SSM - Population Health 4 (2018) 100–116

Contents lists available at ScienceDirect

SSM - Population Health

journal homepage: www.elsevier.com/locate/ssmph

Parental population exposure to historical socioeconomic and political periods and grand-child's birth weight in the Lifeways Cross-Generation Cohort Study in the Republic of Ireland

Cilia Mejia-Lancheros*, John Mehegan, Ricardo Segurado, Celine Murrin, Cecily Kelleher, for the Lifeways Cross-Generation Cohort Study Group.

School of Public Health, Physiotherapy and Sports Science, University College Dublin, Woodview House, Belfield, Dublin 4, Republic of Ireland

ARTICLE INFO

Keywords:
Birthweight
Prenatal exposure
Socioeconomic conditions
Critical periods
Transgenerational transmission.
Transgenerational health

ABSTRACT

Exposure to deprived socioeconomic conditions during the peri-conception and early childhood periods can have a negative long-term impact on individuals' health and that of their progeny. We aimed to examine whether relatives' birth period affected index-child (grand-child) birthweight status in the Lifeways Cross-Generation Cohort in the Republic of Ireland. Participants were 943 mothers and offspring, 890 fathers, 938 maternal grandmothers (MGM), 700 maternal grandfathers (MGF) 537 paternal grandmothers (PGM) and 553 paternal grandfathers (PGF). Index-child's birthweight was sex-for-gestational age standardised (UK1990 population), and then classified into low birthweight (≤10th percentile) and high-birthweight (≥90th percentile) and compared against normal-birthweight (> 10th to < 90th percentiles). Four adult birth periods were considered: The Free State (FS, 1916-1938); Emergency Act (EA, 1939-1946); Post-World War-II Baby-Boom (PWWII-BB, 1947-1964); and Modern Ireland (MI, 1964 onwards). Logistic regression was used to assess the crude and adjusted relationship between index-child's birthweight status and relatives' birth periods.

Overall, there were 8.7% (n = 82) index-children in the low-birthweight category, 77.9% (n = 735) and 13.4% (n = 126) within the normal and high birthweight groups respectively. Index-children whose mothers were born during the PWWII-BB had higher birthweight infants (Crude OR(COR) = 1.81 (1.08–3.03) which remained the case only for male index-children when adjusted for co-variables (Adjusted OR(AOR) = 4.61(1.71–12.42)). Parents' combined PWWII-BB birth period was positively associated with male index-child higher birthweight, even adjusted for maternal characteristics (AOR = 4.60(1.69–12.50)). MGFs born during the EA were more likely to have grandchildren with low birthweight after adjustment for maternal characteristics (AOR = 2.45(1.03-5.85)), particularly for female index-children (AOR = 4.74(1.16–19.25)). Both PGMs and PGFs born during the FS period had higher birthweight grandchildren, adjusted for maternal-related co-variables (PGM, AOR = 3.23(1.21–8.63); PGF, AOR = 3.93(1.11–13.96)), with the effect of PGM more evident in her grand-daughter (AOR = 6.53(1.25–34.04)). In conclusion, there is some evidence that period of grandparental birth is associated with their grandchildren's birthweights, suggesting that transgenerational exposures may be particular to historical context, meriting further exploration.

1. Introduction

In the last decades, many studies have supported the role of early-life events in the aetiological origin of disease and health status (Barker, 2007), suggesting the implication of different mechanisms that span biological, psychosocial, socioeconomic and environmental-related conditions. More recently it has been suggested these exposures may be mediated through genetic and epigenetic factors (Gluckman, Hanson, & Buklijas, 2010; Halfon, Larson, Lu, Tullis, & Russ, 2014). However, the pathways by which such conditions shape transgenerational health patterns are still unclear, since there are few longitudinal or cohort studies with historical and health data for more than two generations.

Studies have shown that exposure to deprived socioeconomic or psychosocial circumstances during the early-years of life might trigger negative health outcomes during adulthood (Ferraro, Schafer, & Wilkinson, 2016; Galobardes, Lynch, & Smith, 2008; Tamayo,

* Corresponding author.
E-mail addresses: cilia.mejialancheros@ucd.ie (C. Mejia-Lancheros), john.mehegan@ucd.ie (J. Mehegan), ricardo.segurado@ucd.ie (R. Segurado), celine.murrin@ucd.ie (C. Murrin), cecily.kelleher@ucd.ie (C. Kelleher).

https://doi.org/10.1016/j.ssmph.2017.11.011
Received 3 April 2017; Received in revised form 3 October 2017; Accepted 27 November 2017
2352-8273/

Christian, & Rathmann, 2010). Moreover, some evidence suggests that significant historic exposures to adverse natural or man-made events (e.g. the Dutch and Chinese famines) may not only affect the exposed individuals' own health over the life course, but also extend across generations, affecting the health status of future children (Huang, Li, Narayan, Williamson, & Martorell, 2010; Painter, Roseboom, & Bleker, 2005; Veenendaal et al., 2013).

The Irish population has experienced significant historical, economic and political events over the 20th century, including the War of Independence and subsequent establishment of the Irish Free State (1916–1938) (Corcoran, 2009), the Emergency period during World War II (WWII) when Ireland was a neutral political state (1939–1946) (Drisceoil, 1996), Post World War-II Baby Boom (1947–1964) (Van Bavel & Reher, 2013) and Modern Ireland from 1964 onwards (Fahey, Fitzgerald, & Maitre, 1998; Gerald, 1999; Whelan, 2013). Many people who were born, raised and lived through these periods may have experienced economic and psychosocial-related constraints or advantages for themselves and those of their households.

The Lifeways cross-generation cohort study in the Republic of Ireland provides the potential to examine cross-generational effects of such period exposures for Irish people over the twentieth century, especially those born and raised during the establishment of the Irish Free State and Emergency Powers Act in the WWII period. This is a three generation cohort study established a priori to examine cross-generational influences on the proband children (index-child) recruited during pregnancy in 2001–3 and several previous analyses have shown grand-parental influences on children's outcomes (Kelleher et al., 2014; McKey et al. 2017; Murrin et al., 2012; Shrivastava et al., 2012; Shrivastava, Murrin, Sweeney, Heavey, & Kelleher, 2013).

In the present analysis we examined whether the birth exposure of grandparents and parents to particular socioeconomic and political periods during the 20th century in Ireland was associated with the index-children's subsequent birthweights.

2. Methods

2.1. Data sources and participants

The Lifeways Cross-Generation Study design, methods, questionnaires and tools as well as follow up have been previously described in detail elsewhere (Kelleher et al., 2014; O'Mahony et al., 2007). The present cross-generation analysis involved the live born index-children of the Lifeways Cross-Generation Study as well as their parents and maternal and paternal grandparents (12 twin pairs were excluded).

Briefly, the Lifeways Cross-Generation Study is a prospective longitudinal study established between October 2001 and January 2003 in the Republic of Ireland, with an average follow up over a decade (2003–2017). The aim of this study was to examine the health status, diet, and lifestyles of parents, offspring and grandparents across the life course and to determine potential cross-generational links and associated risk factors for health outcomes. At baseline, 1132 pregnant mothers were recruited, whose pregnancy resulted in 1092 (94.5%) live born index-children, including 12 sets of twins, the majority of whom (98.2%) were born throughout the year 2002. Using validated questionnaires and follow up reporting forms, mothers provided information related to their own partners and all four lineages of the grandparents, including whether any of these were deceased. Specific gestation, delivery and postnatal associated information of the mother and offspring were also obtained from the hospital, delivery and immunisation records. In addition, the Lifeways Cross Generational Cohort has collected subsequent information of participants at three follow up periods when children averaged 3, 5 and 9 years of age. Finally, all index-child's grandparents were searched for in the General Register Office's database, and if recorded as deceased the date, age and cause of death were recorded.

For the purpose of the present analysis, based on the information available for both the index-child's sex-for-gestational age standardised birthweight (BW) and their relatives' birth period information, the following overall paired samples were separately analysed: (1) 943 index-child and mother pairs; (2) 890 index-child and father pairs; (3) 938 index-child and maternal grandmother (MGM) pairs; (4) 700 index-child and maternal grandfather (MGF) pairs; (5) 537 child and paternal grandmother (PGM) pairs; and (6) 553 index-child and paternal grandfather (PGF) pairs. Additionally, analyses were also performed by grouping grandparental birth period according to family lineage (maternal and paternal grandparents, resulting in following additional sample: 940 index-child and maternal grandparent (MGP)) pairs and 598 index-child and paternal grandparent (PGP) pairs.

For the 943 children with gestational age–for-sex standardised BW, the following grandparents' samples had known or inferred birth period: MGM = 938 (99.4%); MGF = 700 (74.23%); PGM = 537 (56.95%), and PGF = 553 (58.64%). Comparing the index-children with known or inferred grandparental birth period against those with unknown data (neither known, nor inerred) only for the MGF, PGM and PGF (as MGM only had five missing), it was found that children with known MGF's birth period information were more likely to have older mothers than those without valid MGF's birth period information, whilst those index-children with known or inferred birth period data for PGM and PGF tended to have mothers who were slightly older, more highly educated, smoked less and multiparous than those index-children with unknown PGM and PGF birth period information (Table A.1, Appendix A).

2.2. Ethical approval

The Lifeways Cohort received ethical approval for the various baseline and follow-up data collections initially from the ethical committees at the National University of Ireland, Galway; the Coombe Women's Hospital, Dublin; University College Hospital, Galway; the Irish College of General Practitioners; and later from University College Dublin; and St. Vincent's University Hospital, Dublin.

2.3. Main outcome: index-children's birth weight status

The index-children's birth weight status was standardised for sex and gestational age using the British 1990 reference population and using the Cole's LMS method (Cole, Freeman, & Preece, 1995) and LMSgrowth add-in for Microsoft Excel (http://www.healthforallchildren.com/shop-base/shop/software/lmsgrowth/) as the Irish population is more likely to be comparable to the British population rather than to other geographical population groups. Index-child was then classified as low birthweight (LBW) (children under the 10th percentile), normal weight birth weight (children between the 10th and 90th percentile), and high birthweight (HBW) (children over the 90th percentile). The normal weight category was considered the reference group in the analyses. The child's birth weight was recorded by health professionals in the hospital medical registry when the child was born.

2.4. Exposure factors: parental exposure to historical socioeconomic and political periods in Ireland's history

The following four socioeconomic-political periods in Irish history were considered as historically distinct: (1) The Free State (FS) period from 1916 to 1938 (it included the War of Independence and subsequent establishment of the Irish Free State (Corcoran, 2009)); (2) Emergency Powers Act period (EA) from 1939 to 1946 – although remaining conflict neutral during World War II, emergency legislation was in force in Ireland during this period for the rationing of essential goods and services and the control of public order (The electronic Irish Statute Book [eISB], 1939); (3) the Post World War-II Baby Boom (PWWII-BB) from 1947 to 1964 which featured the introduction of a comprehensive health care act and other social reforms; and (4) Modern Ireland (MI) from 1964 onward.

The child's father, mother, and each of the grandparents were allocated to each of the previous exposure periods according to their date of birth (DOB). Of 3131 grandparents with information in the database, exact DOB was known for 1943 individuals (62.10%). In cases where the exact DOB was unknown, the birth period was estimated by taking into account the following (in order of precedence): the birth period of their respective spouse (if known); for maternal grandmothers, the birth period of her daughter (Lifeways mother); the individual's baseline status (alive/deceased); the individual's date of death (if known). From the 1089 non-twin and alive-born Lifeways index-children, the known and estimated DOB of their grandparents was as follows: MGM = 630 with known DOB and 456 estimated; MGF = 493 with known BOD and 310 estimated; PGM = 459 with known DOB and 151 estimated; and PGF = with 361 known DOB and 271 estimated. Two MGMs born before FS and two in MI period, eight MGFs born before FS period, three PGMs and seven PGF born before FS period were excluded in order to maintain the exact period allocation. Then, each grandparent with birth period information was paired with the grandchildren with known standardised birthweight, resulting in the pairs samples as previously described. The number of adults' cohort participants is shown in the supplementary Table A.2 (Appendix A).

The adult birth period exposures were analysed separately for each grandparent and parent (mother, father, MGM, MGF, PGM, PGF) as well as by combined birth periods for parent couples (parents' combined birth period) and for grandparental couples: Maternal grandparents' (MGPs) combined birth period and paternal grandparents' (PGPs) combined birth period. The combining of birth periods was done in order to analyse any overall potential lineage birth period effect on the outcome. The blending of data for both parents and grandparents' combined birth periods was done by giving precedence to the older of the two members. All the crude and adjusted grandparental-related analyses were also performed employing only observed data (parental granparents'birth period based on recorded date of birth (DOB)), supplementary tables (Apendix A).

2.5. Co-variables

2.5.1. Index-child characteristics

Index-child sex (female/ male). Although the Index-child sexwas considered when standardising their BW according British population reference, it was used as an adjusted co-variable in all overall analyses to adjust for any sex-related residual confounding. In addition, Index-child sex was used also for stratifying (female-children/male-children) all the analyses in order to account for potential trangenerational sex-specific effect of the study exposures (Pembrey, 2010; Pembrey et al., 2006).

2.5.2. Maternal characteristics

The following maternal characteristics were chosen, as being known to be key contributing factors in growth development and the pregnancy outcomes. Mother's age at index-child birth (years) was used both to control for any maternal age-related effect on birth outcome and as a general proxy for age of other cohort members. Mother's current smoking status (no/yes) during the first period of pregnancy (self-reported in the baseline questionnaire) was considered as it is well-known to be a strong predictor of offspring birth weight (Juárez & Merlo, 2013). Mother's educational attainment (up to completed secondary school studies and third-level education (university or graduate studies)) was used as an indicator of socioeconomic position (SEP) (Galobardes, Shaw, Lawlor, Lynch, & Davey Smith, 2006) of the mother, since educational level of the mother can directly or indirectly influence the offspring's intrauterine growth development and health (Kramer, Séguin, Lydon, & Goulet, 2000). Moreover, in the context of Lifeways Cohort Study, maternal SEP-related circumstance has been found to be associated with index-child prenatal outcomes including pre-term delivery (Niedhammer *et al.* 2012). Mother's total energy intake (kcal/day) during the first trimester of pregnancy was also taken into account, as maternal dietary patterns during the gestational periods an important contributor for offspring intrauterine development (Ota, Hiroyuki, Mori, Tobe-Gai, & Farrar, 2015). This was estimated from dietary intake recorded using a validated 149-item semi quantitative food frequency questionnaire (FFQ) (Murrin, Shrivastava, & Kelleher, 2013). Mother's parity (zero, one, two or more) was also considered, as a proxy to control for a potential maternal age-related effect and because it has been found to be associated with different adverse neonatal outcomes (Kozuki et al., 2013).

2.5.3. Paternal characteristics

Being the biological father of the index-child was taken into account to perform an additional sensitivity analysis with the paternal and paternal grandparents' birth periods in order to assess whether the potential findings were more likely due to biological outcomes, including possible epigenetic-related mechanisms through the paternal line (Pembrey, 2010; Pembrey, Saffery, & Bygren, 2014).

3. Statistical analysis

The study population characteristics were described across each birth period of the index-child's family members (mother, father, MGM, MGF, PGM, PGF) using percentages for categorical variables, and mean with SD for normally distributed continuous variables (e.g. mother's age) whilst median with the 25th and 75th percentile was used for non-normally distributed continuous variables (e.g., mother's energy and index-child's energy intake). The crude and adjusted associations between adult family members' birth periods and the index-child's birth weight category were assessed by using binomial logistic regression. Index-child-sex, mother's age, mother's smoking status, mother's education, mother's total energy intake (Log-transformed Kcal/day), and mother's parity were included as co-variables in all overall adjusted models. In order to account for potential sex-specific differences, all the analyses were stratified according to index-children's biological sex (female/male). In addition, a sensitivity analysis was repeated in the sample of children with known biological father when paternal and grandparents' period' effects were examined. Finally, as a percentage of the period data for grandparents was imputed, all analyses for grandparents were repeated using the period information calculated based on the known date of birth.

Univariate and bivariate associations were performed assuming a 0.05 alpha level. The goodness of fit of the overall final adjusted models was assessed using the Hosmer–Lemeshow fit test. All the analyses were performed using the Stata 13 software.

Table 1
Description of the study population's characteristics across parents' birth periods.

	N = 943 N	Mother's Birth Period Post World War-II Baby Boom n = 106 (11.24 %) %	Modern Ireland n = 837(88.76%) %	p-value (x^2)	N = 890 N	Father's Birth Period Post World War-II Baby Boom n = 187 (21.01%) %	Modern Ireland n = 703(78.99%) %	p-value (x^2)
Index-child's characteristics								
Birthweight status	**943**				**890**			
Low birthweight (< 10th p)	82	6.60	8.96	0.052	73	5.35	8.96	0.026
Normal birthweight (≥10th to < 90th p)	735	72.64	78.61		697	75.94	78.95	
High birthweight (≥90th p)	126	20.75	12.43		120	18.72	12.09	
Child's sex	**943**				**890**			
Female-child	482	51.89	51.02	0.866	456	53.48	50.64	0.490
Male-child	461	48.11	48.98		434	48.51	49.37	
Mother's characteristics								
Mother's age at child birth[a]	**943**	39.4(± 1.5)	29.4(± 5.1)	< 0.001	**890**	36.5(± 3.6)	29.4(± 5.0)	< 0.001
Mother's age at child birth[b]	**943**	39.1 (38.2-40.3)	30.1(26.1-33.5)	< 0.001	**943**	37.1(34.5- 39.0)	30.0(26.2-33.1)	< 0.001
Mother's education	**922**				**872**			
Up to secondary studies	458	44.66	50.31	0.280	423	47.80	48.70	0.830
Third-level studies	464	55.34	49.69		449	52.20	51.30	
Mother's smoking during 1st trimester of pregnancy	**926**				**873**			
No	723	87.38	76.91	0.016	697	82.61	79.10	0.292
Yes	203	12.62	23.09		176	17.39	20.90	
Mother's energy consumption during 1st trimester of pregnancy (Kcal)[b]	**943**	2324.2 (1871.0–2959.6)	2397.6 (1884.9–3015.0)	0.439	**883**	2296.20 (1871.0–2781.6)	2384.2 (1875.3–3015.5)	0.193
Mother´s parity	**943**				**881**			
Zero	415	13.59	48.31	< 0.001	382	14.84	50.79	< 0.001
One	280	25.24	30.60		269	29.12	30.90	
Two or more	238	61.17	21.08		230	56.04	18.31	

p = percentile.
[a] Mean (SD), p-value: t-test
[b] Median (25th -75th percentiles), p-value: Mann-Whitney test.

4. Results

4.1. Overall description of study population's characteristics

Overall, among the 943 index-children, 8.70% (n = 82) of infants were LBW, 13.36% (n = 735) were HBW and 77.94% (n = 126) had normal BW, 48.89% (n = 461) were males. Likewise, 96.71% (n = 912) of the index-children were known to be the biological child of the father in the study. Regarding maternal characteristics, the mean age of mothers was 30.5 (± SD 5.8) years, their median energy intake during the first trimester of pregnancy was 2379.7 (1879.5–3010.6) Kcal/day. In addition, 21.92% (n = 203) of index-children's mothers were currently smokers during the first trimester of pregnancy, 50.3% (n = 464) had third-level education, and 44.48%(415) were nulliparous.

With respect to relatives' birth periods, the majority of infants had parents born in the MI period (mothers = 88.76%; father = 78.99 %), whilst the majority of the infants' grandparents were born during the FS period (MGM = 33.16%; MGF = 53.71%; PGM = 52.51%; and PGF = 63.29% born during the FS period).

4.2. Distribution of the main population's characteristics across relatives' birth periods

The distribution of population characteristics according maternal and paternal birth periods is shown in Table 1. Mothers born during the MI period were more likely to have a higher percentage of LBW offspring, to be smokers and nulliparous than those born in PWWII-BB. No index-child-sex and mothers' education-related differences were seen. Similarly, index-children with fathers born during the MI period had a significantly high percentage of LBW (Table 1).

The population characteristics by MGM and MGF birth periods are displayed in Table 2. No statistical differences were observed for the index-child's BW status distribution across MGM birth periods. As expected, MGM born during the PWWII-BB had grandchildren with younger and nulliparous mothers than those born during the FS and EA. In contrast, the MGMs born during the FS and EA periods had a higher percentage of grandchildren with better educated mothers, who were less likely to have ever smoked, and with a lower dietary energy intake during their pregnancy than those MGMs born in PWWII-BB. With regard to MGFs, a similar tendency to that observed in MGMs was found (Table 2).

In relation to paternal grandparents (Table 3), PGMs born during the FS and EA periods had a higher proportion of grandchildren born with HBW than those born in PWWII-BB. Except for maternal age and parity, no distribution differences were observed for maternal education, maternal smoking habit and energy intake across the three PGM birth periods (Table 3). PGFs born during the EA tended to have a higher proportion of grandchildren that were LBW, however those born during FS were more likely to have HBW grandchildren. Like PGMs, except for maternal age and parity, no differences in the distribution of the other maternal-related characteristics were observed across PGF birth periods (Table 3).

Table 2
Description of the study population's characteristics across maternal grandparents' birth periods.

		MGM's Birth Period					MGF's Birth Period			
		Free State	Emergency Act	Post World War-II Baby Boom			Free State	Emergency Act	Post World War-II Baby Boom	
	N = 938 N	n = 311 (33.16%) %	347(36.99%) %	n = 280(29.85%) %	p-value (x^2)	N = 700 N	n = 376 (53.71%) %	n = 164(23.43%) %	n = 160(22.86%) %	p-value (x^2)
Index-child's characteristics										
Birthweight status	**938**					**700**				
Low birthweight (< 10th p)	81	6.75	8.93	10.36	0.392	58	7.18	11.59	7.50	0.405
Normal birthweight (≥10th to < 90th p)	732	77.81	78.10	78.21		552	78.72	76.83	81.25	
High birthweight (≥90th p)	125	15.43	12.97	11.43		90	14.10	11.59	11.25	
Child's sex	**938**					**700**				
Female-child	482	51.13	54.76	47.5	0.194	360	53.99	53.05	43.75	0.085
Male-child	456	48.87	45.24	52.5		340	46.01	46.95	56.25	
Mother's characteristics										
Mother's age at child birth[a]	**938**	35.5(± 3.9)	30.9(± 3.5)	24.7(± 4.1)	< 0.001	**700**	34.0(± 4.5)	30.2(± 4.4)	24.4(± 3.8)	< 0.001
Mother's age at child birth[b]	**938**	35.9(33.5-38.2)	31.1(28.6-33.2)	24.5 (21.6-27.8)	< 0.001	**700**	34.5 (31.0-37.2)	31.0(27.7-33.1)	24.1(21.4-27.6	< 0.001
Mother's education	**917**					**690**				
Up to secondary studies	454	44.74	45.70	59.42	0.001	333	47.98	40.63	56.60	0.017
Third-level studies	463	55.26	54.30	40.58		357	52.02	59.38	43.40	0.184
Mother smoking during 1st trimester of pregnancy	**922**					**686**				
No	721	86.60	80.88	65.58	< 0.001	546	85.56	77.30	67.95	< 0.001
Yes	201	13.40	19.12	34.42		140	14.44	22.70	32.05	
Mother's energy consumption during 1st trimester of pregnancy (Kcal)[b]	**932**	2398.1 (1925.4-3044.9)	2261.1 (1814.1-2798.8)	2469.8 (1890.4-3185.1)	0.001	**696**	2364.4 (1875.3-2956.9)	2333.1 (1838.6-2912.0)	2462.1 (1864.4-3172.4)	0.072
Mother´s parity	**928**					**691**				
Zero	411	28.10	40.87	66.43	< 0.001	315	35.41	44.79	70.25	< 0.001
One	279	29.74	33.91	25.63		205	30.81	33.74	22.78	
Two or more	238	42.16	25.22	7.94		171	33.78	21.47	6.96	

p = percentile.
[a] Mean (SD), p-value: ANOVA test
[b] Median (25th–75th percentiles), p-value: Kruskal–Wallis test.

Table 3
Description of the study population's characteristics across paternal grandparents' birth periods.

	PGM's Birth Period					PGF's Birth Period				
	N = 537 N	Free State n = 282(33.16%) %	Emergency Act 132(36.99%) %	Post World War-II Baby Boom n = 123(29.85%) %	p-value (x^2)	N = 553 N	Free State n = 350 (63.29%) %	Emergency Act n = 123(22.24%) %	Post World War-II Baby Boom n = 80(14.47%) %	p-value (x^2)
Index-child's characteristics										
Birthweight status	**537**					**553**				
Low birthweight (< 10th p)	49	7.45	8.33	13.82	0.016	47	6.57	12.20	11.25	0.017
Normal birthweight (≥10th to < 90th p)	413	74.82	78.79	79.67		429	76.57	76.42	83.75	
High birthweight (≥90th p)	75	17.73	12.88	6.50		77	16.86	11.38	5.00	
Child's sex	**537**					**553**				
Female-child	274	54.61	50.00	43.90	0.135	281	53.43	48.78	42.50	0.185
Male-child	263	45.39	50.00	56.10		272	46.57	51.22	57.5	
Mother's characteristics										
Mother's age at child birth[a]	**537**	33.9(± .4.4)	31.3(± 4.0)	26.9(± 4.7)	< 0.001	**553**	33.7(± .4.5)	30.1(± 4.5)	26.4(± 4.8)	< 0.001
Mother's age at child birth[b]	**537**	34.3 (31.4-37.2)	31.7 (28.4-34.1	27.6 (23.1-30.1)	< 0.001	**553**	33.8(31.0-37.0)	30.2 (27.2-33.4)	26.6(22.4-29.5)	< 0.001
Mother's education	**527**					**542**				
Up to secondary studies	240	43.88	41.54	53.78	0.111	251	44.06	48.74	52.56	0.331
Third-level studies	287	56.12	58.46	46.22		291	55.94	51.26	47.44	
Mother smoking during 1st trimester of pregnancy	**530**					**545**				
No	436	83.15	82.31	80.17	0.772	454	85.55	79.34	79.49	0.179
Yes	94	16.85	17.69	19.83		91	14.45	20.66	20.51	
Mother's energy consumption during 1st trimester of pregnancy (Kcal)[b]	**533**	2592.6 (2343.4–2909.6)	2424.7 (1921.6–3002.5)	2456.9 (1867.0–3172.4)	0.272	**549**	2296.2 (1875.3–2884.9)	2475.6 (1889.8–3084.8)	2442.1 (1890.2–3172.6)	0.139
Mother´s parity	**531**					**546**				
Zero	215	30.94	42.42	60.33	< 0.001	216	30.43	51.64	60.76	< 0.001
One	168	30.94	35.61	28.93		173	32.75	29.51	30.38	
Two or more	148	38.13	21.97	10.74		157	36.81	18.85	8.86	

p = percentile.
[a] Mean (SD), p-value: ANOVA test
[b] Median (25th–75th percentiles), p-value: Kruskal–Wallis test.

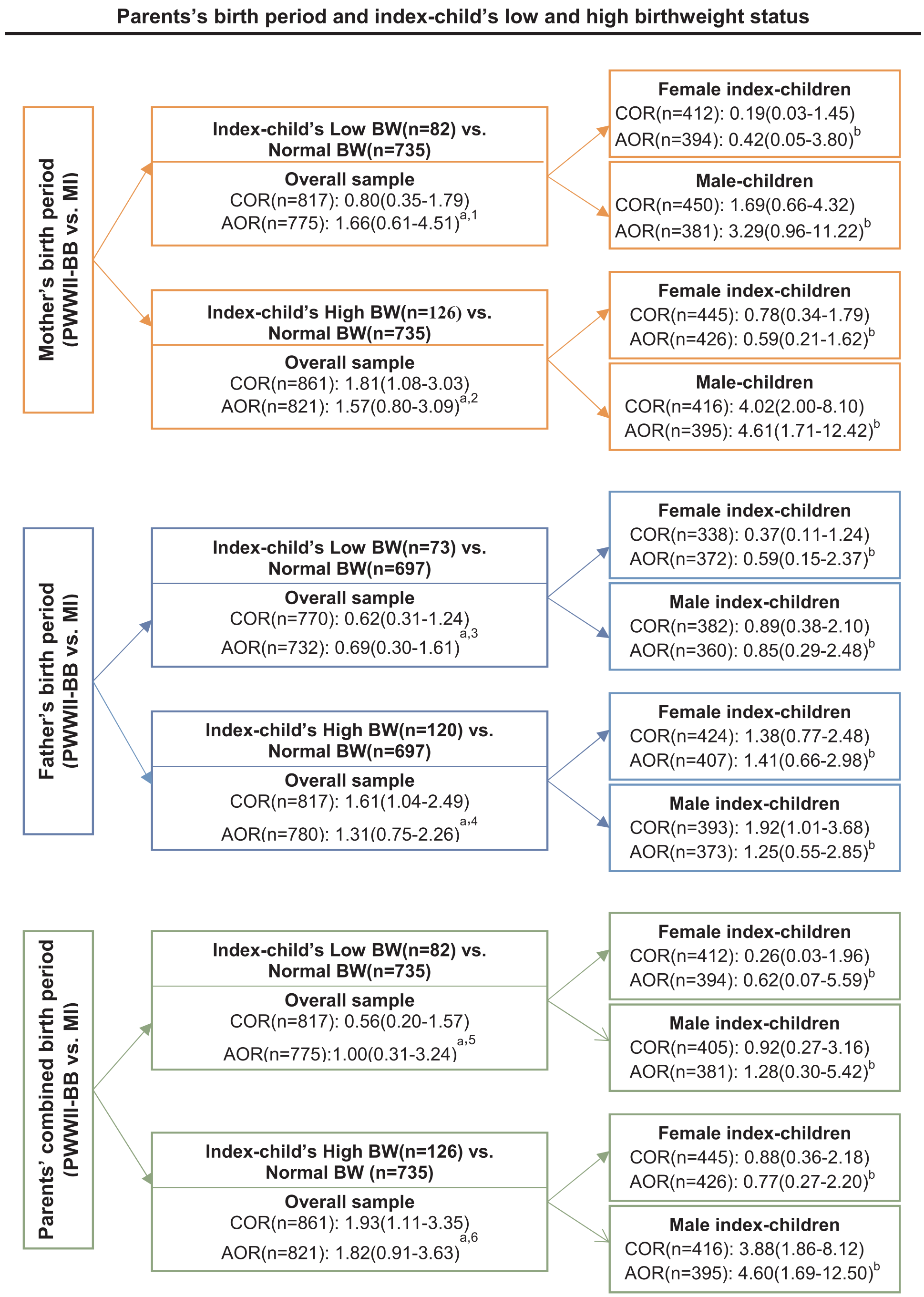

Fig. 1. Associations between parents' birth periods and index-child's birthweight status. PWWII-BB = Post World War-II Baby Boom; MI = Modern Ireland. COR = Crude Odds Ratio; AOR = Adjusted Odds Ratio. BW = Birthweight. Hosmer–Lemeshow fit test (p-value): 1 = 0.873; 2 = 0.328; 3 = 0.674; 4 = 0.937; 5 = 0.480; 6 = 0.429. a. Adjusted for children-sex, mother's age, mother's education, mother smoking, mother's energy consumption during the 1st trimester of pregnancy, and mother´s parity. b. Adjusted for mother's age, mother's education, mother smoking, mother's energy consumption during 1st trimester of pregnancy, and mother´s parity.

4.3. Crude and adjusted association between relatives' birth period and index-child birthweight status

The crude and adjusted associations between grandparental birth periods and the index-child's birthweight status (LBW and HBW) are presented in Figs. 1, 2, 3.

4.3.1. Parents birth period

Overall, mothers born during the PWWII-BB had higher probability of having HBW infants (Crude Odds Ratio (COR): 1.81, 95%CI: 1.08-3.03) compared with those of mothers born in the MI period. However that association did not remain after adjusting for other co-variables, index-child-sex, maternal age, maternal smoking, maternal education, maternal energy intake during the first trimester of pregnancy, and maternal parity (Fig. 1). When the analyses were stratified by index-child-sex, both crude and adjusted associations between mothers born during PWWII-BB and children that were HBW remained significant for index-male-children (adjusted Odds Ratio (AOR): 4.61(1.71-12.42)). As in mothers, the PWWII-BB fathers' birth period tended to be associated with having HBW infants: COR: 1.61 (1.04–2.49) but it did not remain

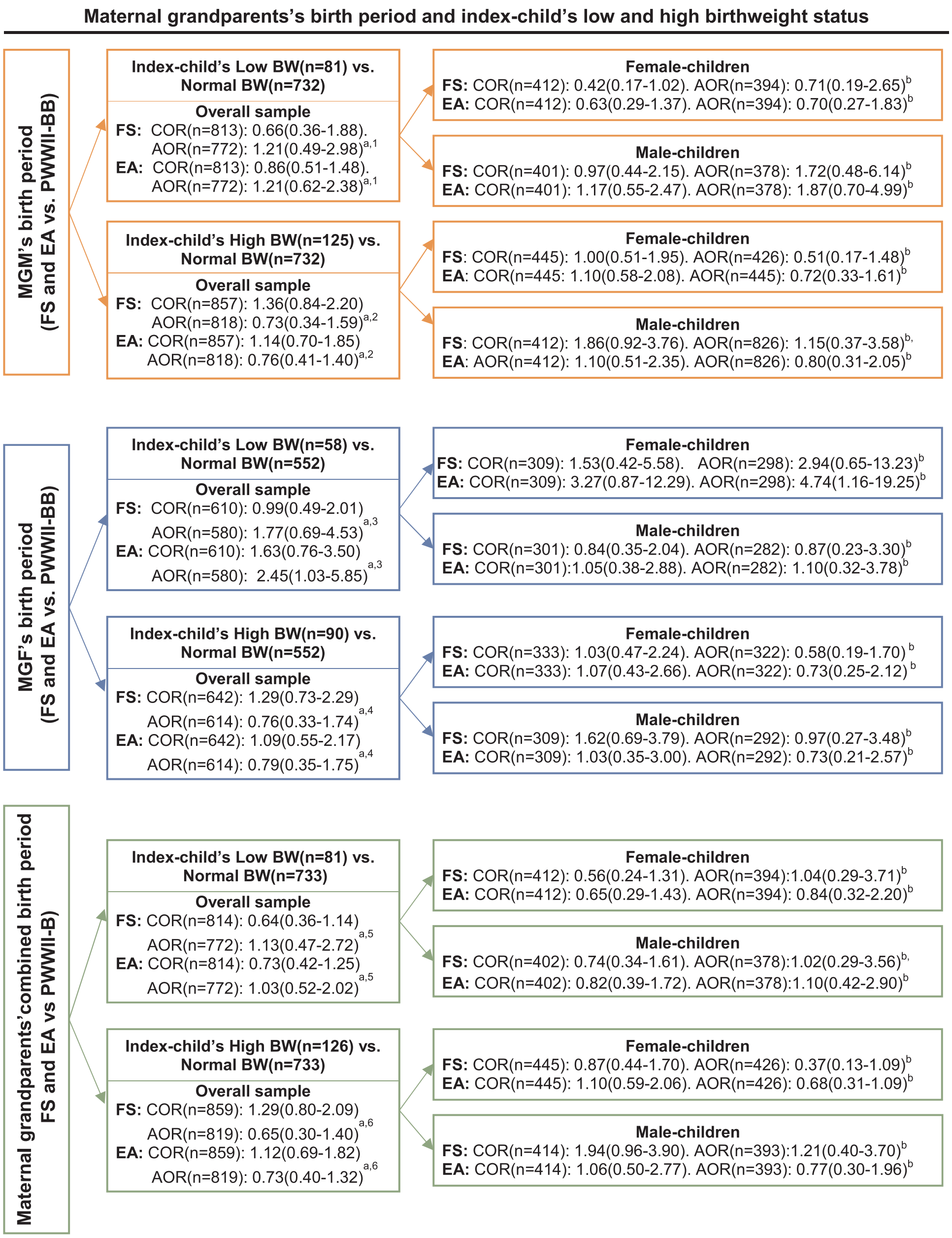

Fig. 2. Associations between maternal grandparents' birth periods and index-child's birthweight status. FS = Free State; EA = Emergency Act Power; PWWII-BB = Post World War-II Baby Boom. COR = Crude Odds Ratio; AOR = Adjusted Odds Ratio. BW = Birthweight. Hosmer–Lemeshow fit test (p-value): 1 = 0.777; 2 = 0.347; 3 = 0.557; 4 = 0.354; 5 = 0.392; 6 = 0.548. a. Adjusted for children-sex, mother's age, mother's education, mother smoking, mother's energy consumption during 1st trimester of pregnancy, and mother´s parity. b. Adjusted for mother's age, mother's education, mother smoking, mother's energy consumption during 1st trimester of pregnancy, and mother´s parity.

after adjusting for co-variables: AOR: 1.31 (0.75–2.26). Finally, when both parents' period was combined, the only associations that remained significant were the associations between parents born in the PWWII-BB period and higher BW in male-index-child: AOR: 4.60 (1.56–10.89) (Fig. 1).

4.3.2. Maternal grandparents' birth period

When comparing MGMs born during the FS and EA periods to those born in the PWIIBB period (Fig. 2), no associations were shown in relation to either LBW or HBW status in their grandchildren. In contrast, MGFs born during the EA showed an adjusted association with their grandchildren's LBW (AOR: 2.45 (1.03–5.85)), being more marked in their granddaughters (AOR: 4.74 (1.16–19.25)). When combining the two maternal grandparents' birth periods (Fig. 2), non-statistically significant relationships between their birth period and the grandchildren's birth status (Fig. 2) were observed.

4.3.3. Paternal grandparents' birth period

Compared with PGMs born in the PWIIBB period (Fig. 3), the PGMs born during the FS showed a significant positive association with grandchildren's HBW in both the crude model (COR: 2.90 (1.33–6.36)) and after adjustment for maternal co-variables (AOR: 3.23 (1.21–8.63)). A positive significant adjusted association was maintained in their granddaughters (AOR: 6.53 (1.25–34.04)) when limiting the analysis to index-child-sex. Similarly to PGMs, PGFs born during FS were associated with their grandchildren's HBW (COR: 3.69 (1.29–10.51), AOR: 3.93 (1.11–13.96)). When combining birth periods for both MGM and MGP (Fig. 3) and after adjusting for maternal

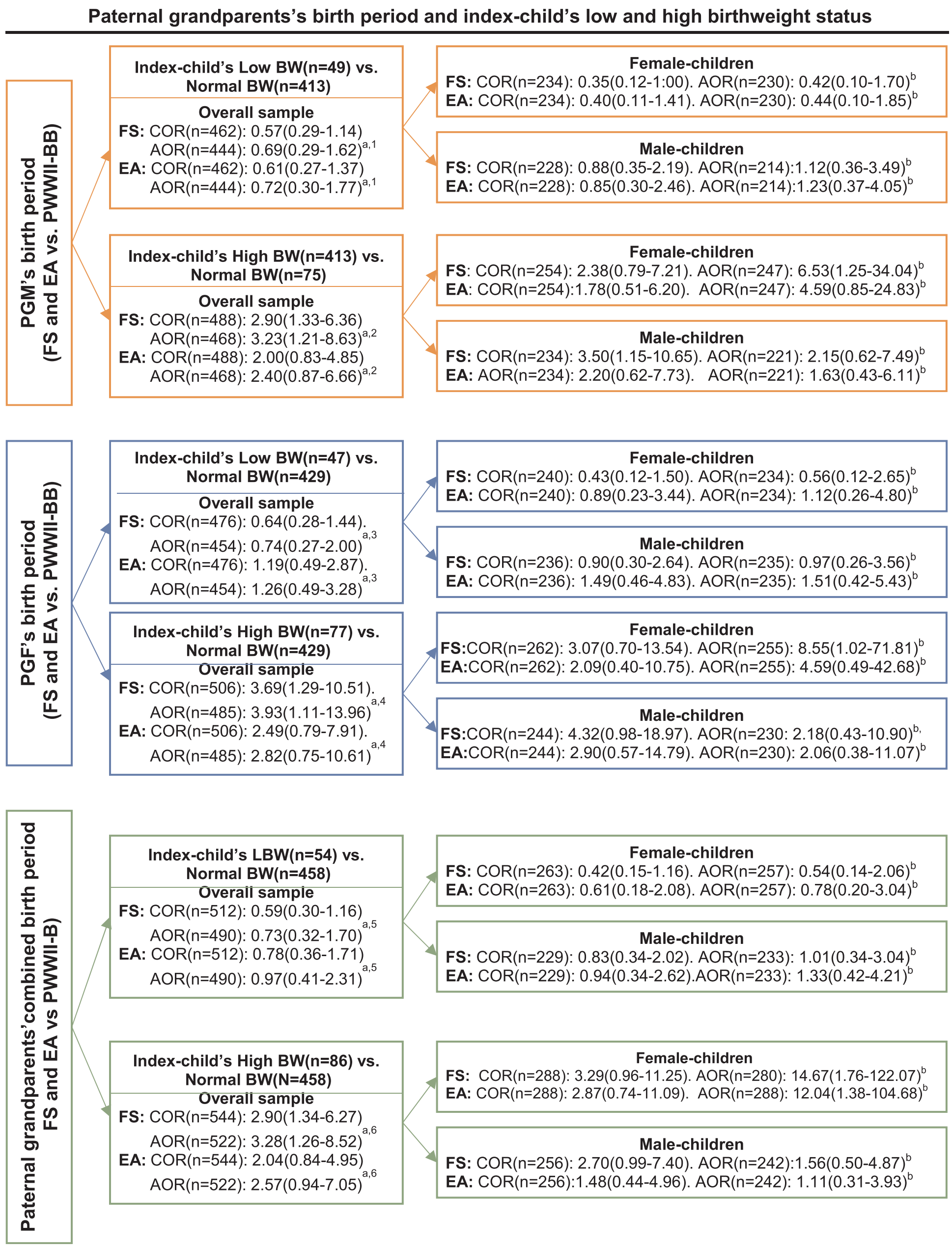

Fig. 3. Associations between paternal grandparents' birth period and index-child's birthweight status. FS = Free State; EA = Emergency Act Power; PWWII-BB = Post World War-II Baby Boom. COR = Crude Odds Ratio; AOR = Adjusted Odds Ratio. BW = Birthweight. Hosmer–Lemeshow fit test (p-value): 1 = 0.360, 2 = 0.553; 3 = 0.095; 4 = 0.132; 5 = 0.070; 6 = 0.933. a. Adjusted for children-sex, mother's age, mother's education, mother smoking, mother's energy consumption during 1st trimester of pregnancy, and mother´s parity. b. Adjusted for mother's age, mother's education, mother smoking, mother's energy consumption during 1st trimester of pregnancy, and mother´s parity.

factors, children with paternal grandparents born in the FS were born with higher birthweight than those with paternal grandparents born in the PWII-BB period (AOR: 3.28 (1.26–8.52)). After stratifiying the analysis to index-child-sex (although the each index-children-sex group has small sample sizes) a significant association was found between paternal grandparents born during both the FS and the EA with their granddaughters' HBW (FS = AOR: 14.67 (1.76–122.07); EA: 12.04 (1.38–104.68)) (Fig. 3).

4.3.4. Results in the children sample with biological father

The results of the analyses for birth periods for fathers and paternal grandparents in the index-children sample with known biological fathers (the following numbers of non-biological children of the study fathers were excluded for the analyses: n = 29 for the analysis related to paternal birth period, n = 12 when analysed related to paternal PGM birth period, and n = 10 when related to PGF birth period) are shown Table A.3, Appendix A. Similar results to those previously described for father, PGM and PGF birth periods, as well as for paternal grandparents combined birth period, were observed.

4.3.5. Results using grandparents' birth period based on the known date of birth

Finally, the crude and adjusted associations between grandparents' (MGM, MGF, PGM, and PGF) birth periods calculated based on the known date of birth are shown in the Table A.4, Table A.5, Table A.6, Table A.7, Table A.8 and Table A.9 (Appendix A). Although with fewer samples available, similar results to those described previously are observed.

5. Discussion

The present study shows that birth period of grandparents is associated with index-children's birth weight, even when maternal characteristics were taken into account. Two contrasting lineage patterns were observed. In the maternal line, maternal grandfathers born in the EA period had higher odds of low birth weight granddaughters. Whilst in the paternal line, both PGM and PGF's FS birth period was significantly associated with having grandchildren with higher birth weights.

Contrasting lineage patterns have been reported in this cohort previously. Dietary aggregation patterns have been shown in the nuclear families, stronger for the mother and in the maternal lines (Shrivastava et al., 2013). Body mass index also shows patterns of association stronger in the maternal line, whereas height is associated with both lineages (Kelly, Murrin, Viljoen, O'Brien, & Kelleher, 2014; Murrin et al., 2012). Whereas maternal grandmothers showed an inverse association with infant birthweight and both stroke and diabetes, paternal grandfathers' mortality patterns were positively associated with higher infant birthweight (Shrivastava et al., 2012). This current analysis provides empirical evidence that these familial patterns may be associated with historical period of exposure of the adult cohort members.

Our results support existing evidence on the transgenerational transmission of the effects of early life experience and circumstance in humans (Pembrey et al., 2014), particularly as few studies have included data from the third generation and even fewer studies have examined effects through the paternal line. Moreover, as Pembrey et al. highlight (Pembrey et al., 2014), transgenerational response might not only be a risk but also a 'protective' adaptation for future generations, which can explain the positive association between some of the grandparental exposure to the adverse conditions in the periods studied here and both grandchildren's high and low birthweight. Furthermore, although the sample size was small following the stratification of our analyses for index-child sex, some sex-specific associations were observed, supporting in part the Pembrey and Champagne hypothesis (Champagne, 2013; Pembrey et al., 2006) that some exposures in critical periods (e.g., preconception and antenatal, and early childhood period) may have sex-specific routes, which might explain to some extent how many health outcomes differ between males and females in humans.

This study did not directly evaluate the potential exposure to nutritional restrictions during the studied periods as other studies have done in similar circumstance in other geographical contexts (e.g. Dutch Hunger Winter of 1944–1945 and the Chinese Great Famine of 1959–1961) (De Rooij, Painter, Holleman, Bossuyt, & Roseboom, 2007; Huang et al., 2010; Painter et al., 2005); however the significant associations found between the FS period of the PGM and PGF and HBW in their grandchildren as well as the positive association between both FS and EA periods of the paternal grandparents when their birth period was combined with the HBW of their granddaughters, are to some extent in line with the suggestion that exposures to hardiness or natural made circumstances may trigger greater growth and survival prospective across generations. For example, in rural China new-borns of mothers exposed to Chinese famine (1959–1961) were heavier and larger (Huang et al., 2010). They only analysed however children's birth linked outcomes in relation to the offspring's mother but not with the father and grandparents. Higher birthweight and BMI values among offspring of prenatally exposed fathers to the Dutch Famine has been also reported (Veenendaal et al., 2013). Our findings might suggest a potential survival effect transmitted from the paternal grandparents though the paternal line (robust male-children with better growth and survival predisposition) expressed in the third-generation children (index-children). From the animal studies and those limited studies in humans, there is growing evidence supporting the transgenerational epigenetic role of the paternal line in the short and long-term health outcome for future generations (Day, Savani, Krempley, Nguyen, & Kitlinska, 2016 ; Li, Tsuprykov, Yang, & Hocher, 2016).

There might also be other plausible biological circumstances that explain these findings. For example, the index-children's parents born in more advantaged socioeconomic times (e.g. Baby Boom period) could have had access to better food supply, and health care services. The introduction of the Health Act in the Republic of Ireland (1947) reformed the health care delivery services and is thought to be one of the main drivers for the improvement of childhood health conditions and status in Ireland (Delaney, 2011). Consistent with this, an age-period-cohort analysis for trends in BMI in the Irish context employing the SLAN surveys of lifestyle, attitudes and nutrition conducted between 1998 and 2007 (Jiang et al., 2013), showed distinct cohort as well as age effects on BMI in adults, with those born between 1950s and 1960s having relatively lower BMIs at equivalent ages than those born in earlier decades, and a strong period influence for latter obesity patterns. Maternal age and parity were considered in all the adjusted models in order to control for maternal cohort effect. Maternal total energy intake during the first trimester of studied children's gestation period was also taken into account, as the maternal energy intake during the pregnancy might influence offspring's birthweight (Parlee & MacDougald, 2014).

Moreover, the transgenerational effect observed between paternal grandparents born during the adverse Free State period and higher birthweight on their grandchildren, might be also due to a survivor effect, as more robust grandmothers produced daughters in turn with higher birth weight children. Stress through an individual's life course may be linked with the stress-neuroendocrine regulatory response (hypothalamic-pituitary-adrenal axis) and stress-linked epigenetics variations, explaining the results observed. There is evidence that stress can be associated with many physical and psychological health consequences such as cardiovascular diseases (Schneiderman, Ironson, & Siegel, 2005) and childhood obesity (Gundersen, Mahatmya, Garasky, & Lohman, 2011). The type of adaptation mechanism response may depend on the type of stressor and time of exposure, prompting many body responses, which in turn might result in different adverse health outcomes. In both acute and chronic stress exposure, hormones, the sympathetic nervous system, the immune system, the inflammatory and cardiovascular function amongst others, are actively involved in the individuals' stress response (Schneiderman et al., 2005).

The transgenerational transmission of the stress effects via epigenetic pathways has been described in animal and human studies, which have documented that exposures to stressful situations or environments can produce long-term diseases and changes or variations in the genes expression that not only prompt both punctual outset and cumulative health disorders in the exposed individuals but also in their future generations (transgenerational stress imprinting) (Bale, 2014; Zucchi, Yao, & Metz, 2012).

The Free State period was associated with violent civil conflict, whilst the Emergency period limited the access to basic goods and services, increasing therefore the possibility that some people might have faced significant food-related constraints during that period. There was also persistent economically-driven emigration during the first half of the twentieth century, a longstanding phenomenon of population depletion in Ireland, whose emigrants were associated with higher rates of cardiovascular disease in their adopted countries (Kelleher et al., 2006; Kelleher, Lynch, Harper, Tay, & Nolan, 2004). This analysis does not address the impact of migration, since it was confined only to families who remained in Ireland.

The association observed between MGFs born during the Emergency Powers Act period and low birthweight in their female-grandchildren particularly, suggests that those who were born and grew up in that period may have experienced certain nutritional restrictions, particularly more disadvantaged people, the consequences of which may have passed through generations and be expressed in the third generation-children. The Irish National Nutrition Survey done in 1948, in fact showed that households of lower social classes and with low income levels had poorer meal patterns and lower consumption of key foods such as meat, eggs, milk, vegetables and fruit (Department of Health, 1948). In the Dutch Famine context, studies have shown that children exposed to maternal famine during the gestational period were more likely to be thinner and shorter as well as developing several negative health outcomes (e.g., coronary heart diseases, adverse lipid profile) later in life (Painter et al., 2005). As it has been explained before, sperm DNA-methylation, sperm RNAs alterations, and histone modification in the sperm, might be part of the epigenetic pathway through which the grandpaternal insult effects can be passed to their children and to their grandchildren (Day et al., 2016; Li et al., 2016).

It is also possible that these observed associations are a consequence of index-mother's unknown behaviour, such as diet-specific patterns during the pregnancy as insufficient, or malnutrition, or cultural factors which might trigger having low birthweight offspring (Abu-Saad & Fraser, 2010). We have consistently shown maternal dietary patterns, including those of maternal grandmothers are associated with offspring outcomes (Kelleher et al., 2014; Shrivastava et al., 2013). In the present study we observed that both mothers and fathers born from 1964 onwards tended to have a higher percentage of offspring with low birthweight. To some extent, this is in line with the findings reported by a study on BMI performed in the Irish context (Jiang et al., 2013). Authors hypothesised that trends may be explained by improvement in childhood nutrition to which later generations have access, prompting to have more "correctly programmed" new-borns. However, it may also be likely that millennial and post-millennial cohorts have been exposed to much unhealthier and less nutritive dietary patterns, in the current obesogenic environment, triggering the "dual" possibility of having offspring with either low or with high birth weights (Black et al., 2008; Popkin, 2006).

5.1. Limitations and strengths

It is important to acknowledge that the following factors can limit our study results. Firstly, it is possible that any grandparental effects are simply a reflection of the fact that older, better educated mothers are more likely to have healthy birth outcomes. We did not undertake a conventional age-period-cohort analysis and there are established problems with collinearity when all three factors are at play (Huang et al., 2015). This is a well-characterised but relatively small cohort study and there are limitations of power and sample size, especially when analyses were stratified by child-sex, the statistical power to detect clear sex-dependent differences in some of the results could be reduced.

It was not possible to examine in more detail the potential accumulated patterns across generations because of the sample size and structure of the data. Moreover, it is possible that some of the associations observed here, are chance findings, due to the fact that multiple statistical tests were performed. The observed associations between grandparental birth period and grandchildren's birth weight could be due to unmeasured maternal factors and residual confounding, though we did adjust for key maternal characteristics such as age, smoking habit, energy intake during the first trimester of pregnancy as well as maternal education (as a core SEP indicator) and parity. It was not possible to use grandparental nutritional intake-related indicators during their own childhoods to evaluate potential nutrition variation during their childhood. However, evidence suggests that there was limited access to basic goods and services, including food products which was imposed by the Emergency Powers Act (eISB, 1939), and a major nutrition survey was undertaken in 1948 precisely because of concern about the nutritional status of the population, showing strong social gradients in dietary patterns (Department of Health, 1948).

There may be an information bias in relation to the delimitation of the historical exposure periods, some authors have suggested for instance that Ireland experienced a later post WW II baby boom period to the late 1970s (Fahey et al., 1998). Despite these limitations, our study is one of the few in the literature with accurate data (demographics, behavioural and medical) for three generations, which is an important source for studying transgenerational disease transmission. As some authors suggest, for a better understanding the transgenerational disease and health patterns transmission, it is important to perform studies with data from more than two generations (Pembrey et al., 2014; Zucchi et al., 2012).

5.2. Conclusion

Findings from this study show some evidence that the period of the grandparental birth is associated with their grandchildren's birthweights, suggesting that transgenerational exposures may be particular to historical contexts, meriting further exploration.

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

The present studied have used data from the participants of the Lifeways Cross-Generation Cohort Study; which have received ethical approval for the various baseline and follow-up data collections initially from the ethical committees at the National University of Ireland, Galway; the Coombe Women's Hospital, Dublin; University College Hospital, Galway; the Irish College of General Practitioners; and later from University College Dublin; and St. Vincent's University Hospital, Dublin.

Appendix A

See appendix Tables A1–A9.

Table A.1
Distribution of the main study population's characteristics across categories of index-children with and without MGF, PGM, PGF's birth period (known or inferred) in the 943-study dataset.

Non-twin and alive-born children sample (N = 943)	N	Maternal Grandfather (MGF) MGF with birth period data[a] N = 700(74.23%) %	MGF without birth period data[b] N = 243(25.77%) %	p-value (x^2)	Paternal Grandmother (PGM) PGM with birth period data[a] N = 537(56.95%) %	PGM without birth period data[b] N = 406(43.05) %	p-value(x^2)	Paternal Grandfather (PGF) PGF with birth period data[a] N = 553(58.64%) %	PGF without birth period data[b] N = 390(41.36%) %	p-value(x^2)
Index-child's characteristics										
Birthweight status	943									
Normal birthweight (≥10th to < 90th p)	82	8.29	9.88	0.513	9.12	8.13	0.678	8.50	8.97	0.819
High birthweight (≥90th p)	735	78.86	75.31		76.91	79.31		77.58	78.46	
Low birthweight (< 10th p)	126	12.86	14.81		13.97	12.56		13.92	12.56	
Child's sex	**943**									
Female-child	482	51.43	50.21	0.743	51.02	51.23	0.950	50.81	51.54	0.826
Male-child	461	48.57	49.79		48.98	48.77		49.19	48.46	
Mother's characteristics										
Mother's age at child birth[c]	943	30.9(5.8)	29.5(5.6)	0.001	31.6(5.2)	29.1(6.7)	0.001	31.8(5.2)	28.7(6.0)	0.001
Mother's education	922									
Up to secondary studies	458	48.26	53.88	0.139	45.54	55.19	0.004	46.31	54.47	0.015
Third-level studies	464	51.74	46.12		54.46	44.81		53.69	45.53	
Mother's smoking during 1st trimester of pregnancy	926									
No	723	79.59	73.75	0.060	82.26	72.47	< 0.001	83.30	70.60	< 0.001
Yes	203	20.41	26.25		17.74	27.53		16.70	29.40	
Mother's energy consumption during 1st trimester of pregnancy (Kcal/day)[d]	**936**	2376.1 (1,869.3-3,008.7)	2,399.2 (1,913.0-3,016.8)	0.639	2,383.0 (1,885.8-2,967.9)	2,375.7 (1,877.7-3,035.7)	0.993	2,367.4 (1,879.5-2,962.7)	2,393.4 (1,879.5-3,040.3)	0.607
Mother´s parity	**933**									
Zero	415	45.59	41.32	0.486	40.49	49.75	0.017	39.56	51.42	0.001
One	280	29.67	30.99		31.64	27.86		31.68	27.65	
Two or more	238	24.75	27.69		27.87	22.39		28.75	20.93	
Being the biological father of the index-child	**943**									
No	31	4.14	0.82		2.23	4.68	0.037	1.81	5.38	0.002
Yes	912	95.86	99.18	0.006[e]	97.77	95.32		98.19	94.62	

p = percentile.
[a] Known or inferred birth period.
[b] Without known or inferred birth period.
[c] Mean (SD), p-value: t-test.
[d] Median (25th–75th percentiles), p-value: Mann-Whitney test.
[e] Fisher's test.

Table A.2
Numbers of mother and fathers according to their own period of birth and those of their parents in the Lifeways Cross-Generation Cohort Study.

Maternal Grandparents	Mothers (n = 1088)		Paternal Grandparents	Fathers (n = 674)		
	1947–1964	After 1964		1939-1946	1947–1964	After 1964
Pre 1916	4	6	**Pre 1916**	0	5	5
1916–1938	202	573	**1916–1938**	2	259	428
1939–1946	13	553	**1939–1946**	0	18	271
1947–1964	0	542	**1947–1964**	0	1	252
After 1964	0	2	**After 1964**	0	0	0

Table A.3
Associations between father and paternal grandparents' birth periods and the index-child's low and high birthweight status in the children sample with biological father.

Index-children Sample with Biological Father **Father's birth period**								
		Index-child's Low BW(n = 72) vs. Normal BW(n = 677)				**Index-child's High BW(n = 117) vs. Normal BW(n = 677)**		
		Overall Sample OR (95%CI)	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**		**Overall Sample OR (95%CI)**	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**
Crude Associations	N = 749				N = 794			
Father born PWWII-BB (vs. MI)		0.61(0.30–1.22)	0.36(0.11–1.21)	0.88(0.37–2.07)		1.61(1.04–2.49)	1.44(0.79–2.59)	1.83(0.96–3.51)
Adjusted Associations	N = 712				N = 758			
Father born PWWII-BB (vs. MI)		0.67(0.29–1.56)[a1]	0.60(0.15–2.40)[b]	0.79(0.27–2.35)		1.35(0.78–2.35)[a2]	1.51(0.71–3.25)[b]	1.25(0.55–2.85)[b]
Paternal grandmother(PGM)'s birth period								
		Index-child's Low BW(n = 48) vs. Normal BW(n = 404)				**Index-child's High BW(n = 73)vs. Normal BW(n = 404)**		
		Overall Sample OR (95%CI)	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**		**Overall Sample OR (95%CI)**	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**
Crude Associations	N = 452				N = 477			
PGM born FS (vs. PWWII-BB)		0.61(0.30–1.22)	0.35(0.12–0.99)	0.99(0.39–2.55)		2.78(1.27–6.11)	2.19(0.72–6.67)	3.51(1.15–10.70)
PGM born EA (vs. PWWII-BB)		0.65 (0.29–1.48)	0.39(0.11–1.40)	0.98(0.33–2.91)		2.02(0.83–4.90)	1.77(0.51- 6.17)	2.24(0.64–7.92)
Adjusted Associations	N = 434				N = 457			
PGM born FS (vs. PWWII-BB)		0.74(0.31–1.79)[a3]	0.43(0.11–1.74)[b]	1.31(0.40–4.32)[b]		3.21(1.19–8.64)[a4]	6.11(1.17–31.95)[b]	2.24(0.64–7.87)[b]
PGM born EA (vs. PWWII-BB)		0.78(0.31–1.92)[a3]	0.44(0.11–1.85)[b]	1.52(0.44–5.17)[b]		2.48(0.90–6.87)[a4]	4.66(0.86–25.14)[b]	1.71(0.46–6.44)[b]
Paternal grandfather(PGF)'s birth period								
		Index-child's Low BW(n = 46) vs. Normal BW(n = 422)				**Index-child's High BW(n = 75) vs. Normal BW(n = 422)**		
		Overall Sample OR (95%CI)	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**		**Overall Sample OR (95%CI)**	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**
Crude Associations	N = 468				N = 497			
PGF born FS (vs. PWWII-BB)		0.65(0.29–1.47)	0.43(0.13–1.51)	0.93(0.31–2.73)		3.63(1.27–10.36)	2.90(0.65–12.82)	4.46(1.01–19.62)
PGF born EA (vs. PWWII-BB)		1.13(0.46–2.77)	0.91(0.24–3.52)	1.36(0.41–4.49)		2.55(0.80–8.09)	2.13(0.41–10.98)	2.97(0.58–15.12)
Adjusted Associations	N = 446				N = 476			
PGF born FS (vs. PWWII-BB)		0.75(0.27–2.04)[a5]	0.56(0.12–2.67)[b]	1.00(0.26–3.79)[b]		3.99(1.12–14.24)[a6]	8.10(0.97–68.02)[b]	2.33(0.46–11.78)[b]
PGF born EA (vs. PWWII-BB)		1.19(0.45–3.16)[a5]	1.14(0.27–4.89)[b]	1.33(0.35–5.01)[b]		2.93(0.78–11.03)[a6]	4.73(0.51–43.91)[b]	2.14(0.40–11.51)[b]
Paternal grandparents(PGPs)' combined birth period								
		Index-child's Low BW(n = 53) vs. Normal BW(n = 449)				**Index-child's High BW(n = 84) vs. Normal BW (n = 449)**		
		Overall Sample OR (95%CI)	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**		**Overall Sample OR (95%CI)**	**Female-children OR (95%CI)**	**Male-children OR (95%CI)**
Crude Associations	N = 502				N = 533			
PGPs born FS (vs. PWWII-BB)		0.63(0.32–1.25)	0.41(0.15–1.15)	0.94(0.37–2.35)		2.79(1.28–6.05)	3.07(0.89–10.52)	2.70(0.98–7.40)
PGPs born EA (vs. PWWII-BB)		0.84(0.38–1.86)	0.61(0.18–2.07)	1.08(0.38–3.09)		2.06(0.85–5.00)	2.86(0.74–11.07)	1.51(0.45–5.07)
Adjusted Associations	N = 480				N = 511			
PGPs born FS (vs. PWWII-BB)		0.79(0.34–1.87)[a7]	0.55(0.14–2.09)[b]	1.17(0.37–3.72)[b]		3.26(1.25–8.51)[a8]	14.05(1.69–117.06)[b]	1.60(0.51–5.05)[b]
PGPs born EA (vs. PWWII-BB)		1.07(0.44–2.58)[a7]	0.78(0.20–3.04)[b]	1.62(0.50–5.31)[b]		2.64(0.96–7.26)[a8]	12.30(1.42–106.83)[b]	1.16(0.33–4.11)[b]

FS: Free State; EA: Emergency Act Power; PWWII-BB: Post World War-II Baby Boom; MI: Modern Ireland.
BW: Birthweight. Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.
Hosmer–Lemeshow fit test (p-value): 1 = 0.838, 2 = 0.906; 3 = 0.307; 4 = 0.685; 5 = 0.066; 6 = 0.220; 7 = 0.135; 8 = 0.912.
[a] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.
[b] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.

Table A.4
Crude and adjusted associations between maternal grandmother (MGM)' birth period based on observed date of birth (DOB) and index-child's low and high birthweight status.

	Index-child Birthweight (BW) Status											
	Index-child's Low BW[a]						**Index-child's High BW**[a]					
	Overall Sample (N = 486)		**Female-Children (n = 241)**		**Male-Children (n = 245)**		**Overall Sample (N = 513)**		**Female-Children (n = 265)**		**Male-Children (n = 248)**	
	n	Low BW(n = 42) vs. Normal BW(n = 444) **OR (95%CI)**	**n**	Low BW(n = 18) vs. Normal BW(n = 223) **OR (95%CI)**	**n**	Low BW(n = 24) vs. Normal BW(n = 221) **OR (95%CI)**	**n**	High BW(n = 69) vs. Normal BW(n = 444) **OR (95%CI)**	**n**	High BW(n = 42) vs. Normal BW(n = 223) **OR (95%CI)**	**n**	High BW(n = 27) vs. Normal BW(n = 221) **OR (95%CI)**
Crude Associations	486		241		245		513		265		248	
MGM's Birth Period based on DOB												
FS (vs. PWII-BB)		0.66(0.30–1.44)		0.39(0.11–1.32)		1.02(0.35–2.95)		1.15(0.63–2.09)		0.94(0.42–2.14)		1.40(0.57–3.42)
EA(vs. PWII-BB)		0.96(0.46–2.02)		0.56(0.18–1.74)		1.52(0.55–4.15)		1.01(0.53–1.92)		1.15(0.51–2.60)		0.67(0.22–2.07)
Adjusted Associations	467		235		232		493					
MGM's Birth Period based on DOB												
FS (vs. PWII-BB)		1.03(0.34–1.37)[b1]		0.67(0.13–3.35)[c]		1.24(0.25–6.13)[c]		0.63(0.25–1.60)[a2]	257	0.43(0.12–1.49)[b]	236	0.95(0.22–4.02)[b]
EA(vs. PWII-BB)		1.21(0.50–2.91)[b1]		0.65(0.18–2.31)[c]		1.86(0.52–6.67)[c]		0.70(0.31–1.57) [a2]		0.76(0.27–2.16)[b]		0.49(0.12–1.99)[b]

Hosmer-Lemeshow fit test (p-value): 1 = 0.321, 2 = 0.691.
[a] Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.
[b] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.
[c] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity

Table A.5
Crude and adjusted associations between maternal grandfather (MGF)' birth period based on observed date of birth (DOB) and index-child's low and high birthweight status.

	Index-child Birthweight(BW) Status											
	Index-child's Low BW[a]						**Index-child's High BW**[a]					
	Overall Sample (N = 373)		**Female-Children (n = 189)**		**Male-Children (n = 184)**		**Overall Sample (N = 396)**		**Female-Children (n = 205)**		**Male-Children (n = 191)**	
	n	Low BW(n = 33) vs. Normal BW(n = 340) **OR (95%CI)**	**n**	Low BW(n = 17) vs. Normal BW(n = 172) **OR (95%CI)**	**n**	Low BW(n = 16) vs. Normal BW(n = 168) **OR (95%CI)**	**n**	High BW(n = 56) vs. Normal BW(n = 340) **OR (95%CI)**	**n**	High BW(n = 33) vs. Normal BW(n = 172) **OR (95%CI)**	**n**	High BW(n = 23) vs. Normal BW(n = 168) **OR (95%CI)**
Crude Associations	373		189		184		396		205		191	
MGF's Birth Period based on DOB												
FS (vs. PWII-BB)		1.06(0.37–3.01)		3.22(0.38–27.60)		0.60(0.15–2.36)		1.18(0.59–2.37)		0.83(0.33–2.08)		1.81(0.60–5.45)
EA(vs. PWII-BB)		2.92(1.10–7.74)		9.57(1.18–77.86)		1.55(0.46–5.21)		1.18(0.55–1.55)		1.06(0.39–2.86)		1.33(0.38–4.64)
Adjusted Associations	353		183		170		377					
MGF's Birth Period based on DOB												
FS (vs. PWII-BB)		2.51(0.67–9.38)[b1]		10.35(0.93–115.25)[c]		0.67(0.10–4.47)[c]		0.98(0.36–2.68)[b2]	199	0.61(0.17–2.25)[c]	178	2.08(0.42–10.39)[c]
EA(vs. PWII-BB)		5.35(1.71–16.72)[b1]		21.22(2.31–194.70)[c]		1.65(0.36–7.67)[c]		1.04(0.41–2.65) [b2]		0.85(0.25–2.88)[c]		1.38(0.30–6.20)[c]

Hosmer-Lemeshow fit test (p-value): 1 = 0.109, 2 = 0.136.
[a] Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.
[b] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.
[c] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity

Table A.6
Crude and adjusted associations between maternal grandparents (MGPs)' combined birth period based on observed date of birth (DOB) and index-child's low and high birthweight status.

	Index-child Birthweight (BW) Status											
	Index-child's Low BW[a]						Index-child's High BW[a]					
	Overall Sample (N = 535)		Female-Children (n = 264)		Male-Children (n = 271)		Overall Sample (N = 565)		Female-Children (n = 287)		Male-Children (n = 278)	
		Low BW(n = 47) vs. Normal BW(n = 488)		Low BW(n = 21) vs. Normal BW(n = 243)		Low BW(n = 26) vs. Normal BW(n = 245)		High BW(n = 77) vs. Normal BW(n = 488)		High BW(n = 44) vs. Normal BW(n = 243)		High BW(n = 33) vs. Normal BW(n = 245)
	n	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**
Crude Associations	535		264		271		565		287		278	
MGPs' Combined Birth Period based on DOB												
FS (vs. PWII-BB)		0.57(0.27–1.21)		0.53(0.18–1.54)		0.63(0.22–1.77)		1.19(0.67–2.12)		0.79(0.35–1.76)		1.83(0.79–4.26)
EA(vs. PWII-BB)		0.89(0.44–1.81)		0.68(0.23–2.02)		1.11(0.44–2.84)		1.14(0.62–2.11)		1.17(0.53–2.58)		0.95(0.35–2.63)
Adjusted Associations	513		257		256		543					
MGPs' Combined Birth Period based on DOB												
FS (vs. PWII-BB)		0.91(0.33–2.47)[b1]		1.00(0.24–4.19)[c]		0.66(0.16–2.82)[c]		0.61(0.26–1.43)[b2]	279	0.26(0.08–0.89)[c]	264	1.43(0.40–5.05)[c]
EA(vs. PWII-BB)		1.17(0.51–2.67)[b1]		0.94(0.29–3.07)[c]		1.18(0.36–3.85)[c]		0.75(0.36–1.60) [b2]		0.61(0.22–1.67)[c]		0.80(0.24–2.69)[c]

Hosmer-Lemeshow fit test (p-value): 1 = 0.756, 2 = 0.707.
[a] Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.
[b] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.
[c] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity

Table A.7
Crude and adjusted associations between paternal grandmother (PGM)' birth period based on observed date of birth (DOB) and index-child's low and high birthweight status.

	Index-child Birthweight (BW) Status											
	Index-child's Low BW[a]						Index-child's High BW[a]					
	Overall Sample (N = 352)		Female-Children (n = 174)		Male-Children (n = 178)		Overall Sample (N = 367)		Female-Children (n = 187)		Male-Children (n = 180)	
		Low BW(n = 33) vs. Normal BW(n = 319)		Low BW(n = 12) vs. Normal BW(n = 162)		Low BW(n = 24) vs. Normal BW(n = 221)		High BW(n = 48) vs. Normal BW(n = 319)		High BW(n = 25) vs. Normal BW(n = 162)		High BW(n = 23) vs. Normal BW(n = 157)
	n	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**	**n**	**OR (95%CI)**
Crude Associations	352		174		178		367		187		180	
PGM's Birth Period based on DOB												
FS (vs. PWII-BB)		0.38(0.15–0.93)		0.19(0.04–0.98)		0.60(0.20–1.79)		2.97(1.17–7.53)		2.47(0.66–9.17)		3.58(0.96–13.40)
EA(vs. PWII-BB)		0.63(0.27–1.46)		0.56(0.15–2.11)		0.69(0.23–2.09)		2.66(1.01–7.04)		2.51(0.64–9.89)		2.78(0.70–11.07)
Adjusted Associations	339		130		167		353					
PGM's Birth Period based on DOB												
FS (vs. PWII-BB)		0.50(0.16–1.54)[b1]		0.18(0.02–1.42)[c]		0.87(0.21–3.56)[c]		3.69(1.09–12.47)[b2]	183	15.05(1.53–148.41)[c]	170	1.76(0.39–7.82)[c]
EA(vs. PWII-BB)		0.78(0.29–2.06)[b1]		0.55(0.11–2.70)[b]		1.17(0.31–4.34)[c]		3.67(1.12–12.01) [b2]		13.68(1.45–129.23)[b]		1.93(0.45–8.37)[c]

Hosmer-Lemeshow fit test (p-value): 1 = 0.780, 2 = 0.380.
[a] Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.
[b] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.
[c] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.

Table A.8
Crude and adjusted associations between paternal grandfather (PGF)' birth period based on observed date of birth (DOB) and index-child's low and high birthweight status.

	Index-child Birthweight(BW) Status											
	Index-child's Low BW[a]						Index-child's High BW[a]					
	Overall Sample (N = 275)		Female-Children (n = 129)		Male-Children (n = 146)		Overall Sample (N = 287)		Female-Children (n = 135)		Male-Children (n = 152)	
	n	Low BW(n = 26) vs. Normal BW(n = 249) OR (95%CI)	n	Low BW(n = 10) vs. Normal BW(n = 119) OR (95%CI)	n	Low BW(n = 16) vs. Normal BW(n = 130) OR (95%CI)	n	High BW(n = 38) vs. Normal BW(n = 249) OR (95%CI)	n	High BW(n = 16) vs. Normal BW(n = 119) OR (95%CI)	n	High BW(n = 22) vs. Normal BW(n = 130) OR (95%CI)
Crude Associations	275		129		146		287		135		152	
PGF's Birth Period based on DOB												
FS (vs. PWII-BB)		0.60(0.21–1.68)		0.36(0.08–1.57)		0.94(0.21–4.20)		3.01(1.00–9.03)		2.16(0.45–10.45)		3.97(0.85–18.51)
EA (vs. PWII-BB)		1.11(0.40–3.10)		0.31(0.05–1.81)		2.52(0.62–10.29)		1.56(0.45–5.43)		0.61(0.08–4.66)		2.83(0.53–15.01)
Adjusted Associations	264		94		137		274					
PGF's Birth Period based on DOB												
FS (vs. PWII-BB)		0.68(0.20–2.38)[b1]		0.72(0.11–4.87)[c]		1.05(0.17–6.50)[c]		3.05(0.75–12.50)[b2]	113	7.21(0.65–80.26)[c]	143	2.05(0.36–11.76)[c]
EA (vs. PWII-BB)		1.24(0.41–3.78)[a1]		0.52(0.07–3.68)[c]		2.84(0.62–13.01)[c]		1.61(0.38–6.85) [b2]		0.98(0.05–18.65)[c]		2.07(0.36–11.81)[c]

Hosmer-Lemeshow fit test (p-value): 1 = 0.695, 2 = 0.060.

[a] Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.

[b] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.

[c] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity

Table A.9
Crude and adjusted associations between paternal grandparents (PGPs)' combined birth period based on observed date of birth (DOB) and index-child's low and high birthweight status.

	Index-child Birthweight (BW) Status											
	Index-child's Low BW[a]						Index-child's High BW[a]					
	Overall Sample (N = 391)		Female-Children (n = 192)		Male-Children (n = 199)		Overall Sample (N = 412)		Female-Children (n = 206)		Male-Children (n = 206)	
	n	Low BW(n = 38) vs. Normal BW(n = 353) OR (95%CI)	n	Low BW(n = 15) vs. Normal BW(n = 177) OR (95%CI)	n	Low BW(n = 26) vs. Normal BW(n = 245) OR (95%CI)	n	High BW(n = 59) vs. Normal BW(n = 353) OR (95%CI)	n	High BW(n = 29) vs. Normal BW(n = 177) OR (95%CI)	n	High BW(n = 30) vs. Normal BW(n = 176) OR (95%CI)
Crude Associations	391		192		199		412		206		206	
PGPs' Combined Birth Period based on DOB												
FS (vs. PWII-BB)		0.36(0.15–085)		0.22(0.05–0.89)		0.53(0.18–1.58)		2.72(1.21–6.12)		2.73(0.75–9.89)		2.87(1.00–8.22)
EA(vs. PWII-BB)		0.78(0.36–1.71)		0.61(0.18–2.08)		0.94(0.34–2.62)		2.04(0.84–4.95)		2.87(0.74–11.09)		1.48(0.44–4.96)
Adjusted Associations	376		143		187		396					
PGPs' Combined Birth Period based on DOB												
FS (vs. PWII-BB)		0.46(0.16–1.30)[b1]		0.36(0.06–2.05)[c]		0.63(0.16–2.48)[c]		2.65(0.94–7.44)[b2]	201	14.04(1.50–131.67)[c]	195	1.32(0.39–4.51)[c]
EA(vs. PWII-BB)		0.94(0.39–2.29)[b1]		0.86(0.21–3.54)[c]		1.31(0.40–4.31)[c]		2.40(0.86–6.67) [b2]		13.80(1.52–125.66)[c]		1.05(0.29–3.77)[c]

Hosmer-Lemeshow fit test (p-value): 1 = 0.700, 2 = 0.940.

[a] Low BW: < 10th percentile; Normal BW: ≥10th to < 90th percentile; High BW: ≥90th p.

[b] Adjusted for child-sex, mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.

[c] Adjusted for mother age, mother's education, mother' smoking, mother's energy consumption during 1st trimester of pregnancy, and mother's parity.

References

Abu-Saad, K., & Fraser, D. (2010). Maternal nutrition and birth outcomes. *Epidemiologic Reviews, 32*, 5–25.

Bale, T. L. (2014). Lifetime stress experience: Transgenerational epigenetics and germ cell programming. *Dialogues in Clinical Neuroscience, 16*, 297–305.

Barker, D. J. P. (2007). The origins of the developmental origins theory. *Journal of Internal Medicine, 261*, 412–417.

Black, R. E., Allen, L. H., Bhutta, Z. A., Caulfield, L. E., de Onis, M., Ezzati, M., et al. (2008). Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet, 371*, 243–260.

Champagne, F. A. (2013). Effects of stress across generations: Why sex matters. *Biological Psychiatry, 73*, 2–4.

Cole, T. J., Freeman, J. V., & Preece, M. A. (1995). Body mass index reference curves for the UK, 1990. *Archives of Disease in Childhood, 73*, 25–29.

Corcoran, D. (2009). Public Policy in an emerging state: The Irish Free State 1922-25. *Irish Journal of Public Policy, 1*〈http://publish.ucc.ie/ijpp/2009/01/corcoran/05/en〉.

Day, J., Savani, S., Krempley, B. D., Nguyen, M., & Kitlinska, J. B. (2016). Influence of paternal preconception exposures on their offspring : through epigenetics to phenotype. *American Journal of Stem Cells, 5*, 11–18.

Delaney, L. (2011). From Angela's Ashes to the Celtic Tiger: Early Life Conditions and Adult Health in Ireland. *J Heal. Eco, 30*, 1–10.

Department of Health. (1948). National nutrition survey: Parts I - VII: complete reports on dietary and clinical surveys. Dublin. 〈http://hdl.handle.net/10147/252421〉.

De Rooij, S. R., Painter, R. C., Holleman, F., Bossuyt, P. M. M., & Roseboom, T. J. (2007). The metabolic syndrome in adults prenatally exposed to the Dutch. *The American Journal of Clinical Nutrition,* 1219–1224.

Drisceoil, D.Ó. (1996). *Censorship in Ireland, 1939-1945: Neutrality, politics, and society.* Cork University Press.

Fahey, T., Fitzgerald, J., & Maitre, B. (1998). The economic and social implications of demographic change. *Journal of The Statistical and Social Inquiry Society of Ireland, 27*, 185–222.

Ferraro, K. F., Schafer, M. H., & Wilkinson, L. R. (2016). Childhood disadvantage and health problems in middle and later life: Early imprints on physical health? *American Sociological Review, 81*, 107–133.

Galobardes, B., Lynch, J. W., & Smith, G. D. (2008). Is the association between childhood socioeconomic circumstances and cause-specific mortality established? Update of a systematic review. *Journal of Epidemiology and Community Health, 62*, 387–390.

Galobardes, B., Shaw, M., Lawlor, D. A., Lynch, J. W., & Davey Smith, G. (2006). Indicators of socioeconomic position (part 1). *Journal of Epidemiology and Community Health, 60*, 95–101.

Gerald, F. (1999). *Understanding Ireland' s Economic Success*. The Economic and Social Research Institute, Dublin (ESRI Working Paper No. 111).

Gluckman, P. D., Hanson, M. A., & Buklijas, T. (2010). A conceptual framework for the developmental origins of health and disease. *J. Dev. Orig. Heal. Dis, 1*, 6–18.

Gundersen, C., Mahatmya, D., Garasky, S., & Lohman, B. (2011). Linking psychosocial stressors and childhood obesity. *Obesity Reviews, 12*, e54–e63.

Halfon, N., Larson, K., Lu, M., Tullis, E., & Russ, S. (2014). Lifecourse health development: Past, present and future. *Maternal and Child Health Journal, 18*, 344–365.

Huang, C., Li, Z., Narayan, K. M. V., Williamson, D. F., & Martorell, R. (2010). Bigger babies born to women survivors of the 1959-1961 Chinese famine: a puzzle due to survival selection? *Journal of Developmental Origins of Health and Disease, 1*, 412–418.

Huang, J. Y., Gavin, A. R., Richardson, T. S., Rowhani-Rahbar, A., Siscovick, D. S., & Enquobahrie, D. A. (2015). Are early-life socioeconomic conditions directly related to birth outcomes? Grandmaternal education, grandchild birth weight, and associated bias analyses. *American Journal of Epidemiology, 182*, 568–578.

Jiang, T., Gilthorpe, M. S., Shiely, F., Harrington, J. M., Perry, I. J., Kelleher, C. C., et al. (2013). Age-period-cohort analysis for trends in body mass index in Ireland. *BMC Public Health, 13*, 889. http://dx.doi.org/10.1186/1471-2458-13-889.

Juárez, S. P., & Merlo, J. (2013). Revisiting the effect of maternal smoking during pregnancy on offspring birthweight: A quasi-experimental sibling analysis in Sweden. *PLoS One, 8*, e61734. http://dx.doi.org/10.1371/journal.pone.0061734.

Kelleher, C. C., Lynch, J. W., Daly, L., Harper, S., Fitz-simon, N., Bimpeh, Y., et al. (2006). The "Americanisation" of migrants: Evidence for the contribution of ethnicity, social deprivation, lifestyle and life-course processes to the mid-20th century Coronary Heart Disease epidemic in the US. *Social Science & Medicine, 63*, 465–484.

Kelleher, C. C., Lynch, J., Harper, S., Tay, J. B., & Nolan, G. (2004). Hurling alone? How social capital failed to save the Irish from cardiovascular disease in the United States. *American Journal of Public Health, 94*, 2162–2169.

Kelleher, C. C., Viljoen, K., Khalil, H., Somerville, R., O'Brien, J., Shrivastava, A., et al. (2014). Longitudinal follow-up of the relationship between dietary intake and growth and development in the Lifeways cross-generation cohort study 2001–2013. *Proceedings of the Nutrition Society, 73*, 118–131.

Kelly, G. E., Murrin, C., Viljoen, K., O'Brien, J., & Kelleher, C. (2014). Body mass index is associated with the maternal lines but height is heritable across family lines in the Lifeways Cross-Generation Cohort Study. *BMJ Open, 4*, e005732.

Kozuki, N., Lee, A. C., Silveira, M. F., Sania, A., Vogel, J. P., Adair, L., et al. (2013). The associations of parity and maternal age with small-for-gestational-age, preterm, and neonatal and infant mortality: A meta-analysis. *BMC Public Health, 13*, S2. http://dx.doi.org/10.1186/1471-2458-13-S3-S2.

Kramer, M. S., Séguin, L., Lydon, J., & Goulet, L. (2000). Socio-economic disparities in pregnancy outcome: Why do the poor fare so poorly? *Paediatric and Perinatal Epidemiology, 14*, 194–210.

Li, J., Tsuprykov, O., Yang, X., & Hocher, B. (2016). Paternal programming of offspring cardiometabolic diseases in later life. *Journal of Hypertension, 34*, 2111–2126.

McKey, S., Heinen, M., Mehegan, J., Somerville, R., Khalil, H., Segurado, R., et al. (2017). Predictors of adults' body mass index and the association with index child's infant birth weight, in the Lifeways Cross-Generation Cohort Study of a thousand families in the Republic of Ireland. *Journal of Developmental Origins of Health and Disease,* 1–9.

Murrin, C., Shrivastava, A., & Kelleher, C. C. (2013). Maternal macronutrient intake during pregnancy and 5 years postpartum and associations with child weight status aged five. *European Journal of Clinical Nutrition, 67*, 670–679.

Murrin, C. M., Kelly, G. E., Tremblay, R. E., Kelleher, C. C., Whitaker, R., Wright, J., et al. (2012). Body mass index and height over three generations: evidence from the Lifeways cross-generational cohort study. *BMC Public Health, 12*, 81.

Niedhammer, I., Murrin, C., O'Mahony, D., Daly, S., Morrison, J. J., & Kelleher, C. C. (2012). Explanations for social inequalities in preterm delivery in the prospective Lifeways cohort in the Republic of Ireland. *European Journal of Public Health, 22*, 533–538.

O'Mahony, D., Fallon, U. B., Hannon, F., Kloeckner, K., Avalos, G., Murphy, A. W., et al. (2007). The Lifeways Cross-Generation Study: Design, recruitment and data management considerations. *Irish Medical Journal, 100*, 3–6.

Ota, E., Hiroyuki, H., Mori, R., Tobe-Gai, R., & Farrar, D. (2015). *Antenatal dietary advice and supplementation to increase energy and protein intake. Cochrane Database System Review*, *9*http://dx.doi.org/10.1002/14651858.CD000032.pub3.

Painter, R. C., Roseboom, T. J., & Bleker, O. P. (2005). Prenatal exposure to the Dutch famine and disease in later life: An overview. *Reproductive Toxicology, 20*, 345–352.

Parlee, Sebastian D., & MacDougald, O. A. (2014). Maternal nutrition and risk of obesity in offspring: The trojan horse of developmental plasticity. *Biochimica et Biophysica Acta, 1842*, 495–506.

Pembrey, M., Saffery, R., & Bygren, L. O. (2014). Human transgenerational responses to early-life experience: Potential impact on development, health and biomedical research. *Journal of Medical Genetics, 51*, 563–572.

Pembrey, M. E. (2010). Male-line transgenerational responses in humans. *Human Fertility, 13*, 268–271.

Pembrey, M. E., Bygren, L. O., Kaati, G., Edvinsson, S., Northstone, K., Sjostrom, M., et al. (2006). Sex-specific, male-line transgenerational responses in humans. *European Journal of Human Genetics, 14*, 159–166.

Popkin, B. M. (2006). Global nutrition dynamics: The world is shifting rapidly toward a diet linked with noncommunicable diseases. *The American Journal of Clinical Nutrition, 84*, 289–298.

Schneiderman, N., Ironson, G., & Siegel, S. D. (2005). Stress and health: Psychological, behavioral, and biological determinants. *Annual Review of Clinical Psychology, 1*, 607–628.

Shrivastava, A., Murrin, C., O'Brien, J., Viljoen, K., Heavey, P., Grant, T., et al. (2012). Grandparental morbidity and mortality patterns are associated with infant birth weight in the Lifeways cross-generation cohort study 2001–2010. *Journal of Developmental Origins of Health and Disease, 3*, 458–468.

Shrivastava, A., Murrin, C., Sweeney, M. R., Heavey, P., & Kelleher, C. C. (2013). Familial intergenerational and maternal aggregation patterns in nutrient intakes in the Lifeways Cross-Generation Cohort Study. *Public Health Nutr, 16*, 1476–1486.

Tamayo, T., Christian, H., & Rathmann, W. (2010). Impact of early psychosocial factors (childhood socioeconomic factors and adversities) on future risk of type 2 diabetes, metabolic disturbances and obesity: A systematic review. *BMC Public Health, 10*, 525.

The electronic Irish Statute Book (eISB) (1939). Emergency Powers Act. 1939. 〈http://www.irishstatutebook.ie/eli/1939/act/2/enacted/en/print.html〉. (Accessed 21 January 2017).

Van Bavel, J., & Reher, D. S. (2013). The baby boom and its causes: What we know and what we need to know. *Population and Development Review, 39*, 257–288.

Veenendaal, M. V. E., Painter, R. C., De Rooij, S. R., Bossuyt, P. M. M., Van Der Post, J. A. M., Gluckman, P. D., et al. (2013). Transgenerational effects of prenatal exposure to the 1944-45 Dutch famine. *BJOG, 120*, 548–553.

Whelan, K. (2013). Ireland's economic crisis the good, the bad and the ugly. *Journal of Macroeconomics, 39*, 424–440.

Zucchi, F. C. R., Yao, Y., & Metz, G. A. (2012). The secret language of destiny: Stress imprinting and transgenerational origins of disease. *Frontiers in Genetics, 3*, 1–12.