of pregnancy among women with Icelandic citizenship during 2001–10, whereas an initial increase in obesity prevalence seemed to level off towards the end of the observation period. Interestingly, we found that prevalence of both maternal risk factors reached their highest prevalence in 2005–06 which

Table 2 Continued smoking at the beginning of second trimester among 1329 pregnancies in Iceland, 2001–10, stratified by maternal socio-demographic characteristics

Socio-demographic characteristics	2001–02 ($N = 162$)		2003–04 ($N = 224$)[a]		2005–06 ($N = 280$)[a]		2007–08 ($N = 306$)[a]		2009–10 ($N = 357$)[a]		OR (95% CI)[b]
	$n_{smokers}$	$\%_{smokers}$	$n_{smokers}$	$\%_{smokers}$	$n_{smokers}$	$\%_{smokers}$	$n_{smokers}$	$\%_{smokers}$	$n_{smokers}$	$\%_{smokers}$	
Age (years)											
<25	9	20.0	8	16.7	9	18.0	9	15.0	12	16.0	0.98 (0.88–1.09)
25–34	9	10.8	7	5.3	32	17.8	16	8.6	14	6.5	0.95 (0.87–1.03)
≥35	4	11.8	6	14.0	4	8.0	1	1.7	5	7.5	0.87 (0.74–1.02)
Parity											
Nulliparous	9	13.4	13	14.0	13	12.6	11	8.5	11	7.4	0.91 (0.82–1.00)
Multipara	13	13.7	8	6.1	32	18.1	15	8.5	20	9.6	0.96 (0.89–1.05)
Citizenship											
Icelandic	22	14.1	20	9.2	42	15.8	23	8.2	22	7.2	0.92 (0.86–0.98)
Foreign	0	0.0	1	16.7	3	20.0	3	11.1	9	17.0	1.09 (0.85–1.39)
Relationship status[c]											
Cohabitating	16	11.1	13	6.7	28	11.6	15	5.9	23	7.6	0.96 (0.89–1.04)
Not cohabitating	6	33.3	8	25.8	17	45.9	11	22.4	8	17.0	0.88 (0.77–0.99)
Occupational status[d]											
Employed	15	13.3	11	6.9	25	12.4	17	7.6	17	6.5	0.93 (0.86–1.01)
Student	0	0.0	3	7.3	6	14.0	3	5.5	5	8.9	1.02 (0.85–1.23)
Unemployed/on disability/homemaker	7	36.8	5	27.8	12	38.7	4	17.4	9	23.1	0.91 (0.80–1.04)
Place of residence[e]											
Urban	12	11.8	14	9.2	25	12.1	16	6.9	22	7.7	0.94 (0.87–1.01)
Rural	9	18.8	7	11.7	19	30.6	10	13.3	9	12.5	0.95 (0.86–1.06)

a: Smoking status missing for one woman.
b: OR presents the crude annual trend of continued smoking in 2001–10 where the independent variable is year (continuous variable).
c: Relationship status missing for 10.
d: Occupational status missing for 24.
e: Residence missing for 36.

Table 3 Trends in obesity (BMI ≥ 30 kg/m^2) at first antenatal weight measurement among 1329 pregnancies in Iceland 2001–10, stratified by maternal socio-demographic characteristics

Socio-demographic characteristics	2001–02 ($N = 162$)[a]		2003–04 ($N = 224$)[b]		2005–06 ($N = 280$)[c]		2007–08 ($N = 306$)[d]		2009–10 ($N = 357$)[e]		OR (95% CI)[f]
	n_{obese}	$\%_{obese}$	n_{obese}	$\%_{obese}$	n_{obese}	$\%_{obese}$	n_{obese}	$\%_{obese}$	n_{obese}	$\%_{obese}$	
Age (years)											
<25	3	6.7	3	6.3	5	10.0	8	13.3	6	8.0	1.02 (0.88–1.18)
25–34	14	16.9	23	17.3	42	23.3	38	20.3	36	16.7	1.00 (0.93–1.07)
≥35	4	11.8	11	25.6	11	22.0	12	20.3	16	23.9	1.06 (0.95–1.18)
Parity											
Nulliparous	4	6.0	8	8.6	16	15.5	18	14.0	23	15.4	1.10 (1.00–1.21)
Multipara	17	17.9	29	22.1	42	23.7	40	22.6	35	16.8	0.99 (0.92–1.05)
Citizenship											
Icelandic	20	12.8	37	17.0	58	21.9	56	20.1	56	18.4	1.04 (0.98–1.10)
Foreign	1	16.7	0	0	0	0	2	7.4	2	3.8	0.91 (0.64–1.28)
Relationship status[g]											
Cohabitating	20	13.9	33	17.1	45	18.6	50	19.5	46	15.2	1.00 (0.95–1.06)
Not cohabitating	1	5.6	4	12.9	13	35.1	7	14.3	10	21.3	1.09 (0.94–1.26)
Occupational status[h]											
Employed	16	14.2	29	18.1	43	21.3	42	18.8	43	16.5	1.01 (0.95–1.07)
Student	0	0	2	4.9	6	14.0	9	16.4	8	14.3	1.20 (1.01–1.43)
Unemployed/on disability/homemaker	3	15.8	6	33.3	7	22.6	5	21.7	7	17.9	0.96 (0.83–1.11)
Place of residence[i]											
Urban	12	11.8	20	13.2	41	19.9	34	14.7	41	14.4	1.01 (0.95–1.08)
Rural	9	18.8	17	28.3	15	24.2	24	32.0	17	23.6	1.02 (0.93–1.12)

a: BMI status missing for five women.
b: BMI status missing for six women.
c: BMI status missing for five women.
d: BMI status missing for 12 women.
e: BMI status missing for 20 women.
f: OR presents the annual trend of obesity at first antenatal weight measurement in 2001–10 where the independent variable is year (continuous variable). All OR are adjusted for gestational date of first weight measurement.
g: Relationship status missing for 10.
h: Occupational status missing for 24.
i: Residence missing for 36.

coincides with a flourishing period in the nation's economy. Following the economic collapse, there was a significant increase in the number of children born, resulting in 2009 being the largest birth cohort ever in Iceland,[28] which might have affected the demographic composition of pregnant women.

Our findings on decreased prevalence of smoking among pregnant women are in line with findings from other Nordic countries, specifically from Denmark, Norway and Sweden.[8] A recent survey among 1111 pregnant Icelandic women shows a 5% prevalence of smoking during pregnancy in 2009–10,[13] which is a slightly lower prevalence than found at the end of our study period (8.7%). However, the aforementioned study is based on questionnaire data where women with higher level of education were overrepresented. The decrease in smoking during pregnancy was confined to women with Icelandic citizenship, whereas no decrease was observed among women of non-Icelandic citizenship. Different cultural background, including language, might potentially act as a barrier in providing antenatal information about the adversities of smoking to women speaking foreign languages. The number of women of childbearing age of non-Icelandic citizenship, mainly Polish, in Iceland doubled in 2001–10.[29] Our findings might therefore motivate a tailored smoking cessation intervention specifically targeted at this group.

We did not observe an overall significant time trend in overweight or obesity in 2001–10, although the increase was significant in two subgroups, namely among nulliparous women and students. Trends in the prevalence of obesity among the general population of Icelandic women indicate a 2-fold increase over the past two decades, from approximately 10% in 1990 to 20% in 2010.[15,30] However, during the most recent years, reports from other countries have indicated that rate of growing prevalence of obesity might be slowing down.[31] Our results are in concordance with results from a population-based study in Sweden where no changes were observed in the rates of overweight or obesity between 2004 and 2008.[32] Similarly, results from a Danish study did not reveal any changes in the rates of overweight or obesity between 1997/1998 and 2004/2005.[33]

Of particular interest is the peak in prevalence of smoking and obesity among women who gave birth in 2005 and 2006. The prevalence of smoking in these 2 years was considerably higher than among women giving birth in the last two time intervals (2007/2008 and 2009/2010). This peak coincides with a boom in Iceland's economy, resulting from a rapid expansion of the country's financial sector.[17] During this expansion, the unemployment rate was at a minimum and the real wage index was constantly rising, a condition which drastically changed in the years following 2007 (figure 1c). Our results correspond with other studies that indicate better health behaviours during times of economic downturn. In a recent study of health behaviours of Icelanders, Ásgeirsdóttir *et al*.[19] found that the economic crisis in Iceland in 2008 led to a reduction in health-compromising behaviours, among them smoking and consumption of fast food, sweets and sugar-sweetened beverages. Similar results were obtained from the survey of dietary habits of Icelanders in 2010–11 where 33.6% of women reported a change in their dietary habits following the economic collapse. These changes were especially in relation to consumption of sweets, beverages and fast food where 51.3%, 46.9% and 63.2%, respectively, reported a decreased intake of these food items following the economic collapse.[30] Yet, another study indicated a slowed down weight gain following a job loss during the economic collapse in Iceland, particularly for females,[34] which further lends support to a levelling off in the prevalence of overweight and obesity among pregnant women in Iceland.

Strength of this study is the objective and prospective measurement found in maternity records of height and weight performed by midwives, which are more reliable than self-reported data. Self-reports have been shown to underestimate weight and overestimate height, resulting in an underestimation of BMI values,[35] whereas height and weight measurements conducted by trained health care practitioners have high reliability.[36] The unavailability of electronic register data on the risk factors under observation limits our study to a relatively small sample that represented an unexposed population in a study on health and birth outcomes of all women previously exposed to sexual violence and subsequently seeking help in the Rape and Trauma Service (RTS) in Iceland. Thus, none of the women in our study population had attended the RTS during the study period possibly yielding somewhat conservative smoking estimates as our previous study indicates that women attending the RTS following sexual violence have been shown to be more likely to be smokers during pregnancy. Of all births in Iceland 2001–10, 1.7% were given by the abovementioned women exposed to sexual violence[23]; a figure unlikely to have a great effect on the smoking estimates observed in this study. A second limitation pertains to the notion that women may be reluctant to disclose their smoking habits during pregnancy due to societal pressures or fear of stigmatization leading to underestimation of the prevalence of smoking. Indeed, studies have shown a discrepancy between self-reported smoking during pregnancy and smoking confirmed by cotinine measurements where the prevalence of smoking is typically underreported in self-reports.[37] It is well possible that increasing negative attitude towards smoking during pregnancy in the past years may have led to biased underestimation of the prevalence of smoking, thus resulting in a false decreasing trend of smoking during pregnancy. However, the trend of smoking among pregnant women in Iceland in 2001–10 is in line with the trend among women of childbearing age in the general population, where the rate decreased by approximately 50% during the same period.[38]

In conclusion, our results indicate that, during a period characterized by dramatic changes in the national economy, the prevalence of continued smoking decreased and the rising prevalence of obesity levelled off among pregnant women in Iceland.

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Conflicts of interest: None declared.

Key points

- Between 2001 and 2010, the annual prevalence of smoking during pregnancy decreased among Icelandic women but not among women of foreign citizenship.
- Maternal smoking and obesity peaked in 2005–06, which coincides with a flourishing period in the nation's economy.

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Paper II

PLOS ONE

RESEARCH ARTICLE

Pregnancy-Induced Hypertensive Disorders before and after a National Economic Collapse: A Population Based Cohort Study

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Abstract

Background

Data on the potential influence of macroeconomic recessions on maternal diseases during pregnancy are scarce. We aimed to assess potential change in prevalence of pregnancy-induced hypertensive disorders (preeclampsia and gestational hypertension) during the first years of the major national economic recession in Iceland, which started abruptly in October 2008.

Methods and Findings

Women whose pregnancies resulted in live singleton births in Iceland in 2005–2012 constituted the study population (N = 35,211). Data on pregnancy-induced hypertensive disorders were obtained from the Icelandic Medical Birth Register and use of antihypertensive drugs during pregnancy, including β-blockers and calcium channel blockers, from the Icelandic Medicines Register. With the pre-collapse period as reference, we used logistic regression analysis to assess change in pregnancy-induced hypertensive disorders and use of antihypertensives during the first four years after the economic collapse, adjusting for demographic and pregnancy characteristics, taking aggregate economic indicators into account. Compared with the pre-collapse period, we observed an increased prevalence of gestational hypertension in the first year following the economic collapse (2.4% vs. 3.9%; adjusted odds ratio [aOR] 1.47; 95 percent confidence interval [95%CI] 1.13–1.91) but not in the subsequent years. The association disappeared completely when we adjusted for aggregate unemployment rate (aOR 1.04; 95% CI 0.74–1.47). Similarly, there was an increase in prescription fills of β-blockers in the first year following the collapse (1.9% vs.3.1%; aOR 1.43; 95% CI 1.07–1.90), which disappeared after adjusting for aggregate unemployment rate

had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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(aOR 1.05; 95% CI 0.72–1.54). No changes were observed for preeclampsia or use of calcium channel blockers between the pre- and post-collapse periods.

Conclusions

Our data suggest a transient increased risk of gestational hypertension and use of β-blockers among pregnant women in Iceland in the first and most severe year of the national economic recession.

Introduction

Pregnancy-induced hypertensive disorders, including preeclampsia and gestational hypertension, are significant sources of maternal, foetal and neonatal morbidity [1, 2]. Antenatal psychosocial stress, such as work stress, anxiety and depression, has been found to play a role in the etiology of these hypertensive disorders [3–9]. Another potential source of psychosocial morbidity for pregnant women is a suboptimal socioeconomic situation [10–12], including macroeconomic recessions. A growing body of literature indicates that macroeconomic conditions influence population health [13, 14], including the health of pregnant women [15].

In the autumn 2008, Icelanders experienced a sudden national economic collapse. From being one of the richest nations in the world, the country suffered a major economic breakdown, affecting all inhabitants of Iceland in some way [16]. Recent studies on the health consequences of the Icelandic economic collapse suggest an increase in depressive symptoms [17, 18] and perceived psychological stress [19], as well as an immediate short-term increase in attendance to a cardiac emergency department [20], among women in particular. Furthermore, results from a recent study suggest an increase in low birth weight deliveries during the first year following the Icelandic economic collapse [21]. Low birth weight is more common in pregnancies complicated by hypertensive disorders [22].

We hypothesized that the 2008 economic collapse in Iceland represented a stressor that might have led to a rise in the incidence of pregnancy-induced hypertensive disorders and corresponding drug use among women. Leveraging the nationwide complete registries of all births and drug utilization, we therefore set out to study whether the prevalence of pregnancy-induced hypertensive disorders and use of antihypertensive drugs during pregnancy changed following the major 2008 economic collapse in Iceland. Further, we aimed to assess whether the potential changes in hypertensive disorders and drug use during pregnancy were due to the aggregate economic conditions.

Methods

Data sources and study population

The study was based on individual level data from the National Medical Birth Register and Medicines Register in Iceland, linked by personal identification numbers, as well as aggregate data on economic indicators from Statistics Iceland [23]. The Medical Birth Register is a population-based register that covers all births in Iceland since 1972. Registered information includes parental-, pregnancy-, and delivery characteristics as well as birth- and neonatal outcomes [24]. Similarly, the Medicines Register is a nationwide prescription register including information on all prescription drugs dispensed from pharmacies in Iceland since 2003 [25]. Included in the study population were women whose pregnancies had reached at least 20

weeks of gestation on September 27th 2004 and all pregnancies from that time-point, subsequently resulting in live singleton births in Iceland between November 29th 2004 throughout December 31st 2012 (N = 35,211). Pregnancy-induced hypertensive disorders are not diagnosed until after 20 gestational weeks and we therefore limited the cohort entry to this time-point in gestation. Information regarding gestational length were lacking from 20 pregnancies which were excluded from the study population.

Outcome variables

1. **Pregnancy-induced hypertensive disorders.** Medical conditions during pregnancy are registered in the Medical Birth Register according to the International Classification of Disease, 10th revision [ICD-10][26]. The primary outcomes of the present study were pregnancy-induced hypertensive disorders, including gestational hypertension and preeclampsia. Gestational hypertension [ICD-10 code O13] is defined as newly diagnosed hypertension (systolic blood pressure [SBP] ≥140 mmHg; diastolic blood pressure [DBP] ≥90 mmHg) after 20 weeks of gestation. Preeclampsia is defined as pre-existing or gestational hypertension concurring with significant proteinuria (>300 mg protein in 24 hour urine sample). In the present study, women were classified as having preeclampsia if they had been diagnosed with pre-existing hypertensive disorder with superimposed preeclampsia [ICD-10 code O11], preeclampsia [ICD-10 code O14], or eclampsia [ICD-10 code O15].
2. **Prescription fills of antihypertensive drugs.** As a secondary study outcome we used prescriptions fills for antihypertensive drugs. For the women included in the study, we extracted all prescriptions of β-blockers (Anatomical Therapeutic Chemical (ATC) code C07) and calcium channel blockers (ATC code C08), filled after 20 gestational weeks onwards. Substances belonging to abovementioned ATC drug codes are Labetalol and Nifedipine, which are two of the most commonly used drugs for treating hypertensive disorders during pregnancy [27].

Explanatory variable

The Icelandic economic collapse was a swift and sudden event, allowing us to pin down the beginning of the crisis to a distinct time point, i.e. the first week of October 2008. In our main analyses, we used calendar time to approximate the economic collapse, categorizing time into a pre-collapse period (unexposed to the economic collapse) and four separate post-collapse years (exposed, to a varying extent, to the economic recession). As pregnancy-induced hypertensive diseases do not occur before 20 weeks of gestation we used ≥20 gestational weeks as an indicator of where to locate each pregnancy with respect to exposure to the economic crisis. The aggregate economic indicators were on quarterly or yearly basis, while the timing of births was on weekly basis (not the actual date of birth). Thus, the beginning of the 4th quarter 2008 (28th of September) was used as a marker of the economic collapse as data on the economic climate showed dramatic changes between the third and fourth quarters of 2008 [23]. The pre-collapse group consisted of pregnancies with a gestational length of 20 weeks or more between September 27th 2004 and September 28th 2008. The four separate post-collapse groups were defined similarly, including all pregnancies having reached at least 20 gestational weeks during i) September 29th 2008–September 27th 2009 (post-collapse year 1), ii) September 28th 2009 –October 3rd 2010 (post-collapse year 2), iii) October 4th 2010 –October 2nd 2011 (post-collapse year 3) and iv) October 3rd 2011 –October 1st 2012 (post-collapse year 4). To further explore the associations between the outcomes of interest (gestational hypertension and β-blockers) and

the timing of the economic collapse, we divided the first post-collapse year in two 6 months periods, each including pregnancies with a gestational length of 20 weeks or more during I) September 29th 2008 –March 29th 2009 and II) March 30th 2009 –September 28th 2009.

Covariates

Information on covariates were retrieved from the Medical Birth Register, including calendar week of birth, gestational length, maternal age at delivery (continuous and grouped by <25; 25–34; ≥35 years), gravidity (primigravida; multigravida), relationship status (cohabitating with other parent; not cohabitating with other parent), maternal place of residence (urban; rural), employment status (employed; student; not working [homemaker/unemployed/on disability]), citizenship (Icelandic; foreign), diabetes mellitus (pre-existing diabetes [ICD-10 code O24.0–24.3]; gestational diabetes [ICD-10 code O24.4–24.9]), pre-existing hypertension [ICD-10 code O10] and infant's sex [28]. Gestational length was determined by ultrasound measurement before the 21st week of gestation for 99.9% of the study population. For 37 pregnancies, gestational length was based on women's self-reported last menstrual period. In order to control for seasonality, we used quarters of the calendar year.

In order to further capture if the potential influence of time on the outcomes was due to macroeconomic changes, we used aggregate economic indicators as the unit of analysis. The economic indicators tested were national unemployment rate and gross domestic product (GDP), as traditional measures of economic conditions. However, as the Icelandic collapse resulted in a debt crisis at the national and individual levels [16], we also tested the balance of accounts and rates of homes that finds it very difficult to make ends meet (i.e. to cover expenses through the pay period) or have defaults on loans or rent. The unemployment rate and GDP were on a quarterly basis while the other indicators were on a yearly basis.

Data analysis

We calculated descriptive statistics for all maternal and pregnancy-related characteristics, contrasting frequencies across exposure groups. Chi-square and one-way ANOVA were used to assess differences in the distribution of maternal and pregnancy-related characteristics.

In order to examine the impact of the economic collapse on the outcome variables, we used logistic regression analyses to calculate the crude and adjusted odds ratios (ORs) and corresponding 95% confidence intervals [CIs] for each outcome contrasting the four separate post-collapse years with the pre-collapse period. The total number of calendar weeks during the study period, beginning on September 27th 2004, was used to address potential time-trends in the aggregate explanatory variables as well as in the prevalence of the outcome variables. The final regression models were adjusted for I) maternal age, gravidity and time-trend, II) maternal age, gravidity, time-trend, diabetes, pre-existing hypertension, relationship status, place of residence, employment status, citizenship and infant sex, III) maternal age, gravidity, time-trend and aggregate economic indicators, if associated with index outcome in a supplementary analysis. We did not adjust for seasonality in our main regression models as the exposure categories were equally balanced with respect to calendar time. However, the effect of seasonality on the outcomes of interest was explored in a supplementary analysis. Similarly, adjusting for seasonality, logistic regression models were created in order to further explore the odds ratio of gestational hypertension and prescription fills for β-blockers in months 1–6 and months 7–12 following the economic collapse, compared with the pre-collapse period.

Further, in a supplementary analysis we used logistic regression analyses to estimate the crude and adjusted ORs and corresponding 95% CIs to assess the association between each aggregate economic indicator, i.e. unemployment rate, GDP, balance of accounts, rates of

either finding it very difficult making ends meet or having defaults on loans or rent, and the study outcomes irrespective of the defined exposure categories. We adjusted for all maternal and pregnancy-related covariates separately to determine which of the covariates affected the measured association. We then constructed three different regression models adjusting for i) time-trend, ii) time-trend, maternal age and gravidity and iii) time-trend, maternal age, gravidity, diabetes, pre-existing hypertension [ICD-10 code O10], relationship status, place of residence, employment status, citizenship and infant sex.

All the data analyses were performed using IBM SPSS Statistic 20.

The study was approved by the Icelandic National Bioethics committee (VSNb2013010002/03.07), the Data Protection Authority (2012121499HGK/—) and the Directorate of Health (1301064/5.6.1/gkg). An informed consent from women in the study population was not obtained as all personal information was anonymized and de-identified prior to analysis.

Results

Table 1 shows the demographic and pregnancy-related characteristics of women across exposure categories. After the economic collapse, pregnant women in Iceland were slightly older, less likely to be employed, less likely to be of Icelandic citizenship and less likely to cohabit with the other parent, as compared with pregnant women before the collapse (Table 1).

The overall prevalence of pregnancy-induced hypertensive disorders remained stable during the study period. However, when gestational hypertension and preeclampsia were examined separately, an increase was observed for gestational hypertension from 2.1% (74 of 4,166) to 2.6% (114 of 4,383), while the prevalence of preeclampsia decreased from 3.8% (159 of 4,166) to 3.2% (139 of 4,383) (Fig 1). During the whole study period, 0.3% (104/35,211) of women were diagnosed with both gestational hypertension and preeclampsia, a proportion which was equal across exposure categories (Table 1). Fig 2 shows an increase over time in the prevalence of filled prescriptions for antihypertensive drugs among the study population.

After adjusting for time-trend and other available covariates, we observed increased odds of pregnancy-induced hypertensive disorders (aOR = 1.03 [1.00–1.06]), gestational hypertension (aOR = 1.09, 95% CI [1.05–1.13]) and prescription fills for β-blockers (aOR = 1.08, 95% CI [1.04–1.13]) with each percentage point increase in unemployment (S1 Appendix). Unemployment rate was not associated with preeclampsia or prescription fills for calcium channel blockers. No associations were observed between the other aggregate economic indicators and outcomes of interest (S1 Appendix).

Adjusting for maternal age, gravidity and time-trend, we observed a statistically significant increase in gestational hypertension during post-collapse year 1 ($aOR_{year\ 1}$ = 1.47, 95% CI [1.13–1.91]), as compared with the pre-collapse period (Table 2). Adding other maternal- and pregnancy related covariates did not affect this association, while it disappeared (aOR_{year1} = 1.04, 95% CI [0.74–1.47]) when adding aggregate unemployment rate to the model. We found no association between the economic collapse and gestational hypertension during the subsequent post-collapse years or with overall pregnancy-induced hypertensive disorders or preeclampsia during any of the post-collapse years (Table 2).

The pattern of prescription fills of β-blockers across exposure categories was similar to what was observed for gestational hypertension (Table 3). The odds of filling a prescription for β-blockers were increased by 43% only during post-collapse year 1 ($aOR_{year\ 1}$ = 1.43, 95% CI [1.07–1.90]); an increase which disappeared when adjusting for aggregate unemployment rate (Table 3).

Furthermore, the economic collapse did not seem to impact on the prevalence of prescription fills for calcium channel blockers beyond the observed time trend of increase; after adjustment

Table 1. Maternal background characteristics of live singleton births in the study population in Iceland between November 29th 2004 and December 31st 2012.

Maternal & obstetric characteristics	Pre-collapse years[a] N = 17,447		Post-collapse year 1[b] N = 4,990		Post-collapse year 2[c] N = 4,664		Post-collapse year 3[d] N = 4,295		Post-collapse year 4[e] N = 3,815		*p*-value
Mean maternal age [SD]	28.92 [5.50]		29.12 [5.45]		29.40 [5.47]		29.27 [5.45]		29.45 [5.43]		<0.001*
	Births, *n*	**Births, %**	**Births, *n***	**Births, %**	**Births, *n***	**Births, %**	**Births, *n***	**Births, %**	**Births, *n***	**Births, %**	
Maternal age (years)											
<25	3,915	22.4	1,021	20.5	904	19.4	855	19.9	733	19.2	<0.001**
25–34	10,600	60.8	3,111	62.3	2,861	61.3	2,664	62.0	2,364	62.0	
≥35	2,932	16.8	858	17.2	899	19.3	776	18.1	718	18.8	
Gravidity											
Primigravida	7,075	40.6	2,021	40.5	1,840	39.5	1,662	38.7	1,523	39.9	0.184
Multigravida	10,372	59.4	2,969	59.5	2,824	60.5	2,633	61.3	2,292	60.1	
Relationship status											
Cohabitating with other parent	14,872	85.2	4,192	84.0	3,893	83.5	3,478	81.0	3,080	80.7	0.006
Not cohabitating with other parent	2,442	14.0	744	14.9	721	15.5	645	15.0	575	15.1	
Missing	133	0.8	54	1.1	50	1.1	172	4.0	160	4.2	
Maternal place of residence											
Capital area	11,244	64.4	3,328	66.7	3,054	65.5	2,810	65.4	2,489	65.2	0.510
Rural area	5,936	34.0	1,653	33.1	1,594	34.2	1,464	34.1	1,311	34.4	
Missing	267	1.5	9	0.2	16	0.3	21	0.5	15	0.4	
Maternal employment status											
Employed	13,123	75.2	3,665	73.4	3,312	71.0	3,027	70.5	2,689	70.5	<0.001
Student	2,841	16.3	836	16.8	834	17.9	758	17.6	717	18.8	
Homemaker/on disability/ unemployed	1,438	8.2	489	9.8	518	11.1	509	11.9	406	10.6	
Missing	45	0.3	0	0	0	0	1	<0.001	3	0.1	
Maternal citizenship											
Icelandic	15,886	91.1	4,332	86.8	4,105	88.0	3,769	87.8	3,336	87.4	<0.001
Foreign	1,561	8.9	658	13.2	559	12.0	526	12.2	479	12.6	
Infant's sex											
Boy	8,975	51.4	2,531	50.7	2,423	52.0	2,258	52.6	1,954	51.2	0.447
Girl	8,467	48.5	2,459	49.3	2,240	48.0	2,037	47.4	1,861	48.8	
Missing	5	<0.001	0		1	<0.001	0		0		
Diabetes											
Pre-existing diabetes	63	0.4	22	0.4	19	0.4	17	0.4	21	0.6	0.593
Gestational diabetes	485	2.8	196	3.9	188	4.0	195	4.5	161	4.2	<0.001
Hypertensive disorders of pregnancy											
Pre-existing hypertension	212	1.2	69	1.4	56	1.2	47	1.1	46	1.2	<0.489
Pregnancy-induced hypertension***	1,003	5.7	318	6.4	270	5.8	261	6.1	228	6.0	0.540
Gestational hypertension	422	2.4	193	3.9	144	3.1	133	3.1	117	3.1	<0.001
Preeclampsia	629	3.6	141	2.8	141	3.0	138	3.2	126	3.3	0.048
Cardiovascular drugs											
β-blockers (C07)	336	1.9	156	3.1	115	2.5	92	2.1	106	2.8	<0.001

(*Continued*)

Table 1. (*Continued*)

Maternal & obstetric characteristics	Pre-collapse years[a] N = 17,447		Post-collapse year 1[b] N = 4,990		Post-collapse year 2[c] N = 4,664		Post-collapse year 3[d] N = 4,295		Post-collapse year 4[e] N = 3,815		*p*-value
Calcium channel blockers (C08)	71	0.4	34	0.7	28	0.6	40	0.9	60	1.6	<0.001

*Based on one-way ANOVA.

**Based on chi-square test.

*** Of those diagnosed with pregnancy-induced hypertensive disorder 48; 16; 15; 10; 15 were both diagnosed with gestational hypertension and preeclampsia

Included in the collapse groups are women with singleton pregnancies with gestational length of 20 weeks or more during [a]September 27th 2004–September 28th 2008, [b]September 29th 2008 –September 27th 2009, [c]September 28th 2009 –October 3rd 2010, [d]October 4th 2010 –October 2nd 2011, [e]October 3rd 2011 –October 1st 2012.

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for maternal age, gravidity and time-trend, the positive crude increase in calcium channel blockers disappeared and even reversed in post-collapse year 2 (Table 2). Further adjustment for seasonality did not significantly change the association between the economic collapse and the outcomes of interest (S2 Appendix and S3 Appendix). When exploring the odds ratios of gestational hypertension and prescription fills for β-blockers in finer time-period during the first year following the economic collapse, we observed similar point estimates for months 1–6 and months 7–12 (gestational hypertension: $aOR_{months1-6}$ = 1.36, 95% CI [1.00–1.85]; $aOR_{months7-12}$ = 1.44, 95% CI [1.05–1.97] and β-blockers: $aOR_{months1-6}$ = 1.37, 95% CI [0.98–1.92]; $aOR_{months7-12}$ = 1.31, 95% CI [0.92–1.85]) (S4 Appendix).

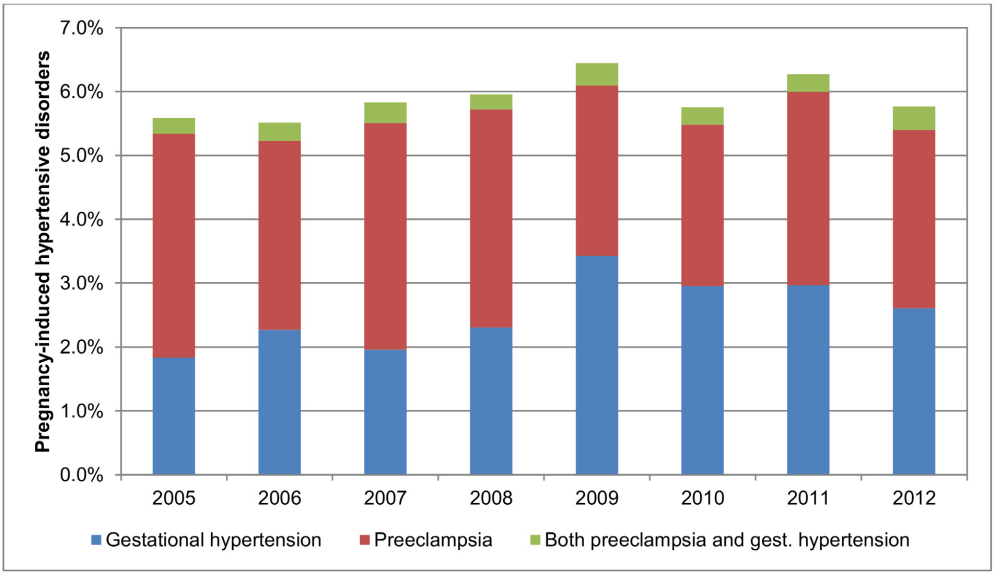

Fig 1. Prevalence of overall pregnancy-induced hypertensive disorders, gestational hypertension and preeclampsia in Iceland, 2005–2012.

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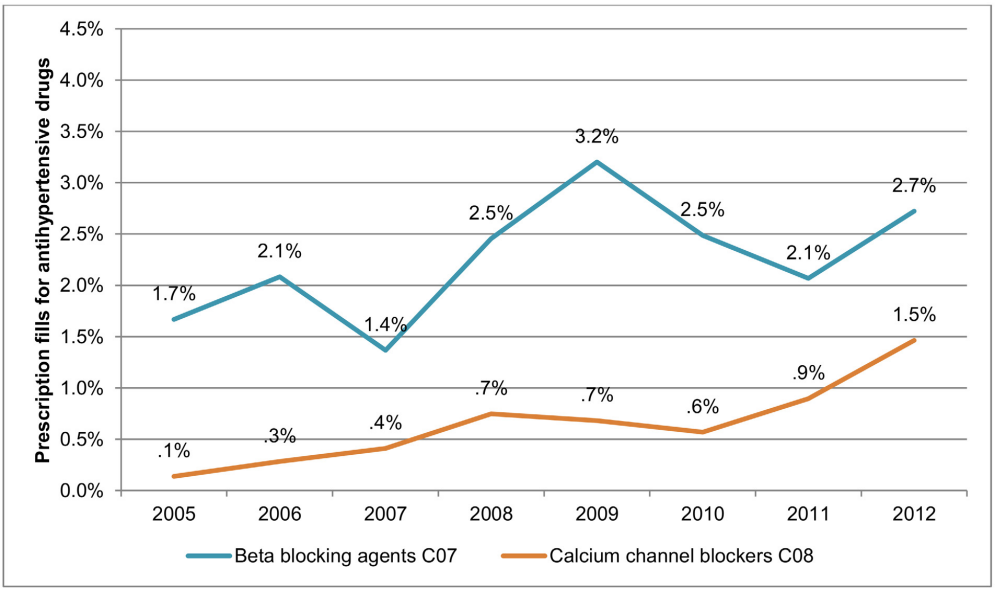

Fig 2. Prevalence of prescription fills for β-blockers and calcium channel blockers among pregnant women in Iceland 2005–2012, after gestational week 20.

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Discussion

In this nationwide study of women with live singleton births in Iceland during a time of severe economic fluctuation, we observed a transient increase in the risk of gestational hypertension and prescription fills for β-blockers during the first year following the economic collapse, but no such increase was detected for preeclampsia. In parallel with the development of the macro-economic conditions, this initial increase in gestational hypertension seemed to level off with years passing from the severe economic collapse. Indeed, our findings suggest that the increase risk of gestational hypertension at the first year of the crisis may be explained by changing aggregate unemployment rates, reflecting the severity of the economic crisis at this time point.

The dramatic economic collapse in Iceland in 2008 affected the whole Icelandic population in one way or another and recent studies suggest considerable influence on mental health [17–19] and reproductive outcomes [21]. Our findings on increased risk of gestational hypertension and corresponding drug use after the economic collapse add to this litterature and are in line with the findings of previous studies indicating an association between psychosocial stress and pregnancy-induced hypertensive disorders [3–9]. Most [3–9], but not all studies [29], have found high levels of perceived stress, work-related stress, depression and anxiety to be associated with pregnancy-induced hypertensive disorders. A large population based study by László et al. found severe psychosocial stress to be associated with a modest increase in preeclampsia [7], while other hypertensive diseases of pregnancy were not reported. We did not observe any association between the economic collapse and risk of preeclampsia.

The pathways through which stress could affect pregnancy-induced hypertensive disorders are not fully understood. Stress can influence health behaviours of affected individuals to the worse, resulting in higher levels of smoking, less exercise and poorer diet [30]. In addition,

Table 2. The odds ratios [OR] and 95% confidence intervals [CI] of (A) overall pregnancy-induced hypertensive disorders, (B) gestational hypertension and (C) preeclampsia in each of the four post-collapse years following the economic collapse in Iceland compared with pre-collapse period.

Regression models	Pre-collapse period[a] OR [95% CI]	Post-collapse year 1[b] OR [95% CI]	Post-collapse year 2[c] OR [95% CI]	Post-collapse year 3[d] OR [95% CI]	Post-collapse year 4[e] OR [95% CI]
(A) Pregnancy-induced hypertensive disorders					
Crude	1.00 [ref.]	1.12 [0.98–1.27]	1.01 [0.88–1.16]	1.06 [0.92–1.22]	1.04 [0.90–1.21]
Model I*	1.00 [ref.]	1.13 [0.94–1.37]	1.03 [0.82–1.30]	1.11 [0.84–1.47]	1.08 [0.78–1.50]
Model II**	1.00 [ref.]	1.13 [0.93–1.36]	1.02 [0.81–1.29]	1.10 [0.83–1.46]	1.06 [0.76–1.48]
Model III***	1.00 [ref.]	0.96 [0.74–1.23]	0.86 [0.65–1.15]	0.96 [0.70–1.31]	0.99 [0.70–1.38]
(B) Gestational hypertension					
Crude	1.00 [ref.]	1.62 [1.37–1.93]	1.29 [1.06–1.56]	1.29 [1.06–1.57]	1.28 [1.04–1.57]
Model I*	1.00 [ref.]	1.47 [1.13–1.91]	1.11 [0.79–1.55]	1.09 [0.72–1.63]	1.02 [0.63–1.64]
Model II**	1.00 [ref.]	1.44 [1.11–1.87]	1.08 [0.77–1.52]	1.05 [0.69–1.58]	0.99 [0.61–1.61]
Model III***	1.00 [ref.]	1.04 [0.74–1.47]	0.78 [0.52–1.17]	0.81 [0.52–1.26]	0.85 [0.52–1.38]
(C) Preeclampsia					
Crude	1.00 [ref.]	0.78 [0.65–0.94]	0.83 [0.69–1.00]	0.89 [0.74–1.07]	0.91 [0.75–1.11]
Model I*	1.00 [ref.]	0.86 [0.67–1.11]	0.97 [0.72–1.31]	1.09 [0.76–1.56]	1.15 [0.76–1.74]
Model II**	1.00 [ref.]	0.86 [0.66–1.10]	0.97 [0.71–1.31]	1.11 [0.77–1.59]	1.12 [0.73–1.72]
Model III***	1.00 [ref.]	0.88 [0.62–1.23]	0.99 [0.67–1.45]	1.11 [0.73–1.67]	1.16 [0.75–1.79]

* Adjusted for maternal age, gravidity and time in weeks [time-trend].

** Simultaneously adjusted for maternal age, gravidity, time in weeks, sex, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship.

***Adjusted for maternal age, gravidity, time in weeks and aggregate unemployment rate.

Included in the collapse groups are women with singleton pregnancies with gestational length of 20 weeks or more during [a]September 27th 2004–September 28th 2008, [b]September 29th 2008 –September 27th 2009, [c]September 28th 2009 –October 3rd 2010, [d]October 4th 2010 –October 2nd 2011, [e]October 3rd 2011 –October 1st 2012.

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physiology of individuals experiencing stress may also be affected [12]. Over-activation of the hypothalamic-pituitary-adrenal axis and the autonomous nervous system at times of stress leads to a corresponding rise in the concentrations of cortisol and nor-epinephrine, which act upon different organ systems and may cause pathophysiological changes, including hypertension and cardiovascular disease in non-pregnant populations [12]. Such pathophysiologic reactions, in combination with altered behaviours of pregnant women, may offer explanation to our findings.

It is unclear why we observed an association between the economic collapse and gestational hypertension but not to preeclampsia, yet two explanations seem most plausible. Firstly, if viewed as separate diseases with different aetiologies, it is possible that mechanisms underlying gestational hypertension are more sensitive to stress compared with mechanisms underlying preeclampsia. Secondly, from the perspective that the gestational hypertension is merely a milder form of preeclampsia, it is possible that the economic collapse was not a stressor of sufficient magnitude to cause the more severe form of the disorder.

The β-blocking agent Labetalol is the first line of treatment of pregnancy-induced hypertensive disorders in Iceland. In most cases the calcium channel blocker, Nifedipine, is prescribed if treatment with Labetalol has proven insufficient or is not tolerated by the pregnant woman. However, during the last 10 years, Nifedipine has increasingly been used for treatment of

Table 3. The odds ratios [OR] and 95% confidence intervals [CI] of (A) prescription fills for β-blockers and (B) prescription fills for calcium channel blockers in pregnancies during each of the four post-collapse years following the economic collapse in Iceland compared with pre-collapse period.

Regression models	Pre-collapse period[a] OR [95% CI]	Post-collapse year 1[b] OR [95% CI]	Post-collapse year 2[c] OR [95% CI]	Post-collapse year 3[d] OR [95% CI]	Post-collapse year 4[e] OR [95% CI]
(A) β-blockers (C07)					
Crude	1.00 [ref.]	1.64 [1.36–1.99]	1.29 [1.04–1.60]	1.12 [0.88–1.41]	1.46 [1.17–1.82]
Model I*	1.00 [ref.]	1.43 [1.07–1.90]	1.05 [0.72–1.52]	0.87 [0.55–1.37]	1.06 [0.62–1.80]
Model II**	1.00 [ref.]	1.49 [1.11–2.00]	1.12 [0.76–1.64]	0.91 [0.56–1.46]	1.10 [0.64–1.89]
Model III***	1.00 [ref]	1.05 [0.72–1.54]	0.77 [0.49–1.20]	0.67 [0.41–1.10]	0.91 [0.53–1.55]
(B) Calcium channel blockers					
Crude	1.00 [ref.]	1.68 [1.11–2.53]	1.48 [0.95–2.29]	2.30 [1.56–3.39]	3.91 [2.77–5.52]
Model I*	1.00 [ref.]	0.67 [0.38–1.18]	0.38 [0.18–0.81]	0.40 [0.16–0.97]	0.45 [0.16–1.31]
Model II**	1.00 [ref.]	0.62 [0.35–1.11]	0.36 [0.17–0.76]	0.32 [0.13–0.79]	0.39 [0.13–1.14]
Model III***	1.00 [ref.]	1.07 [0.49–2.31]	0.63 [0.25–1.62]	0.60 [0.21–1.67]	0.59 [0.19–1.81]

* Adjusted for maternal age, gravidity and time in weeks [time-trend].

** Simultaneously adjusted for maternal age, gravidity, time in weeks, sex, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship.

***Adjusted for maternal age, gravidity, time in weeks and aggregate unemployment rate.

Included in the collapse groups are women with singleton pregnancies with gestational length of 20 weeks or more during [a]September 27th 2004–September 28th 2008, [b]September 29th 2008 –September 27th 2009, [c]September 28th 2009 –October 3rd 2010, [d]October 4th 2010 –October 2nd 2011, [e]October 3rd 2011 –October 1st 2012

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contractions during pregnancy, which might explain the time-trend observed for calcium channel blockers in our study.

The available data in our study are not informative on potential underlying mechanisms although they suggest that the influence of this societal stressor on pregnancy-induced hypertensive disorders was rapid and transient, although further exploitation of the time during the first year following the collapse did not reveal much difference of the effect between women who were pregnant in the first and second half-year after the collapse. The observed increase in gestational hypertension and in prescription fills for β-blockers in the first year following the economic collapse disappeared entirely when we adjusted for the aggregate unemployment level. This finding is supported by a line of studies linking pregnancy-induced hypertensive disorders, particularly preeclampsia, to socioeconomic difficulties [31–35]. To our knowledge, our study is the first to examine the effect of a major macroeconomic downturn on pregnancy-induced hypertensive disorders. Yet, there are some studies [14, 36–38], although not all [39–41], that have provided evidence of increased cardiovascular morbidity and mortality in the general population during times when the economy is bad. Based on self-reports from a nationally representative cohort of approximately 4000 Icelanders from the Health and Well-being study, Asgeirsdottir et al. reported a modest increase in self-reported hypertension in the first year following the economic collapse in 2008 among men, but not among women [42]. However, it is indeed possible that pregnant women are particularly vulnerable to the socioeconomic adversities brought about by a national economic crisis.

Study strengths and limitations

This study leverages the National Medical Birth Register and Medicines Register in Iceland to accomplish a population based cohort study of all pregnancies resulting in live singleton births

in Iceland during eight years of follow-up. These registries are a rich source of information regarding health and drug use of pregnant women and their offspring, enabling collection of data independent of the exposure categories, i.e. timing of the economic collapse. The detailed information in the Medical Birth Register allowed us to account for potential confounding factors. In order to enhance internal validity of the study, we restricted the study population to singleton pregnancies as previous studies indicate higher risk of hypertensive disorders in multiple pregnancies. Furthermore, we adjusted for potential time-trend in the study outcomes in the statistical analyses. Thus, the observed increase in gestational hypertension and prescription fills for β-blockers is unlikely to be explained by secular trends in the detection rate of the diseases or prescribing practices among health care professionals in Iceland.

A limitation of this study is the lack of accessible data on smoking, body mass index and other behavioral factors that might possibly influence the observed increase in gestational hypertension. Many of these behavioral risk factors are strongly associated with pregnancy-induced hypertensive disorders, although some in opposite direction [43]. A sudden decrease in maternal smoking or increase in overweight or obesity among women of childbearing age, could theoretically have contributed to the increase in the prevalence of gestational hypertension among women who were pregnant in the first year following the economic collapse. However, in a recent study on the prevalence of smoking, overweight and obesity among pregnant women in Iceland between 2001 and 2010, a reduction in maternal smoking was observed whereas the mean body mass index of pregnant women remained relatively stable [44]. The same decreasing trend in smoking has been reported among the general population following the economic collapse in Iceland [45, 46]. Loss of resources may lead to worsened nutrition or decreased attention to personal health [47]. In recent studies of health behaviors of Icelanders following the economic collapse, a decrease in health-compromising behaviors, such as smoking, consumption of fast food, sugar-sweetened beverages, sweets or alcohol, was reported. Some health-promoting factors were found to increase after the collapse, such as consumption of fish oil and getting enough sleep, while the intake of fruits and vegetables decreased [45, 48]. Thus, we cannot rule out that a sudden nutritional deterioration or an altered risk behavior may have contributed to the observed increase in gestational hypertension. A second limitation pertains to the fact that only pregnancies resulting in live births were included in the study. Women with hypertensive disorders of pregnancy have higher rates of stillbirths than women with normal blood pressure [49]. Therefore, the observed increase in gestational hypertension in the first year following the economic collapse might have led to an increase in stillbirths, which potentially could have resulted in an underestimation of the observed effect. However, the stillbirth rate in Iceland is very low, on average 3.5 per 1000 births during the study period [24]. A rate of this magnitude is unlikely to significantly impact the observed effect estimates. Thirdly, we cannot rule out potential misclassification of the hypertensive outcomes. It is possible that women with preeclampsia were temporarily misclassified as having gestational hypertension, explaining the observed increase in the first year following the economic collapse. However, such misclassification is unlikely as preeclampsia is a severe condition that poses both mother and fetus at high risk, requiring high intensity maternal care. Moreover, it is unlikely that such misclassification would be limited only to the first year following the collapse. Fourthly, as this is a quasi-experimental design we are unable to control for other potential factors that might have been occurring at the same time as the economic collapse, affecting the outcomes of interest. However, the collapse of the financial system in Iceland was by far the most notable event occurring at that time and other important changes that may have occurred in Iceland around that time are likely to be consequences of the collapse. Lastly, our study is based on an entire nation exposed to a specific economic collapse. All economic fluctuations have their own characteristics, the distinct features of the collapse in Iceland included

currency- and household debt crisis. Thus, these findings cannot be readily generalized to other populations of pregnant women undergoing economic recessions.

Conclusions

In summary, the results suggest a transient increase in gestational hypertension and use of β-blockers among pregnant women in Iceland in the first year following the national economic collapse. The severity of the aggregate economic climate at that time with a gradual yet slow recovery during the following years is a likely explanation for the observed pattern.

Supporting Information

S1 Appendix. The association between aggregate macroeconomic indicators in Iceland and (A) overall pregnancy-induced hypertensive disorders, (B) gestational hypertension, (C) pre-eclampsia, (D) prescription fills for β-blockers, (E) prescription fills for calcium channel blockers, among the women in the study population giving birth to live born singletons between November 29th 2004 and December 31st 2012.
(DOCX)

S2 Appendix. The odds ratios [OR] and 95% confidence intervals [CI] of (A) overall pregnancy-induced hypertensive disorders, (B) gestational hypertension and (C) preeclampsia in each of the four post-collapse years following the economic collapse in Iceland compared with pre-collapse period, adjusted for seasonality.
(DOCX)

S3 Appendix. The odds ratios [OR] and 95% confidence intervals [CI] of (A) prescription fills for β-blockers and (B) prescription fills for calcium channel blockers in pregnancies during each of the four post-collapse years following the economic collapse in Iceland compared with pre-collapse period, adjusted for seasonality.
(DOCX)

S4 Appendix. The odds ratios [OR] and 95% confidence intervals [CI] of (A) gestational hypertension and (B) β-blockers in the first and second half year following the economic collapse in Iceland compared with pre-collapse period
(DOCX)

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Author Contributions

Conceived and designed the experiments: VHE UAV TLA AH SHL RIB SC HZ. Analyzed the data: VHE UAV SHL HZ. Wrote the paper: VHE UAV TLA AH SHL RIB SC HZ.

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S1 Appendix. The association between aggregate macroeconomic indicators in Iceland and (A) overall pregnancy-induced hypertensive disorders, (B) gestational hypertension, (C) preeclampsia, (D) prescription fills for β-blockers, (E) prescription fills for calcium channel blockers, among the women in the study population giving birth to live born singletons between November 29th 2004 and December 31st 2012

	Regression models			
	Crude	**Model I***	**Model II****	**Model III*****
	OR [95% CI]	**OR [95% CI]**	**OR [95% CI]**	**OR [95% CI]**
(A) Pregnancy-induced hypertensive disorders				
Aggregate unemployment (%)[α]	1.018 [0.999-1.037]	1.025 [0.997-1.053]	1.029 [1.001-1.057]	1.029 [1.001-1.058]
Gross domestic product (milliard ISK) [α]	1.000 [0.999-1.001]	1.000 [0.997-1.002]	0.999 [0.996-1.002]	0.999 [0.996-1.002]
Balance of account (milliard ISK) [β]	1.000 [1.000-1.001]	1.000 [0.999-1.001]	1.000 [0.999-1.001]	1.000 [0.999-1.001]
Very difficult making ends meet (%)[β]	1.004 [0.990-1.018]	0.997 [0.974-1.021]	1.000 [0.977-1.024]	0.999 [0.987-1.012]
Defaults on loans or rent (%)[β]	1.003 [0.993-1.013]	1.000 [0.985-1.016]	1.002 [0.987-1.018]	1.003 [0.987-1.018]
(A) Gestational hypertension				
Aggregate unemployment (%)[α]	1.082 [1.053-1.111]	1.085 [1.045-1.126]	1.089 [1.049-1.130]	1.088 [1.047-1.129]
Gross domestic product (milliard ISK) [α]	1.002 [1.001-1.003]	0.999 [0.996-1.003]	0.999 [0.995-1.003]	0.999 [0.995-1.003]
Balance of account (milliard ISK) [β]	1.001 [1.000-1.002]	1.000 [0.999-1.001]	1.000 [0.999-1.001]	1.000 [0.999-1.001]

Very difficult making ends meet (%)[β]	1.036 [1.016-1.056]	1.012 [0.979-1.046]	1.014 [0.981-1.048]	1.012 [0.979-1.046]
Defaults on loans or rent (%)[β]	1.026 [1.012-1.041]	1.010 [0.989-1.032]	1.012 [0.990-1.034]	1.011 [0.989-1.033]
(B) Preeclampsia				
Aggregate unemployment (%)[α]	0.964 [0.941-0.989]	0.969 [0.934-1.005]	0.972 [0.937-1.009]	0.973 [0.937-1.010]
Gross domestic product (milliard ISK) [α]	0.999 [0.998-1.000]	0.999 [0.996-1.003]	0.999 [0.995-1.002]	0.999 [0.995-1.002]
Balance of account (milliard ISK) [β]	0.999 [0.999-1.000]	1.000 [0.999-1.001]	1.000 [0.999-1.001]	1.000 [0.999-1.001]
Very difficult making ends meet (%)[β]	0.976 [0.958-0.994]	0.982 [0.951-1.013]	0.985 [0.955-1.017]	0.987 [0.956-1.019]
Defaults on loans or rent (%)[β]	0.984 [0.971-0.997]	0.991 [0.972-1.011]	0.993 [0.974-1.013]	0.994 [0.975-1.015]
C) β-blockers				
Aggregate unemployment (%)[α]	1.077 [1.045-1.109]	1.070 [1.026-1.115]	1.072 [1.028-1.118]	1.083 [1.038-1.131]
Gross domestic product (milliard ISK) [α]	1.003 [1.001-1.004]	1.002 [0.998-1.006]	1.002 [0.998-1.006]	1.002 [0.998-1.006]
Balance of account (milliard ISK) [β]	1.000 [0.999-1.001]	0.999 [0.998-1.000]	0.999 [0.998-1.000]	0.999 [0.998-1.000]
Very difficult making ends meet (%)[β]	1.025 [1.003-1.048]	0.977 [0.941-1.014]	0.978 [0.942-1.016]	0.985 [0.948-1.024]
Defaults on loans or rent (%)[β]	1.015 [0.999-1.031]	0.982 [0.958-1.006]	0.983 [0.959-1.007]	0.988 [0.963-1.013]
D) Calcium channel blockers				
Aggregate unemployment (%)[α]	1.092 [1.034-1.153]	0.892 [0.825-0.963]	0.892 [0.826-0.964]	0.898 [0.830-0.973]
Gross domestic product (milliard ISK) [α]	1.012 [1.009-1.015]	1.011 [1.004-1.019]	1.011 [1.004-1.019]	1.012 [1.004-1.020]
Balance of account (milliard ISK) [β]	1.003 [1.001-1.005]	0.997 [0.995-0.999]	0.997 [0.995-0.999]	0.997 [0.995-0.999]

Very difficult making ends meet (%)[β]	1.096 [1.054-1.140]	0.881 [0.819-0.948]	0.881 [0.819-0.948]	0.878 [0.814-0.947]
Defaults on loans or rent (%)[β]	1.063 [1.032-1.095]	0.917 [0.875-0.962]	0.917 [0.875-0.962]	0.915 [0.872-0.961]

*Adjusted for time in weeks (time-trend).

** Adjusted for maternal age, gravidity and time in weeks [time-trend].

*** Simultaneously adjusted for maternal age, gravidity, time in weeks, gender, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship.

[α] On Quarterly basis

[β] On yearly basis

S2 Appendix. The odds ratios [OR] and 95% confidence intervals [CI] of (A) overall pregnancy-induced hypertensive disorders, (B) gestational hypertension and (C) preeclampsia in each of the four post-collapse years following the economic collapse in Iceland compared with pre-collapse period, adjusted for seasonality.

Regression models	Pre-collapse period[a]	Post-collapse year 1[b]	Post-collapse year 2[c]	Post-collapse year 3[d]	Post-collapse year 4[e]
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
(A) Pregnancy-induced hypertensive disorders					
Crude	1.00 [ref.]	1.12 [0.98-1.27]	1.01 [0.88-1.16]	1.06 [0.92-1.22]	1.04 [0.90-1.21]
Model I*	1.00 [ref.]	1.13 [0.94-1.36]	1.03 [0.81-1.30]	1.11 [0.83-1.47]	1.09 [0.78-1.52]
Model II**	1.00 [ref.]	1.12 [0.93-1.36]	1.02 [0.80-1.29]	1.10 [0.82-1.47]	1.06 [0.76-1.49]
Model III***	1.00 [ref.]	1.11 [0.83-1.49]	1.02 [0.74-1.40]	1.10 [0.79-1.53]	1.09 [0.77-1.53]
(B) Gestational hypertension					
Crude	1.00 [ref.]	1.62 [1.37-1.93]	1.29 [1.06-1.56]	1.29 [1.06-1.57]	1.28 [1.04-1.57]
Model I*	1.00 [ref.]	1.47 [1.13-1.91]	1.11 [0.79-1.57]	1.09 [0.72-1.65]	1.04 [0.64-1.70]
Model II**	1.00 [ref.]	1.44 [1.10-1.87]	1.08 [0.77-1.52]	1.05 [0.69-1.59]	1.01 [0.62-1.65]
Model III***	1.00 [ref.]	1.12 [0.76-1.65]	0.85 [0.55-1.32]	0.90 [0.57-1.41]	0.95 [0.59-1.56]
(C) Preeclampsia					
Crude	1.00 [ref.]	0.78 [0.65-0.94]	0.83 [0.69-1.00]	0.89 [0.74-1.07]	0.91 [0.75-1.11]

Model I*	1.00 [ref.]	0.86 [0.67-1.11]	0.97 [0.71-1.31]	1.09 [0.76-1.57]	1.16 [0.76-1.77]
Model II**	1.00 [ref.]	0.85 [0.66-1.11]	0.97 [0.71-1.32]	1.11 [0.77-1.61]	1.13 [0.74-1.75]
Model III***	1.00 [ref.]	1.10 [0.73-1.64]	1.24 [0.80-1.93]	1.32 [0.85-2.06]	1.29 [0.82-2.02]

* Adjusted for maternal age, gravidity, time in weeks [time-trend] and seasonality.

** Simultaneously adjusted for maternal age, gravidity, time in weeks, seasonality, sex, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship.

***Adjusted for maternal age, gravidity, time in weeks, seasonality and aggregate unemployment rate.

Included in the collapse groups are women with singleton pregnancies with gestational length of 20 weeks or more during [a]September 27th 2004 - September 28th 2008, [b]September 29th 2008 – September 27th 2009, [c]September 28th 2009 – October 3rd 2010, [d]October 4th 2010 – October 2nd 2011, [e]October 3rd 2011 – October 1st 2012.

S3 Appendix. The odds ratios [OR] and 95% confidence intervals [CI] of (A) prescription fills for β-blockers and (B) prescription fills for calcium channel blockers in pregnancies during each of the four post-collapse years following the economic collapse in Iceland compared with pre-collapse period, adjusted for seasonality.

Regression models	Pre-collapse period[a]	Post-collapse year 1[b]	Post-collapse year 2[c]	Post-collapse year 3[d]	Post-collapse year 4[e]
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
(A) β-blockers (C07)					
Crude	1.00 [ref.]	1.64 [1.36-1.99]	1.29 [1.04-1.60]	1.12 [0.88-1.41]	1.46 [1.17-1.82]
Model I*	1.00 [ref.]	1.41 [1.05-1.89]	1.03 [0.70-1.51]	0.85 [0.53-1.36]	1.04 [0.60-1.79]
Model II**	1.00 [ref.]	1.46 [1.08-1.97]	1.10 [0.74-1.62]	0.88 [0.54-1.43]	1.07 [0.61-1.86]
Model III***	1.00 [ref]	1.09 [0.71-1.69]	0.80 [0.49-1.31]	0.71 [0.42-1.19]	0.96 [0.55-1.65]
(B) Calcium channel blockers					
Crude	1.00 [ref.]	1.68 [1.11-2.53]	1.48 [0.95-2.29]	2.30 [1.56-3.39]	3.91 [2.77-5.52]
Model I*	1.00 [ref.]	0.66 [0.37-1.19]	0.38 [0.17-0.82]	0.38 [0.15-0.98]	0.42 [0.14-1.29]
Model II**	1.00 [ref.]	0.64 [0.37-1.10]	0.42 [0.21-0.86]	0.41 [0.17-0.97]	0.50 [0.18-1.35]
Model III***	1.00 [ref.]	1.23 [0.47-3.21]	0.70 [0.23-2.10]	0.60 [0.20-1.86]	0.52 [0.16-1.70]

* Adjusted for maternal age, gravidity, time in weeks [time-trend] and seasonality.

** Simultaneously adjusted for maternal age, gravidity, time in weeks,seasonality, sex, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship.

***Adjusted for maternal age, gravidity, time in weeks, seasonality and aggregate unemployment rate.

Included in the collapse groups are women with singleton pregnancies with gestational length of 20 weeks or more during [a]September 27th 2004 - September 28th 2008, [b]September 29th 2008 – September 27th 2009, [c]September 28th 2009 – October 3rd 2010, [d]October 4th 2010 – October 2nd 2011, [e]October 3rd 2011 – October 1st 2012.

S4 Appendix. The odds ratios [OR] and 95% confidence intervals [CI] of (A) gestational hypertension and (B) β-blockers in the first and second half year following the economic collapse in Iceland compared with pre-collapse period.

Regression models	Pre-collapse period[a] OR [95% CI]	4th quarter 2008 & 1st quarter 2009[b] OR [95% CI]	2nd quarter 2009 & 3rd quarter 2009[c] OR [95% CI]
(A) Gestational hypertension			
Crude	1.00 [ref.]	1.52 [1.21-1.92]	1.70 [1.36-2.12]
Model I*	1.00 [ref.]	1.36 [1.00-1.85]	1.44 [1.05-1.97]
Model II**	1.00 [ref.]	1.34 [0.99-1.83]	1.40 [1.02-1.93]
Model III***	1.00 [ref.]	1.04 [0.66-1.67]	1.16 [0.76-1.77]
(B) β-blockers			
Crude	1.00 [ref.]	1.63 [1.26-2.10]	1.66 [1.30-2.12]
Model I*	1.00 [ref.]	1.37 [0.98-1.92]	1.31 [0.92-1.85]
Model II**	1.00 [ref.]	1.46 [1.03-2.06]	1.37 [0.96-1.96]
Model III***	1.00 [ref.]	1.13 [0.67-1.91]	1.12 [0.70-1.80]

* Adjusted for maternal age, gravidity, time in weeks [time-trend] and seasonality.

** Simultaneously adjusted for maternal age, gravidity, time in weeks, seasonality, sex, diabetes, pre-existing hypertension, relationship status, place of residence, employment status and citizenship.

***Adjusted for maternal age, gravidity, time in weeks, seasonality and aggregate unemployment rate.

Included in the collapse groups are women with singleton pregnancies with gestational length of 20 weeks or more during [a]September 27th 2004 - September 28th 2008, [b]September 29th 2008 – March 29th 2009, [c]March 30th 2009 – September 29th 2009

Paper III

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PLOS ONE

Low Birth Weight, Small for Gestational Age and Preterm Births before and after the Economic Collapse in Iceland: A Population Based Cohort Study

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Abstract

Objective: Infants born small for gestational age (SGA) or preterm have increased rates of perinatal morbidity and mortality. Stressful events have been suggested as potential contributors to preterm birth (PB) and low birth weight (LBW). We studied the effect of the 2008 economic collapse in Iceland on the risks of adverse birth outcomes.

Study design: The study population constituted all Icelandic women giving birth to live-born singletons from January 1st 2006 to December 31st 2009. LBW infants were defined as those weighing <2500 grams at birth, PB infants as those born before 37 weeks of gestation and SGA as those with a birth weight for gestational age more than 2 standard deviations (SD's) below the mean according to the Swedish fetal growth curve. We used logistic regression analysis to estimate odds ratios [OR] and corresponding 95 percent confidence intervals [95% CI] of adverse birth outcomes by exposure to calendar time of the economic collapse, i.e. after October 6th 2008.

Results: Compared to the preceding period, we observed an increased adjusted odds in LBW-deliveries following the collapse (aOR = 1.24, 95% CI [1.02, 1.52]), particularly among infants born to mothers younger than 25 years (aOR = 1.85, 95% CI [1.25, 2.72]) and not working mothers (aOR = 1.61, 95% CI [1.10, 2.35]). Similarly, we found a tendency towards higher incidence of SGA-births (aOR = 1.14, 95% CI [0.86, 1.51]) particularly among children born to mothers younger than 25 years (aOR = 1.87, 95% CI [1.09, 3.23]) and not working mothers (aOR = 1.86, 95% CI [1.09, 3.17]). No change in risk of PB was observed. The increase of LBW was most distinct 6–9 months after the collapse.

Conclusion: The results suggest an increase in risk of LBW shortly after the collapse of the Icelandic national economy. The increase in LBW seems to be driven by reduced fetal growth rate rather than shorter gestation.

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Introduction

Infants born small for gestational age or preterm have increased risks of perinatal morbidity and mortality [1] and of somatic diseases that can last throughout childhood and into adulthood [2,3].

It is widely believed that a woman's emotional and psychological environment during the prenatal period can affect fetal development. Numerous studies have examined this hypothesis by obtaining associations between emotional and stressful life events during the prenatal period and adverse birth outcomes. However, results of these studies are inconsistent, with some studies reporting that adverse life events increase risks of poor pregnancy outcomes [4–14] and others reporting no association [15,16] or the opposite [17].

Whether economic conditions during the prenatal period have adverse effects on infant health has been less investigated. Deheeja and Llers-Muney reported a reduced incidence of adverse birth outcomes during periods of high unemployment [18]. Margerison-Zilko et al. recently reported that unexpected economic contraction (measured as unexpectedly high monthly unemployment rate) early in pregnancy was associated with a decrease in birth weight [19]. Other studies have found either null associations [20,21] or higher risks of low birth weight and neonatal mortality following recessions or involuntary unemployment [22–24].

On October 6th 2008 the Icelandic prime minister informed the nation of an unusually swift and severe economic collapse in a dramatic manner and the government took over its three largest banks. The largely unforeseen collapse of the Icelandic economy

Table 1. Maternal characteristics during the study period, before and after Oct 6th 2008.

Maternal characteristics	Category of characteristics	Precrisis (N = 11,111)		Postcrisis (N = 5,160)		*p*-value*
Mean age (SD)		**29.01 (5.55)**		**29.24 (5.54)**		**0.016****
		Births, *n*	**Births, %**	**Births, *n***	**Births, %**	
Age (year)	<25	2,454	22.09	1,055	20.45	0.036**
	25–34	6,734	60.61	3,160	61.24	
	≥35	1,923	17.31	945	18.31	
Parity	Nulliparous	4,324	38.92	1,966	38.10	0.072
	Primiparous	3,929	35.36	1,779	34.48	
	Multiparous	2,858	25.72	1,415	27.41	
Relationship status[£]	Cohabitating with father	9,422	86.38	4,182	84.18	<0.001***
	Single	1,485	13.62	786	15.82	
Place of residence[¥]	Rural	3,799	34.53	1,715	33.27	0.119
	Urban	7,203	65.47	3,438	66.73	
Employment status[β]	Working	8,247	75.23	3,783	74.48	0.312
	Not working	2,716	24.77	1,296	25.52	
Diabetes	No	10,783	97.05	4,953	95.99	0.001***
	Pre-existing	47	0.43	21	0.42	
	Gestational diabetes	281	2.53	186	3.60	
Hypertension	No	10,290	92.61	4,721	91.49	0.045**
	Pre-existing	151	1.36	82	1.59	
	Pregnancy-induced-hypertension	670	6.03	357	6.92	

[£]Missing values n = 396 were excluded from analysis.
[¥]Missing values n = 116 were excluded from analysis.
[β]Missing values n = 229 were excluded from analysis.
**p*-values are based on Chi-square test, except for maternal age where independent sample t-test was used.
**Difference is statistically significant within p = 0.05.
***Difference is statistically significant equal to or within p = 0.001.
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with its associated rapid rise in unemployment and increase in household debt represents a potentially powerful stressor that may have adversely affected birth outcomes. Using the nationwide Medical Birth Registry, we examined the effect of the 2008 economic collapse in Iceland on infant health, as measured by low birth weight, preterm birth and small-for-gestational age birth.

Materials and Methods

Population

All Icelandic women registered in the National Icelandic Birth Registry from January 1st 2006 to December 31st 2009 (N = 16,616) were considered. We excluded women with multiple pregnancies (n = 298) and stillbirths (n = 47), leaving a total of 16,271 eligible women in the study.

Outcome assessment

Information on birth weight in grams and gestational length in days was obtained from the Birth Registry. Low birth weight (LBW) was defined as less than 2,500 grams at birth and preterm birth (PB) as a delivery before 37 completed gestational weeks (259 days of gestation). For 16,228 births (>99.9%), length of gestation was based on ultrasound measurement before the 21st week of gestation. In 7 pregnancies, gestational age could be estimated on the basis of last menstrual period. It could not be determined for 8 cases. Small-for-gestational age (SGA), a proxy for intrauterine growth restriction, was defined as infants with birth weight more than 2 standard deviations (SD) below the mean for gestational age according to the sex-specific Swedish fetal growth curve [25], which has been shown to be applicable for Icelandic fetuses [26]. Fetal growth rate index (Z scores) was also assessed by using methods previously described [25].

Explanatory variables

The study period was dichotomized with pre-crisis period ("unexposed"), spanning from January 1st 2006 to October 5th 2008, and post-crisis period ("exposed"), spanning from October 6th 2008 to December 31st 2009. The pre- and post-crisis groups will hereafter be referred to as the unexposed (reference group) and the exposed group, respectively.

Potential covariates

Information on covariates was obtained from the National Medical Birth Registry. Maternal characteristics obtained from the registry were: place of delivery; maternal age at delivery; parity (nulli-, primi- and multiparous); relationship status (mother cohabitating with father or not); employment status (employed or not employed (student/housewife/unemployed/on disablement benefit)); residence (living in the capital area or not). Maternal and infants' diseases were classified according to the International Classification of Diseases, tenth revision (ICD-10). Pregnancy-related diseases known to influence fetal growth included essential hypertension (ICD-10 code O10-O11), gestational hypertension and preeclampsia (ICD-10 codes O12-O15) and pre-gestational and gestational diabetes mellitus (ICD-10 codes O24.0-O24.2 and

Table 2. Obstetric characteristics during the study period, before and after Oct 6th 2008.

Obstetric characteristics	Category of characteristics	Precrisis (N = 11,111)		Postcrisis (N = 5,160)		*p*-value*
Mean birth weight (g) (SD)		**3,693.7 (569.38)**		**3,665.7 (570.31)**		**0.003**
Mean gestational length$^{\Phi}$ (days) (SD)		**279.54 (12.10)**		**279.02 (11.91)**		**0.023**
		Births, *n*	**Births, %**	**Births, *n***	**Births, %**	
Mode of delivery	Vaginal	9,279	83.51	4,344	84.18	0.278
	Caecerian section	1,832	16.49	816	15.82	
Infant's gender$^{\epsilon}$	Male	5,763	51.88	2,630	50.97	0.281
	Female	5,346	48.12	2,530	49.03	
Apgar 5min	7–10	10,868	97.82	5,050	97.87	0.850
	<7	242	2.18	110	2.13	
Congenital malformation	No	10,716	96.44	4,964	96.22	0.440
	Yes	395	3.56	196	3.78	
Early neonatal death (<7 days)	No	11,102	99.92	5,157	99.94	0.617
	Yes	9	0.08	3	0.06	
Low birth weight (<2500 g)	No	10,873	97.53	5,005	97.0	0.046
	Yes	274	2.47	155	3.0	
Small-for-gestational age	No	10,950	98.64	5,083	98.51	0.505
	Yes	151	1.36	77	1.49	
Preterm birth (<37 weeks)	No	10,619	95.64	4,918	95.31	0.342
	Yes	484	4.36	242	4.69	

$^{\Phi}$Missing values n = 8.
$^{\epsilon}$Missing values n = 2.
*p-values are based on Chi-square test, except for birth weight and gestational length where linear regression analysis, adjusted for maternal age, parity and seasonality was used. Significance level is 0.05.
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O24.4). Obstetric information obtained was: mode of delivery (vaginal or cesarean delivery), infants' sex, Apgar score at 5 minutes, vaginal induction of delivery (ICD-10 code O83.8), congenital malformations and chromosomal abnormalities (ICD-codes Q00-99) and early neonatal death (defined as death of a live-born infant within 7 days from birth). In order to account for seasonal variation of birth weight, the years were divided into four seasons and births occurring in the same season were grouped together.

Statistical analysis

We calculated descriptive statistics for all maternal and obstetric characteristics as well as for the outcome variables, contrasting frequencies before and after the economic collapse. Differences in characteristics by exposure groups were explored using the Chi-square test for categorical variables and independent sample t-test was used for maternal age. Linear regression analysis was used for the continuous outcome variables gestational length and birth weight, adjusting for maternal age, parity and seasonality. One-way ANOVA tests with post-hoc Tukey's test were conducted to assess the homogeneity of birth weight and gestational length between seasons.

Logistic regression analyses were used to calculate adjusted odds ratios (aOR) and their 95% confidence intervals [CI's] for LBW, PB and SGA in the exposed period. In model I, adjustments were made for variables assessed as possible confounders: maternal age, parity and seasonality. In models II and III, we explored whether possible increased risks of adverse birth outcomes were mediated by other maternal factors or diseases during pregnancy all which, in fact, may have been influenced by the crisis. In model II, we therefore also adjusted for: hypertension and diabetes, and in model III we added relationship status, residence, employment status into the model. Analysis involving LBW and PB were also adjusted for infant's sex in models II and III. We used linear regression models to estimate changes in the fetal growth rate index across exposure categories. In order to explore further the risk of adverse birth outcomes among certain subgroups, we performed logistic regression analyses where we stratified for each of the following maternal characteristics: age, parity, relationship status, place of residence and employment status. The model used in the analyses was also adjusted for age (continuous), parity and seasonal variations (model I).

To further explore whether associations between PB, SGA and LBW differed depending on, when in gestation the collapse hit, we divided the study period into intervals of three months and compared those giving birth in a particular intervals in 2008 and 2009 with those giving birth in the same time intervals in 2006 and 2007. Each time interval in 2008 and 2009 averaged 1,050 births. In the comparison groups, the corresponding time intervals in 2006 and 2007 averaged 1,974 births.

In order to refine our exploration of potential crisis effects, we also used date of conception (instead of date of birth) to sort pregnancies according to exposure to the economic crisis. For example, women who conceived in the time period January – March 2008 (exposed to the crisis in the 3rd trimester) were grouped together and compared to women who became pregnant January – March 2005, 2006 and 2007 (unexposed) etc.

Further, in an attempt to detect a possible time-trend in LBW, SGA and PB that might falsely lead to measured exposure effects, we used linear regression analysis to calculate the monthly trend of

Table 3. The separate and combined effect of covariates on the odds ratio of low birth weight, small for gestational age and preterm birth during the two study periods, before and after October 6th 2008.

Covariates	Low birth weight (<2500 g)	Small for gestational age (SGA)	Preterm birth (<37 weeks)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Model I*	1.25 (1.02–1.53)	1.14 (0.86–1.51)	1.08 (0.92–1.26)
Model II**	1.22 (0.99–1.50)	1.11 (0.83–1.47)	1.06 (0.90–1.24)
Model III***	1.17 (0.95–1.45)	1.09 (0.82–1.46)	1.03 (0.87–1.22)
Crude	1.23 (1.00–1.50)	1.10 (0.83–1.45)	1.08 (0.92–1.26)
Seasonal variation	1.24 (1.01–1.52)	1.13 (0.86–1.50)	1.08 (0.92–1.26)
Maternal age	1.23 (1.01–1.50)	1.10 (0.83–1.45)	1.08 (0.92–1.27)
Parity	1.23 (1.01–1.50)	1.10 (0.84–1.46)	1.08 (0.92–1.27)
Sex	1.22 (1.00–1.50)	[α]	1.08 (0.93–1.27)
Diabetes	1.22 (1.00–1.49)	1.10 (0.83–1.45)	1.07 (0.92–1.26)
Hypertension	1.20 (0.98–1.46)	1.06 (0.81–1.40)	1.07 (0.91–1.25)
Relationship status	1.19 (0.97–1.46)	1.10 (0.83–1.45)	1.08 (0.92–1.26)
Place of residency	1.21 (0.99–1.48)	1.10 (0.84–1.46)	1.06 (0.91–1.25)
Employment status	1.22 (0.99–1.49)	1.09 (0.83–1.45)	1.07 (0.91–1.26)

[α]SGA is inherently adjusted for infant's sex.
*Odds ratio adjusted for seasonal variation, maternal age and parity.
**Odds ratio adjusted for seasonal variation, maternal age, parity, sex, diabetes and hypertension.
***Odds ratio adjusted for seasonal variation, maternal age, parity, sex, diabetes, hypertension, relationship status, place of residency and employment status.
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each birth outcome in the pre-crisis period. This model was adjusted for maternal age and parity.

Additional analysis was conducted to examine the effect of the shock on fetuses that were in utero on the day of the collapse. The exposed group consisted only of those women who were pregnant on October 6th 2008. Women, pregnant on October 6th 2006 and 2007, were considered unexposed. Similar analysis was carried out to examine the effect of the crisis on women who became pregnant during the post-crisis period and gave birth in the last 7 months of 2009. The reference group consisted of women who became pregnant after October 6th 2006 and gave birth the following year.

Ethical considerations

The study was approved by the Icelandic National Bioethics Committee (VSNb2010050014/03.7), the Data Protection Authority (2010050499LSL/–) and the Directorate of Health (2010050296/5.6.1/HBS/hbs).

Results

Among all 16,271 infants; 11,111 (68%) were in the unexposed group and 5,160 (32%) were in the exposed group. Table 1 and 2 present the maternal and obstetric characteristics by exposure status. Following the economic collapse, we observed a statistically significant increase in maternal age as well as a tendency towards higher parity. Compared to the pre-crisis period, mothers giving birth following the economic collapse were more likely to be single, and to have pregnancy-induced hypertension and gestational diabetes (table 1).

The infants born in the period of the economic crisis weighed, on average, 28 grams less than infants in the reference group (table 2). There was also a small but statistically significant difference in mean gestational length between births in the exposed and unexposed periods. No differences were observed with respect to maternal residence, mode of delivery, sex of infants, Apgar score at 5 minutes, congenital malformation or early neonatal death. Post-hoc Tukey's test showed a statistically significant seasonal variation of both birth weight and gestational length in the pre-crisis period but not in post-crisis period ($p<0.05$ and $p>0.05$, respectively).

The rates of infants born with low birth weight (<2,500 grams) before and after the collapse were 2.5% and 3.0%, respectively. Table 3 shows the results for multivariate logistic regression analysis. When adjusting for maternal age, parity and seasonality (model I) we observed a statistically significant increase in the odds of LBW during the post-crisis period (aOR = 1.25 95% CI [1.02, 1.53]). When we further adjusted for other, possibly mediating variables (models II and III), the difference loses significance but remains elevated (aOR 1.17 95% CI [0.95, 1.45). Rates of preterm born infants were 4.3% before and 4.6% after the economic collapse. This difference was not statistically significant (table 3). Rates of SGA before and after the crisis were 1.4% and 1.5%, respectively. When applying logistic regression analysis, we found no significant association between time of crisis and risk of SGA (table 3) and aOR indicated relatively small differences (e.g., aOR 1.10).

Additional analysis was conducted to estimate the change in fetal growth rate index between pre- and post-crisis groups. Compared to the reference group, infants born in time of crisis, had a decreased fetal growth rate ($\beta = -0.004$; $p = 0.032$). This decrease was particularly distinct for women giving birth in the time period April – June 2009 ($\beta = -0.015$; $p = 0.001$).

Figure 1 presents results from logistic regressions of LBW, SGA and PB around the economic collapse in three-month intervals, 3 intervals before the economic collapse (January 1st– October 5th 2008) and 5 intervals after the collapse (October 6th 2008–December 31st 2009), using identical calendar times from 2006 and 2007 (combined) as reference periods. The first three comparisons are thus between before collapse time periods and can be viewed partly as falsification tests, for which we do not expect to see statistically significant results. After the economic collapse, we observed a statistically significant increased odds of

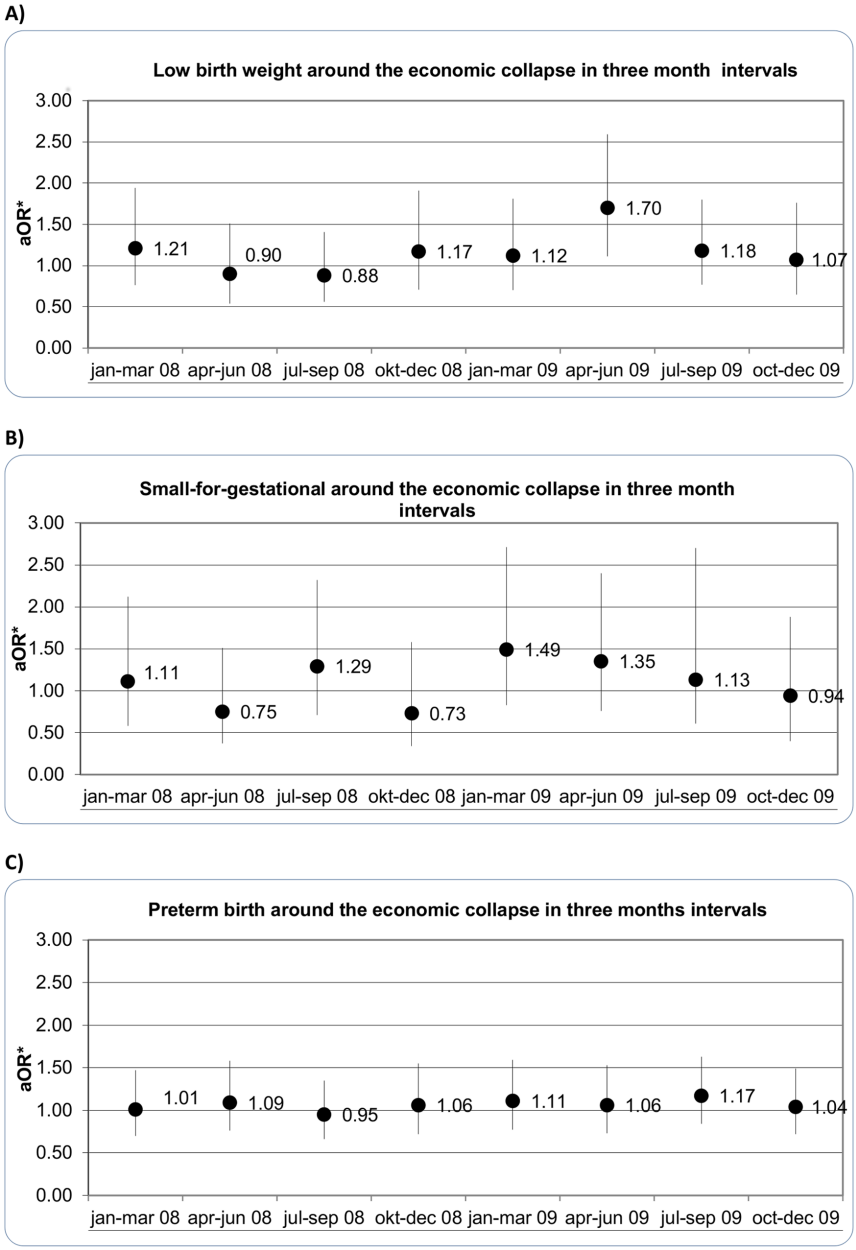

Figure 1. Odds ratio and 95% CI for (a) low birth weight, (b) small-for-gestational age and (c) preterm birth infants in Iceland for 8 three months intervals, prior to and after the economic collapse compared with the same intervals from each of two years before.
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LBW (aOR = 1.70, 95% CI [1.11, 2.59]) among women who were in their 1st trimester when the crisis began, giving birth in the time interval April – June 2009, which is 6–9 months after the beginning of the crisis (figure 1a). A tendency towards increased odds of SGA was observed among women in their 2nd and 1st trimester during the onset of the crisis, giving birth in the time intervals January – March 2009 and April – June 2009, respectively (figure 1b). There were no associations observed

Table 4. Adjusted odds ratio of low birth weight, small-for-gestational age and preterm birth during the study period, before and after Oct 6th 2008, stratified by maternal characteristics.

Characteristics	Category of characteristics	aOR_{LBW}* (95% CI)	aOR_{SGA}* (95% CI)	aOR_{PB}* (95% CI)
Age (year)	<25	**1.85 (1.25–2.72)****	**1.87 (1.09–3.23)****	1.13 (0.81–1.58)
	25–34	1.05 (0.79–1.39)	0.81 (0.54–1.23)	1.06 (0.86–1.31)
	≥35	1.20 (0.78–1.87)	1.34 (0.76–2.37)	1.08 (0.75–1.55)
Parity	nulliparous	1.26 (0.95–1.68)	1.06 (0.73–1.55)	1.15 (0.91–1.45)
	primiparous	1.10 (0.74–1.64)	1.14 (0.63–2.06)	1.02 (0.74–1.39)
	multiparous	1.45 (0.95–2.23)	1.36 (0.74–2.50)	1.04 (0.75–1.43)
Relationship status	Cohabiting with father	1.15 (0.91–1.47)	1.18 (0.85–1.64)	1.02 (0.85–1.23)
	Single	1.36 (0.90–2.06)	1.01 (0.57–1.79)	1.20 (0.85–1.71)
Place of resident	rural	**1.53 (1.07–2.20)****	1.33 (0.81–2.18)	0.94 (0.70–1.26)
	urban	1.11 (0.87–1.43)	1.06 (0.75–1.50)	1.12 (0.92–1.35)
Employment status	In work	1.13 (0.88–1.45)	0.94 (0.66–1.32)	1.06 (0.88–1.29)
	Not working	**1.61 (1.10–2.35)****	**1.86 (1.09–3.17)****	1.11 (0.81–1.51)

*OR adjusted for maternal age; parity and seasonal variation.
**Statistically significant difference between the time periods.
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between PB and stressors of the collapse in any of the three months intervals (figure 1c).

When classifying births according to date of conception rather than date of birth we obtained similar results. Women who conceived in the time period July – September 2008 and gave birth in April – June 2009 had increased risk of LBW and SGA but not of PB (appendix S1).

This pattern is also consistent with the results obtained from the analysis of fetuses on the day of the collapse, where a tendency towards increased risk of LBW and SGA deliveries was observed but not PB. Infants, conceived during the crisis, were not at increased risk of LBW, SGA or PB (appendix S2).

Table 4 presents multivariate adjusted odds ratios of LBW, SGA and PB during the crisis period stratified by age, parity, relationship status, place of residence and employment. Among mothers younger than 25 years, we observed a statistically significantly increased odds of giving birth to LBW and SGA infants during the crisis period as compared to before the crisis (aOR = 1.85, 95% CI [1.25, 2.72]; aOR = 1.87, 95% CI [1.09, 3.23], respectively). Similarly, if mothers were not working, corresponding post-collapse risks were increased (aOR = 1.61, 95% CI [1.10, 2.35]; aOR = 1.86, 95% CI [1.09, 3.17], respectively) compared to mothers not working prior to the collapse. Exposed mothers living outside the capital area also had increased odds of having a LBW compared to unexposed mothers (aOR = 1.53, 95% CI [1.07, 2.20]). There was no statistically significant difference in the odds of PB in any subgroups during vs. before the economic collapse and adjusted odds ratios were relatively small (close to 1).

Finally, our linear regression analysis indicated no time-trends in LBW ($F = 0.137$; $p = 0.714$), SGA ($F = 0.001$; $p = 0.972$) and PB ($F = 1.11$; $p = 0.301$) in the pre-crisis period.

Discussion

The results from this nationwide study indicate a decrease in mean birth weight as well as an increased rate of LBW deliveries in Iceland in the months following the economic collapse. This effect was mainly observed among relatively young mothers and mothers without a job. Women, in their 1st trimester of pregnancy, at the time of the swift and dramatic collapse seemed most affected. This is in accordance with findings of Glynn et al., Lederman et al., Margerison-Zilko et al. and Mansour and Reed in their studies of major adverse life events effects on birth outcomes [6,12,19,27]. Although, limited by small numbers, our findings suggest that the increase in LBW is driven by intrauterine growth restriction rather than shorter gestation. In an analysis of the unemployment crisis in Sweden in the 1990s, Bergmark and Palme identified subgroups that experienced greater welfare loss during the crisis. They found that young adults and single mothers (and immigrants), subgroups that already were socially and economically vulnerable, were particularly disadvantaged in terms of welfare resources [28]. These findings are in line with our findings which indicate that the increase in LBW and SGA births during the crisis period was considerable among young mothers (<25 years) and those without employment, compared with the same subgroups from before the collapse. Indeed, unemployment rates have been highest in this age group in Iceland during the crisis and rose up to 21% in the 2nd quarter of 2009 and in 2010 [29]. Though, it should be

acknowledged that due to the drastic rise in unemployment rates, the individuals constituting the group "not working" in the pre-crisis period might be different from those in the post-crisis period. Therefore, the positive association between the group not working and LBW should be interpreted with caution.

Dooley and Prause reported a decrease in birth weight of infants born to women who shifted from adequate employment to underemployment during pregnancy [24]. Furthermore, Catalano et al. found increased risk of very LBW infants among parents where the father was unemployed [30] and lastly, Jansen et al. found a decrease in mean birth weight among offspring of students and women receiving disability benefits [31].

It should be noted that the "not working" group in our study is heterogeneous, consisting of unemployed, disabled, housewives and students. This grouping may therefore not be comparable to other studies examining the effect of unemployment on birth outcomes. However, the largest group was students and it can be argued that being a student in Iceland at this time might have been a proxy for unemployment, as many of those who lost their jobs during the crisis subsequently went to school.

During the crisis, women living in rural areas were at higher risk of having a LBW than women living in urban areas. Since the impact of the crisis was in the beginning most severe for inhabitants living in the capital area and nearby areas, the opposite was expected. A possible explanation may be that the rural area category included a relatively densely populated area in the south-west part of Iceland, Suðurnes, which was hit especially hard by the economic crisis. Unemployment rate in Suðurnes was 13–14% in 2009, the highest in Iceland.

Hypertension has been identified as a risk factor for LBW, SGA and PB [32,33]. The incidence of hypertension diagnosed during pregnancy did increase following the collapse but when hypertension was added to the models, the results did not indicate that the observed increases in LBW and SGA were altogether mediated via hypertension. Several other mechanisms may explain the observed association between the economic recession and increase in LBW/SGA. The economic collapse may have increased the stress levels among pregnant women causing direct physiological changes to the endocrine, immune and cardiovascular systems; changes that may affect the process of gestation to the worse [34,35]. Furthermore, it is well recognized that stressful conditions, such as income shocks, may promote adverse health behaviors, e.g. smoking, drinking etc. [36,37], thus acting as mediators between the stress caused by the economic collapse and the observed increase in LBW and SGA.

Validity

This study leverages the National Medical Birth Registry to accomplish a population-based cohort study of all pregnant Icelandic women giving birth in Iceland in a four year time period. A multitude of information on the mother and child has been systematically collected to the registry since 1973, and this data collection is independent of exposure level, i.e. time of economic recession. Several measures were taken in order to further enhance the internal validity of this study. In order to make the cohort homogenous with regard to birth weight and length of gestation, we excluded all stillbirths and multiple gestations. Furthermore, our sample included only Icelandic women, as the literature indicates that risks of IUGR and PB may differ by ethnicity. Practically all pregnant women undertook ultrasound scanning around the 20th week of pregnancy, and possible measurement errors of gestational length should be non-differential between the exposed and unexposed groups. Almost all (99%) births occur in hospitals or at local health clinics, resulting in accurate measurement of birth weight. The richness of information in the Medical Birth Registry allows us to control for most major confounding factors and our time trend analysis also indicates a somewhat stable rate of LBW before the economic collapse. Thus, we finally decided that changes occurring in most covariates (cohabitation, working–status, diabetes and hypertension) may actually be a consequence of the economic collapse and therefore in the causal chain between stress and LBW/SGA.

A limitation of this study is the lack of information on maternal smoking, alcohol, and nutritional habits during pregnancy. Smoking during pregnancy is causally associated with risk of LBW and IUGR [33,38,39]. Furthermore, some researchers have suggested that stressful circumstances are often alleviated by adverse health behavior, such as smoking [36,37]. However, McClure et al. and Asgeirsdottir et al. report a significant reduction in the prevalence of smoking in Iceland between 2007 and 2009 among a representative cohort of 3755 Icelanders [40,41]. Further, we did not have information on pre-pregnancy maternal weight. Low pre-pregnancy weight is associated with both SGA and LBW and high pre-pregnancy weight is associated with gestational diabetes and pregnancy-induced hypertensive diseases like preeclampsia, which often leads to SGA and PB [42–44]. Studies have indicated an increase in the prevalence of overweight and obesity among the Icelandic population over the last decades [45]. However, there are indications of a healthier lifestyle among Icelanders following the economic collapse in 2008, i.e. less consumption of fast food and sugar sweetened drinks [41]. Thus, it could be postulated that the short-term increase in LBW might be mediated by changes in body weight or smoking in the general population after the economic collapse. On the other hand, our previous study clearly indicates an increase in high stress levels among Icelandic women after the collapse [46] which strengthens our interpretation that the shock of the dramatic economic collapse may have contributed to the observed short-term increase in LBW. Nevertheless, further studies are needed to address if the effect of the economic crisis on LBW is mediated through altered behavior, exposure to heightened levels of stress hormones or both.

Conclusion/Implication

The results of this study add important knowledge on how birth outcomes are affected when mothers are exposed to significant economic shocks such as the economic collapse that occurred practically overnight in Iceland. Our results suggest that the economic meltdown was an important stressor that increased the risk of LBW deliveries, especially for women in the 1st trimester of pregnancy. The increase in LBW seemed to be driven by fetal growth restriction rather than by shortened gestation. The crisis appeared to have the largest effect on younger women (<25 years) and women who were not employed.

These findings suggest that the effect of the crisis on LBW was short lived, as women who were exposed during later periods of their pregnancy or who completed the pregnancy in the post-crisis period were relatively unaffected. However, further studies with longer follow-up are needed for definite conclusion, particularly to observe whether the effect for young and vulnerable women is persistent. The findings have implications for public health practice and clinical management of pregnant women, particularly young women and women in a vulnerable situation on the labor market.

Supporting Information

Appendix S1 Odds ratios and 95% CI for (a) low birth weight, (b) small-for-gestational age and (c) preterm birth infants, born to Icelandic women in time of economic collapse. Women are grouped together by their date of conception into 5 three-months intervals; each period is contrasted with the combined time-intervals from the previous years.
(TIF)

Appendix S2. a) *Table 1*– The effect of covariates on the odds ratio of low birth weight, small for gestational age and preterm birth among women who were pregnant on October 6th 2008 (n = 3130) compared with women who were pregnant on October 6th in the two previous years (n = 6083). **b**) *Table 2*– The effect of covariates on the odds ratio of low birth weight, small for gestational age and preterm birth among women who became pregnant after October 6th 2008 and gave birth in the last 6 months of 2009 (n = 2030) compared with women who became pregnant after October 6th 2006and gave birth in the last 6 months of 2007 (n = 1898).
(DOCX)

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Author Contributions

Conceived and designed the experiments: VHE TLA RIB RK SC UAV. Analyzed the data: VHE TLA RIB RK SC UAV. Contributed reagents/materials/analysis tools: VHE UAV. Wrote the paper: VHE UAV. Drafted the manuscript: VHE TLA RIB RK SC UAV. Responsible for the final manuscript: VHE TLA RIB RK SC UAV. Acquired the data: VHE UAV.

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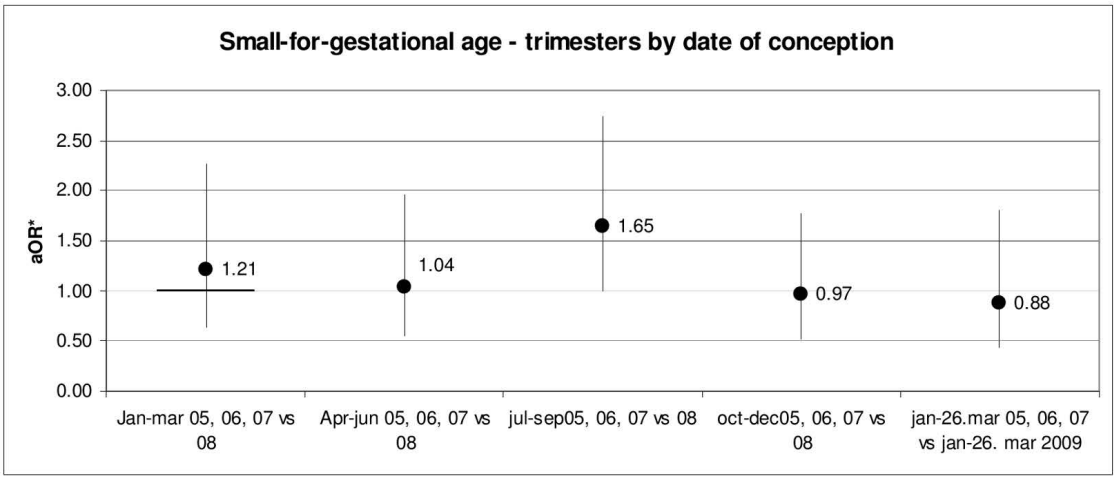
A)

B)



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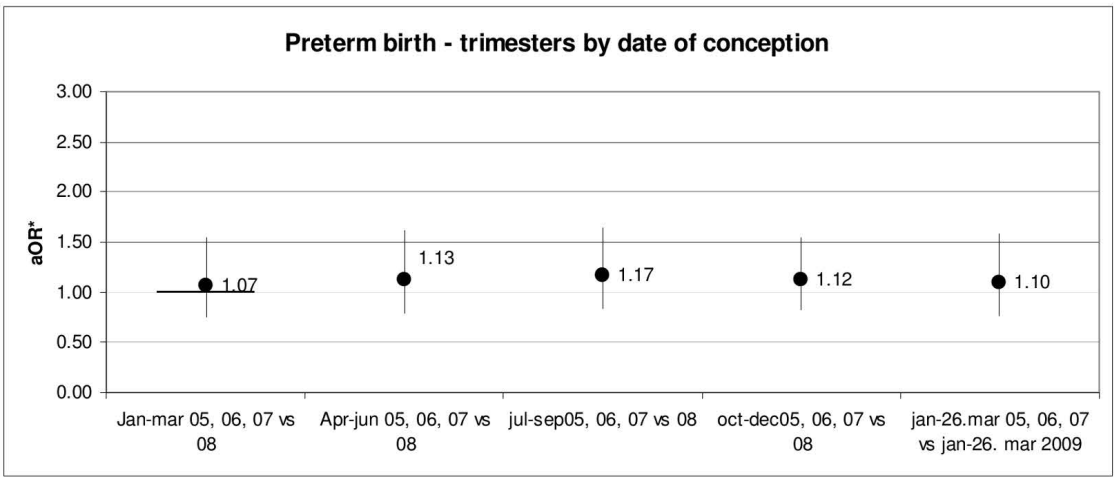

Supplementary appendix 1 - Odds ratios and 95% CI for (a) low birth weight, (b) small-for-gestational age and (c) preterm birth infants, born to Icelandic women in time of economic collapse. Women are grouped together by their date of conception into 5 three-months intervals; each period is contrasted with the combined time-intervals from the previous years.

Supplementary appendix 2

Table 1 - The effect of covariates on the odds ratio of low birth weight, small for gestational age and preterm birth among women who were pregnant on October 6th 2008 (n=3130) compared with women who were pregnant on October 6th in the two previous years (n=6083).

Covariates	Low birth weight (<2500 g) OR (95% CI)	Small for gestational age (SGA) OR (95% CI)	Preterm birth (<37 weeks) OR (95% CI)
Crude	1.25 (0.95 - 1.66)	1.30 (0.90 - 1.88)	1.05 (0.84 - 1.31)
Model I*	1.25 (0.95 - 1.66)	1.31 (0.91 - 1.90)	1.05 (0.84 - 1.31)
Model II**	1.23 (0.92 - 1.63)	1.27 (0.88 - 1.84)	1.03 (0.83 - 1.29)
Model III***	1.18 (0.88 - 1.59)	1.27 (0.87 - 1.85)	1.01 (0.80 - 1.27)

α SGA is inherently adjusted for infant's sex
* Odds ratio adjusted for seasonal variation, maternal age and parity.
** Odds ratio adjusted for seasonal variation, maternal age, parity, sex, diabetes and hypertension.
*** Odds ratio adjusted for seasonal variation, maternal age, parity, sex, diabetes, hypertension, relationship status, place of residency and employment status.

Table 2 - The effect of covariates on the odds ratio of low birth weight, small for gestational age and preterm birth among women who became pregnant after October 6th 2008 and gave birth in the last 6 months of 2009 (n=2030) compared with women who became pregnant after October 6th 2006and gave birth in the last 6 months of 2007 (n=1898).

Covariates	Low birth weight (<2500 g) OR (95% CI)	Small for gestational age (SGA) OR (95% CI)	Preterm birth (<37 weeks) OR (95% CI)
Crude	1.05 (0.75 - 1.48)	0.94 (0.56 - 1.57)	1.06 (0.81 - 1.39)
Model I*	1.06 (0.75 - 1.48)	0.94 (0.56 - 1.58)	1.07 (0.81 - 1.40)
Model II**	1.05 (0.74 - 1.48)	0.94 (0.54 - 1.59)	1.06 (0.81 - 1.39)
Model III***	1.08 (0.75 - 1.54)	1.06 (0.60 - 1.86)	1.10 (0.83 - 1.45)

α SGA is inherently adjusted for infant's sex
* Odds ratio adjusted for seasonal variation, maternal age and parity.
** Odds ratio adjusted for seasonal variation, maternal age, parity, sex, diabetes and hypertension.
*** Odds ratio adjusted for seasonal variation, maternal age, parity, sex, diabetes, hypertension, relationship status, place of residency and employment status

Paper IV

Increase in small for gestational age births during an economic recession: a nationwide cohort study in Iceland

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Running title: Increase in SGA births following an economic recession

ABSTRACT

Objective: Macroeconomic fluctuations have shown various effects on population health, but the evidence base for their influence on birth outcomes is scarce and inconclusive. The aim of this nationwide cohort study was to explore potential long-term changes in birth outcomes during the economic recession in Iceland, which started abruptly in 2008 with gradual alleviation over the following years.

Design: A population-based cohort study from October 2002 to September 2012.

Population: All singleton live birth infants in Iceland as identified by the Icelandic Medical Register (N=43 693).

Methods: With the pre-recession period as a reference, we used logistic regression analysis to calculate the adjusted odds ratios (aOR) and 95% confidence intervals (CI) of adverse birth outcomes separately for the 1st year and years 2-4 of the recession.

Main outcome measures: Low birth weight (LBW), preterm birth (PB) and small for gestational age (SGA)

Results: The prevalence of LBW increased from 2.4% in the pre-recession period to 3.1% in the first recession year (aOR_{year1} 1.35, 95% CI 1.12-1.63), while the prevalence of LBW in the 2nd to 4th recession years was 2.5% ($aOR_{years2-4}$ 1.07, 95% CI 0.93-1.24). We noted a sustained rise in SGA births (10.0% pre-recession vs. 11.2% in 1st and 10.9% in 2nd to 4th recessions years) yielding an aOR_{year1} 1.11 (95% CI 1.00-1.23) and $aOR_{years2-4}$ 1.08 (95% CI 1.01-1.16), respectively. These point estimates were attenuated when adding aggregate economic indicators to the regression models. No change was observed with respect to the prevalence of PB.

Conclusions: These findings lend support to the notion that major macroeconomic downturns may negatively influence fetal growth.

Keywords: Macroeconomic recessions; low birth weight; small for gestational age; preterm birth; unemployment rate

INTRODUCTION

Fetal growth and birth outcomes are to a considerable extent influenced by maternal environmental conditions. Socioeconomically disadvantaged women are more likely to give birth to low birth weight [1] and preterm infants [2], compared with their more advantaged

counterparts. Furthermore, parents who go from adequate employment to underemployment shortly before or during pregnancy are more likely to have lighter infants. [3, 4]

Studies examining the association between macroeconomic conditions and birth outcomes have yielded inconclusive results. Some studies have reported a reduction in birth weight following decreased employment security during pregnancy [5, 6] and during economic downturns, measured as aggregate unemployment rate [7, 8] and gross domestic product (GDP). [9] Other have not found an association between the aggregate unemployment rate and infant birth weight [10, 11] or even observed better health among infants conceived in times of high unemployment rate. [12] These inconsistent findings may be due to differences in methodology and completeness of outcome ascertainment, as well as differences in study populations or the nature of the economic conditions that pregnant women are exposed to.

Iceland was hit hard by the 2008 global economic recession with an even larger rate of economic decline than in Spain and Ireland. [13] In early October 2008 the nation experienced a swift financial collapse, resulting in the country's three largest banks defaulting within the same week. [14] The collapse had considerable effects on the macroeconomic environment in Iceland; a threefold increase in the unemployment rate immediately following the collapse and a 6.5% decrease in GDP in 2009, the first year of the recession. [13, 15] Previous studies on infants born during the first year following the 2008 economic collapse in Iceland indicated an increase in low birth weight (LBW) infants, particularly among women who were in the first trimester of pregnancy when the collapse hit [16, 17], among young women and women not working a labour-market job. [16] Building on these previous studies, we sought to examine whether the 2008 Icelandic economic collapse and the associated aggregate economic environment affected new-born health beyond the first year of the recession. More specifically, we aimed to assess potential changes in LBW, preterm birth

(PB), and small for gestational age (SGA) during the first four years of the economic recession.

METHODS

Data sources and study population

The study leveraged individual-level data from the Icelandic Medical Birth Registry [18] as well as aggregate data on economic indicators from Statistics Iceland. [19] All singleton pregnancies, resulting in live births after gestational week 22 in Iceland between September 30th, 2002, and September 30th, 2012, were included in the study population (N=43 693).

Outcome variables

The main outcome variables were LBW, PB and SGA. LBW was defined as birth weight below 2500 g and PB as delivery before gestational week 37. Gestational length was determined with an ultrasound for >99.9% of all pregnancies. Information on gestational length was missing for 33 live births, which were excluded from analyses of PB. SGA, a proxy for intrauterine growth restriction, was defined as fetal growth rate index in the lowest 10th percentile according to sex-specific fetal growth curves. [20] A cut-off value for the lowest 10th percentile of the fetal growth rate index among live born singletons in the pre-recession group was calculated and used as a reference in order to identify infants categorised as SGA. Information regarding gestational age or sex of infant was missing for 44 live births, which were excluded from analyses of SGA.

Explanatory variables

The start of the economic recession in Iceland was a swift and distinct event, allowing us to pin down the beginning of the recession to an exact time point, i.e. the first week of October 2008. The aggregate economic indicators used in this study were available on a quarterly basis, while the timing of births was on a weekly basis (not the actual date of birth).

Thus, the first week of October 2008, with a start date on the 29th of September (and coinciding with the beginning of the 4th quarter of the year 2008), was used as a marker of the economic collapse, as data on the economic climate showed dramatic changes between the third and fourth quarters of 2008 (21). In our main analyses, we categorised time into a pre-recession period (unexposed to the economic recession) and a recession period (exposed to the economic recession). In order to meet the main objectives of the study (i.e. to assess the immediate and longer-term association between the recession and birth outcomes), the recession period was further divided into two separate periods, recession year 1 and recession years 2-4. The pre-recession period consisted of singleton births occurring between September 30th, 2002, and September 28th, 2008. The two separate recession periods included all live births occurring between i) September 29th, 2008, and September 27th, 2009 (recession year 1), ii) September 28th, 2009, and September 30th, 2012 (recession years 2-4).

Covariates

Information on covariates was obtained from the Medical Birth Registry. Demographic background characteristics included were gravidity (primigravida, multigravida), maternal age (both continuous and grouped by <25; 25-34; ≥35 years), relationship status (cohabitating with other parent; not cohabitating), maternal citizenship (Icelandic; foreign), parental employment status (both employed; one employed/one not working a labour-market job [student/homeworker/on disability/unemployed]; neither working a labour-market job), and maternal place of residence (capital; rural). Information on parental socioeconomic variables (relationship status, citizenship, employment status, and residence) was collected on average at gestational week 13. Maternal conditions during pregnancy were classified according to the International Classification of Disease, tenth revision [ICD-10]. Included in the study were pregnancy related diseases known to influence fetal growth or gestational length, including pre-existing hypertension [ICD-10 code O10], gestational (non-proteinuric) hypertension

[ICD-10 codes O13, O16], preeclampsia [ICD-10 codes O11, O14, O15], pre-existing and gestational diabetes mellitus [ICD-10 codes O24.0-O24.3 and O24.4-O24.9, respectively]. The categorization of hypertensive disorders of pregnancy was mutually exclusive; if women had more than one diagnosis, preeclampsia overruled both gestational hypertension and pre-existing hypertension, and gestational hypertension overruled pre-existing hypertension. Obstetric information obtained were calendar week of birth, mode of delivery (vaginal; elective caesarean [ICD-10 code O82.0]; emergency caesarean [ICD-10 codes O82.1, O82.2]), infants sex, 5 minutes Apgar score (<7; ≥7), and congenital malformation (ICD-10 codes Q00-Q99).

In order to capture whether the potential influence of time on birth outcomes was due to changes in the surrounding macroeconomic climate, we explored aggregate economic indicators as mediators. The economic indicators used were national unemployment rate and GDP on a quarterly basis, as traditional measures of economic conditions.

Data analysis

Descriptive statistics were calculated for all parental- and pregnancy related characteristics, contrasting frequencies across exposure categories. Differences between pre-recession and recession periods were assessed with χ^2-test for the categorical variables and one-way ANOVA for mean maternal age. Time trend was visually inspected by plotting the quarterly average prevalence of LBW, PB and SGA and fitting a loess curve, with a 95% confidence interval (CI), through the data points. Further, the potential time trend in LBW, PB, and SGA was assessed in a supplementary analysis using a Poisson regression analyses to calculate the change per year (relative risks, 95% CIs), separately for the pre-recession and recession periods. Likelihood ratio tests were used to assess differences in average prevalence before and after the economic collapse.

Logistic regression analyses were used to calculate the adjusted odds ratio (aOR) and 95% CIs for LBW, PB, and SGA in each of the two recession periods with the pre-recession period as a reference. In model 1, adjustments were made for maternal age (continuous) and gravidity. In model 2, we also adjusted for relationship status, maternal residence, maternal citizenship, parental employment status, hypertensive disorders of pregnancy, congenital malformation, gestational- and pre-existing diabetes, in addition to maternal age and gravidity. In models 3 and 4, we assessed the role of surrounding economic conditions on the observed associations between the timing of the economic collapse and birth outcomes. Supplementary logistic regression analysis was performed to examine the association between the aggregate economic indicators (GDP and unemployment rate) and birth outcomes. In this supplementary analysis, aggregate indicators associated with the index outcome at significance level 0.10 were introduced separately into model 1 (model 3: GDP; model 4: unemployment rate), with focus on potential changes in the explanatory coefficients. Finally, as a previous study (16) indicated that the association between the economic collapse and birth outcomes differed by subgroups of women in the first recession year (i.e. young women and women not working a labour-market job were more affected), we conducted stratified logistic regression analyses by parental demographic characteristics and maternal medical conditions during pregnancy. Data analyses were performed using SPSS Statistic for Windows version 20 and 22 and R version 3.2.2. The study was approved by the Icelandic National Bioethics committee, the Data Protection Authority and the Directorate of Health.

RESULTS

Compared with the pre-recession period, women giving birth during the recession (year 1 and years 2-4) were more likely to be older and of foreign citizenship. During the recession years, there was a distinct increase of births among parents not working a labor-market job. We observed an increase in pregnancies with gestational diabetes and gestational

hypertension as well as infants with congenital malformation during the recession period. In contrast, there was a decrease in preeclampsia during the recession period compared with pre-precession period. Further, fewer women underwent emergency or elective cesarean sections during the recession years compared with the years before (Table 1).

Figure 1 shows the prevalence of the three main birth outcomes under study (LBW, PB, SGA) fitted by quarters of each calendar year throughout the whole study period. All outcomes followed a similar pattern during the pre-recession years: an upward trend, which for LBW peaked in the latter half of 2008, but remained elevated for SGA throughout the recession (Figure 1). No time trend was observed for the birth outcomes when examined separately by pre-recession and recession periods. When testing whether there was a difference between the average prevalence of the birth outcomes in the pre-recession and recession periods, SGA was found to be higher after the economic collapse (likelihood ratio test=10.65; p=0.001). No such difference in the average prevalence for LBW and PB was observed (Table S1).

Adjusting for maternal age, gravidity, socioeconomic factors and medical conditions, an increase in LBW was observed during the first recession year (model 2: aOR 1.35, 95% CI 1.12-1.63) but not in the three subsequent recession years (model 2: aOR 1.07, 95% CI 0.93-1.24) (Table 2). Adjusting for the same covariates, an increase was found for SGA in the first year of the recession (model 2: aOR 1.11, 95% CI 1.00-1.23), which lasted throughout recession years 2-4 (model 2: aOR 1.08, 95% CI 1.01-1.16). A tendency towards increase in PB was observed in the first recession year (model 2: aOR 1.12, 95% CI 0.97-1.31) (Table 2), but not in subsequent years.

The association between the aggregate economic indicators and birth outcomes, assessed in the supplementary analysis, showed an association between unemployment rate and SGA and

a weak association of GDP with LBW and SGA (Table S2). When GDP was added as a covariate to the analysis of LBW, the ORs decreased and became insignificant (Table 2, model 3). The observed increase in SGA risk remained unchanged when GDP was added to the model (Table 2, model 3) but when we added unemployment rate as a covariate, the risk increase was essentially eliminated (aOR_{year1} 1.04, 95% CI 0.89-1.21; $aOR_{year2-4}$ 1.00 95% CI 0.86-1.16) (Table 2, model 4).

When examining the association between the economic collapse and birth outcomes stratified by subgroups, the point estimates varied considerably by parental employment status. Compared with the pre-recession period, infants of parents, where only one parent was working a labor-market job, had increased odds of LBW during the first year of the recession (aOR_{year1} 1.66, 95% CI 1.19-2.31). This increase was even greater when neither parent was working and lasted through recession years 2-4 (aOR_{year1} 2.36, 95% CI 1.00-5.55; $aOR_{years2-4}$ 2.88, 95% CI 1.61-5.14). A similar pattern was observed for odds of SGA by employment status of the parents although the point estimates were lower (Table 3).

DISCUSSION

Main findings

The results of this nationwide study on birth outcomes in Iceland following the economic collapse in 2008 indicate an upward trend in LBW and SGA births, which started in parallel with the declining economic conditions the year before the collapse. The rise in LBW and SGA births peaked during the first, and most severe, year of the economic recession with a lasting increase in SGA births throughout the four recession years under study. These findings suggest that the economic collapse had a negative effect on fetal growth, which may to a large extent be explained by adverse macroeconomic conditions.

Strengths and limitations

The major strength of this study is that it leverages on the Medical Birth Registry of Iceland, allowing a prospective collection of information on the health of all women giving birth in Iceland and their offspring during ten years of follow up, independent of the economic collapse. The Medical Birth Registry has collected comprehensive information on pregnancy- and delivery characteristics as well as birth outcomes since 1973 (18). The study population was limited to singleton pregnancies, as adverse birth outcomes are more likely to arise in multiple gestations.

A limitation of the study is the lack of information regarding the maternal behaviour and pre-pregnancy weight during pregnancy. Studies of the health consequences of the Icelandic economic collapse indicate that the health behaviour in general did not change for the worse [13, 21], and our previous findings of reduced smoking and maternal weight among pregnant women in Iceland do not indicate that the behavioural pattern changed differently for the pregnant population [22]. Another limitation of the study is the ecological nature of the exposure. We used calendar time to approximate the economic recession as well as economic indicators, assuming that they affect all women in the study population equally. Obtaining more accurate measurement of the financial situation for each woman in the study would have been the ideal approach. Furthermore, we are unable to control for other factors that might have occurred in Iceland during the same time as the economic collapse, potentially also affecting the outcomes of interest. However, the collapse of the Icelandic financial system was by far the most distinguished event at that time; other changes in environment were likely consequences of the collapse, thus factors in the causal chain rather than independent exposures. Lastly, our study is based on one nation exposed to a specific economic recession. All economic fluctuations have their own features, and the findings of this study may therefore not be readily generalised to other populations of pregnant women undergoing economic recessions.

Interpretation

Our findings on increased prevalence of LBW and SGA are in line with some [3-9], but not all [10-12], previous studies, which indicated an association between unemployment rate and decreased birth weight. Also in line with our findings are results from two individual level studies demonstrating that a parental shift from adequate employment to underemployment before or during pregnancy, can negatively affect birth weight. [3, 4] Lindo [4] hypothesised that the adverse effect of fathers' job displacement on their offspring's birth weight may suggest a contagion effect on their pregnant partners. Indeed, studies support the hypothesis that partners of dismissed workers may experience stress to a similar degree as the affected worker. [23, 24] This is reflected in our findings which suggest a dose-response association between employment status of both parents and LBW; the observed association was greatest when neither parent was working a labour-market job. Furthermore, our findings of increased risk of LBW and SGA among infants of parents with low socioeconomic status are in line with evidence from Spain, suggesting widening inequalities in birth outcomes following the 2008 economic recession. [25]

The direct person-to-person transmission of stress in response to job displacement is important to keep in mind when discussing potential mechanisms for the observed findings. There were signs of economic difficulties during the year leading up to the economic collapse [26], which resulted in a dramatic increase in national unemployment rates during the first months following the collapse [15] and employment insecurity for many more. Although it is challenging to disentangle potential mechanisms leading to the observed increase in LBW and SGA in the present study, it is possible that the increased level of stress, in response to threatened or actual job loss, decreased income and general worry regarding one's economic situation, serves as an explanation for the findings. A wide array of research based on different methodological approaches has linked maternal exposure to chronic stress during

pregnancy with adverse pregnancy outcomes [27, 28], in particular with growth restriction, while acute stress has been found to be more strongly associated with PB [27]. A possible difference in effects of acute vs. chronic stress on birth outcomes might explain the observed indication of increased risk of PB only during the first year of the recession (acute stress) while the increased risk of SGA was lingering throughout the study period (chronic stress). There are, indeed, indications of worsened psychological health following the Icelandic economic collapse as manifested by an increased level of stress [29] and depressive symptoms [30], particularly among unemployed women.

Other potential mechanisms by which economic contraction can affect infant health outcomes at birth include changes in women's health behaviour [31, 32] and medical risk factors [33], as well as a change in the composition of the pregnant population [12], and in utilization of healthcare. [34] In this study, we did not have information on maternal health behaviours, such as smoking, diet, or maternal body weight. However, in a recent study on the prevalence of smoking and maternal weight among pregnant women in Iceland between 2001 and 2010, we noted a reduction in smoking during pregnancy while the prevalence of overweight and obesity remained relatively stable [22]. Furthermore, recent studies indicate, if anything, a positive change in health behaviour of Icelanders following the 2008 economic collapse, i.e. less smoking and alcohol intake, and consumption of more nutritious food. [13, 21] In the current study, we observed some difference in the demographic composition of the pregnant population (e.g. age, citizenship, employment status) as well as in the medical risk factor profile between the pre-recession and recession periods. Further, the findings indicate that infants born to the most vulnerable groups of women (i.e. young women, not employed, not cohabitating, and those with medical conditions prior to or during pregnancy) may have been disproportionally affected by the economic recession. However, adjusting for these factors in the main analyses did not have considerable impact on the point estimates.

Inadequate health care is a predictor of worse birth outcomes, in general. [35] In Iceland, antenatal care is a publicly funded service where women attend in a uniform manner every 2nd to 4th weeks of pregnancy. This service did not change despite cuts in public spending following the economic collapse, making a decrease in maternal care attendance rates of the pregnant women an unlikely explanation for the observed increase in LBW and SGA.

CONCLUSION

In summary, our findings suggest that the economic recession in Iceland, starting in 2008, was associated with a seemingly persistent increase in rates of SGA births. The compromised fetal growth in babies born during this period of major national crisis seems to have been driven by changed macroeconomic conditions. The findings have implications for public health practice and clinical management of pregnant women, suggesting a need for increased support to the pregnant population during stressful situations and, in particular, to young women and women in a vulnerable situation on the labour market.

Word count: 3278

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DISCLOSURE OF INTERESTS

The authors declare that no competing interests exists.

AUTHOR CONTRIBUTION

Aquired the data: VHE, HZ, UAV. Conceived and designed the research: VHE, HZ, UAV, TLA, SC, AH. Analyzed the data: VHE, SHL, UAV, TLA, HZ. Drafted the manuscript: VHE, UAV, HZ, SC, TLA. Responsible for the final manuscript: VHE, HZ, TLA, UAV, SHL, SC, AH.

DETAILS OF ETHICS APPROVAL

The study was approved by the Icelandic National Bioethics committee (VSNb2013010002/03.07), the Data Protection Authority (2012121499HGK/--) and the Directorate of Health (1301064/5.6.1/gkg). An informed consent from participants in the study was not obtained as all personal information was anonymized and de-identified prior to analysis. All procedures performed in the study were in accordance with the ethical standards with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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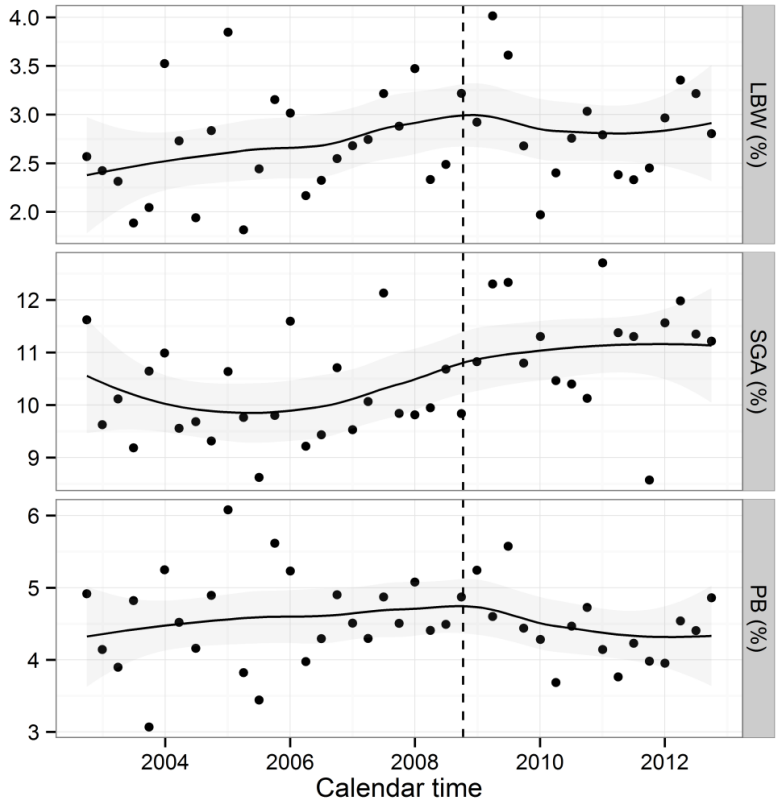

Figure 1 Each point represents the quarterly average prevalence and the 95% confidence intervals (shadowed area) of a) low birth weight (LBW, <2500 g), b) small for gestational age[b] (SGA, <10th pct) and c) preterm birth[a] (PB, <37 weeks) of 43 693 live singleton births in Iceland fitted with a loess curve against time, 2002-2012. The vertical dashed line represents the economic collapse

(missing for [a]33 and [b]44 infants)

Table 1 Demographic and Obstetric Characteristics of All Singleton Live Births (N=43 693) in Iceland between September 30th, 2002, and September 30th, 2012.

Characteristics	Pre-recession period N=25 265		Recession year 1 N=4 763		Recession years 2-4 N=13 665		*P*-value[a]
Mean maternal age [SD]	28.9 [5.5]		29.2 [5.5]		29.3 [5.4]		<0.001
	n	**%**	**n**	**%**	**n**	**%**	
Maternal age (years)							
<25	5821	23.0	995	20.9	2688	19.7	<0.001
25-34	15 267	60.4	2920	61.3	8456	61.9	
≥35	4177	16.6	848	17.8	2521	18.4	
Gravidity							
Primigravida	10 161	40.2	1922	40.4	5404	39.5	0.385
Multigravida	15 104	59.8	2841	59.6	8261	60.5	
Maternal relationship status							
Cohabitating	21 397	84.7	4004	84.1	11 237	82.2	0.310
Not cohabitating	3751	14.8	704	14.8	2060	15.1	
Missing	117	0.5	55	1.2	368	2.7	
Maternal place of residence							
Capital area	15 813	62.6	3154	66.2	8952	65.5	0.005
Rural area	8719	34.5	1600	33.6	4657	34.1	
Missing	733	2.9	9	0.2	56	0.4	
Maternal citizenship							
Icelandic	23 453	92.8	4169	87.5	11 974	87.6	<0.001
Foreign	1812	7.2	594	12.5	1691	12.4	
Parental employment status							
Both parents working	17 515	69.3	3354	70.4	8830	64,6	<0.001

One parent working	6156	24.4	1196	25.1	3971	29.1	
Neither parent working	1031	4.1	211	4.4	853	6.2	
Missing	563	2.2	2	<0.01	11	0.1	
Diabetes							
Pre-existing diabetes	93	0.4	18	0.4	60	0.4	0.786
Gestational diabetes	680	2.7	173	3.6	572	4.2	<0.001
Hypertensive disorders[b]							
Pre-existing hypertension	292	1.2	67	1.4	158	1.2	0.223
Gestational hypertension	502	2.0	150	3.1	409	3.0	<0.001
Preeclampsia	942	3.7	157	3.3	402	2.9	<0.001
Infant‘s sex							
Male	12 966	51.3	2414	50.7	7070	51.7	0.437
Female	12 288	48.6	2349	49.3	6594	48.3	
Missing	11	<0.01	0		1	<0.01	
Apgar score 5-min (<7)	592[c]	2.3	94	2.0	266	1.9	0.022
Congenital malformation	952	3.8	175	3.7	582	4.3	<0.039
Mode of delivery							
Vaginal	21 119	83.6	3988	83.7	11 681	85.5	<0.001
Elective caesarian section	1587	6.3	295	6.2	739	5.4	
Emergency caesarian section	2559	10.1	480	10.1	1245	9.1	

[a]Difference between exposure categories (*P*-value) is based on one-way ANOVA for maternal age (continuous) and chi-square test for the categorical variables.

[b]Gestational hypertension (ICD 13 & 16); preeclampsia (ICD code 11, 14, 15). Hypertensive diagnoses are mutually exclusive – women who are both with the diagnoses O10 and O13, O16 are categorized as having gestational hypertension. Similarly, preeclampsia overrides both gestational hypertension and preexisting hypertension.

[c]1 missing

Table 2 The number and adjusted odds ratios [OR] and 95% confidence intervals [CI] of a) low birth weight, b) preterm birth and c) small for gestational age among 43 693 live born singletons during the economic recession in Iceland compared with pre-recession period

	Pre-recession period		**Recession period**			
			Year 1		Years 2-4	
	N=25 265		N=4763		N=13 665	
	OR	95% CI	OR	95% CI	OR	95% CI
a) Low birth weight, n (%)	605	(2.4)	148	(3.1)	346	(2.5)
Model I[a]	1.00	ref.	1.30	1.08, 1.56	1.05	0.92, 1.21
Model II[b]	1.00	ref.	1.35	1.12, 1.63	1.07	0.93, 1.24
Model III[c]	1.00	ref.	1.19	0.94, 1.50	0.94	0.76, 1.18
b) Preterm birth, n (%)	1080	(4.3)	(226)	(4.7)	557	(4.1)
Model I[a]	1.00	ref.	1.11	0.96, 1.29	0.95	0.86, 1.05
Model II[b]	1.00	ref.	1.12	0.97, 1.31	0.94	0.85, 1.05
c) Small for gestational age, n (%)	2532	(10.0)	535	(11.2)	1492	(10.9)
Model I[a]	1.00	ref.	1.13	1.02, 1.25	1.10	1.03, 1.18
Model II[b]	1.00	ref.	1.11	1.00, 1.23	1.08	1.01, 1.16
Model III[c]	1.00	ref.	1.13	1.00, 1.28	1.10	0.98, 1.23
Model IV[d]	1.00	ref.	1.04	0.89, 1.21	1.00	0.86, 1.16

[a]Adjusted for maternal age (continuous) and gravidity.

[b]Adjusted for maternal age (continuous), gravidity, relationship status, maternal residence, maternal citizenship, parental employment status, hypertensive disorders (4 cat.), diabetes (3 cat.), congenital malformation.

[c]Adjusted for maternal age (continuous), gravidity and gross domestic product (associated with low birth weight and small for gestational age in supplementary analyses).

[d]Adjusted for maternal age (continuous), gravidity and unemployment rate (associated with SGA in supplementary analysis).

Table 3 Adjusted odds ratio [OR] and 95% confidence interval [CI] of a) low birth weight and b) small for gestational age among 43 693 Icelandic live born singletons during the first four year of the economic recession, stratified by parental characteristics and maternal disorders during pregnancy

Characteristics	**Pre-recession period**		**Recession period**				**Recession period**			
			Low birth weight				**Small for gestational age**			
			Year 1		Years 2-4		Year 1		Years 2-4	
	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI	OR[a]	95% CI
Maternal age										
<25 years old	1.00	ref.	1.73	1.23-2.43	1.18	0.90-1.55	1.24	1.02-1.51	1.14	0.99-1.31
25-34 years old	1.00	ref.	1.06	0.82-1.37	1.03	0.86-1.23	1.11	0.97-1.27	1.17	1.07-1.27
≥35 years old	1.00	ref.	1.53	1.03-2.26	1.00	0.74-1.36	1.05	0.82-1.34	0.86	0.72-1.02
Relationship status										
Cohabitating	1.00	ref.	1.17	0.94-1.44	1.01	0.87-1.18	1.12	1.00-1.26	1.10	1.02-1.19
Not cohabitating	1.00	ref.	1.94	1.36-2.76	1.20	0.90-1.59	1.17	0.94-1.47	1.08	0.92-1.26
Residence										

Capital area	1.00	ref.	1.17	0.93-1.47	0.95	0.80-1.12	1.20	1.07-1.36	1.11	1.02-1.21
Rural area	1.00	ref.	1.55	1.14-2.10	1.22	0.97-1.53	0.98	0.81-1.18	1.08	0.96-1.22
Parental employment status										
Both parents working	1.00	ref.	1.19	0.94-1.49	0.93	0.78-1.10	1.12	0.99-1.27	1.07	0.98-1.16
One parent working	1.00	ref.	1.66	1.19-2.31	1.20	0.94-1.54	1.16	0.96-1.41	1.10	0.97-1.26
Neither parent working	1.00	ref.	2.36	1.00-5.55	2.88	1.61-5.14	1.28	0.80-2.04	1.61	1.22-2.14
Diabetes										
No	1.00	ref.	1.28	1.06-1.55	1.04	0.90-1.19	1.12	1.01-1.23	1.10	1.03-1.18
Pre-existing diabetes	1.00	ref.	1.07	0.12-9.85	0.86	0.20-3.80	1.17	0.23-6.02	0.61	0.18-2.10
Gestational diabetes	1.00	ref.	1.99	0.79-5.02	1.61	0.80-3.24	2.04	1.16-3.62	1.27	0.82-1.98
Hypertension[b]										
No	1.00	ref.	1.19	0.94-1.49	1.08	0.92-1.27	1.13	1.01-1.26	1.12	1.04-1.21
Pre-existing hypertension	1.00	ref.	1.95	0.76-5.01	1.79	0.85-3.75	1.43	0.72-2.85	1.41	0.84-2.36
Pregn.- induced hypertension	1.00	ref.	1.38	0.98-1.95	0.90	0.69-1.18	1.01	0.76-1.34	0.91	0.74-1.12

[a]Adjusted for maternal age and gravidity.

[b]Diagnoses of hypertensive disorders are mutually exclusive where, in case of two diagnoses, pregnancy, induced hypertension overrides preexisting hypertension.

Table S1 The trend of the average prevalence before (I) and after (II) the economic collapse and (III) the difference between the average prevalence of a) low birth weight, b) preterm birth, and c) small for gestational age assessed separately in the pre-recession and recession periods

Birth outcomes	**(I) Change per year before the economic collapse[a]**		**(II) Change per year after the economic collapse[b]**		**(III) Difference between the average prevalence before and after the economic collapse**
	Risk ratio	95% CI[c]	Risk ratio	95% CI	Likelihood ratio test (*P*-value)
a) Low birth weight	1.03	0.98-1.07	0.98	0.91-1.05	2.45 (0.12)
b) Preterm birth	1.01	0.98-1.04	0.96	0.91-1.02	0.07 (0.79)
c) Small for gestational age	1.00	0.98-1.03	1.01	0.97-1.04	10.7 (<0.01)

[a]Time period before the collapse: September 30th 2002 - and September 28st 2008.

[b]Time period after the collapse: September 28st 2008-October 1st 2012.

[c]CI: confidence interval

Table S2 The correlation between the aggregate macroeconomic indicators and a) low birth weight, b) preterm birth and c) small for gestational age among live birth singletons in Iceland, between September 30th, 2002, and October 1st, 2012.

	Regression models			
	Crude	Model I[a]	Model II[b]	Model III[c]
	OR[d] 90% CI[e] (*P*-value)	OR 90% CI (*P*-value)	OR 90% CI (*P*-value)	OR 90% CI (*P*-value)
a) Low birth weight				
Gross domestic product (milliard ISK) [f]	1.00 1.00-1.00 (0.03)	1.00 1.00-1.00 (0.04)	1.00 1.00-1.00 (0.06)	1.00 1.00-1.00 (0.05)
Aggregate unemployment (%)[g]	1.02 0.99-1.04 (0.21)	1.02 0.99-1.04 (0.21)	1.01 0.99-1.04 (0.31)	1.03 0.99-1.08 (0.11)
b) Preterm birth				
Gross domestic product (milliard ISK)[f]	1.00 1.00-1.00 (0.99)	1.00 1.00-1.00 (0.93)	1.00 1.00-1.00 (0.72)	1.00 1.00-1.00 (0.97)
Aggregate unemployment (%)[g]	0.99 0.97-1.01 (0.47)	0.99 0.97-1.01 (0.48)	0.99 0.97-1.01 (0.32)	0.99 0.97-1.01 (0.42)
c) Small for gestational age				
Gross domestic product (milliard ISK)[f]	1.00 1.00-1.00 (0.05)	1.00 1.00-1.00 (0.01)	1.00 1.00-1.00 (0.16)	1.00 1.00-1.00 (0.07)
Aggregate unemployment (%)[g]	1.03 1.01-1.04 (<0.01)	1.03 1.01-1.04 (<0.01)	1.02 1.01-1.03 (0.01)	1.02 1.01-1.04 (<0.01)

[a]Adjusted for maternal age, gravidity.
[b]Simultaneously adjusted for maternal age, gravidity, relationship status, place of residence, parental employment status and citizenship.
[c]Simultaneously adjusted for maternal age, gravidity, relationship status, place of residence, parental employment status and citizenship, diabetes and hypertension and congenital malformation.
[d]OR: odds ratio. [e]CI: confidence interval.
[f]On quarterly basis from September 30th, 2002 [g]On quarterly basis from January 1st, 2003

Study approvals

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Tilv.: VSNb2010050009/03.7

Texti:

Á fundi sínum 29.01.2013 fjallaði Vísindasiðanefnd um umsókn þína dags. 14.01.2013, vegna viðbótar við ofangreinda rannsóknaráætlun. Í erindinu þínu kemur fram að óskað er eftir leyfi nefndarinnar fyrir frekari úrvinnslu gagna sem notuð hafa verið í doktorsverkefni Agnesar Gísladóttur;Fæðingarútkomur kvenna sem hafa orðið fyrir kynferðisofbeldi. Um er að ræða tvö viðbótarmarkmið sem miða að því að fá svör við eftirfarandi spurningum:

1. Hefur orðið breyting á líkamsþyngdarstuðli ófrískra kvenna í kjölfar íslenska efnahagshrunsins?

2. Hafa orðið breytingar á tíðni reykinga, áfengis-eða vímuefnaneyslu meðal ófrískra kvenna í kjölfar efnahagskreppunnar?

Fram kemur að vinnslugrunnurinn er á ópersónugreinanlegu formi og inniheldur gögn sem svarað gætu ofangreindum spurningum. Upplýsinga um líkamsþyngdarstuðul, reykingar, áfengis- og vímuefnaneyslu var aflað með því að lesa mæðraskrár, en þessar upplýsingar eru ekki til í rafrænni skráningu. Um er að ræða gögn um meðgöngu og fæðingu um 900 kvenna með sögu um kynferðisofbeldi sem og 1700 kvenna án slíkrar sögu sem valdar voru af handahófi til samanburðar.

Vísindasiðanefnd hefur farið yfir bréf þitt og gerir ekki athugasemdir við tilgreindar breytingar. Viðbót nr. 1 ásamt fylgigögnum við ofangreinda rannsókn, er endanlega samþykkt af Vísindasiðanefnd.

Áréttað er að ábyrgðarmanni ber að láta stofnanir, sem áður hafa veitt leyfi vegna framkvæmdar rannsóknarinnar, vita af ofangreindri breytingu á rannsóknaráætluninni.

Með kveðju,
f.h. Vísindasiðanefndar,

Gísli Ragnarsson, varaformaður

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Heimild

til handa embætti landlæknis
- vinnsla upplýsinga úr fæðingaskrá og lyfjagagnagrunni landlæknis, samkeyrsla viðkvæmra persónuupplýsinga og miðlun viðkvæmra persónuupplýsinga

til handa rannsakanda
- vinnsla viðkvæmra persónuupplýsinga

I.
Upphafleg umsókn og frekari bréfaskipti

1.
Móttekin umsókn

Persónuvernd hefur borist umsókn, dags. 21. desember 2012, frá Unni Önnu Valdimarsdóttur, prófessor og forstöðumanni Miðstöðvar í lýðheilsuvísindum við Háskóla Íslands, og Védísi Helgu Eiríksdóttur, doktorsnema í lýðheilsuvísindum, um leyfi til aðgangs að fæðingaskrá landlæknis, lyfjagagnagrunni landlæknis, upplýsingum úr skattgrunnskrá frá Hagstofu Íslands, sem og samkeyrslu framangreindra gagna, vegna rannsóknarinnar „Áhrif íslenska efnahagshrunsins á heilsu barnshafandi kvenna og fæðingarútkomur".

Í umsókninni er tilgangi fyrirhugaðrar vinnslu lýst á eftirfarandi hátt:

> „Rannsóknin er verkefni Védísar Helgu Eiríksdóttur til doktorsgráðu í lýðheilsuvísindum. Efnahagshrunið í október 2008 var einstakt í umfangi og hraða og leiða má að því líkur að það hafi haft áhrif á líf flestra landsmanna á einhvern hátt. Rannsóknir hafa leitt í ljós að streituvaldandi

atburðir og áföll á meðgöngu geta haft neikvæð áhrif á meðgöngulengd og fæðingaþyngd. Fáar rannsóknir hafa hins vegar verið gerðar á tengslum efnahagsáfalla og þessara sömu óhagstæðu fæðingarútkomna. Niðurstöður fyrri rannsóknar á vegum umsækjenda benda til þess að tíðni léttburafæðinga hafi aukist í kjölfar efnahagsáfallsins 2008. Tilgangur þessarar rannsóknar er að varpa frekara ljósi á mögulegar afleiðingar efnahagshrunsins á heilsu barnshafandi kvenna (t.d. háþrýsting) og nýbura (t.d. fæðingarþyngd) til langs tíma, auk þeirra þátta sem gætu miðlað slíkum áhrifum. Sérstök áhersla verður lögð á áhættu meðal viðkvæmra hópa, s.s. ungra, atvinnulausra og einhleypra mæðra. Ennfremur verður kannað hvort konur sem upplifa tekjumissi á meðgöngu séu í aukinni hættu á að eignast léttbura eða fyrirbura."

Samkvæmt umsókninni er fyrirhugað að rannsóknarúrtak verði valið með eftirfarandi hætti:

„Um er að ræða lýðgrundaða ferilrannsókn þar sem unnið verður með dulkóðuð gögn. Ekki verður á neinu stigi rannsóknar haft samband við þátttakendur hennar beint, enda ómögulegt að rekja upplýsingar rannsóknar til einstaklinga. Þar af leiðandi verður ekki aflað upplýsts samþykkis þátttakenda.

Hvað þátttakendur varðar munu upplýsingar um allar barnshafandi íslenskar konur úr fæðingaskrá, sem eignuðust einbura á tímabilinu 1. janúar 2002 til 31. desember 2012 verða notaðar til rannsóknarinnar. Sé gert ráð fyrir að meðaltali 4300 einburafæðingum árlega er fjöldi rannsóknarþýðis u.þ.b. 47 þúsund barnshafandi konur auk afkvæma þeirra. Upplýsingar um konur með erlent ríkisfang sem fæða barn hér á landi verða ekki notaðar til rannsóknarinnar þar sem þeirra fyrri lífsreynsla og upplifun gæti haft áhrif á framvindu meðgöngu og fæðingarútkomur og þ.a.l. valdið bjögun. Af sömu ástæðu eru íslenskar konur sem búsettar eru erlendis við fæðingu barna þeirra ekki hafðar með í úrtaki.

Lyfjagagnagrunnur embættis landlæknis verður notaður til að safna upplýsingum um notkun á blóðþrýstingslækkandi lyfjum á meðgöngu hjá öllum konum sem eignuðust einbura á rannsóknartímabilinu. Auk þess mun verða óskað eftir upplýsingum úr skattgrunnskrá Hagstofu Íslands um tekjur/tekjumissi hjá rannsóknarhóp með það að marki að kanna möguleg tengsl tekjumissis og óhagstæðs heilsufars barnshafandi kvenna og fæðingaútkoma."

Samkvæmt umsókninni er fyrirhugað að gagnagrunnsstjóri embættis landlæknis afli upplýsinga úr fæðingaskrá embættisins og lyfjagagnagrunni embættisins, um allar konur sem fæddu einbura á tímabilinu 1. janúar 2002 til 31. desember 2012, í þeim tilgangi að samkeyra þær við upplýsingar sem gagnagrunnsstjóri landlæknis móttekur frá Hagstofu Íslands úr skattgrunnskrá um sama hóp einstaklinga. Mun embætti landlæknis í kjölfarið afhenda rannsakendum rannsóknargögnin að lokinni samkeyrslu þeirra, án kennitalna. Eru rannsóknarlok áætluð í lok árs 2015.

Samkvæmt umsókninni munu rannsakendur varðveita móttekin gögn frá landlækni á tölvutæku formi á læstri skrifstofu Miðstöðvar Háskóla Íslands í lýðheilsuvísindum á meðan rannsókn stendur og að rannsókn lokinni. Forstöðumaður Miðstöðvar í lýðheilsuvísindum og ábyrgðarmaður þessarar umsóknar mun hafa umráðarétt á rannsóknargögnum og einungis vinnsluaðilar munu hafa aðgang að þeim gögnum sem hér um ræðir.

2.
Bréfaskipti við Unni Önnu Valdimarsdóttur,
embætti landlæknis og Hagstofu Íslands

Með bréfi, dags. 18. apríl 2013, óskaði Persónuvernd nánari upplýsinga um framkvæmd rannsóknarinnar. Barst stofnuninni svarbréf Unnar Önnu, dags. 29. apríl 2013, þann 2. maí 2013.

Með bréfi, dags. 17. maí sl., óskaði Persónuvernd eftir afstöðu Unnar Önnu til þess að afrúna þær breytur sem gætu orðið til þess að upplýsingar yrðu persónugreinanlegar, sér í lagi þegar litið er til allra breyta í heild sinn, t.d. um fæðingardag barns, póstnúmer móður, aldur móður og ríkisfang beggja foreldra. Í svarbréfi rannsakanda, dags. 4. júní sl., segir:

„[...T]il þess að koma í veg fyrir að rannsakendur gætu mögulega, með mikilli fyrirhöfn, auðkennt þá einstaklinga sem hér um ræðir, þá leggjum við til að rúnna af tvær af fjórum umræddum breytum án þess að vísindalegt gildi (og þar með siðferðilegt) rannsóknarinnar skerðist. Annars vegar væri um að ræða póstnúmer móður; og leggjum við þar til grófari flokkun, s.s. stór-Reykjavíkursvæði/Akureyri/Reykjanes/dreifbýli. Hins vegar væri um að ræða ríkisfang móður og föður; þar sem við leggjum til tvíkosta skiptingu í íslenskt ríkisfang/erlent ríkisfang.

Grófari flokkun á öðrum breytum sem um var rætt í bréfi Persónuverndar (t.d. aldri móður), myndi óumflýjanlega leiða til aukinnar áhættu á ónákvæmum niðurstöðum eða í versta falli röngum niðurstöðum. Það er með því engu móti ásættanlegt vísindalega - og á sér engin fordæmi í okkar fyrri rannsóknum (með leyfi Persónuverndar) - að framkvæma umrædda rannsókn án umræddra upplýsinga."

Í kjölfar fundar sem haldinn var með rannsakendum þann 12. júlí 2013 óskaði Persónuvernd eftir nánari rökstuðningi fyrir þeirri upplýsingaöflun sem hér um ræðir úr skrám landlæknis og Hagstofu Íslands. Í svarbréfi Unnar Önnu, dags. 14. ágúst 2013, segir m.a.:

„[...E]ru rannsakendur reiðubúnir að koma til móts við sjónarmið Persónuverndar á eftirfarandi hátt: Við munum óska eftir upplýsingum úr lyfjagagnagrunni um úttekt á lyfjaflokkunum hjarta- og æðasjúkdómalyf (ATC flokkur C) og geðlyf (ATC flokkur N05 og N06). Í stað nákvæmrar lyfjategundar fallast rannsakendur á að fá afhentar upplýsingar um lyfjaflokk sem afmarkast af 4 stigs ATC flokkun (s.s. SRI þunglyndislyf, ATC flokkur N06AB) meðal ófríska kvenna á rannsónartímanum, á vikubasis frá þremur mánuðum fyrir getnað og út meðgöngu. Nákvæm dagsetning lyfjaávísunar og lyfjaúttektar verður því algjörlega afmáð en vegna þess að lyfjanotkun getur verið mis-áhættusöm eftir því hvenær á meðgöngu lyf eru tekin, óskum við eftir því að geta aðgreint lyfjanotkun eftir því hvenær á meðgöngu lyfið er notað. [...]

Við höfum þegar samþykkt að afrúna breytur um póstnúmer móður, ríkisfang móður og föður, ásamt lyfjaupplýsingum[...]. Við leggjum til við embætti landlæknis að rúnna af fæðingardag barns í rannsóknargrunninum við tveggja daga bil og vikubil. Nákvæm dagsetning fæðingar verður því algjörlega afmáð en þessi nálgun gerir okkur kleift að viðhalda eins mikilli nákvæmni og hægt er í áhrifum tíma á fæðingarútkomur. [...]

Eftir ítarlega skoðun á breytulista rannsóknarinnar föllumst við einnig á að fara ekki fram á upplýsingar um áður umbeðna breytu varðandi hjúskaparstétt foreldra. Afrúnun annarra breyta teljum við ekki mögulega án þess að raska verulega vísindalegu gildi rannsóknarinnar."

Í ljósi framangreinds svarbréfs rannsakenda óskaði Persónuvernd eftir upplýsingum frá embætti landlæknis með bréfi, dags. 24. september 2013, um afstöðu embættisins til þess að rúnna af breytur úr lyfjagagnagrunni og fæðingaskrá með þeim hætti sem Unnur Anna lýsti í bréfi, dags. 14. ágúst sl., áður en gögnin yrðu afhent rannsakanda.

Í svarbréfi landlæknis, dags. 18. október 2013, kemur fram að embættið hafi samþykkt með bréfi, dags. 14. janúar 2013 að heimila rannsakendum aðgang að upplýsingum úr fæðingaskrá og lyfjagagnagrunni landlæknis sem voru nánar tilgreindar í breytulista er fylgdi með áðurnefndu bréfi embættisins til Persónuverndar. Þá segir að embættið setji ávallt þau skilyrði að framsetning og birting upplýsinga sem byggja á gögnum úr gagnagrunnum landlæknis séu með þeim hætti að ekki sé hægt að rekja til einstaklinga. Er það skylda rannsakenda að uppfylla þessi skilyrði landlæknis. Í umræddri rannsókn hafi landlæknir aftur á móti sett það viðbótarskilyrði að ábyrgðarmaður rannsóknarinnar setji inn reiknaða breytu í stað raunverulegs fæðingardags barns og afmái í kjölfarið skráðan fæðingardag. Aðferðafræði við þessa aðgerð skuli borin undir embættið og þarf embættið að samþykkja hana áður en gögn verða afhent rannsakendum. Að öðru leyti telji landlæknir ekki þörf á að afrúna eða meðhöndla á annan hátt aðrar breytur úr fæðingaskrá eða lyfjagagnagrunni áður en gögn verða afhent.

Var rannsakanda, Unni Önnu, tilkynnt um framangreinda afstöðu landlæknis með bréfi Persónuverndar, dags. 12. nóvember 2013, og henni bent á að embætti landlæknis bæri ábyrgð á afhendingu viðkvæmra persónuupplýsinga úr umræddum skrám og myndi því Persónuvernd halda áfram með efnislega afgreiðslu umsóknarinnar, m.t.t. athugasemda landlæknis um úrvinnslu þeirra gagna sem yrðu afhent rannsakendum, þar á meðal um skráningu upplýsinga um fæðingardag barns.

Með tölvupósti, mótteknum þann 15. nóvember 2013, staðfesti embætti landlæknis að samkeyrslan hjá embættinu yrði framkvæmd í samræmi við verklag embættisins og rannsóknargrunnur afhentur án kennitalna en með einkvæmum númerum í stað þeirra til rannsakanda.

Með tölvupóstum, mótteknum dagana 7. og 11. febrúar 2014, samþykktu embætti landlæknis og Hagstofa Íslands að afhending og samkeyrsla upplýsinga frá embættunum yrði breytt með eftirfarandi hætti:

1) Gögn úr fæðingaskrá eru samkeyrð við lyfjagagnagrunn á kennitölum hjá embætti landlæknis.
2) Í gagnasettinu sem til verður við þessa samkeyrslu er hverri kennitölu úthlutað einkvæmu rannsóknarnúmeri. Sér gagnagrunnsstjóri landlæknis um að úthluta umræddum rannsóknarnúmerum.
3) Hagstofu Íslands er sent skjal frá embætti landlæknis með kennitölum og rannsóknarnúmerum, þ.e. hvaða rannsóknarnúmer samsvarar hvaða kennitölu. Þegar móttaka skjalsins er staðfest af Hagstofunni eyðir gagnagrunnsstjóri landlæknis upprunalega skjalinu.
4) Kennitölum er því næst eytt úr gagnasettinu hjá embætti landlæknis en einungis verða eftir rannsóknarnúmerin.
5) Hagstofa Íslands finnur þau gögn sem þaðan er óskað, n.t.t. úr skattgrunnskrá Hagstofunnar, með því að nota kennitölulistann úr skjalinu frá landlækni með kennitölum og rannsóknarnúmerum.
6) Hagstofan eyðir loks kennitölum úr gagnasettinu sem til verður þar en sendir gögnin til embættis landlæknis einungis með rannsóknarnúmerunum.
7) Gagnasett Hagstofu og gagnasett embættis landlæknis eru samkeyrð á rannsóknarnúmerum hjá embætti landlæknis (hvorug skráin væri með kennitölum). Sér gagnagrunnsstjóri um að framkvæma umrædda samkeyrslu.
8) Rannsakandi, Unnur Anna Valdimarsdóttir, fær afhent gagnasett með rannsóknarnúmerum eingöngu frá gagnagrunnsstjóra landlæknis, n.t.t. án kennitalna.

II.
Leyfisskyld vinnsla

Af framangreindu er ljóst að í rannsókninni felst öflun upplýsinga um einstaklinga úr lyfjagagnagrunni landlæknis. Samkvæmt 9. mgr. 27. gr. lyfjalaga nr. 93/1994, sbr. 3. mgr. 15. gr. laga nr. 74/1997 um réttindi sjúklinga, þarf leyfi Persónuverndar til aðgangs að lyfjagagnagrunni landlæknis í þágu vísindarannsókna.

Þá verður einnig aflað upplýsinga úr fæðingaskrá landlæknis. Fæðingaskrá er varðveitt á Landspítala en embætti landlæknis skipuleggur skrána og er ábyrgðarmaður hennar, sbr. 1. tölul. 2. mgr. og 4. mgr. 8. gr. laga nr. 41/2007 um landlækni. Samkvæmt 8. mgr. sömu greinar, sbr. 3. mgr. 15. gr. laga nr. 74/1997 um réttindi sjúklinga, þarf leyfi Persónuverndar til aðgangs að þeirri skrá.

Er fyrirhugað að embætti landlæknis afhendi Hagstofu Íslands skjal með kennitölum og einkvæmum rannsóknarnúmerum, svo að Hagstofa geti sótt upplýsingar úr skattgrunnskrá um umrædda einstaklinga. Leyfi Persónuverndar þarf fyrir slíkri miðlun viðkvæmra persónuupplýsinga, sem varðveittar eru hjá stjórnvaldi, til Hagstofu Íslands í þágu rannsókna skv. 8. tölul. 1. mgr. 4. gr. reglna nr. 712/2008 um tilkynningarskylda og leyfisskylda vinnslu persónuupplýsinga, sbr. 33. gr. laga nr. 77/2000.

Auk þess er fyrirhugað að láta gagnagrunnsstjóra embættis landlæknis framkvæma samkeyrslu á upplýsingum úr lyfjagagnagrunni og fæðingaskrá við mótteknar upplýsingar úr skattgrunnskrá frá Hagstofu Íslands. Samkvæmt ákvæði 1. tölul. 1. mgr. 4. gr. reglna nr. 712/2008 um tilkynningarskylda og leyfisskylda vinnslu persónuupplýsinga, sbr. 33. gr. laga nr. 77/2000, er samkeyrsla skráa, sem hefur að geyma viðkvæmar persónuupplýsingar við aðra skrá, hvort sem sú hefur að geyma almennar eða viðkvæmar persónuupplýsingar, háð leyfi Persónuverndar. Slík samkeyrsla er þó ekki leyfisskyld ef samkeyrðar eru skrár sama ábyrgðaraðila, þó að undanskildum miðlægum skrám sem innihalda viðkvæmar persónuupplýsingar, eða ef einvörðungu eru samkeyrðar upplýsingar úr þjóðskrá um nafn, kennitölu, fyrirtækjanúmer, heimilisfang, aðsetur og póstnúmer. Í ljósi þess að samkeyrðar verða upplýsingar úr tveimur skrám landlæknis við upplýsingar úr skattgrunnskrá Hagstofu Íslands er umrædd samkeyrsla háð leyfi Persónuverndar. Hefur Hagstofa Íslands samþykkt að afhenda upplýsingar með einkvæmum rannsóknarnúmerum til gagnagrunnsstjóra landlæknis, sem mun í kjölfarið annast samkeyrslu við önnur gögn rannsóknarinnar.

Þá er jafnframt fyrirhugað að láta gagnagrunnsstjóra embættis landlæknis afhenda Unni Önnu Valdimarsdóttur rannsakanda rannsóknargrunn án kennitalna að lokinni samkeyrslu upplýsinga úr fæðingaskrá, lyfjagagnagrunni og skattgrunnskrá Hagstofu Íslands. Telur Persónuvernd að þær upplýsingar sem embætti landlæknis hyggst afhenda rannsakanda án kennitalna séu engu að síður persónurekjanlegar, í skilningi laga nr. 77/2000, þar sem eftir standi í rannsóknargrunninum óafrúnaðar breytur að mestu leyti sem saman veiti persónugreiningu hinna skráðu. Samkvæmt ákvæði 8. tölul. 1. mgr. 4. gr. reglna nr. 712/2008 um tilkynningarskylda og leyfisskylda vinnslu persónuupplýsinga er miðlun viðkvæmra persónuupplýsinga, sem varðveittar eru hjá stjórnvöldum, í þágu rannsókna háð skriflegri heimild Persónuverndar. Á framangreint við um afhendingu rannsóknargrunns með persónugreinanlegum viðkvæmum persónuupplýsingum frá embætti landlæknis til rannsakanda. Þá þarf einnig leyfi Persónuverndar, samkvæmt 9. tölul. 1. mgr. 9. gr. laga nr. 77/2000, fyrir vinnslu viðkvæmra persónuupplýsinga sé hún nauðsynleg vegna tölfræði- eða vísindarannsókna, enda sé persónuvernd tryggð með tilteknum ráðstöfunum eftir því sem við á. Á framangreint við um vinnslu rannsakanda, Unnar Önnu, á þeim upplýsingum sem hún móttekur í rannsóknargrunni frá landlækni.

Stofnunin bindur leyfi til handa landlækni og Unni Önnu Valdimarsdóttur rannsakanda þeim skilyrðum sem hún telur nauðsynleg hverju sinni.

III.
Leyfi og leyfisskilmálar er varða embætti landlæknis

- um vinnslu upplýsinga úr fæðingaskrá og lyfjagagnagrunni landlæknis, miðlun viðkvæmra persónuupplýsinga til Hagstofu Íslands, samkeyrslu viðkvæmra persónuupplýsinga og miðlun viðkvæmra persónuupplýsinga til rannsakanda

Í samræmi við 8. mgr. 8. gr., sbr. 1. tölul. 2. mgr. sömu greinar laga nr. 41/2007 um landlækni, 9. mgr. 27. gr. lyfjalaga nr. 93/1994, sbr. 3. mgr. 15. gr. laga nr. 74/1997 um réttindi sjúklinga, og 1.

og 8. tölul. 1. mgr. 4. gr. reglna nr. 712/2008, sbr. 33. gr. laga nr. 77/2000, er embætti landlæknis, f.h. Unnar Önnu Valdimarsdóttur rannsakanda, veitt heimild til tiltekinnar vinnslu persónuupplýsinga í fæðingaskrá landlæknis og lyfjagagnagrunni landlæknis í þágu rannsóknarinnar „Áhrif íslenska efnahagshrunsins á heilsu barnshafandi kvenna og fæðingarútkomur". Nánar tiltekið er embættinu heimilað að afla tiltekinna upplýsinga úr skránum, miðla kennitölulista til Hagstofu Íslands og loks samkeyra mótteknar upplýsingar úr skattgrunnskrá frá Hagstofu Íslands við áðurnefndar upplýsingar úr lyfjagagnagrunni og fæðingaskrá í þágu sömu rannsóknar.

Er gagnagrunnsstjóra embættis landlæknis heimilt að finna kennitölur kvenna sem fæddu einbura á tímabilinu 1. janúar 2002 til 31. desember 2012 úr fæðingaskrá landlæknis til þess að afla eftirfarandi upplýsinga úr fæðingaskrá:

Úr fæðingaskrá landlæknis

Meðganga
- Lengd meðgöngu skv. síðustu tíðum
- Lengd meðgöngu skv. ómun

Fæðing
- Dagsetning fæðingar
- Númer fæðingar
- Fæðingarstaður
  - heiti stofnunar
  - utan fæðingastofu
- Lengd fæðingar (mín)
- Áður fætt lifandi
- Áður fætt andvana
- Tala fyrri fósturláta
- Upphaf fæðingar
- Afbrigði fæðingar - móðir
- Íhlutun/meðferð/aðgerðir í fæðingu

Móðir
- Aldur
- Staða/Atvinna
- Íslenskt/erlent ríkisfang
- Sambýli móður og föður
- Búseta (stór-Reykjavíkursvæði/Akureyri/Reykjanes/dreifbýli)
- Sjúkdómsgreiningar móður

Faðir
- Staða/atvinna
- Íslenskt/erlent ríkisfang

Barn
- Kyn barns
- Barn fæddist lifandi/andvana
- Fjöldi barna í fæðingu
- Þyngd við fæðingu
- Lengd við fæðingu
- Ummál höfuðs
- Barn dó - dánardagsetning
- Apgar 1 mín
- Apgar 5 mín
- Heilbrigt barn

Sjúkdómsgreiningar barns (ICD kóði)

Að því loknu er embætti landlæknis heimilt að nota kennitölur sömu kvenna til að afla eftirfarandi upplýsinga úr lyfjagagnagrunni landlæknis:

Úr lyfjagagnagrunni landlæknis
Upplýsingar um úttektir á lyfjaflokkunum hjarta- og æðasjúkdómalyf (ATC flokkur C) og geðlyf (ATC flokkur N05 og N06) meðal ófrískra kvenna á rannsóknartímabilinu, á vikubili, frá 90 dögum fyrir dagsetningu síðustu blæðinga (LMP) til loka meðgöngu/fæðingu barns. Ekki verða sóttar upplýsingar úr lyfjagagnagrunni um lyfjategund, dagsetningu lyfjaávísunar eða dagsetningu lyfjaúttektar.

Er landlækni í kjölfarið heimilt að afhenda Hagstofu Íslands kennitölur þeirra kvenna sem eru í framangreindu úrtaki rannsóknarinnar með eftirfarandi hætti:

1) Hagstofu Íslands er sent skjal frá embætti landlæknis með kennitölum og rannsóknarnúmerum, þ.e. hvaða rannsóknarnúmer samsvarar hvaða kennitölu. Þegar móttaka skjalsins er staðfest af Hagstofunni eyðir gagnagrunnastjóri landlæknis upprunalega skjalinu.
2) Kennitölum er því næst eytt úr gagnasettinu hjá embætti landlæknis en einungis verða eftir rannsóknarnúmerin.

Þegar Hagstofa Íslands hefur aflað upplýsinga úr skattgrunnskrá um konur í úrtaki rannsóknarinnar er landlækni heimilað að framkvæma samkeyrslu á eftirfarandi upplýsingum úr skattgrunnskrá sem hann móttekur frá Hagstofu Íslands með rannsóknarnúmerum en án kennitalna, við upplýsingar úr lyfjagagnagrunni og fæðingaskrá sem varðveittar eru undir rannsóknarnúmerum hjá gagnagrunnsstjóra landlæknis:

Úr skattgrunnskrá Hagstofu Íslands
Upplýsingar sem berast gagnagrunnsstjóra embættis landlæknis frá Hagstofu Íslands um tekjur á ársgrundvelli hjá þeim konum, og mökum þeirra (þar sem við á), sem eignuðust einbura á rannsóknartímabilinu, n.t.t. persónunúmer, fjölskyldunúmer, kyn, fjöldi barna, launatekjur, tekjur af atvinnurekstri, laun, tekjuár, reiknað endurgjald, hjúskapur, skattur og áætlun.

Leyfi þetta gildir til **31. desember 2015** og er bundið eftirfarandi skilyrðum:

1. Ábyrgðaraðili að vinnslu persónuupplýsinga
Embætti landlæknis (sem hér eftir kallast leyfishafi) telst vera ábyrgðaraðili þessa hluta vinnslunnar í skilningi 4. tölul. 2. gr. laga nr. 77/2000. Fer landlæknir með allt fyrirsvar gagnvart Persónuvernd um alla þætti er varða þetta leyfi, þ.á m. álitaefni, er upp kunna að rísa, um það hvort vinnsla persónuupplýsinga hafi verið í samræmi við lög, reglur og ákvæði þessa leyfis.

2. Lögbundnir leyfisskilmálar
a. Ábyrgðarmaður fæðingaskrár og lyfjagagnagrunns skal varðveita yfirlit yfir þær upplýsingar sem veittur er aðgangur að í þágu rannsóknar þessarar til þess að geta síðar uppfyllt upplýsingaskyldu gagnvart hinum skráðu í samræmi við 18. gr. laga nr. 77/2000.
b. Leyfi þetta er bundið því skilyrði að siðanefnd, eða eftir atvikum vísindasiðanefnd, hafi lagt mat á rannsóknina og látið í té skriflegt álit sitt þess efnis að hvorki vísindaleg né siðfræðileg sjónarmið mæli gegn framkvæmd hennar, sbr. 3. mgr. 15. gr. laga nr. 74/1997, sbr. 4. mgr. 2. gr. sömu laga.

3. Lögmæt vinnsla persónuupplýsinga og þagnarskylda

a. Leyfishafi ber ábyrgð á því að vinnsla persónuupplýsinga vegna rannsóknarinnar fullnægi ávallt kröfum 1. mgr. 7. gr. laga nr. 77/2000.
b. Farið skal með upplýsingar úr fæðingskrá, sem skráðar eru vegna rannsóknarinnar, í samræmi við lög nr. 77/2000, lög nr. 74/1997 um réttindi sjúklinga, lög nr. 34/2012 um heilbrigðisstarfsmenn og lög nr. 55/2009 um sjúkraskrár og reglna settra með stoð í þeim lögum. Hvílir þagnarskylda á leyfishafa og öðrum þeim sem koma að rannsókninni um heilsufarsupplýsingar sem unnið er með, sbr. 15. gr. laga nr. 53/1988. Þagnarskylda helst þótt látið sé af störfum við rannsóknina.

4. Afhending kennitölulista til Hagstofu Íslands og samkeyrsla við kvæmra persónuupplýsinga hjá landlækni

a. Eftir að landlæknir hefur fundið úrtak rannsóknarinnar úr fæðingaskrá landlæknis, eins og lýst er í upphafi III. kafla í leyfi þessu, er honum heimilt að skrá umræddar breytur úr fæðingaskrá í rannsóknargrunn undir kennitölum.
b. Við rannsóknargrunninn bætir gagnagrunnsstjóri landlæknis næst tilgreindar breytur úr lyfjagagnagrunni landlæknis um sama hóp einstaklinga, eins og einnig er lýst í upphafi III kafla í leyfi þessu.
c. Embætti landlæknis er næst heimilt að miðla lista með kennitölum og einkvæmum rannsóknarnúmerum til Hagstofu Íslands með öuggum hætti með hliðsjón af eðli gagnanna.
d. Upplýsingar úr skattgrunnskrá frá Hagstofu Íslands, sem sendar eru til gagnagrunnsstjóra embættis landlæknis, skulu sendar honum með öruggum hætti og án kennitalna. Sér gagnagrunnsstjóri Hagstofunnar um afhendingu upplýsinganna til embættis landlæknis. Mun Hagstofan eyða mótteknum upplýsingum frá landlækni um kennitölur einstaklinga í úrtaki rannsóknarinnar, áður en upplýsingar úr skattgrunnskrá verða afhentar embætti landlæknis á einkvæmum rannsóknarnúmerum.
e. Þegar gagnagrunnsstjóri, f.h. embættis landlæknis, hefur móttekið umrædd gögn frá Hagstofunni er honum heimilt að bæta þeim upplýsingum úr skattgrunnskrá við rannsóknargrunn landlæknis, undir einkvæmum rannsóknarnúmerum, þ.e. án kennitalna.
f. Skal gagnagrunnsstjóri landlæknis gæta að því að kennitölum einstaklinga í úrtaki rannsóknarinnar, sé eytt um leið og Hagstofa Íslands hefur staðfest móttöku á kennitölulista frá embætti landlækni, eins og lýst er í upphafi III. kafla í leyfi þessu. Að fenginni slíkri staðfestingu er landlækni einungis heimilt að varðveita upplýsingar í rannsóknargrunni án kennitalna.
g. Ber gagnagrunnsstjóra landlæknis að eyða öllum mótteknum upplýsingum frá Hagstofu Íslands í þágu rannsóknarinnar að samkeyrslu lokinni skv. e-lið þessarar greinar.

5. Afhending rannsóknargagna til rannsakenda

a. Embætti landlæknis er heimilt að afhenda rannsakanda framangreindar upplýsingar úr fæðingaskrá, lyfjagagnagrunni og skattgrunnskrá Hagstofu Íslands að lokinni samkeyrslu þeirra, sbr. 4. gr., **með rannsóknarnúmerum eingöngu en án kennitalna, persónunúmera eða fjölskyldunúmera eða annarra persónuauðkenna.**
b. Ef upplýsingarnar eru afhentar rannsakendum út úr húsi landlæknis ber að gera það með öruggum hætti með hliðsjón af eðli gagnanna.
c. Eðli málsins samkvæmt tekur þessi hluti leyfisins eingöngu til vinnslu tiltekinna upplýsinga úr skrám landlæknis og skattgrunnskrá Hagstofu Íslands, samkeyrslu þeirra og loks afhendingu upplýsinga með einkvæmum rannsóknarnúmerum til rannsakanda en ekki til eftirfarandi vinnslu rannsakanda á upplýsingunum í þágu vísindarannsóknar sinnar. Er nánar fjallað um skilmála til handa rannsakanda, varðandi úrvinnslu gagna frá landlækni, í kafla IV.
d. Þrátt fyrir c-lið þessarar greinar ber landlækni að veita rannsakanda, Unni Önnu Valdimarsdóttur, fyrirmæli um að skrá reiknaða breytu í rannsóknargögn í stað raunverulegs fæðingardags barns og afmá í kjölfarið fæðingardag úr rannsóknargrunninum sem hún fær afhentan frá landlækni að lokinni samkeyrslu, sbr. bréf landlæknis, dags. 18. október 2013 og

skilmála í c-lið 2. gr. í IV. kafla í leyfi þessu.

6. Auðkenning, varðveisla og eyðing rannsóknargagna

a. Er gagnagrunnsstjóra embættis landlæknis heimilt við framkvæmd rannsóknar þessarar að skrá og varðveita *tímabundið* sérstaka skrá, greiningarlykil, sem tengir saman upplýsingar um kennitölur einstaklinga og rannsóknarnúmer á meðan verið er að útbúa rannsóknargrunn. Slíkan greiningarlykil skal ávallt varðveita aðskilda frá öðrum rannsóknargögnum og má ekki afhenda neinum öðrum, svo sem rannsakendum.
b. Þegar Hagstofa Íslands hefur staðfest móttöku á kennitölulista frá embætti landlæknis, en eigi síðar en við lok gildistíma leyfis þessa, ber gagnagrunnsstjóra landlæknis að eyða kennitölum úr þeim rannsóknargögnum sem hann hefur undir höndum, þ.á m. greiningarlykli. Að fenginni framangreindri staðfestingu Hagstofu Íslands fer vinnsla landlæknis á upplýsingum í rannsóknargrunni, bæði fyrir og eftir móttöku upplýsinga á einkvæmum rannsóknarnúmerum frá Hagstofu Íslands, einungis fram á **einkvæmum rannsóknarnúmerum**, eins og lýst er í upphafi III. kafla í leyfi þessu.
c. Persónuvernd getur gert úttekt á því hvort farið sé að fyrirmælum b-liðar þessarar greinar um eyðingu kennitalna. Til þess getur stofnunin notið aðstoðar sérfræðings í upplýsingaöryggi, sbr. og g-lið 8. gr. hér á eftir.

7. Öryggi við vinnslu persónuupplýsinga

Leyfishafa ber að gera viðeigandi tæknilegar og skipulagslegar öryggisráðstafanir til að vernda persónuupplýsingar gegn óleyfilegum aðgangi í samræmi við 11. og 12. gr. laga nr. 77/2000. Þar er meðal annars áskilið að:

a. beita skuli ráðstöfunum sem tryggja nægilegt öryggi miðað við áhættu af vinnslunni og eðli þeirra gagna sem verja á, með hliðsjón af nýjustu tækni og kostnaði við framkvæmd þeirra, og
b. tryggja skuli að áhættumat og öryggisráðstafanir við vinnslu persónuupplýsinga séu í samræmi við lög, reglur og fyrirmæli Persónuverndar um hvernig tryggja skal öryggi upplýsinga, þ.m.t. þá staðla sem hún ákveður að skuli fylgt.

Leyfishafi ber ábyrgð á því að hver sá er starfar í umboði hans og hefur aðgang að persónuupplýsingum vinni aðeins með þær í samræmi við skýr fyrirmæli sem hann gefur og að því marki að falli innan skilyrða leyfis þessa, nema lög mæli fyrir á annan veg, sbr. 3. mgr. 13. gr. laga nr. 77/2000.

8. Almennir skilmálar

a. Ávallt skal tryggt að rannsóknargögn séu varðveitt á tryggum stað og aðeins þar sem lögum samkvæmt er heimilt að varðveita þau.
b. Leyfishafi ber ábyrgð á að farið sé með öll persónuauðkennd gögn sem sjúkragögn í samræmi við lög, reglur og ákvæði þessa leyfis.
c. Leyfishafi skal ábyrgjast að engir aðrir en hann fái í hendur persónugreinanleg gögn sem sérstaklega verður aflað í þágu þessarar rannsóknar.
d. Leyfishafa ber að tilkynna Persónuvernd tafarlaust ef upp kemur öryggisbrestur varðandi þær persónuupplýsingar sem leyfi þetta tekur til.
e. Óski leyfishafi þess að hætta rannsókn ber honum að tilkynna það til Persónuverndar á skriflegan og sannanlegan hátt. Skal þá tilgreina hvort þeim persónuupplýsingum, sem unnar voru á grundvelli þessa leyfis, hafi verið eytt. Að öðrum kosti úrskurðar Persónuvernd um hvort persónuupplýsingunum skuli eytt eða þær varðveittar með ákveðnum skilyrðum.
f. Leyfishafa ber að veita Persónuvernd, starfsmönnum og tilsjónarmönnum hennar allar umbeðnar upplýsingar um vinnslu persónuupplýsinga sé eftir því leitað, svo sem í þágu eftirlits eða vegna meðferðar mála sem tengjast vinnslunni.
g. Persónuvernd getur látið gera úttekt á því hvort leyfishafi fullnægi skilyrðum laga nr. 77/2000

og reglna sem settar eru samkvæmt þeim eða einstökum fyrirmælum. Getur Persónuvernd ákveðið að hann skuli greiða þann kostnað sem af því hlýst. Persónuvernd getur einnig ákveðið að leyfishafi greiði kostnað við úttekt á starfsemi, við undirbúning útgáfu vinnsluleyfis og annarrar afgreiðslu. Persónuvernd skal þá gæta þess að sá sérfræðingur, sem framkvæmir umrædda úttekt, undirriti yfirlýsingu um að hann lofi að gæta þagmælsku um það sem hann fær vitneskju um í starfsemi sinni og leynt ber að fara eftir lögum eða eðli máls. Brot á slíkri þagnarskyldu varðar refsingu samkvæmt 136. gr. almennra hegningarlaga. Þagnarskyldan helst þótt látið sé af starfi.

h. Leyfi þetta er háð því skilyrði að einungis verði safnað þeim upplýsingum sem *nauðsynlegar* eru vegna rannsóknarinnar.

i. Brot á ákvæðum leyfis þessa getur m.a. varðað því að leyfið verði fellt niður.

IV.
Leyfi og leyfisskilmálar
sem varða rannsakanda (Unni Önnu Valdimarsdóttur)

- um vinnslu upplýsinga frá embætti landlæknis

Í samræmi við 9. tölul. 1. mgr. 9. gr. laga nr. 77/2000 er Unni Önnu Valdimarsdóttur heimiluð vinnsla upplýsinga er henni berast frá embætti landlæknis að lokinni samkeyrslu upplýsinga úr fæðingaskrá landlæknis, lyfjagagnagrunni landlæknis og skattgrunnskrá Hagstofu Íslands vegna rannsóknarinnar „Áhrif íslenska efnahagshrunsins á heilsu barnshafandi kvenna og fæðingarútkomur", sbr. III. kafla í leyfi þessu.

Vill Persónuvernd árétta að með leyfi þessu er rannsakanda **hvorki veitt heimild til aðgangs að fæðingaskrá, lyfjagagnagrunni landlæknis né skattgrunnskrá Hagstofu Íslands.**

Leyfi þetta gildir til **31. desember 2015** og er bundið eftirfarandi skilyrðum:

1. Ábyrgðaraðilar að vinnslu persónuupplýsinga
Unnur Anna Valdimarsdóttir (hér eftir nefnd leyfishafi), telst vera ábyrgðaraðili þessa hluta vinnslunnar í skilningi 4. tölul. 2. gr. laga nr. 77/2000. Fer hún með allt fyrirsvar gagnvart Persónuvernd um alla þætti er varða þetta leyfi, þ.á m. álitaefni, er upp kunna að rísa, um það hvort vinnsla persónuupplýsinga hafi verið í samræmi við lög, reglur og ákvæði þessa leyfis.

2. Lögmæt vinnsla persónuupplýsinga og þagnarskylda

a. Leyfishafi ber ábyrgð á því að vinnsla persónuupplýsinga vegna rannsóknarinnar fullnægi ávallt kröfum 1. mgr. 7. gr. laga nr. 77/2000.

b. Farið skal með mótteknar upplýsingar frá landlækni að lokinni samkeyrslu, sbr. lýsingu í III. kafla í leyfi þessu, sem skráðar eru vegna rannsóknarinnar, í samræmi við lög nr. 77/2000. Hvílir þagnarskylda á leyfishafa og öðrum þeim sem koma að rannsókninni um upplýsingar sem unnið er með. Þagnarskylda helst þótt látið sé af störfum við rannsóknina.

c. Taki háskólanemar eða aðrir, sem ekki teljast til löggiltra heilbrigðisstétta, þátt í framkvæmd rannsóknarinnar skulu þeir undirrita sérstaka þagnarskylduyfirlýsingu, þar sem þeir m.a. ábyrgjast að tilkynna leyfishafa ef í rannsóknargögnum eru viðkvæmar persónuupplýsingar um þá sem eru eða hafa verið maki viðkomandi, skyldir eða mægðir henni í beinan legg eða að öðrum lið til hliðar eða tengdir henni með sama hætti vegna ættleiðingar. Er viðkomandi þá óheimilt að kynna sér gögn um þá einstaklinga. Leyfishafa eða fulltrúa hennar ber að votta rétta undirskrift hlutaðeigandi og dagsetningu slíkrar yfirlýsingar og varðveita hana. Leyfishafa ber að afhenda Persónuvernd afrit af slíkri yfirlýsingu þegar og ef stofnunin kallar eftir henni. Þagnarskyldan er byggð á 3. mgr. 35. gr. laga nr. 77/2000. Á heimasíðu Persónuverndar er að finna staðlað eyðublað fyrir þagnarskylduyfirlýsingu. Ef

þagnarskylduyfirlýsingum er ekki skilað innan tilskilins frests getur Persónuvernd afturkallað leyfi þetta.

3. Auðkenning rannsóknargagna

a. Þegar leyfishafi tekur við upplýsingum frá embætti landlæknis að lokinni samkeyrslu, sbr. lýsingu í III. kafla í leyfi þessu (einkum a-lið 5. gr.), ber henni að ganga úr skugga um að í þeim séu ekki skráðar kennitölur, persónunúmer eða fjölskyldunúmer.
b. Þegar þær heilbrigðisupplýsingar, sem leyfi þetta tekur til, hafa verið skráðar í rannsóknargögn leyfishafa skal leyfishafi tryggja að þar liggi ekki fyrir auðkenning á því frá hvaða einstaklingi upplýsingarnar stafa, t.d. með samansafni upplýsinga sem gera kleift að afhjúpa hver hinn skráði er. Er framangreint einnig í samræmi við afstöðu landlæknis um framsetningu og birtingu upplýsinga sem byggja á gögnum úr gagnagrunnum landlæknis.
c. Ber leyfishafa jafnframt að gæta að skilyrði embættis landlæknis, sbr. bréf, dags. 18. október 2013, um að skrá reiknaða breytu í rannsóknargögn í stað raunverulegs fæðingardags barns og afmá í kjölfarið fæðingardag úr rannsóknargrunninum sem hún fær afhentan frá landlækni að lokinni samkeyrslu, sbr. einnig d-lið 5. gr. í III. kafla í leyfi þessu.

4. Varveisla og eyðing persónuupplýsinga

a. Að rannsókn lokinni, þó eigi síðar en við lok gildistíma leyfis þessa hinn **31. desember 2015**, skal öllum upplýsingum sem leyfishafi fær frá embætti landlæknis vegna rannsóknar þessarar eytt.
b. Persónuvernd getur gert úttekt á því hvort farið sé að fyrirmælum a-liðar þessarar greinar um eyðingu upplýsinga. Til þess getur stofnunin notið aðstoðar sérfræðings í upplýsingaöryggi, sbr. og g-lið 6. gr. hér á eftir.

5. Öryggi við vinnslu persónuupplýsinga

Leyfishafa ber að gera viðeigandi tæknilegar og skipulagslegar öryggisráðstafanir til að vernda persónuupplýsingar gegn óleyfilegum aðgangi í samræmi við 11. og 12. gr. laga nr. 77/2000. Þar er meðal annars áskilið að:

a. beita skuli ráðstöfunum sem tryggja nægilegt öryggi miðað við áhættu af vinnslunni og eðli þeirra gagna sem verja á, með hliðsjón af nýjustu tækni og kostnaði við framkvæmd þeirra, og
b. tryggja skuli að áhættumat og öryggisráðstafanir við vinnslu persónuupplýsinga séu í samræmi við lög, reglur og fyrirmæli Persónuverndar um hvernig tryggja skal öryggi upplýsinga, þ.m.t. þá staðla sem hún ákveður að skuli fylgt.

Leyfishafi ber ábyrgð á því að hver sá er starfar í umboði hennar og hefur aðgang að persónuupplýsingum vinni aðeins með þær í samræmi við skýr fyrirmæli sem hún gefur og að því marki að falli innan skilyrða leyfis þessa, nema lög mæli fyrir á annan veg, sbr. 3. mgr. 13. gr. laga nr. 77/2000.

6. Almennir skilmálar

a. Ávallt skal tryggt að rannsóknargögn séu varðveitt á tryggum stað og aðeins þar sem lögum samkvæmt er heimilt að varðveita þau.
b. Leyfishafi ber ábyrgð á að farið sé með öll persónuauðkennd gögn sem sjúkraskrárgögn í samræmi við lög, reglur og ákvæði þessa leyfis.
c. Leyfishafi skal ábyrgjast að engir aðrir en hún, eða aðili sem starfar á hennar vegum, fái í hendur persónugreinanleg gögn sem unnið verður með í tengslum við þessa rannsókn.
d. Leyfishafa ber að tilkynna Persónuvernd tafarlaust ef upp kemur öryggisbrestur varðandi þær persónuupplýsingar sem leyfi þetta tekur til.
e. Óski leyfishafi eftir því að hætta rannsókn ber henni að tilkynna það til Persónuverndar á skriflegan og sannanlegan hátt. Skal þá tilgreina hvort öllum þeim persónuupplýsingum, sem

unnar voru upp úr þeim gögnum sem veittur var aðgangur að á grundvelli þessa leyfis, hafi verið eytt. Að öðrum kosti úrskurðar Persónuvernd um hvort persónuupplýsingunum skuli eytt eða þær varðveittar með ákveðnum skilyrðum.

f. Leyfishafa ber að veita Persónuvernd, starfsmönnum og tilsjónarmönnum hennar allar umbeðnar upplýsingar um vinnslu persónuupplýsinga sé eftir því leitað, svo sem í þágu eftirlits eða vegna meðferðar mála sem tengjast vinnslunni.

g. Persónuvernd getur látið gera úttekt á því hvort leyfishafi fullnægi skilyrðum laga nr. 77/2000 og reglna sem settar eru samkvæmt þeim eða einstökum fyrirmælum. Getur Persónuvernd ákveðið að hún skuli greiða þann kostnað sem af því hlýst. Persónuvernd getur einnig ákveðið að leyfishafi greiði kostnað við úttekt á starfsemi, við undirbúning útgáfu vinnsluleyfis og annarrar afgreiðslu. Persónuvernd skal þá gæta þess að sá sérfræðingur, sem framkvæmir umrædda úttekt, undirriti yfirlýsingu um að hann lofi að gæta þagmælsku um það sem hann fær vitneskju um í starfsemi sinni og leynt ber að fara eftir lögum eða eðli máls. Brot á slíkri þagnarskyldu varðar refsingu samkvæmt 136. gr. almennra hegningarlaga. Þagnarskyldan helst þótt látið sé af starfi.

h. Leyfi þetta er háð því skilyrði að einungis verði unnið með þær upplýsingum sem *nauðsynlegar* eru vegna rannsóknarinnar.

i. Brot á ákvæðum leyfis þessa getur m.a. varðað því að leyfið verði fellt niður.

Virðingarfyllst

Helga Grethe Kjartansdóttir

Afrit:
Hagstofa Íslands
Hrafnhildur Arnkelsdóttir, skrifstofustjóri
félagsmálasvið
Borgartúni 21a
150 Reykjavík

VÍSINDASIÐANEFND

Hafnarhúsið, Tryggvagata 17
101 Reykjavík,

Sími: 551 7100, Bréfsími: 551 1444

netfang: visindasidanefnd@vsn.stjr.is

Unnur Anna Valdimarsdóttir
Grenimel 2
107 Reykjavík

Reykjavík 12. febrúar 2013
Tilv.: VSNb2013010002/03.07

Efni: 13-002-S1 Áhrif íslenska efnahagshrunsins á heilsu barnshafandi kvenna og fæðingaútkomur.

Vísindasiðanefnd þakkar svarbréf þitt, dags. 28.01.2013 vegna áðursendra athugasemda við ofangreinda rannsóknaráætlun sbr. bréf nefndarinnar dags. 15.91.2013. Í bréfinu koma fram svör og skýringar til samræmis við athugasemdir Vísindasiðanefndar og því fylgdu endurbætt gögn.

Fjallað var um svarbréf þitt og önnur innsend gögn á fundi Vísindasiðanefndar 29.01.2013.

Rannsóknaráætlunin er endanlega samþykkt af Vísindasiðanefnd.

Vísindasiðanefnd bendir rannsakendum vinsamlegast á að birta VSN tilvísunarnúmer rannsóknarinnar þar sem vitnað er í leyfi nefndarinnar í birtum greinum um rannsóknina.

Jafnframt fer Vísindasiðanefnd fram á að fá send afrit af, eða tilvísun í, birtar greinar um rannsóknina. Rannsakendur eru minntir á að tilkynna rannsóknarlok til nefndarinnar.

Áréttað er að allar fyrirhugaðar breytingar á þegar samþykktri rannsóknaráætlun þurfa að koma inn til nefndarinnar til umfjöllunar.

Jafnframt ber ábyrgðarmanni að láta stofnanir, sem veitt hafa leyfi vegna framkvæmdar rannsóknarinnar eða öflunar gagna vita af fyrirhugðum breytingum.

Með kveðju,
f.h. Vísindasiðanefndar,

Gísli Ragnarsson, varaformaður

Embætti landlæknis
Directorate of Health

Unnur Anna Valdimarsdóttir
Háskóla Íslands, Stapa v/ Hringbraut
101 Reykjavík

Reykjavík, 14. janúar 2013
1301064/5.6.1/gkg

Efni: Aðgangur að gögnum úr fæðingaskrá og lyfjagagnagrunni vegna vísindarannsóknar

Embætti landlæknis vísar til umsóknar þinnar sem barst embættinu 4. janúar 2013, þar sem farið er fram á að fá aðgang að gögnum úr fæðingaskrá og lyfjagagnagrunni vegna rannsóknarinnar *„Áhrif íslenska efnahagshrunsins á heilsu barnshafandi kvenna og fæðingaútkomur."*
Úr fæðingaskrá var óskað eftir gögnum um allar fæðingar á árunum 2002-2012. Úr lyfjagagnagrunni var óskað eftir gögnum um útleystar lyfjaávísanir á háþrýstingslyf og geðlyf fyrir þær konur sem í rannsóknarhópnum verða, á því tímabili sem afmarkast af 90 dögum fyrir síðustu blæðingar til loka meðgöngu/fæðingar barns. Í fylgiskjali er að finna lista yfir þær breytur sem óskað var eftir úr ofangreindum skrám.

Landlæknir sér því ekkert til fyrirstöðu að umsækjandi fái aðgang að umræddum ópersónugreinanlegum gögnum, með vísan í 1. mgr. 8 gr. laga um landlækni og lýðheilsu nr. 41/2007 og 9. tölulið 9. gr. laga um persónuvernd og meðferð persónuupplýsinga nr. 77/2000.

Jafnframt var óskað eftir því að samkeyrsla gagna úr ofangreindum skrám við gögn úr skattgrunnskrá Hagstofu Íslands yrði framkvæmd hjá Embætti landlæknis. Fallist er á þá beiðni, að fengnu leyfi Hagstofu Íslands fyrir afhendingu gagna úr skattgrunnskrá.
Verkferli við afmörkun rannsóknarhóps og við samkeyrslur verður í samræmi við lýsingar rannsakanda í umsóknum til Persónuverndar og Vísindasiðanefndar og í samræmi við reglur Embættis landlæknis.

Leyfi þetta er háð því skilyrði að rannsóknin fái leyfi Persónuverndar og Vísindasiðanefndar. Afrit af báðum leyfum þurfa að berast Embætti landlæknis áður en aðgangur er veittur að umbeðnum gögnum. Vinnsluaðili Fæðingarskrár er Landspítali og að uppfylltum ofangreindum skilyrðum skal úrtakið útbúið þar.

Virðingarfyllst,

Lilja Sigrún Jónsdóttir
staðgengill sviðsstjóra
heilbrigðisupplýsingasviði

Afrit: Persónuvernd
Vísindasiðanefnd

LANDLÆKNISEMBÆTTIÐ
Directorate of Health

Unnur Anna Valdimarsdóttir
Stapi v/Hringbraut
101 Reykjavík

Seltjarnarnesi, 29. júní 2010
2010050296/5.6.1/HBS/hbs

Efni: Aðgangur að gögnum úr Fæðingaskrá vegna rannsóknarinnar: "Áhrif efnahagshrunsins á Íslandi 2008 á tíðni fyrirbura og léttburafæðinga".

Landlæknisembættið vísar til umsóknar þinnar sem barst þann 26. maí s.l. Í umsókninni er óskað eftir aðgangi að gögnum úr Fæðingaskrá vegna rannsóknar á áhrifum efnahagshrunsins á Íslandi 2008 á tíðni fyrirbura og léttburafæðingar, þegar leyfi Vísindasiðanefndar og Persónuverndar liggja fyrir. Þær upplýsingar sem óskað er eftir varða allar barnshafandi íslenskar konur úr Fæðingaskrá, sem eignast hafa lifandi fædd börn á tímabilinu 1. október 2006 til 31. desember 2009.

Landlæknisembættið sér því ekkert til fyrirstöðu að umsækjandi fái aðgang að umræddum gögnum með vísan í 9. tölulið 9. gr. laga um persónuvernd og meðferð persónuupplýsinga nr. 77/2000, að því tilskyldu að rannsóknin fái leyfi Persónuverndar og Vísindasiðanefndar. Afrit af báðum leyfum þurfa að berast Landlæknisembættinu áður en aðgangur er veittur að umbeðnum gögnum.

Virðingarfyllst,

Sigríður Haraldsdóttir
Sviðsstjóri heilbrigðistölfræðisviðs

Afrit: Védís Helga Eiríksdóttir
Vísindasiðanefnd
Persónuvernd

VÍSINDASIÐANEFND

Vegmúla 3, 108 Reykjavík,

Sími: 551 7100, Bréfsími: 551 1444

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Unnur Anna Valdimarsdóttir, dósent og
forstöðumaður
Grenimel 2
107 Reykjavík

Reykjavík 22. júní 2010
Tilv.: VSNb2010050014/03.7

Efni: Varðar: 10-081-afg Áhrif efnahagshrunsins á Íslandi 2008 á tíðni fyrirburaléttburafæðinga.

Á fundi sínum 22.06.2010 fjallaði Vísindasiðanefnd um umsókn þína dags. 27.05.2010, vegna ofangreindrar rannsóknaráætlunar. Meðrannsakendur þínir eru Dr. Tinna Laufey Ásgeirsdóttir, Ragnheiður Bjarnadóttir og Védís Helga Eiríksdóttir, meistaranemi.

Vísindasiðanefnd gerir eftirfarandi athugasemdir við rannsóknaráætlunina:

1. Leyfi Landlæknis hefur ekki borist nefndinni.

Rannsóknin verður tekin til frekari afgreiðslu hjá Vísindasiðanefnd þegar henni hefur borist undirritað svarbréf við ofangreindum athugasemdum, ásamt endurbættum fylgigögnum sem nefndin óskar eftir hverju sinni, lita skal leiðréttingar með litapenna í þeim gögnunum sem send eru inn. Þessi gögn eiga að berast nefndinni í 3 eintökum.

Upplýsingar um skilafresti má nálgast á heimasíðu nefndarinnar, www.visindasidanefnd.is. Vinsamlegast athugið að óheimilt er að hefja framkvæmd rannsóknar fyrr en endanlegt samþykki Vísindasiðanefndar fyrir henni hefur verið veitt.

Með kveðju,
f.h. Vísindasiðanefndar,
Eiríkur Baldursson.
dr. Eiríkur Baldursson, framkvæmdastjóri

Háskóli Íslands - Miðstöð í lýðheilsuvísindum
Dr. Unnur Anna Valdimarsdóttir
Stapa v/Hringbraut
101 Reykjavík

Persónuvernd

Rauðarárstíg 10 105 Reykjavík
sími: 510 9600 bréfasími: 510 9606
netfang: postur@personuvernd.is
veffang: personuvernd.is

Reykjavík, 1. júlí 2010
Tilvísun: 2010050499LSL/--

Heimild skv. 3. mgr. 15. gr. laga nr. 74/1997, sbr. 8. mgr. 8. gr. laga nr. 41/2007.

I.
Umsókn

Persónuvernd barst umsókn dr. Unnar Önnu Valdimarsdóttur, dósents og forstöðumanns, f.h. Miðstöðvar í lýðheilsuvísindum, Ragnheiðar Bjarnadóttur, fæðingalæknis á Landspítala, og dr. Tinnu Laufeyjar Ásgeirsdóttur, lektors og umsjónarmanns MS náms í heilsufræðum við Háskóla Íslands, dags. 27. maí 2010, um heimild til aðgangs að fæðingaskrá landlæknis í þágu rannsóknar undir heitinu: „Áhrif efnahagshrunsins á Íslandi 2008 á tíðni fyrirbura og léttburafæðinga".

Tilgangur vinnslunnar er skoða nýgengi fyrirbura- og léttburafæðinga í kjölfar efnahagskreppunnar í október 2008 og bera saman við nýgengi undanfarinna ára. Þýði rannsóknarinnar verða allar barnshafandi íslenskar konur sem eignuðust lifandi fædd börn á tímabilinu frá 1. október 2006 til 31. desember 2009 samkvæmt fæðingskrá landlæknis. Áætlað er að um fimmtán þúsund fæðingar sé að ræða. Eingöngu er um aftursýna rannsókn að ræða.

Þær upplýsingar sem fyrirhugað er að afla úr fæðingaskrá eru fæðingardagur, aldur móður við fæðingu, fjöldi þungana fyrir fæðingu, hjúskaparstaða og starf móður, króníski sjúkdómar móður, sjúkdómar á meðgöngu, fjöldi barna í fæðingu, kyn barns, lengd og þyngd barns, upphaf fæðingar, gangur fæðingar, erfiðleikar í fæðingu og sjúkdómar greindir á meðgögnu og í ár eftir fæðingu.

Varðandi skráningu persónuauðkenna og varðveislu rannsóknargagna segir í umsókn að

ábyrgðarmaður fæðingaskrár muni dulkóða upplýsingarnar úr skránni og afhenda rannsakendum. Verður greiningarlykli eytt að dulkóðun gagnanna lokinni.

Þann 1. júlí 2010 barst Persónuvernd yfirlýsing landlæknis þess efnis að hann sé hlynntur því fyrir sitt leyti að ofangreindir rannsakendur fái aðgang að gögnum fæðingaskrár í þágu rannsóknar þessarar.

II.
Lögmæti vinnslunnar

Fæðingaskrá er varðveitt á Landspítala en landlæknisembættið skipuleggur skrána og er ábyrgðarmaður hennar, sbr. 4. tölul. 2. mgr. og 4. mgr. 8. gr. laga nr. 41/2007 um landlækni. Samkvæmt 8. mgr. sömu greinar fer um aðgang að skránni í þágu vísindarannsókna eftir ákvæði 3. mgr. 15. gr. laga nr. 74/1997 um réttindi sjúklinga og því þarf leyfi Persónuverndar til aðgangs að þeirri skrá.

III.
Leyfi og leyfisskilmálar

Persónuvernd hefur nú ákveðið, m.a. að virtum ákvæðum 29., 33. og 34. gr. í formálsorðum persónuverndartilskipunarinnar nr. 95/46/EB, 9. tölul. 1. mgr. 9. gr. laga nr. 77/2000 um persónuvernd og meðferð persónuupplýsinga, að veita dr. Unni Önnu Valdimarsdóttur, Ragnheiði Bjarnadóttur og dr. Tinnu Laufeyju Ásgeirsdóttur umbeðna heimild til aðgangs að fæðingaskrá í þágu rannsóknarinnar: „Áhrif efnahagshrunsins á Íslandi 2008 á tíðni fyrirbura og léttburafæðinga“ skv. 3. mgr. 15. gr. laga nr. 74/1997, sbr. 8. mgr. 8. gr. laga nr. 41/2007.

Leyfi þetta gildir til 1. mars 2011 og er bundið eftirfarandi skilyrðum:

1. Ábyrgðaraðilar að vinnslu persónuupplýsinga

Dr. Unnur Anna Valdimarsdóttir, f.h. Miðstöðvar í lýðheilsuvísindum, Ragnheiður Bjarnadóttir og dr. Tinna Laufey Ásgeirsdóttir (sem hér eftir kallast leyfishafar), teljast vera ábyrgðaraðilar vinnslunnar í skilningi 4. tölul. 2. gr. laga nr. 77/2000. Fer dr. Unnur Anna Valdimarsdóttir með allt fyrirsvar gagnvart Persónuvernd um alla þætti er varða þetta leyfi, þ.á m. álitaefni, er upp kunna að rísa, um það hvort vinnsla persónuupplýsinga hafi verið í samræmi við lög, reglur og ákvæði þessa leyfis.

2. Lögbundnir leyfisskilmálar

Þegar leyfishafar fara þess á leit við ábyrgðarmann fæðingaskrár að fá aðgang að viðkomandi sjúkraskrám ber þeim að framvísa leyfi þessu.

a. Ábyrgðarmaður fæðingaskrár skal varðveita yfirlit yfir þær upplýsingar sem veittur er aðgangur að í þágu rannsóknar þessarar til þess að geta síðar uppfyllt upplýsingaskyldu gagnvart hinum skráðu í samræmi við 18. gr. laga nr. 77/2000.
b. Leyfi þetta er bundið því skilyrði að ábyrgðarmaður fæðingaskrár hafi lýst því yfir að hann sé því samþykkur fyrir sitt leyti að leyfishafar fái aðgang að henni.
c. Leyfi þetta er bundið því skilyrði að siðanefnd, eða eftir atvikum vísindasiðanefnd, hafi lagt mat á rannsóknina og látið í té skriflegt álit sitt þess efnis að hvorki vísindaleg né siðfræðileg sjónarmið mæli gegn framkvæmd hennar, sbr. 3. mgr. 15. gr. laga nr. 74/1997, sbr. 4. mgr. 2. gr. sömu laga.

3. Lögmæt vinnsla persónuupplýsinga og þagnarskylda

a. Leyfishafar bera ábyrgð á því að vinnsla persónuupplýsinga vegna rannsóknarinnar fullnægi ávallt kröfum 1. mgr. 7. gr. laga nr. 77/2000.

b. Farið skal með upplýsingar úr fæðingskrá, sem skráðar eru vegna rannsóknarinnar, í samræmi við lög nr. 77/2000, lög nr. 74/1997 um réttindi sjúklinga, læknalög nr. 53/1988 og lög nr. 41/2007 og reglan settra með stoð í þeim lögum. Hvílir þagnarskylda á leyfishöfum og öðrum þeim sem koma að rannsókninni um heilsufarsupplýsingar sem unnið er með, sbr. 15. gr. laga nr. 53/1988. Þagnarskylda helst þótt látið sé af störfum við rannsóknina.
c. Taki háskólanemar eða aðrir, sem ekki teljast til löggiltra heilbrigðisstétta, þátt í framkvæmd rannsóknarinnar skulu þeir undirrita sérstaka þagnarskylduyfirlýsingu, þar sem þeir m.a. ábyrgjast að tilkynna leyfishöfum ef í rannsóknargögnum eru viðkvæmar persónuupplýsingar um þá sem eru eða hafa verið maki viðkomandi, skyldir eða mægðir honum í beinan legg eða að öðrum lið til hliðar eða tengdir honum með sama hætti vegna ættleiðingar. Er viðkomandi þá óheimilt að kynna sér gögn um þá einstaklinga. Leyfishöfum eða fulltrúa þeirra ber að votta rétta undirskrift hlutaðeigandi og dagsetningu slíkrar yfirlýsingar og koma henni til Persónuverndar innan tveggja vikna frá útgáfu leyfis þessa eða frá því viðkomandi hefur störf við rannsóknina. Þagnarskyldan er byggð á 3. mgr. 35. gr. laga nr. 77/2000. Á heimasíðu Persónuverndar er að finna staðlað eyðublað fyrir þagnarskylduyfirlýsingu. Ef þagnarskylduyfirlýsingum er ekki skilað innan tilskilins frests getur Persónuvernd afturkallað leyfi þetta.

4. Auðkenning rannsóknargagna

a. Í rannsóknargögn má skrá upplýsingar um fæðingarmánuð, fæðingarár og kyn hvers sjúklings.
b. Óheimilt er að skrá í rannsóknargögn upplýsingar um nöfn sjúklinga, nafnnúmer, heimilisföng, símanúmer, fax-númer, tölvupóstföng eða annað sambærilegt.
c. Þegar þær heilbrigðisupplýsingar, sem leyfi þetta tekur til, hafa verið skráðar í rannsóknargögn, og eftir atvikum verið staðreynt að þær séu réttar, og gögnin að öðru leyti verið fullgerð, skal tryggja að þar liggi ekki fyrir auðkenning á því frá hvaða einstaklingi upplýsingarnar stafa, s.s. með eyðingu kennitalna.

5. Öryggi við vinnslu persónuupplýsinga

Leyfishöfum ber að gera viðeigandi tæknilegar og skipulagslegar öryggisráðstafanir til að vernda persónuupplýsingar gegn óleyfilegum aðgangi í samræmi við 11. og 12. gr. laga nr. 77/2000. Þar er meðal annars áskilið að:

a. beita skuli ráðstöfunum sem tryggja nægilegt öryggi miðað við áhættu af vinnslunni og eðli þeirra gagna sem verja á, með hliðsjón af nýjustu tækni og kostnaði við framkvæmd þeirra, og
b. tryggja skuli að áhættumat og öryggisráðstafanir við vinnslu persónuupplýsinga séu í samræmi við lög, reglur og fyrirmæli Persónuverndar um hvernig tryggja skal öryggi upplýsinga, þ.m.t. þá staðla sem hún ákveður að skuli fylgt.

Leyfishafar bera ábyrgð á því að hver sá er starfar í umboði þeirra og hefur aðgang að persónuupplýsingum vinni aðeins með þær í samræmi við skýr fyrirmæli sem þeir gefa og að því marki að falli innan skilyrða leyfis þessa, nema lög mæli fyrir á annan veg, sbr. 3. mgr. 13. gr. laga nr. 77/2000.

6. Almennir skilmálar

a. Ávallt skal tryggt að rannsóknargögn séu varðveitt á tryggum stað og aðeins þar sem lögum samkvæmt er heimilt að varðveita þau.
b. Leyfishafar bera ábyrgð á að farið sé með öll persónuauðkennd gögn sem sjúkragögn í samræmi við lög, reglur og ákvæði þessa leyfis.
c. Leyfishafar skulu ábyrgjast að engir aðrir en þeir fái í hendur persónugreinanleg gögn sem sérstaklega verður aflað í þágu þessarar rannsóknar.
d. Óski leyfishafar þess að hætta rannsókn ber þeim að leggja þetta leyfi inn til Persónuverndar

á skriflegan og sannanlegan hátt. Skal þá tilgreina hvort þeim persónuupplýsingum, sem unnar voru á grundvelli þessa leyfis, hafi verið eytt. Að öðrum kosti úrskurðar Persónuvernd um hvort persónuupplýsingunum skuli eytt eða þær varðveittar með ákveðnum skilyrðum.

e. Leyfishöfum ber að veita Persónuvernd, starfsmönnum og tilsjónarmönnum hennar allar umbeðnar upplýsingar um vinnslu persónuupplýsinga sé eftir því leitað í þágu eftirlits. Brot á ákvæði þessu getur varðað afturköllun á leyfinu.

f. Persónuvernd getur látið gera úttekt á því hvort leyfishafar fullnægi skilyrðum laga nr. 77/2000 og reglna sem settar eru samkvæmt þeim eða einstökum fyrirmælum. Getur Persónuvernd ákveðið að þeir skuli greiða þann kostnað sem af því hlýst. Persónuvernd getur einnig ákveðið að leyfishafar greiði kostnað við úttekt á starfsemi, við undirbúning útgáfu vinnsluleyfis og annarrar afgreiðslu. Persónuvernd skal þá gæta þess að sá sérfræðingur, sem framkvæmir umrædda úttekt, undirriti yfirlýsingu um að hann lofi að gæta þagmælsku um það sem hann fær vitneskju um í starfsemi sinni og leynt ber að fara eftir lögum eða eðli máls. Brot á slíkri þagnarskyldu varðar refsingu samkvæmt 136. gr. almennra hegningarlaga. Þagnarskyldan helst þótt látið sé af starfi.

g. Leyfi þetta er háð því skilyrði að einungis verði safnað þeim upplýsingum sem *nauðsynlegar* eru vegna rannsóknarinnar.

Virðingarfyllst

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