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The Long-Term Effects of In-Utero Exposure to Rubella

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Abstract

A large body of research in economics and other disciplines considers the role of early-life circumstances in shaping later-life outcomes. The foetal origins hypothesis establishes that certain health conditions in later adulthood can be linked to in-utero development. In this paper, we contribute to the evidence on the foetal origins hypothesis by examining the later-life impact of a rubella outbreak that occurred in Ireland in 1956. Rubella is a contagious viral disease that displays mild symptoms and is generally inconsequential in childhood or adulthood. However, a rubella infection in early pregnancy poses a significant risk of damage to the foetus. Matching the outcomes of individuals born in 1955 to 1958 who are in the 2016 Irish Census to the county-level rubella incidence rate that was prevailing when respondents were in utero, we find that a 1% increase in the rubella incidence rate when in utero is associated with a 0.03% to 0.17% increase in the probability of having lower levels of educational attainment, being in poor health and having a disability in later life.

JEL Codes: I10, I18, J13

Key words: in-utero; rubella; Ireland; later-life health

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1. Introduction

A large body of research in economics considers the role of early-life circumstances in shaping later-life outcomes. Poorer health and socio-economic status in early life has been shown to be associated with a higher risk of later-life ill-health (Almond and Mazumder, 2005; Case and Paxson, 2011; Grimard et al., 2010; Iveson et al., 2020; McCrory et al., 2015; Wen and Gu, 2011), lower educational and occupational attainment (Black et al., 2007; Nelson, 2010; Scholte et al., 2015), lower cognition (Kim et al., 2017; Zhang et al., 2018) and even poorer social outcomes such as marriage rates (Brandt et al., 2016). A key dimension of the debate on the role of early-life circumstances concerns the impact of in-utero conditions. Originally attributed to Barker, the foetal origins hypothesis establishes that certain chronic health conditions in later adulthood such as stroke and ischaemic heart disease can be linked to in-utero development (Barker, 1990; Barker and Osmond, 1987, 1986). It is argued that the in-utero environment (and in particular nutrition during pregnancy) predisposes the foetus to have particular metabolic characteristics, which can lead to future disease (Almond and Currie, 2011).

However, much of the early research on the foetal origins hypothesis has been criticised for reliance on studies using observational or cross-sectional data (Almond and Currie, 2011). Establishing causality is not easy in this setting as it is likely that those with poor in-utero environments also have (unobserved) characteristics that may lead them to have poorer later-life outcomes, e.g., genetic endowments, parental investments in early life, etc. In this case, estimates of the impact of foetal health on later-life outcomes might be biased (overstating the importance of foetal health). One solution is to use an exogenous source of variation in foetal health, e.g., a random health shock that occurs during pregnancy. Previous research that exploits natural experiments that mimic a random shock in pregnancy include those examining the impact of the 1918 and 1957 influenza pandemics (Almond, 2006; Almond and Currie, 2011; Almond and Mazumder, 2005; Kelly, 2011; Lin and Liu, 2014; Nelson, 2010), the 1946/1947 Dutch famine (Scholte et al., 2015), the 1950-1953 Korean War (Lee, 2014), the 1958-1961 Chinese Famine (Kim et al., 2017), maternal fasting during Ramadan (Almond and Mazumder, 2011) and the 2014/2015 Flint Water Crisis (Grossman and Slusky, 2019; Wang et al., 2019).

In this paper, we contribute to the evidence on the foetal origins hypothesis by examining the later-life impact of a rubella outbreak that occurred in Ireland in 1956. Rubella is a contagious viral disease that displays mild symptoms including rash, fever and swollen glands although it is estimated that

more than 50 per cent of cases can be asymptomatic (Bouthry et al., 2014). It occurs most often in children and young adults (Galazka, 1991). The rubella virus is transmitted by airborne droplets when infected people sneeze or cough. While symptoms are mild, a rubella infection just before conception and in early pregnancy can result in low birth weight, prematurity, miscarriage, foetal death or congenital defects known as congenital rubella syndrome (CRS) (Kennedy and Clarke, 2018; Siegel and Fuerst, 1966).[1] The risk to the foetus decreases with gestational age, and defects are rare when infection occurs after the 18th week of gestation (Bouthry et al., 2014; Miller, 1991).[2] Among the consequences of rubella in early pregnancy are foetal death and CRS.[3] A 32 year follow-up of 125 adults with CRS in the US reported ophthalmic damage as the most common disorder (78 per cent), followed by sensorineural deafness (66 per cent), psychomotor retardation (62 per cent) and cardiac defects (58 per cent). Additionally, CRS is associated with autoimmune diseases, and several studies have reported an increased risk for diabetes and thyroid diseases (Bouthry et al., 2014; Plotkin, 2006). There is no treatment for rubella but the disease is preventable with vaccination (which became available from 1969 (CDC, 2010)). In Ireland, a vaccine against rubella was introduced (for girls between their 12th and 14th birthdays) in 1971, and a Measles, Mumps and Rubella (MMR) vaccine was added to the national immunisation schedule in 1988 (Jennings and Thornton, 1993; Kennedy and Clarke, 2018; O'Dwyer et al., 2013).

Due to the impact of vaccination, the WHO has ruled that rubella has been effectively eliminated in Ireland[4], although small numbers of imported cases are sometimes reported (the latest data from the European Centre for Disease Control show that two cases were reported over the period March 2019 – February 2020).[5] As of 2019, 81 of the 194 WHO member states had achieved rubella elimination, and an additional six had been verified as having controlled rubella. However, these countries

[1] The association between rubella in pregnancy and congenital anomalies was first reported by an Australian ophthalmologist in 1941 (Gregg, 1991).

[2] It is estimated that 85 per cent of mothers infected with rubella in the first trimester of pregnancy will deliver a child with congenital defects (Bouthry et al., 2014). This figure comes from a large prospective study of maternal infection and foetal outcomes during the 1978/1979 rubella epidemic in the UK. The results showed that the risk of having a rubella-damaged child was 90 per cent if infection occurs between 2 and 10 weeks, 34 per cent between 11 and 12 weeks, 17 per cent between 13 and 16 weeks and 3 per cent between 17 and 18 weeks (Bouthry et al., 2014; Miller, 1991).

[3] CRS is clinically confirmed in an infant if a qualified physician detects at least two of the following complications in the infant: cataract(s), congenital glaucoma, congenital heart disease, loss of hearing, or pigmentary retinopathy, or one of those complications and one of the following: purpura, splenomegaly, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease, or jaundice that begins within 24 hours after birth (CDC, 2010).

[4] https://apps.who.int/iris/bitstream/handle/10665/337779/WHO-EURO-2020-1421-41171-55983-eng.pdf?sequence=2&isAllowed=y

[5] https://www.ecdc.europa.eu/sites/default/files/documents/measles-rubella-monthly-report-april-2020.pdf

accounted for only 24 per cent of the world's population. Over the 11 year period between 2007 and 2018, just under 140,000 cases of rubella were reported worldwide (Patel et al., 2020). Rubella infection in pregnancy is therefore still a concern in many parts of the world (Toizumi et al., 2017).

Using data from the 2016 Irish Census of Population, we examine the impact of in-utero exposure to rubella during the 1956 outbreak on a variety of health and educational outcomes measured nearly 60 years later. We match outcomes of individuals born in 1955 to 1958 who are in the 2016 Irish Census to the county-level rubella incidence rate that was prevailing when respondents were in utero.[6] We use two identification strategies. First, we model the relationship between in-utero rubella incidence and adult health and educational attainment in a probit regression framework. Second, we use instrumental variable (IV) estimation to address potential omitted-variable bias and measurement-error bias in rubella incidence. We find that a 1% increase in the rubella incidence rate when in utero is associated with a 0.03% to 0.17% increase in the probability of having lower levels of educational attainment, being in poor health and having a disability in later life.

This paper makes a number of contributions to the literature. It is the first paper in the economics literature to focus on the long-term effects of rubella exposure in pregnancy. In contrast to other studies of the foetal origins hypothesis in the economics literature, the fact that gestational age is a key determinant of foetal damage from rubella means that we can test a more refined hypothesis (i.e., that rubella exposure in early pregnancy leads to poorer health and socio-economic outcomes in later-life). Second, the nature of the outbreak in 1956 means that we can exploit geographical and temporal variation in order to identify causal effects. We match historical Department of Health data on rubella notifications by quarter and county with 2016 Census data that includes county of birth, year of birth, month of birth, educational attainment, self-reported health and disability. Internationally, the Irish Census is rare in including a question on self-reported health. The sample is also large, comprising 10 per cent of the population in that year. In contrast, studies in the medical literature are typically based on a relatively small number of observations, i.e., mothers with a diagnosis of rubella in pregnancy or babies born with CRS, and often lack a control group. Our approach is more comprehensive as we

[6] The county is the main administrative local area in Ireland. In 2016, there were 34 counties that ranged in population size from 31,972 (Leitrim) to 553,165 (Dublin city).

focus on an exogenous source of potential exposure to rubella in pregnancy (this approach is also more likely to capture asymptomatic cases, mildly affected cases and un-reported cases).[7]

This paper is structured as follows. Section 2 provides further context on the 1956 rubella outbreak in Ireland. Section 3 describes the empirical methodology. Section 4 presents results, Section 5 discusses the results and Section 6 summarises and concludes.

2. The 1956 Rubella Outbreak in Ireland

Rubella became a notifiable disease in Ireland in 1948. Clinical diagnosis of rubella is difficult because similar rashes occur in other viral infections and in allergic reactions, and a laboratory diagnosis is therefore essential (Bouthry et al., 2014). The rubella virus was first isolated in 1962, which allowed for the development of methods for antibody detection thereafter (Cradock-Watson, 1991). Therefore, prior to 1962, identification of rubella infection was done on the basis of reported symptoms and it is likely that the true incidence of the disease was underreported (Jennings and Thornton, 1993). In Ireland, notifications are compiled by practicing physicians and notified to the local medical officer of health/director of public health. Figure 1 illustrates the number of rubella cases reported per annum in Ireland throughout the 1950s. The 1956 outbreak can be clearly identified, with a near five-fold increase in annual cases compared to the next-highest year (1952). While the number of cases may appear low, the fact that diagnostic tests were not available, and that approximately 50 per cent of cases can be asymptomatic, means that the incidence figures reported in Figure 1 are likely to be underestimated.

<FIGURE 1 AROUND HERE>

The 1956 rubella outbreak began in the early months of the year.[8] The outbreak affected primarily urban areas of the country, although there were outbreaks in more rural counties too (e.g., Tipperary).

[7] There have been a number of analyses of the foetal origins hypothesis (and the impact of early-life conditions more generally) in the Irish context. (Pringle, 1998) examine the association between deaths from ischaemic heart disease in those aged 55-64 between 1981 and 1990 in Ireland and infant mortality around the time of their birth (between 1916 and 1935). The analysis is conducted at the county level. A weak, but statistically non-significant, correlation was found. (Delaney et al., 2011) also use infant mortality rates to proxy early-life living conditions, and examine the association between infant mortality rates and later-life disability (using data from the 2002 and 2006 Census of Population). They found a strong association between early-life infant mortality rates in the respondent's county of birth and later life disability, with the effects strongest for those from lower socio-economic groups.

[8] Before the vaccination era, rubella typically occurred in the spring (Bouthry et al., 2014).

Figure 2 shows how the number of cases started to increase in the first quarter, reached a peak in the second quarter of the year, before falling off sharply from July onwards. Section 3 discusses in greater detail how we use this temporal and geographical variation in rubella exposure to identify effects on later-life health and educational attainment.

<FIGURE 2 AROUND HERE>

Other infectious diseases were common in Ireland in the 1950s. Throughout the 1950s, diseases such as tuberculosis, measles, pertussis (whooping cough), scarlet fever and diarrhoea were recorded in large numbers in Ireland (see Table A1 in Appendix). Tuberculosis was a major focus of public health attention in Ireland throughout the first half of the 20th century, reflecting the high incidence and death rates associated with the disease. While death rates had been falling steadily since the 1930s, in 1950 the death rate was still amongst the highest in Europe, and substantially higher than the rates in Britain and Northern Ireland (Department of Health, 1956). Table A1 illustrates that while there were other infectious disease outbreaks in the 1950s (most notably measles in 1959), the 1956 outbreak of rubella was not accompanied by other infectious disease outbreaks.

The risk of mortality in early life in the 1950s in Ireland was also considerably higher than it is today. In Figure 3, data on early neonatal (within 24 hours), neonatal (within the first month) and infant (within the first year) mortality rates (per 1,000 live births) are presented. As is evident from the data, there was a steady improvement in the infant mortality rate throughout the 1950s, with the rate falling from 46 per 1,000 live births in 1951 to 32 per 1,000 live births in 1959.[9] Nonetheless, the rate of infant mortality in Ireland in 1959 was still considerably higher than that in Northern Ireland (28), England and Wales (22) and Scotland (28) (Central Statistics Office, 1950-1959). The rates of early neonatal and neonatal mortality were more stable over the decade. We discuss early neonatal, neonatal and infant mortality rates around the time of the 1956 rubella outbreak in greater detail in Section 5.

<FIGURE 3 AROUND HERE>

[9] In 2020, the rate of infant mortality in Ireland was 2.7 per 1,000 live births (Central Statistics Office, 2021).

3 Empirical Methodology

We match outcomes of individuals born in 1955 to 1958 who are in the 2016 Irish Census (aged 58 to 60 at Census interview date) to the county-level rubella incidence rate that was prevailing when respondents were in utero. We use two estimation strategies. First, we model the relationship between rubella incidence and adult outcomes in a probit regression framework. Second, we use instrumental variable estimation.

3.1 Probit Model

We assume that adult health and educational attainment are a function of exposure to rubella in utero. The model also controls for sex, year of birth, county of birth fixed effects and month of birth fixed effects. In regression form:

$$\Pr(Y_{ijt} = 1) = \phi\left(\beta\, RubellaUtero_{jt} + \gamma_j + \delta_m + \rho\, X_i + \epsilon_{ijt}\right) \qquad \text{(Eq. 1)}$$

Where Y_{ijt} is a (binary) outcome for individual i in the 2016 Census born in county j in time t. $RubellaUtero_{jt}$ is the county-level rubella incidence rate (i.e., notifications per 10,000 population) that was prevailing when individuals born in county j in time t were in utero (in early pregnancy). γ_j are county of birth fixed effects. δ_m are month of birth fixed effects. X_i is a vector of control variables which include sex and year of birth. We cluster standard errors at county level. The function linking the left- and right-hand sides of Eq. (1) is assumed to be cumulative normal. Therefore, the model is estimated using probit regression.

3.2 IV-Probit Model

One concern is that the estimates of RubellaUtero in Eq. 1 might be biased if RubellaUtero is: (i) correlated with important unobservable factors; and/or (ii) measured with error, e.g., the number of cases of rubella notified to the Irish Department of Health in a certain quarter is an underestimate or an overestimate of the true incidence of rubella in that quarter. To allay concerns of omitted-variable bias and measurement error bias in rubella incidence, we then estimate an IV-probit model. The key requirement of IV estimation is the availability of at least one variable, Z (instrument), which has the following three key properties: (1) variation in Z is associated with variation in RubellaUtero; (2) variation in Z is not associated with variation in Y (apart from the indirect route via RubellaUtero); and

(3) variation in Z is not associated with variation in unmeasured variables that affect RubellaUtero and Y.

We estimate an IV-Probit model with the first stage equation:

$$RubellaUtero_{jt} = \alpha_0 + \alpha_1 Z_{jt} + \gamma_j + \delta_m + \tau X_i + \eta_{ijt} \quad \text{(Eq. 2)}$$

Where Z_{jt} is the instrumental variable employed in our analysis. This variable is described in detail in Section 3.3. γ_j, δ_m and X_i are the same set of variables of Eq. 1. Finally, in the second-stage equation we estimate Eq.1 using the predicted values of RubellaUtero from Eq. 2.

3.3 Variables

Adult Health and Educational Attainment

We focus on four outcomes. The first outcome is self-reported health, which has been consistently shown to be an accurate and reliable predictor of mortality (Ganna and Ingelsson, 2015). Census respondents are asked to rate their health on a five-point scale. The responses individuals can choose from are: very good; good; fair; bad and very bad. We dichotomise responses so that the outcome 'poor health' is equal to one for respondents who report to be in bad or very bad health; zero otherwise.

The second outcome is having a disability. Census respondents are asked to report whether they have any long-lasting condition or disability. If respondents report a disability, they are assigned a value of one. Otherwise, they are assigned a value of zero.

The third outcome is work-related disability. Census respondents are asked to report their current labour market status and can choose from the following options: working for payment or profit; looking for first regular job; unemployed; student; looking after home/family; retired from employment; unable to work due to permanent sickness or disability; and other. If respondents (aged 58 to 60) report to be unable to work due to permanent sickness or disability, they are assigned a value of one. Otherwise, they are assigned a value of zero.

The fourth outcome is highest level of education attained. Respondents are asked to choose the highest level of education attained from the following list: no formal education, primary, lower secondary, upper secondary, technical or vocational, advanced certificate, higher certificate, ordinary

degree, honours degree, postgraduate degree or doctorate. Responses are dichotomised so that individuals who have at most primary education are assigned a value of one; and individuals who have attained at least lower secondary education are assigned a value of zero.

Rubella Exposure in Utero

In the 1950s, rubella notifications were reported quarterly by the Irish Department of Health. The four quarters were: January-March; April-June; July-September; October-December. In the 2016 Census micro-data at our disposal, month of birth is grouped into six categories. These are: January-February; March-April; May-June; July-August; September-October and November-December. [10] To align data from the two sources, and to reflect the timing and length of pregnancies, and the timing of rubella exposure (typically in Spring), we aggregate quarterly rubella notifications into two semesters: January-June and July-December. We also aggregate the six months of birth into two semesters: March-August and September-February.

We then calculate RubellaUtero as follows. For those born in March-August of year t, RubellaUtero is the average incidence rate in the county of birth for the period July-December of year t-1. For those born between September of year t and February of year t+1, RubellaUtero is the average rubella incidence rate in the county of birth for the period January-June of year t. Therefore, rubella incidence rate is 'lagged'. This is because our aim is to provide a measure of exposure to rubella in utero – and specifically in early pregnancy – not at birth.

Control Variables

The model also controls for sex, year of birth, county of birth fixed effects and month of birth fixed effects. County of birth fixed effects are included to control for time-invariant county characteristics that could be correlated with both exposure to rubella and later-life educational attainment, health or disability. In the 2016 Census micro-data at our disposal, a total of 26 counties of birth are identified.[11] Month of birth fixed effects are included as a proxy for factors that do vary by month of birth (or month of conception) but are not measured in the Census and could affect later-life

[10] Due to data protection issues, this was the most disaggregated level of data available for month of birth.
[11] These are: Carlow; Cavan; Clare; Cork; Donegal; Dublin; Galway; Kerry; Kildare; Kilkenny; Laois; Leitrim; Limerick; Longford; Louth; Mayo; Meath; Monaghan; Offaly; Roscommon; Sligo; Tipperary; Waterford; Westmeath; Wexford and Wicklow.

outcomes. For example, poor nutritional intake and maternal infections from respiratory disease during the winter months might compromise outcomes among those born in springtime (Costa and Lahey, 2005). As explained above, a total of six "months of birth" are available in our data.

Instrumental Variable

It is possible that the statistical approach outlined in Eq. 1 may still lead to biased estimates. One main concern is that rubella notifications were measured with some degree of error. Crucially for our analysis, not all counties experienced the 1956 rubella outbreak. We exploit this specific source of variation and instrument rubella incidence with a dummy variable which is equal to one if the respondent was born in a county that experienced the rubella outbreak in 1956 and was in utero when the rubella outbreak occurred. As illustrated in Figure 2 above, the rubella outbreak occurred in January to June 1956. This implies that respondents born in September 1956 to February 1957 were most likely to be in utero – and in early pregnancy– when the outbreak occurred. Therefore, our instrumental variable is a dummy variable equal to one if the respondent was born in September 1956 to February 1957 in a county that experienced the rubella outbreak; zero otherwise.

Next, we need to identify which counties experienced the 1956 rubella outbreak and which did not. Figure 4 shows the rubella incidence rate by county in 1956. The rubella outbreak was most severe in Dublin, where more than 15 cases per 10,000 population were recorded, followed by counties Meath, Kildare, Cork, Limerick and Tipperary, where between 2.5 and 15 cases of rubella per 10,000 population were recorded. Between 2 and 2.5 notifications per 10,000 population were recorded in Westmeath, Cavan and Waterford. The remaining counties experienced less than 2 and most often less than 1 notifications per 10,000 population.

<FIGURE 4 AROUND HERE>

The data in Figure 4 suggest that six counties experienced a rubella outbreak in 1956. These were Dublin, Meath, Kildare, Cork, Limerick and Tipperary. In these counties, a minimum of 2.5 notifications of rubella per 10,000 population were reported. However, an important note of caution is needed. Compared to the other Irish counties, Dublin had a very high rate of disease in the 1950s. Table 1 shows the notifications of various infectious diseases in Dublin in the 1950s as a percentage of the

total number of notifications in Ireland. To illustrate, 70.7% of notifications of dysentery in 1952 were recorded in Dublin. The remaining 29.3% were recorded in the rest of the country. Similarly, 59.4%, of notifications of measles in 1955 were recorded in Dublin. The remaining 40.6% were reported in the rest of the country. However, only around 23 to 25% of the population was living in Dublin in these years. Therefore, infectious diseases were considerably more widespread in Dublin than in the rest of the country.

<TABLE 1 AROUND HERE>

Figure 5 provides further evidence of how different Dublin was to other counties during the 1950s. It shows the neonatal mortality rate for congenital malformations in counties that experienced and did not experience the 1956 rubella outbreak. Counties that experienced the outbreak are divided into two groups: (1) Dublin; and (2) the other counties that experienced the 1956 rubella outbreak. These are Cork, Limerick, Tipperary, Meath and Kildare. The figure shows that both Dublin and the other 'treated' counties experienced a higher mortality rate in 1956 than the 'control' counties. This is to be expected as the 'treated' counties experienced a rubella outbreak in 1956. However, in Dublin the neonatal mortality rate for congenital malformations also spiked two years later, in 1958. This violates a key assumption of our analysis. This assumption is that 'everything else' was trending smoothly around the 'treatment period' for 'treated' and 'control' counties. Therefore, based on the evidence of both Table 1 and Figure 5, we exclude Dublin from our analysis.

<FIGURE 5 AROUND HERE>

The geographical and temporal variation in rubella notifications is explored further in Figure 6. For each semester of birth, two points are shown. The red point displays the rubella incidence rate that was prevailing when those born in a certain semester were in utero in counties that did experience the 1956 rubella outbreak. The green point displays the rubella incidence rate that was prevailing when those born in a certain semester were in utero in counties that did not experience the 1956 rubella outbreak. As explained above, Dublin is excluded. The vertical dotted line denotes the cohorts of main interest in our analysis, i.e. cohorts born between September 1955 and February 1958. Figure 6 shows that around 5.9 in 10,000 population were diagnosed with rubella when the cohort born in

September 1956 to February 1957 were in utero. This is the highest figure in the period in focus. The rate for the same birth cohort in counties that were not affected by the outbreak was 0.4.

< FIGURE 6 AROUND HERE>

3.4 Summary

To summarise, we estimate two separate models for each of our four binary outcome variables. The first model is a probit model, where our explanatory variable of interest is the county-level rubella incidence rate that was prevailing when respondents were in utero. The second model is an IV-probit model. In our baseline IV analysis, we instrument rubella incidence rate with a dummy variable which is equal to 1 if the respondent was born in the period September 1956 to February 1957 in one of the following five counties: Cork, Limerick, Tipperary, Meath and Kildare; and 0 otherwise. In both probit and IV-probit estimations, the sample includes individuals who participated in the 2016 Irish Census and who were born between September 1955 and February 1958 in a county that was not Dublin (N=7769). These are individuals aged between 58 and 60 at Census interview date (24th April 2016). In both probit and IV-probit models, county of birth fixed effects are included and standard errors are clustered at the county level.

4 Results

4.1 Descriptive Statistics

Descriptive statistics for all the regression variables are presented in Table 2. Statistics are also presented separately for individuals born in counties that were affected by the 1956 rubella outbreak (N=2720) and individuals born in counties which were not affected by the 1956 rubella outbreak (N=5049). The results of a test for the difference in means or proportions between the two groups of counties are shown in column (5). Five birth cohorts are included in the analysis: the cohort who was in utero when the rubella outbreak occurred (born in 'September 1956 to February 1957'), two older cohorts and two younger cohorts. The older cohorts were born in the semesters 'September 1955 to February 1956' and 'March 1956 to August 1956'. The younger cohorts were born in the semesters 'March 1957 to August 1957' and 'September 1957 to February 1958'.

Three points about Table 2 are worth making. The first is that as expected there is a sizeable difference in rubella incidence rate between the two groups of counties. The incidence rate is 1.51 for individuals born in counties that experienced the outbreak. This compares to an incidence rate of 0.52 for individuals born in counties that did not experience the outbreak. This difference is statistically highly significant ($p<1\%$). As illustrated in Figure 6, this difference is mainly driven by the 1956 outbreak. Second, the share of individuals born in the two groups of counties are well balanced in terms of both year of birth and share of males/females ($p>10\%$). Third, health and educational attainment outcomes are poorer for cohorts born in counties affected by the 1956 outbreak. However, whilst the difference in the shares reporting a disability or a work disability is statistically significant, the difference in the shares reporting poor health or a low educational attainment is not.

<TABLE 2 AROUND HERE>

4.2 Regression Results

Baseline Probit and IV-Probit Models

The regression estimates of our baseline probit and IV-probit models are summarized in Table 3. Columns (1), (3), (5) and (7) show probit regression estimates. Columns (2), (4), (6) and (8) show second-stage IV-probit estimates. For all specifications, elasticities are reported for our main explanatory variable of interest: RubellaUtero. Coefficients are then reported for RubellaUtero, YearBirth and Male. Clustered standard errors are reported in parentheses. The clustering is at the level of the county of birth. The IV first-stage F statistics is reported at the bottom of the table. OLS regression is used to estimate the first-stage equation. Probit regression is used to estimate the second-stage equation. Coefficients for all explanatory variables are reported in Table A2 and Table A3 in Appendix.

The results of Table 3 show that in both probit and IV-probit estimations, there is a positive relationship between exposure to rubella in utero and the probability of being in poor health, having a disability and being unable to work because of a disability in later life (aged 58 to 60) and having attained a low level of educational attainment. In general, the estimates are larger in magnitude in the IV estimations compared to the probit estimations. To illustrate, for the outcome of self-reported health, the elasticity of RubellaUtero is equal to 0.107 in the probit specification of column (1). This means that an increase of 1% in rubella notifications per 10,000 population when in utero is associated

with a 0.107% increase in the probability of being in poor health in later-life. The elasticity of RubellaUtero is equal to 0.170 in the IV-probit specification of column (2). This implies that an increase of 1% in rubella notifications per 10,000 population when in utero is associated with a 0.17% increase in the probability of being in poor health in later-life. In our analysis, the IV specification estimates the average effect of rubella incidence when in utero on later-life outcomes for the group of individuals who were in utero in the affected counties when the rubella outbreak occurred, but who would have not been affected had the outbreak not been in place.

The elasticities of RubellaUtero with respect to the other three dependent variables are somewhat smaller in magnitude, ranging between 0.03 and 0.08. The statistics from the first-stage equation reported at the bottom of Table 3 confirm that the instrument is not weak. The results of Table 3 also indicate that male gender and year of birth are important predictors of educational attainment, but are not important predictors of self-reported health and disability status. In the regressions of columns (7) and (8), male gender has a positive sign whereas year of birth has a negative sign. Therefore, the probability of having attained a low level of education is higher for males than for females and is higher for (slightly) older cohorts. We do not find these results surprising. Evidence that Irish men born in the 1950s are less educated than their female counterparts and that there is a clear time gradient in educational attainment for these cohorts has been found elsewhere (for example, see (Barrett et al., 2011).

<TABLE 3 AROUND HERE>

4.3 Robustness Checks

To consider the robustness and the validity of the estimates of Table 3, five sets of additional regressions are estimated. The relevant elasticities from these additional regressions are shown in Table 4. Columns (1), (3), (5) and (7) show probit regression estimates. Columns (2), (4), (6) and (8) show second-stage IV-probit estimates. The IV first-stage F statistics is reported at the bottom of the table. Coefficients for the main explanatory variables of interest, Male and YearBirth are reported in Table A4 in Appendix.

The first set of regressions is based on a wider time window. It includes individuals who were born between September 1953 and February 1960. A total of 20,426 Irish-born individuals aged between

53 and 60 at Census interview date are included in this analysis. The second set of regression employs an alternative IV. The instrumental variable is now equal to one also for individuals born in September 1956 to February 1957 in the following three counties: Westmeath, Cavan and Waterford. As shown in Figure 4, in 1956 the rubella incidence rate in these three counties ranged between 2 and 2.5. A total of 122 individuals in our baseline sample were born in one of these three counties in the period September 1956 to February 1957. Therefore, compared to the specifications of Table 3, the instrumental variable is now equal to one for an additional 122 individuals. The key points about the first and second set of robustness checks shown in Table 4, Panel (1) and Panel (2) is that they confirm the baseline regressions shown in Table 3.

In the third set of regressions, the explanatory variable of interest is exposure to rubella in the semester of birth. Therefore, rubella exposure is no longer lagged. For those born in January-June of year t, RubellaBirth is the average incidence rate in the county of birth for the period January-June of year t. For those born in July-December of year t, RubellaBirth is the average incidence rate in the county of birth for the period July-December of year t. In the IV estimation, the instrumental variable is a dummy variable equal to one for those born in January-June 1956 in counties that were affected by the rubella outbreak, 0 otherwise. The results of Table 4, Panel (3) show that there is no statistically significant relationship between rubella incidence in the semester of birth and later life health, disability and educational attainment. Only the elasticity of column (2) is statistically significant at the 5% level. However, it has a negative sign. The findings of Table 4, Panel (3) are in line with our expectations as the literature shows that generally rubella is an inconsequential disease if contracted by the mother in later pregnancy or by a new-born.

In the fourth and fifth sets of regressions, the explanatory variable of interest is exposure to scarlet fever in utero. Evidence shows that the risk to the foetus if the expectant mother has scarlet fever during pregnancy is low (Watkins, 2004).[12] Therefore, we do not expect to find any relationship between exposure to scarlet fever in utero and later life health or disability and educational attainment. A scarlet fever outbreak occurred in Ireland in the first and second quarter of 1953, thus potentially affecting in utero those who were born in September 1953 to February 1954. The incidence of scarlet fever was highest (i.e., above 6), and higher than in any other year, in the following six counties: Carlow, Cork, Wexford, Kilkenny, Sligo, Kildare. In the IV regressions of Table 4, Panel (4)

[12] See also https://www.nhs.uk/conditions/scarlet-fever/.

and Panel (5), incidence of scarlet fever is instrumented with a dummy variable equal to one if the individual was born in September 1953 to February 1954 in one of the six counties that experienced the 1953 scarlet fever outbreak; zero otherwise. The regressions of Panel (4) include individuals born in September 1953 to February 1956. The regressions of Panel (5) include individuals born in September 1953 to February 1960. In line with our expectations, no evidence of a statistically significant relationship between in-utero exposure to scarlet fever and later-life health or disability and educational attainment is found.

< TABLE 4 AROUND HERE>

5 Discussion

In this paper, we investigated the long-term effects of in-utero exposure to rubella. Rubella is a contagious viral disease that displays mild symptoms and is generally inconsequential in childhood or adulthood. However, a rubella infection in early pregnancy poses a significant risk of damage to the foetus. Using historic data on rubella infections linked to the 2016 Irish Census of Population, we found that a 1% increase in the rubella incidence rate when in utero is associated with a 0.03% to 0.17% increase in the probability of having lower levels of educational attainment, being in poor health and having a disability in later life.

There are two potential pathways through which rubella infection in pregnancy may lead to poorer outcomes in later life. First, via the direct effect of rubella infection in early pregnancy. As discussed earlier, rubella infection in early pregnancy leads to a high probability of giving birth to a baby with CRS. Miscarriages and stillbirths may also occur. The second pathway is via the indirect effects of rubella infection in early pregnancy. (Almond and Currie, 2011) note that maternal infections in pregnancy can affect foetal health by diverting maternal energy towards fighting infection, by restricting food intake, or through negative consequences arising from the body's own inflammatory response. Other behavioural changes may also be possible; for example, parents of rubella-affected children may invest more in their affected child to compensate for their disability.[13] Behaviour during

[13] There is some evidence of 'compensatory' behaviour in previous research; in an analysis of the impact of exposure to polio infection in early life, (Gensowski et al., 2019) find that while childhood disability increases the likelihood of early retirement and disability pension receipt at age 50, paralytic polio survivors are more likely to obtain a university degree and to go on to work in white-collar and computer-demanding jobs than their non-paralytic counterparts. These results are consistent with individuals making educational and occupational choices that reflect a shift in the comparative advantage of cognitive versus physical skills.

and after pregnancy may also change in response to a health shock such as a rubella infection, e.g., it may make the mother more aware of good health during the remainder of her pregnancy. However, we believe that this indirect pathway is less likely in this instance as rubella infection is generally a mild infection for the mother (although very damaging to the foetus if it occurs in early pregnancy) and it is estimated that approximately 50 per cent of cases are asymptomatic.

Therefore, assuming that our results represent largely a direct effect of rubella infection in early pregnancy on later-life outcomes, we need to make sure that our results reflect the effect of exposure to the 1956 rubella outbreak in early pregnancy, and not some other factor that is correlated with exposure and with later-life health and socio-economic outcomes. In addition, three sources of potential selection need to be considered (namely, selection in terms of pregnancy, birth and premature later-life mortality), to ensure that the cohort we observe in 2016 that were exposed to the 1956 outbreak do not differ from surrounding cohorts in terms of their composition that may bias the estimated results. We first discuss threats to identification, before moving on to a discussion of possible selection effects.

The identifying assumption for the probit analysis is that the change in rubella notifications in 1956 compared to their long-run trend is exogenous. County and time fixed effects should account for unobserved factors such as the distribution of socioeconomic status and public health resources that differ across counties and time. In order for some omitted factor to be driving the results, it would have to vary in exactly the same nonlinear pattern as rubella exposure, differentially affect those in utero in the early months of 1956, and not before or thereafter. Furthermore, for the IV analysis, this factor would have to vary at the county level also. Possible factors include institutional or policy changes that were implemented at the same time as rubella exposure. While the 1940s and 1950s were a period of considerable policy development in Irish healthcare (Barrington, 1987; Delaney et al., 2011; McGovern, 2016), our review of the literature suggests no obvious health policy changes around the 1956 outbreak. While the 1956 Health Act did include provisions around the extension of healthcare eligibility to mothers and children, these were largely continuations of trends towards greater public provision and financing of healthcare in Ireland that had been initiated in the late 1940s (Barrington, 1987).

Three potential sources of selection need to be considered. The first is selection in pregnancy, whereby families responded to the outbreak of rubella by changing behaviour during pregnancy or before, either in order to prevent conception or to prevent infection once pregnant. While this cannot be tested empirically, we believe it is unlikely that this type of behaviour change would be a significant factor in this instance for a at least two reasons. First, the sale and importation of artificial contraceptives had been banned in Ireland in 1935, and only fully legalised in 1985 (Barrington, 1987). Second, there was very little public discussion at the time (in terms of news reporting or public health advice) (Department of Health, 1957) about the outbreak, so it is unlikely that potentially-affected women would have modified their fertility behaviour, or behaviour in pregnancy, in an attempt to prevent infection.

Selection in birth is a more serious issue, as the consequences of maternal infection with rubella in the first trimester of pregnancy are severe. Indeed, (Almond and Currie, 2011) note that estimates of the effects of foetal health shocks are generally conservative when the shock also increases mortality. As noted above, it is estimated that 85 per cent of mothers infected with rubella in the first trimester of pregnancy will deliver a child with congenital defects, with congenital deafness being the most common condition. Infection during the first trimester also results in significantly higher incidence of spontaneous abortions and stillbirths (Bouthry et al., 2014; Miller, 1991). While data on stillbirths (and miscarriages) for the exposed and non-exposed cohorts are not available, we first compare the rates of infant (under 1 year), neonatal (under 1 month) and early neonatal (under 24 hours) mortality for the 1956 and 1957 cohorts to see if they differ systematically from the rates observed for surrounding cohorts (data presented earlier in Figure 3). The data shows that the rate of infant mortality was trending strongly downwards over the period 1954-1959, with the exception of a rise in 1958, before declining again in 1959. The rates of neonatal and early neonatal mortality were more stable overall across years. Notwithstanding the fact that we cannot disaggregate the 1956 or 1957 mortality figures by month of birth (to more closely align with in utero exposure to the rubella outbreak), there is no clear discontinuity in infant, neonatal or early neonatal mortality observed in 1956 or 1957 in comparison with surrounding years.

For early neonatal and infant mortality, it is possible to examine cause of death, and in particular causes of death that might be associated with rubella infection (congenital malformations and immaturity). Figure A1 shows that for early neonatal deaths (in the first 24 hours of life), the share of deaths accounted for by congenital malformations increased over time, from 15 per cent of all early

neonatal deaths in 1955 to 23 per cent in 1959. While the shares in 1956 and 1957 were higher than in 1955, the shares continued to rise into 1958 and 1959. The share of deaths accounted for by immaturity remained stable over the period. See Figure A2 for corresponding figures for infant mortality. Finally, it is possible to focus on deaths from congenital malformations, which allows us to identify if the 'treated' counties experienced a differential trend in deaths from congenital malformations that might bias our results (by changing the composition of the surviving cohort). As illustrated earlier in Figure 5, rates of death from congenital malformations in the 'treated' counties were higher in 1956 than in the 'control' counties. While some of the 'treated' group will have been born in early 1957, it does appear that deaths from congenital malformations were higher in the period coinciding with the rubella outbreak of 1956. This means that our estimates must be interpreted as lower bounds of the effect of rubella exposure in utero on later-life health and educational attainment.

Selection in terms of premature mortality in later life is the third potential source of selection that needs to be considered. To test for this, we gather data from each Census of Population from 1961 (the first after the 1956 outbreak) to 2016 and compare the sizes and growth rates of the treated and control cohorts through time. Identifying the treated and control cohorts in the published Census of Population data is complicated however as the data only identify individuals by their reported age on the Census date (which is in April), rather than their precise date of birth (or even month and year of birth). In addition, the timing and spread of the rubella outbreak in 1956 meant that some of those exposed in utero were born in 1956, and some in early 1957, and only certain counties were affected. Without detailed data on date of birth, or even month and year of birth for each Census, and on county of birth, we cannot further disaggregate the 1956 and 1957 cohorts. Nonetheless, in Appendix Figures A3 and A4, we compare the size and growth rates of the 1956 and 1957 cohorts over the period 1961 – 2016 with the size and growth rates of the surrounding cohorts (1954, 1955, 1958, 1959). The data shows that there is no clear discontinuity in the evolution of the 1956 and 1957 cohorts in comparison with the 1954, 1955 or 1958 cohorts over the period 1961-2016 (the 1959 cohort continues to increase in size after 2006). All cohorts declined in size until about 1991 (consistent with the large net emigration figures that were a feature of the Irish economy over much of the period from 1961 to 1991)[14], before starting to increase slightly during the economic boom in the late 1990s and early 2000s (when net immigration reached its highest ever levels, many of whom were returning Irish

[14] See Figure A5 for data on the components of population change (natural increase and net migration) over the period 1951-2016 in Ireland.

migrants). It is only when the 1954-1958 cohorts reached their 50s after around 2006 that their sizes started to decline once again (which may be driven both by mortality and net emigration as result of the financial crisis).

6 Conclusion

A large body of research in economics and other disciplines considers the role of early-life circumstances in shaping later-life outcomes. The foetal origins hypothesis establishes that certain chronic health conditions in later adulthood can be linked to in-utero development (Barker, 1990; Barker and Osmond, 1987, 1986). However, much of the early research on the foetal origins hypothesis has been criticised for reliance on studies using observational or cross-sectional data. Using an exogenous source of variation in foetal health (i.e., a rubella outbreak that occurred in Ireland in 1956), we investigate the long-term effects of in-utero exposure to rubella on a variety of later-life outcomes. Rubella is a contagious viral disease that displays mild symptoms and is generally inconsequential in childhood or adulthood. However, a rubella infection in early pregnancy poses a significant risk of damage to the foetus. Matching the outcomes of individuals born in 1955 to 1958 who are in the 2016 Irish Census to the county-level rubella incidence rate that was prevailing when respondents were in utero, we find that a 1% increase in the rubella incidence rate when in utero is associated with a 0.03% to 0.17% increase in the probability of having lower levels of educational attainment, being in poor health and having a disability in later life. In addition to providing further evidence on the foetal origins hypothesis, the analyses in this paper also provide useful insights for healthcare providers and policymakers in the countries where rubella infection has yet to be eliminated or controlled, and where rubella infection in pregnancy poses a serious risk to the developing foetus; these countries account for the vast majority (76 per cent) of the global population.

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TABLES AND FIGURES

Table 1 Notifications of Infectious Diseases (Dublin as % of Total), 1952-1960

	1952	1953	1954	1955	1956	1957	1958	1959	1960
Acute Anterior Poliomyelitis	16.7%	20.8%	28.0%	37.0%	21.8%	16.3%	36.7%	35.9%	54.9%
Diarrhoea and enteritis (children <2 ys of age)	64.6%	76.2%	55.9%	73.0%	78.6%	79.2%	84.9%	82.3%	78.1%
Diphtheria	27.5%	0.0%	79.4%	87.0%	93.9%	93.8%	88.7%	92.9%	92.6%
Dysentery	70.7%	44.5%	71.0%	42.7%	48.9%	55.3%	83.9%	65.9%	71.9%
Erysipelas	55.9%	51.5%	47.4%	50.9%	46.6%	48.2%	49.3%	57.9%	36.8%
Infective Hepatitis	54.9%	59.4%	52.5%	44.4%	63.3%	59.0%	52.2%	49.0%	52.4%
Infective Mononucleosis	87.7%	86.8%	79.2%	85.2%	62.5%	75.9%	79.6%	84.7%	60.8%
Influenza Pneumonia	57.1%	21.6%	20.3%	34.9%	2.7%	35.0%	32.5%	23.6%	25.0%
Measles	46.1%	50.8%	43.9%	59.4%	53.9%	46.3%	25.4%	40.7%	52.8%
Rubella	88.7%	82.3%	77.9%	63.8%	87.6%	52.8%	72.9%	45.5%	66.4%
Scabies	75.8%	87.4%	80.9%	95.3%	89.5%	93.0%	96.0%	93.0%	91.6%
Scarlet Fever	23.5%	29.4%	45.3%	46.7%	49.4%	49.2%	49.4%	55.0%	50.2%
Whooping Cough	59.8%	62.2%	24.3%	58.8%	57.1%	31.1%	47.1%	57.3%	31.2%

Source: Authors' Calculations from Department of Health, 1950-1955 and 1956-1960

Table 2 Descriptive Statistics, Cohorts Born September 1955 to February 1958

	(1)	(2)	(3)	(4)	(5)
	Variable Measurement	All counties	Born in counties affected by the 1956 outbreak?		p value of test (3)–(4)=0
			Yes	No	
Dependent Variables					
PoorHealth	Dummy variable: 1 for bad/very bad health; 0 for very good /good/fair health	2.9%	3.3%	2.7%	>0.10
AnyDis	Dummy variable: 1 for any long-lasting condition or disability; 0 otherwise	17.7%	19.5%	16.7%	<0.01
WorkDis	Dummy variable: 1 for unable to work due to permanent sickness or disability; 0 otherwise	10.5%	12.4%	9.5%	<0.01
LowEduc	Dummy variable: 1 for at most primary education; 0 otherwise	15.3%	15.6%	15.1%	>0.10
Independent Variables					
RubellaUtero	Rubella incidence rate (per 10,000 population) in county of birth when respondent was in utero	0.87 (1.86)	1.51 (2.38)	0.52 (1.39)	<0.01
YearBirth	Year of Birth	1956 (0.78)	1956 (0.79)	1956 (0.77)	>0.10
Male	Dummy variable: 1 for male; 0 for female	49.6%	49.8%	49.5%	>0.10
Instrumental Variable					
IV	Dummy variable: 1 for individuals born in September 1956 to February 1957 in a county that experienced the 1956 rubella outbreak; 0 otherwise	6.7%	19.0%	0.0%	--
Number of observations		7769	2720	5049	

Note: the counties that experienced the 1956 rubella outbreak are: Cork, Limerick, Kildare, Meath and Tipperary. Dublin is excluded from the analysis.

Table 3 Probit and IV-Probit Regression Estimates, Baseline Model, Cohorts Born 1955 to 1958

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Estimation:	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit
Dependent variable:	PoorHealth	PoorHealth	AnyDis	AnyDis	WorkDis	WorkDis	LowEduc	LowEduc
Elasticity								
RubellaUtero	0.107***	0.170***	0.035***	0.051***	0.031	0.078***	0.038***	0.065***
	[0.026]	[0.034]	[0.013]	[0.015]	[0.027]	[0.023]	[0.011]	[0.017]
Coefficient								
RubellaUtero	0.056***	0.088***	0.029***	0.043***	0.022	0.053***	0.029***	0.050***
	[0.014]	[0.017]	[0.011]	[0.013]	[0.019]	[0.016]	[0.009]	[0.013]
Male	-0.055	-0.052	0.007	0.008	-0.003	-0.002	0.128***	0.129***
	[0.050]	[0.050]	[0.039]	[0.039]	[0.042]	[0.042]	[0.046]	[0.046]
YearBirth	-0.004	-0.011	-0.013	-0.014	-0.01	-0.012	-0.051**	-0.052**
	[0.036]	[0.039]	[0.023]	[0.023]	[0.031]	[0.033]	[0.021]	[0.021]
First-stage IV F Statistics	--	27.7	--	27.7	--	27.7	--	28.0
N	7769	7769	7769	7769	7769	7769	7504	7504

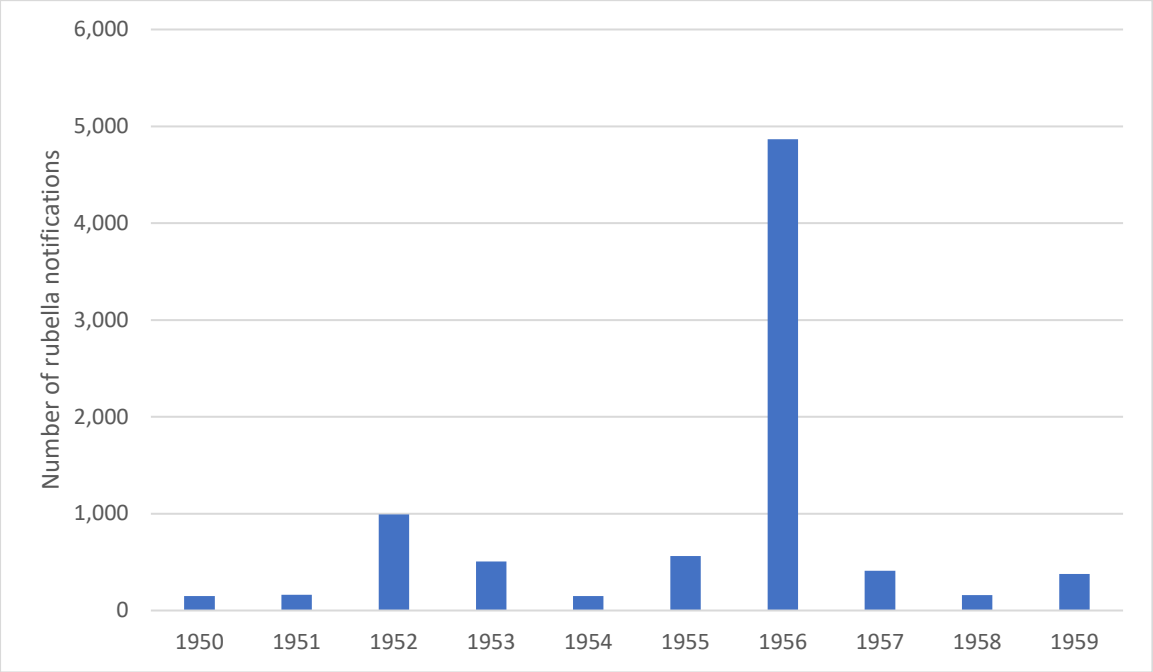
Note: county of birth fixed effects and month of birth fixed effects are included. Standard errors are clustered at county level.
* p<0.10; ** p<0.05; ***p<0.01

Table 4 Probit and IV-Probit Regression Elasticity Estimates, Robustness Checks

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Estimation:	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit
Dependent variable:	PoorHealth	PoorHealth	AnyDis	AnyDis	WorkDis	WorkDis	LowEduc	LowEduc
Baseline (see Table 5)								
RubellaUtero	0.107***	0.170***	0.035***	0.051***	0.031	0.078***	0.038***	0.065***
	[0.026]	[0.034]	[0.013]	[0.015]	[0.027]	[0.023]	[0.011]	[0.017]
Robustness checks:								
(1) Explanatory Variable of Interest is Exposure to Rubella in Utero, Cohorts Born 1953 to 1960								
RubellaUtero	0.037***	0.074***	0.010**	0.026***	0.012	0.037***	0.008	0.029***
	[0.009]	[0.020]	[0.005]	[0.007]	[0.008]	[0.011]	[0.005]	[0.007]
First-stage IV F Statistics		28.3		28.3		28.3		28.6
N	20426	20426	20426	20426	20426	20426	19472	19472
(2) Explanatory Variable of Interest is Exposure to Rubella in Utero, Alternative Geographical Definition of IV, Cohorts Born 1955 to 1958								
RubellaUtero	0.107***	0.168***	0.035***	0.055***	0.031	0.089***	0.038***	0.061***
	[0.026]	[0.043]	[0.013]	[0.017]	[0.027]	[0.026]	[0.011]	[0.017]
First-stage IV F Statistics	--	19.4	--	19.4	--	19.4	--	19.5
N	7769	7769	7769	7769	7769	7769	7504	7504
(3) Explanatory Variable of Interest is Exposure to Rubella at Birth, Cohorts Born 1955 to 1958								
RubellaBirth	-0.045	-0.107**	-0.013	-0.024	-0.006	-0.033	-0.001	-0.008
	[0.039]	[0.053]	[0.012]	[0.018]	[0.016]	[0.023]	[0.009]	[0.010]
First-stage IV F Statistics	--	27.2	--	27.2	--	27.2	--	27.3
N	7769	7769	7769	7769	7769	7769	7504	7504
(*4) Explanatory Variable of Interest is Exposure to Scarlet Fever in Utero, Cohorts Born 1953 to 1956*								
ScFeverUtero	0.07	0.087	0.037	0.039	0.043	0.072	-0.025	-0.014
	[0.108]	[0.106]	[0.043]	[0.064]	[0.039]	[0.050]	[0.024]	[0.049]
First-stage IV F Statistics	--	63.0	--	63.0	--	62.9	--	62.9
N	7742	7742	7742	7742	7742	7742	7444	7444
(5) *Explanatory Variable of Interest is Exposure to Scarlet Fever in Utero, Cohorts Born 1953 to 1960*								
ScFeverUtero	-0.004	0.029	0.007	0.014	0.004	0.029	-0.019	-0.009
	[0.063]	[0.060]	[0.021]	[0.032]	[0.023]	[0.025]	[0.016]	[0.024]
First-stage IV F Statistics	--	80.7	--	80.7	--	80.7	--	80.4
N	20426	20426	20426	20426	20426	20426	19472	19472

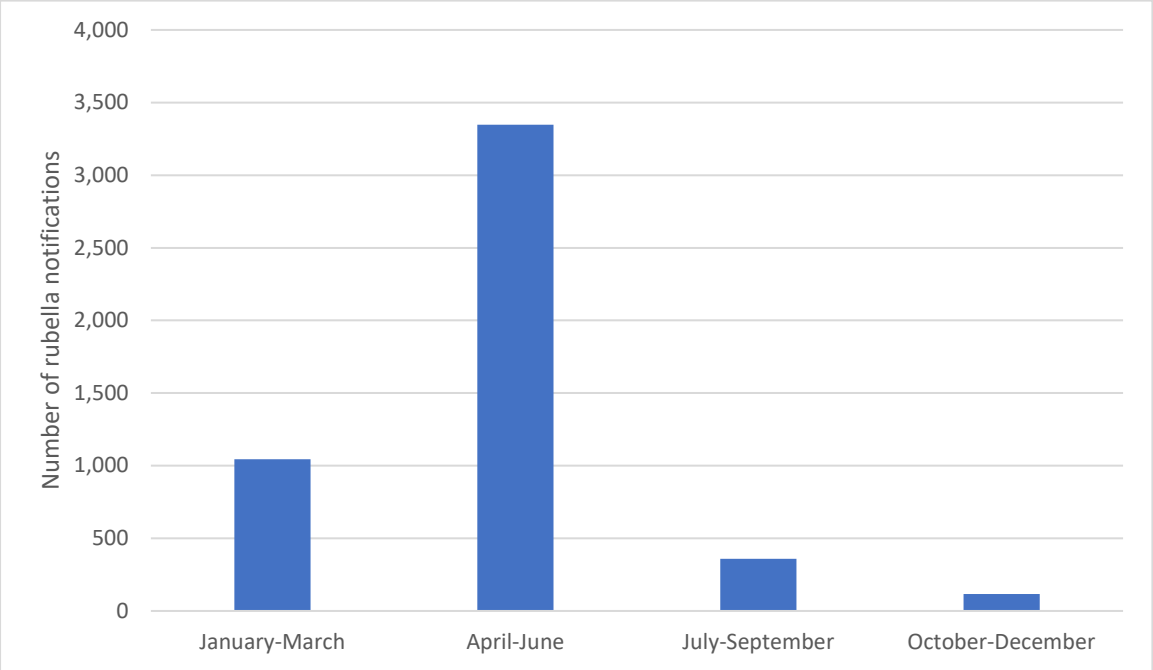
Note: county of birth fixed effects, month of birth fixed effects and controls for sex and year of birth are included in all models. Standard errors are clustered at county level. * p<0.10; ** p<0.05; ***p<0.01

Figure 1 Annual Notifications of Rubella, Ireland, 1950-1959



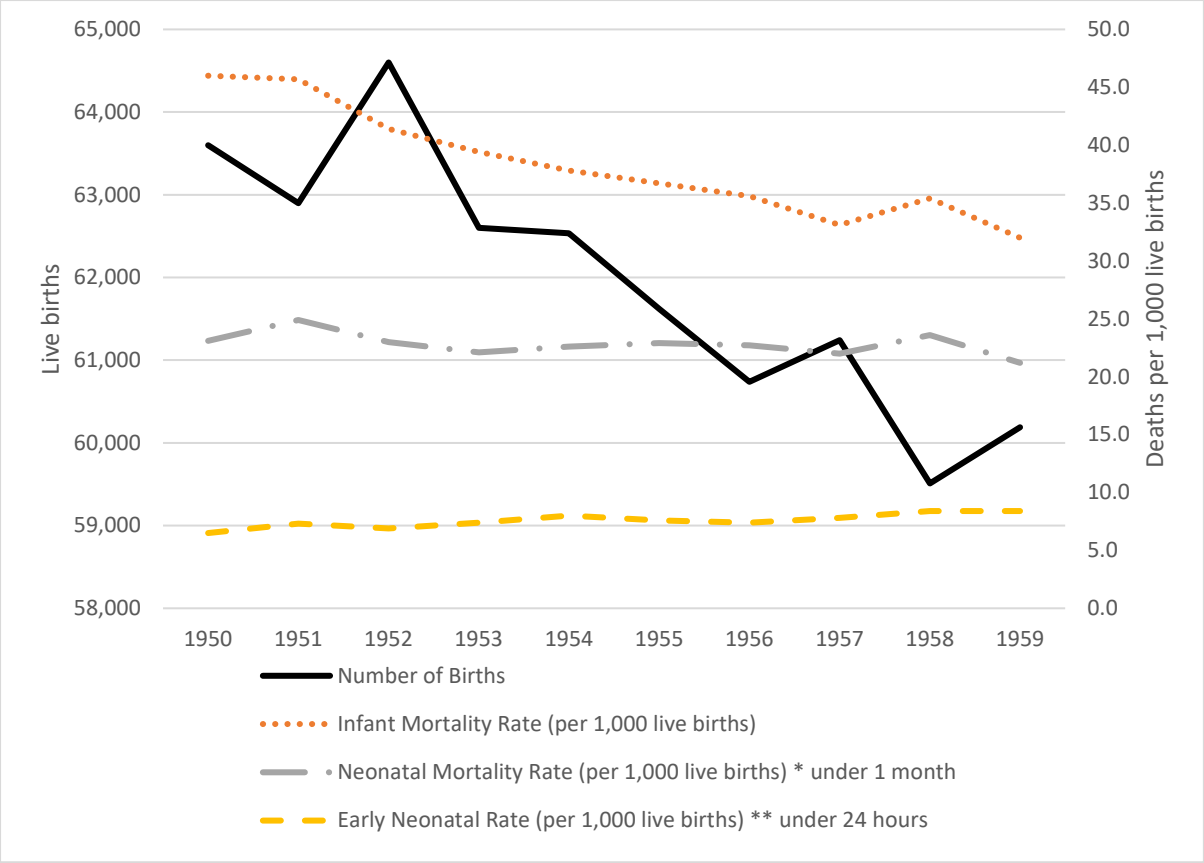
Source: Department of Health, 1950-1955 and 1956-1960

Figure 2 Quarterly Notifications of Rubella, Ireland, 1956



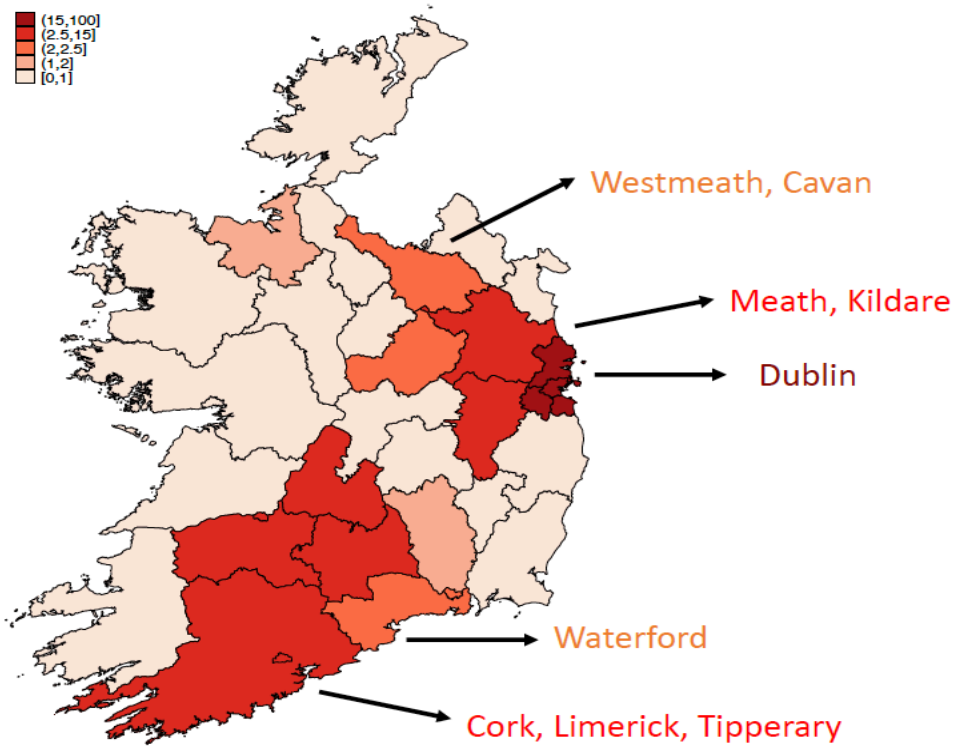
Source: Department of Health, 1956-1960

Figure 3 Number of live births, and early neonatal, neonatal and infant mortality rates, Ireland, 1950-1959



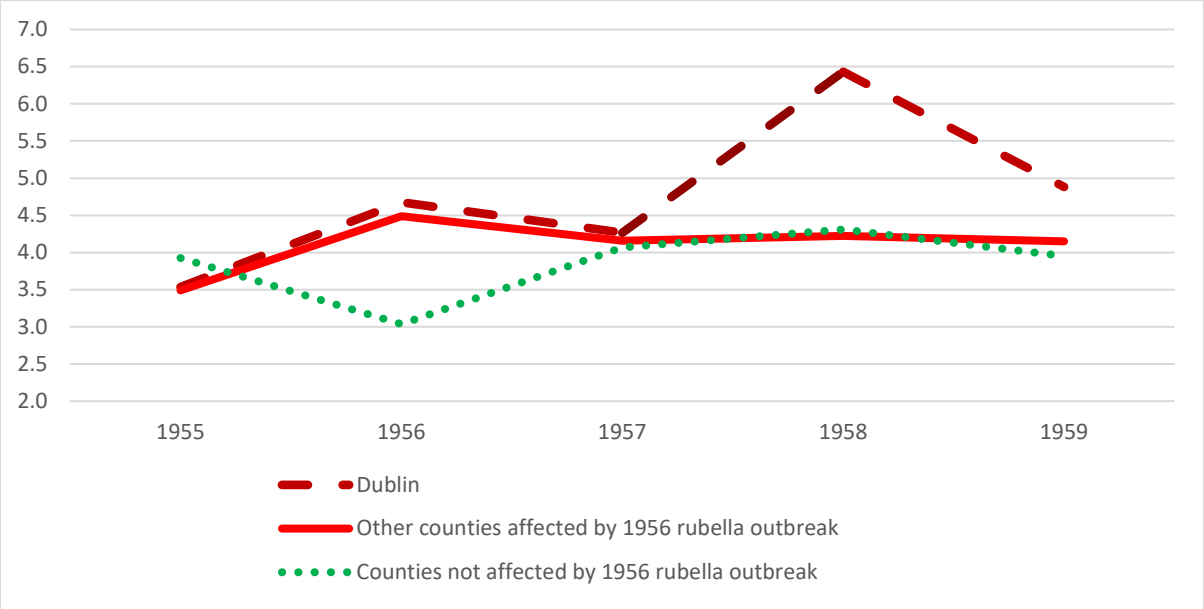
Source: Central Statistics Office, 1950-1959

Figure 4 Rubella Incidence by County, 1956



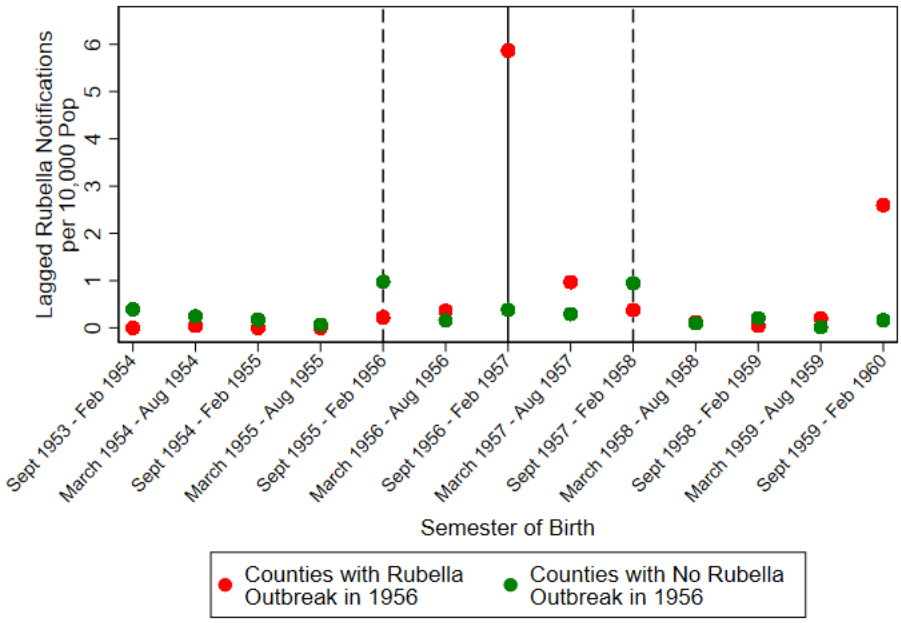
Source: Authors' calculations from Central Statistics Office, 1950-1959
Note: rubella incidence is defined as notifications per 10,000 population

Figure 5 Neonatal Mortality Rate (Congenital Malformations), 1955-1959



Source: Central Statistics Office, 1950-1959
Note: other counties affected by 1956 rubella outbreak are: Cork, Limerick, Kildare, Meath and Tipperary

Figure 6 Rubella Incidence Rate when In Utero by Semester of Birth, 1953-1960



Source: Authors' Calculations from 2016 Irish Census Microdata and Department of Health, 1950-1955 and 1956-1960.
Note: the counties that experienced the 1956 rubella outbreak are: Cork, Limerick, Kildare, Meath and Tipperary. Dublin is excluded from the analysis. The term lagged is used to indicate that rubella incidence refers to the period in which individuals born in a certain semester were in utero, not in the semester of birth.

Appendix

Table A1 Notifications of Infectious Diseases (per 10,000 population), Ireland, 1950-1960

	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960
Acute Anterior	0.7	0.2	0.3	0.8	0.3	0.4	1.8	0.5	0.9	0.1	0.6
Diarrhoea and enteritis (children <2 ys of age)	3.7	5.2	4.3	4.7	3.3	5.2	3.6	4.4	4.9	5.5	4.7
Diphtheria	0.5	0.3	0.1	0.1	0.1	0.3	0.8	0.3	0.2	0.2	0.2
Dysentery	0.1	0.1	0.3	0.4	0.7	0.5	0.3	0.6	0.8	1.1	1.0
Erysipelas	1.2	1.0	1.0	0.9	0.7	0.6	0.7	0.6	0.5	0.4	0.4
Infective Hepatitis	0.7	0.5	1.1	1.5	1.1	1.0	1.7	1.5	1.7	2.0	4.4
Infective Mononucleosis	0.4	0.3	0.2	0.2	0.3	0.3	0.2	0.2	0.3	0.5	0.5
Influenza Pneumonia	0.0	2.5	0.2	0.6	0.4	0.7	0.5	2.3	0.7	1.0	0.5
Measles	23.6	21.4	35.2	28.0	38.3	25.2	27.6	25.4	18.3	53.2	6.3
Rubella	0.5	0.6	3.4	1.7	0.5	1.9	16.8	1.4	0.6	1.3	1.7
Scabies	1.9	1.7	1.1	1.1	0.8	0.7	1.1	0.9	1.3	1.1	1.2
Scarlet Fever	12.4	8.3	10.2	9.2	5.3	3.9	3.5	3.5	4.0	4.2	3.4
Whooping Cough	12.2	13.4	14.8	16.2	6.9	11.7	17.5	6.2	5.0	15.5	8.4

Source: Department of Health, 1950-1955 and 1956-1960

Table A2 Probit and IV-Probit Coefficients [Standard Errors], Baseline Model, Cohorts Born 1955 to 1958

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Estimation:	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit
Dependent variable:	PoorHealth	PoorHealth	AnyDis	AnyDis	WorkDis	WorkDis	LowEduc	LowEduc
RubellaUtero	0.056***	0.088***	0.029***	0.043***	0.022	0.053***	0.029***	0.050***
	[0.014]	[0.017]	[0.011]	[0.013]	[0.019]	[0.016]	[0.009]	[0.013]
Male	-0.055	-0.052	0.007	0.008	-0.003	-0.002	0.128***	0.129***
	[0.050]	[0.050]	[0.039]	[0.039]	[0.042]	[0.042]	[0.046]	[0.046]
YearBirth	-0.004	-0.011	-0.013	-0.014	-0.01	-0.012	-0.051**	-0.052**
	[0.036]	[0.039]	[0.023]	[0.023]	[0.031]	[0.033]	[0.021]	[0.021]
BornJanFeb	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.
BornMarApr	0.017	0.054	0.039	0.052	0.02	0.055	0.075	0.094
	[0.109]	[0.112]	[0.071]	[0.070]	[0.065]	[0.061]	[0.066]	[0.069]
BornMayJun	0.133	0.165*	0.015	0.027	0.042	0.075	-0.075*	-0.057
	[0.088]	[0.090]	[0.070]	[0.072]	[0.076]	[0.076]	[0.044]	[0.049]
BronJulAug	0.164**	0.202***	-0.073	-0.06	0.049	0.085	-0.034	-0.014
	[0.071]	[0.072]	[0.081]	[0.080]	[0.071]	[0.066]	[0.048]	[0.053]
BornSepOct	-0.077	-0.083	0.025	0.025	-0.021	-0.022	-0.07	-0.07
	[0.113]	[0.113]	[0.063]	[0.063]	[0.070]	[0.072]	[0.059]	[0.060]
BornNovDec	0.031	0.021	-0.019	-0.02	0.069	0.067	0.039	0.039
	[0.096]	[0.096]	[0.056]	[0.056]	[0.068]	[0.068]	[0.049]	[0.051]
BornCarlow	-0.401***	-0.433***	0.249***	0.232***	0.113***	0.066***	0.218***	0.185***
	[0.033]	[0.026]	[0.016]	[0.017]	[0.027]	[0.023]	[0.011]	[0.020]
BornCavan	-0.571***	-0.605***	-0.282***	-0.307***	-0.310***	-0.378***	0.220***	0.184***
	[0.047]	[0.038]	[0.023]	[0.024]	[0.037]	[0.030]	[0.017]	[0.026]
BornClare	0.266***	0.228***	-0.137***	-0.156***	-0.169***	-0.218***	-0.357***	-0.387***
	[0.028]	[0.031]	[0.020]	[0.021]	[0.034]	[0.026]	[0.017]	[0.023]
BornCork	0.065***	0.021	0.077***	0.060***	0.067**	0.028	-0.036***	-0.063***
	[0.025]	[0.027]	[0.015]	[0.016]	[0.027]	[0.023]	[0.011]	[0.016]
BornDonegal	0.231***	0.240***	0.032***	0.036***	0.092***	0.102***	0.497***	0.502***
	[0.007]	[0.007]	[0.004]	[0.004]	[0.006]	[0.004]	[0.004]	[0.005]
BornGalway	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.	Ref. Cat.
BornKerry	-0.356***	-0.353***	-0.102***	-0.101***	-0.221***	-0.217***	-0.077***	-0.075***
	[0.008]	[0.008]	[0.002]	[0.002]	[0.004]	[0.004]	[0.003]	[0.003]
BornKildare	0.338***	0.300***	0.170***	0.163***	0.006	-0.017	0.319***	0.306***
	[0.011]	[0.018]	[0.008]	[0.009]	[0.012]	[0.012]	[0.007]	[0.009]
BornKilkenny	0.142***	0.136***	0.110***	0.106***	-0.100***	-0.107***	-0.020***	-0.027***
	[0.008]	[0.010]	[0.004]	[0.004]	[0.008]	[0.007]	[0.003]	[0.006]
BornLaois	-0.003	-0.025	-0.107***	-0.117***	-0.171***	-0.202***	0.017**	-0.003
	[0.022]	[0.021]	[0.012]	[0.012]	[0.021]	[0.016]	[0.008]	[0.015]
BornLeitrim	-0.330***	-0.318***	-0.329***	-0.325***	-0.261***	-0.251***	-0.141***	-0.136***
	[0.014]	[0.014]	[0.009]	[0.009]	[0.014]	[0.013]	[0.004]	[0.003]
BornLimerick	0.285***	0.239***	0.128***	0.114***	0.209***	0.172***	0.173***	0.148***
	[0.020]	[0.025]	[0.012]	[0.014]	[0.021]	[0.019]	[0.010]	[0.015]
BornLongford	0.390***	0.402***	0.205***	0.210***	-0.034***	-0.020**	0.059***	0.067***
	[0.009]	[0.007]	[0.006]	[0.007]	[0.010]	[0.009]	[0.005]	[0.006]
BornLouth	0.306***	0.317***	0.183***	0.188***	0.120***	0.132***	0.191***	0.197***
	[0.008]	[0.007]	[0.006]	[0.006]	[0.006]	[0.006]	[0.006]	[0.007]
BornMayo	0.227***	0.233***	-0.179***	-0.177***	-0.104***	-0.098***	0.050***	0.053***
	[0.007]	[0.007]	[0.002]	[0.002]	[0.003]	[0.003]	[0.003]	[0.003]
BornMeath	-0.213***	-0.250***	-0.044*	-0.071***	0.002	-0.061*	0.251***	0.208***
	[0.058]	[0.043]	[0.026]	[0.027]	[0.042]	[0.034]	[0.020]	[0.029]
BornMonagan	0.263***	0.269***	-0.030***	-0.027***	-0.088***	-0.080***	0.191***	0.195***
	[0.006]	[0.007]	[0.004]	[0.005]	[0.006]	[0.006]	[0.005]	[0.005]
BornOffaly	0.500***	0.504***	0.055***	0.057***	-0.016***	-0.010**	0.179***	0.182***
	[0.005]	[0.005]	[0.004]	[0.004]	[0.004]	[0.004]	[0.003]	[0.002]
BornRoscommon	0.355***	0.364***	0.201***	0.205***	0.090***	0.099***	-0.081***	-0.076***

	[0.007]	[0.008]	[0.003]	[0.003]	[0.006]	[0.005]	[0.005]	[0.006]
BornSligo	0.426***	0.415***	0.191***	0.187***	0.041***	0.033***	0.234***	0.227***
	[0.007]	[0.008]	[0.005]	[0.006]	[0.007]	[0.006]	[0.004]	[0.004]
BornTipperary	0.374***	0.325***	0.105***	0.089***	0.074***	0.035	0.002	-0.026*
	[0.021]	[0.027]	[0.013]	[0.015]	[0.022]	[0.021]	[0.011]	[0.015]
BornWaterford	0.229***	0.209***	0.053***	0.047***	-0.087***	-0.102***	0.054***	0.043***
	[0.012]	[0.016]	[0.006]	[0.006]	[0.012]	[0.011]	[0.005]	[0.008]
BornWestmeath	0.025***	0.016*	-0.011	-0.013**	-0.188***	-0.194***	0.053***	0.049***
	[0.007]	[0.010]	[0.007]	[0.006]	[0.008]	[0.007]	[0.003]	[0.003]
BornWexford	0.280***	0.290***	0.143***	0.148***	0.063***	0.073***	0.234***	0.240***
	[0.008]	[0.008]	[0.004]	[0.005]	[0.007]	[0.005]	[0.003]	[0.004]
BornWicklow	-0.053***	-0.050***	0.083***	0.084***	0.098***	0.101***	0.128***	0.129***
	[0.007]	[0.007]	[0.003]	[0.003]	[0.005]	[0.006]	[0.003]	[0.003]
Constant	6.319	19.369	25.347	26.968	17.552	22.818	98.500**	99.960**
	[70.486]	[75.635]	[44.494]	[45.475]	[61.460]	[64.782]	[40.281]	[41.823]
N	7769	7769	7769	7769	7769	7769	7504	7504

Note: Standard errors are clustered at county level. * p<0.10; ** p<0.05; ***p<0.01

Table A3 First-Stage IV Coefficients [Standard Errors], Baseline Model, Cohorts Born 1955 to 1958

	(1)	(2)
Estimation:	OLS	OLS
Dependent variable:	RubellaUtero	RubellaUtero
IV	5.262***	5.294***
	[0.810]	[0.813]
Male	-0.026	-0.034
	[0.025]	[0.026]
YearBirth	0.078	0.074
	[0.195]	[0.195]
BornJanFeb	Ref. Cat.	Ref. Cat.
BornMarApr	-0.229	-0.224
	[0.210]	[0.214]
BornMayJun	-0.23	-0.24
	[0.224]	[0.227]
BronJulAug	-0.235	-0.239
	[0.225]	[0.227]
BornSepOct	0.091	0.085
	[0.179]	[0.180]
BornNovDec	0.071	0.063
	[0.218]	[0.216]
BornCarlow	1.362***	1.352***
	[0.006]	[0.005]
BornCavan	1.839***	1.843***
	[0.010]	[0.009]
BornClare	1.617***	1.657***
	[0.007]	[0.007]
BornCork	0.165	0.153
	[0.153]	[0.153]
BornDonegal	-0.284***	-0.284***
	[0.010]	[0.007]
BornGalway	Ref. Cat.	Ref. Cat.
BornKerry	-0.099***	-0.103***
	[0.008]	[0.007]
BornKildare	-0.251**	-0.219*
	[0.120]	[0.112]
BornKilkenny	0.322***	0.321***
	[0.013]	[0.012]
BornLaois	0.939***	0.992***
	[0.015]	[0.012]
BornLeitrim	-0.222***	-0.219***
	[0.034]	[0.033]
BornLimerick	-0.117	-0.132
	[0.169]	[0.175]
BornLongford	-0.361***	-0.365***
	[0.012]	[0.011]
BornLouth	-0.353***	-0.355***
	[0.006]	[0.005]
BornMayo	-0.116***	-0.118***
	[0.010]	[0.010]
BornMeath	1.175***	1.179***

	[0.134]	[0.137]
BornMonagan	-0.258***	-0.260***
	[0.009]	[0.010]
BornOffaly	-0.174***	-0.172***
	[0.009]	[0.007]
BornRoscommon	-0.286***	-0.285***
	[0.003]	[0.008]
BornSligo	0.272***	0.272***
	[0.009]	[0.007]
BornTipperary	0.069	0.058
	[0.155]	[0.157]
BornWaterford	0.495***	0.501***
	[0.006]	[0.006]
BornWestmeath	0.189***	0.191***
	[0.007]	[0.008]
BornWexford	-0.311***	-0.308***
	[0.008]	[0.010]
BornWicklow	-0.049***	-0.045***
	[0.011]	[0.010]
Constant	-152.036	-144.867
	[380.959]	[381.769]
N	7769	7504

Note: IV is a dummy variable which is equal to one if the respondent was born in a county that experienced the rubella outbreak in 1956 and was in utero when the rubella outbreak occurred. The sample size in column (2) is smaller (N=7504) as the outcome variable of the second-stage equation is LowEduc. Standard errors are clustered at county level. * p<0.10; ** p<0.05; ***p<0.01

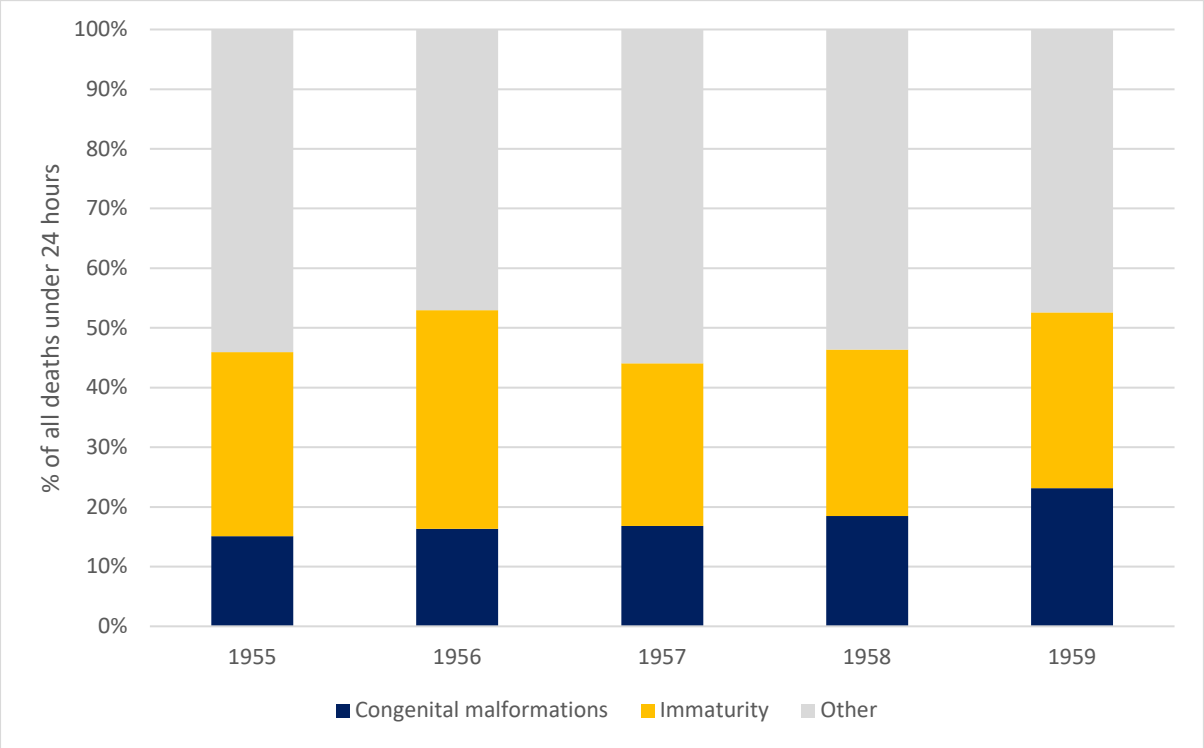
Table A4 Probit and IV-Probit Regression Coefficients [Standard Errors], Robustness Checks

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Estimation:	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit	Probit	IV-Probit
Dependent variable:	PoorHealth	PoorHealth	AnyDis	AnyDis	WorkDis	WorkDis	LowEduc	LowEduc
(1) Explanatory Variable of Interest is Exposure to Rubella in Utero, Cohorts Born 1953 to 1960								
RubellaUtero	0.036***	0.071***	0.015**	0.038***	0.016	0.047***	0.011	0.039***
	[0.009]	[0.020]	[0.007]	[0.011]	[0.011]	[0.014]	[0.008]	[0.009]
Male	0.029	0.03	0.028	0.028	0.01	0.01	0.185***	0.185***
	[0.029]	[0.029]	[0.025]	[0.025]	[0.028]	[0.028]	[0.041]	[0.040]
YearBirth	-0.026**	-0.027**	-0.031***	-0.032***	-0.030***	-0.031***	-0.069***	-0.071***
	[0.011]	[0.012]	[0.007]	[0.007]	[0.008]	[0.009]	[0.006]	[0.007]
First-stage IV F Statistics		28.3		28.3		28.3		28.6
N	20426	20426	20426	20426	20426	20426	19472	19472
(2) Explanatory Variable of Interest is Exposure to Rubella in Utero, Alternative Geographical Definition of IV, Cohorts Born 1955 to 1958								
RubellaUtero	0.056***	0.087***	0.029***	0.046***	0.022	0.060***	0.029***	0.047***
	[0.014]	[0.022]	[0.011]	[0.014]	[0.019]	[0.018]	[0.009]	[0.013]
Male	-0.055	-0.052	0.007	0.008	-0.003	-0.002	0.128***	0.129***
	[0.050]	[0.050]	[0.039]	[0.039]	[0.042]	[0.042]	[0.046]	[0.046]
YearBirth	-0.004	-0.01	-0.013	-0.015	-0.01	-0.013	-0.051**	-0.052**
	[0.036]	[0.038]	[0.023]	[0.023]	[0.031]	[0.034]	[0.021]	[0.021]
First-stage IV F Statistics	--	19.4	--	19.4	--	19.4	--	19.5
N	7769	7769	7769	7769	7769	7769	7504	7504
(3) Explanatory Variable of Interest is Exposure to Rubella at Birth, Cohorts Born 1955 to 1958								
RubellaBirth	-0.023	-0.054**	-0.011	-0.02	-0.004	-0.023	-0.001	-0.007
	[0.019]	[0.026]	[0.010]	[0.015]	[0.011]	[0.016]	[0.007]	[0.008]
Male	-0.056	-0.056	0.006	0.006	-0.004	-0.004	0.127***	0.127***
	[0.049]	[0.049]	[0.039]	[0.039]	[0.042]	[0.042]	[0.047]	[0.047]
YearBrith	-0.02	-0.038	-0.017	-0.023	-0.011	-0.022	-0.047**	-0.051**
	[0.040]	[0.041]	[0.025]	[0.024]	[0.034]	[0.036]	[0.023]	[0.024]
First-stage IV F Statistics	--	27.2	--	27.2	--	27.2	--	27.3
N	7769	7769	7769	7769	7769	7769	7504	7504
(*4) Explanatory Variable of Interest is Exposure to Scarlet Fever in Utero, Cohorts Born 1953 to 1956*								
ScFeverUtero	0.011	0.013	0.009	0.01	0.009	0.015	-0.006	-0.003
	[0.017]	[0.016]	[0.011]	[0.016]	[0.008]	[0.011]	[0.006]	[0.012]
Male	0.056	0.056	0.093**	0.093**	0.038	0.038	0.222***	0.222***
	[0.063]	[0.063]	[0.041]	[0.041]	[0.049]	[0.048]	[0.051]	[0.052]
YearBirth	-0.033	-0.028	-0.038	-0.037	-0.043*	-0.032	-0.101***	-0.096***
	[0.046]	[0.048]	[0.033]	[0.037]	[0.025]	[0.028]	[0.027]	[0.032]
First-stage IV F Statistics	--	63.0	--	63.0	--	62.9	--	62.9
N	7742	7742	7742	7742	7742	7742	7444	7444
(5) *Explanatory Variable of Interest isl Exposure to Scarlet Fever in Utero, Cohorts Born 1953 to 1960*								
ScFeverUtero	-0.001	0.007	0.003	0.005	0.001	0.009	-0.007	-0.003
	[0.015]	[0.014]	[0.008]	[0.012]	[0.007]	[0.008]	[0.006]	[0.009]

Male	0.029	0.029	0.028	0.028	0.01	0.01	0.184***	0.184***
	[0.029]	[0.029]	[0.025]	[0.025]	[0.028]	[0.028]	[0.041]	[0.041]
YearBirth	-0.023**	-0.02	-0.029***	-0.027***	-0.028***	-0.024***	-0.072***	-0.070***
	[0.011]	[0.013]	[0.006]	[0.007]	[0.007]	[0.009]	[0.006]	[0.006]
First-stage IV F Statistics	--	80.7	--	80.7	--	80.7	--	80.4
N	20426	20426	20426	20426	20426	20426	19472	19472

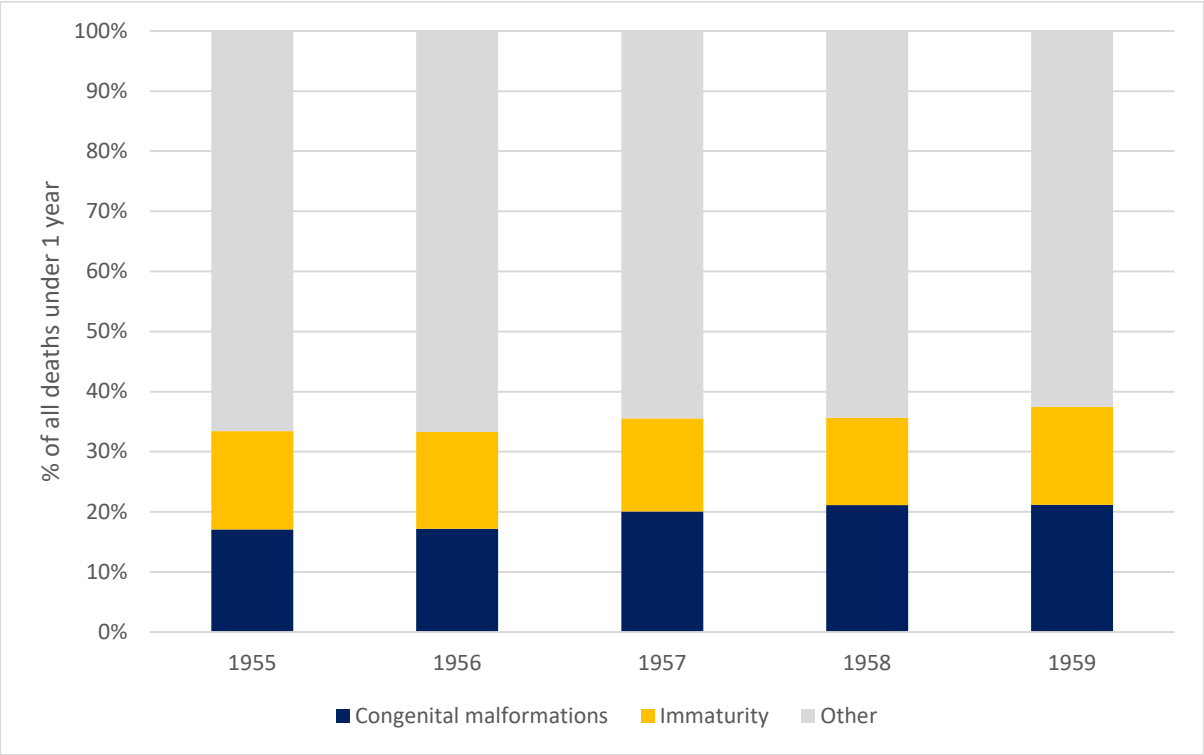
Note: county of birth fixed effects and month of birth fixed effects. Standard errors are clustered at county level. * p<0.10; ** p<0.05; ***p<0.01

Figure A1 Causes of Early Neonatal Mortality (%), 1954-1959



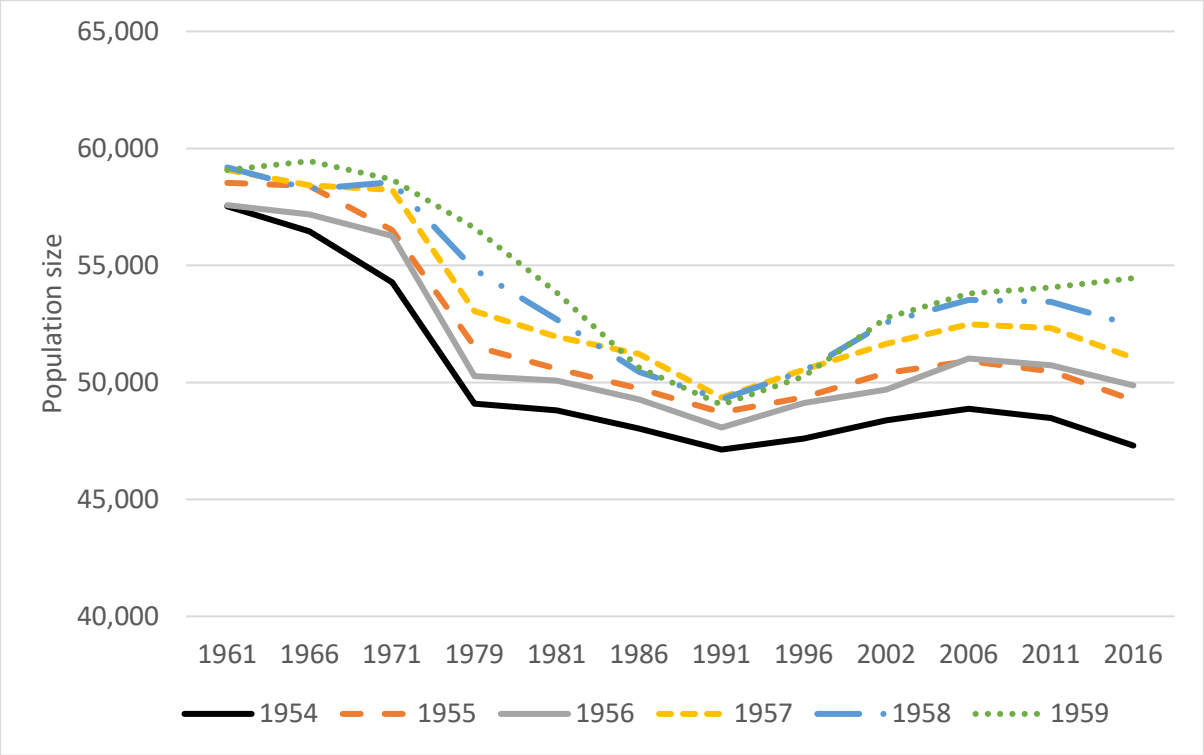
Source: Central Statistics Office, 1950-1959

Figure A2 Causes of Infant Mortality (%), 1954-1959



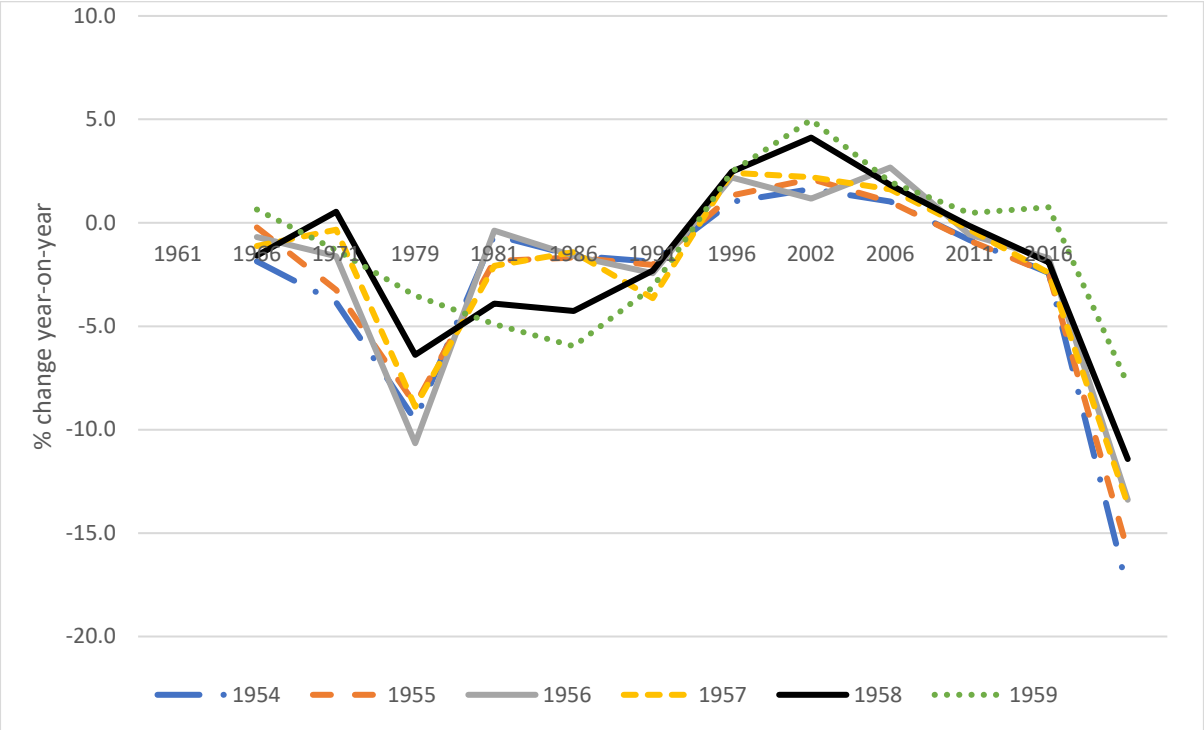
Source: Central Statistics Office, 1950-1959

Figure A3 Population Cohort Sizes, 1961 – 2016



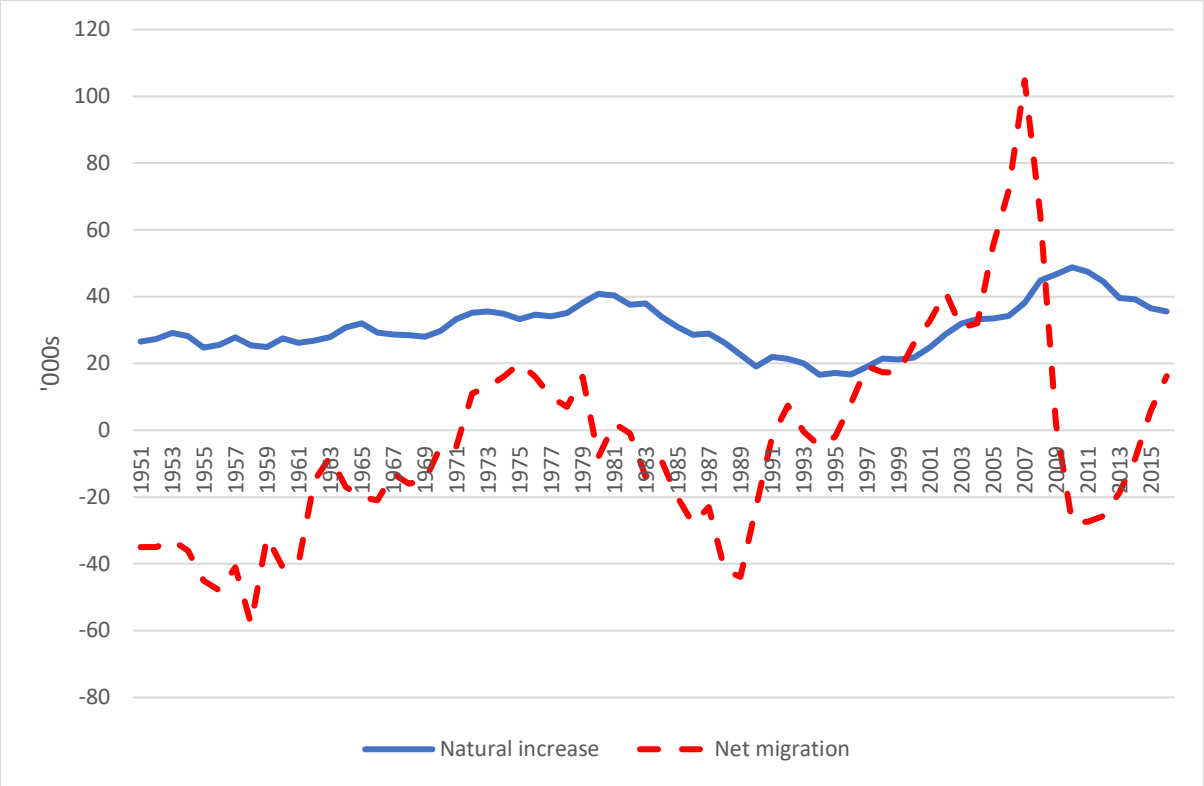
Source: Central Statistics Office, 1961-2016

Figure A4 Population Cohort Growth Rates, 1961-2016



Source: Central Statistics Office, 1961-2016

Figure A5 Components of Population Change (all ages/birth cohorts), 1951-2016



Source: Central Statistics Office, 1950-1959 and 1960-2016