The Second World War and Epigenetic
Part 1: Low Sugar Intake a Thousand Days After Conception Reduced T2DM and Hypertension in Adults

'An event study approach' trailing the sugar consumption after the sudden opening of candy shops in the UK in 1953

To become an expert in 'an event study approach,' world history might be your most favored high school topic before graduating as a medical doctor at the university, writing a master's thesis in public health, and gaining a Ph.D. in statistics. Historical knowledge will tell you where and when a vast population went through a catastrophe, placing survivors under almost intolerable stress. You compare those who survived and lived further on under more pleasant circumstances with those who did not experience the catastrophe. Finally, you have to look for a source of information that allows you to run sophisticated statistics through it, enabling you to finally publish a paper in a journal with a high impact factor.

Outlay

Whether the authors of a recent publication in the Science journal looked back on such a career outlined here is unknown. However, they used the tools mentioned above to select a particular event at the end of the Second World War, compare a specific group of individuals who lived through the event, and use data from a large Biobank to compare the exposed group with those not exposed. To comprehend the true value of the recent 'event study approach,' a closer look at the Second World War is helpful.

Second World War

The war, so far, was the 'bloodiest conflict in human history' and divided the world into two major groups of nations fighting each other consisting of the USA, the British Empire, the Soviet Union, and France on one side and the "Axis Powers of Hitler Germany, Italy under Mussolini and Imperial Japan, on the other side lasting from 1939 (2480) to 1945 (2488). The actional starting point was the German army's invasion of Poland in September. Japan invaded China in 1938 (2481). In June 1941 (2484), Germany attacked the Soviet Union out of the blue because the two nations had a pact of non-aggression before (1). In December 1941, Japan decimated the Pacific Fleet of the USA at Pearl Harbor, opening the Second World War in the Pacific.

UK during the Second World War

Britain was drawn into the war quite reluctantly. Prime Minister Chamberlain had to admit that his appeasement policy with Hitler failed and declared war on Germany due to the invasion of Poland on the 3rd of September 1939. On that day, an English ship, SS Athena, sank, attacked by the German 'Kriegsmarine,' causing 128 civilians to die. That marked the 4th of September as the beginning of the Battle of Atlantic, the most extended campaign of the war up to 1945. German submarines attacked throughout the war, the naval forces of the enemy and convoys of ships

delivering goods to the British Island, and, later, when the USA assisted the war in Russia with war material and weapons.

In May 1940 (2483), Chamberlain was forced to resign, and Churchill took over in a snap decision. At that time, the British minister of foreign affairs refused to be selected for the position. Churchill had to lead Britain through the 'Blitzkrieg' while Germany invaded Belgium, the Netherlands, Norway, and France, which surrendered. The British expedition force in France, in a dramatic rescue operation at Dunkirk, returned to England. Further developments of the war, such as the bombing of the cities in England by the Germans and later the German towns by the Allied air forces, are still in the memory of those who are still alive and experienced these events as very young children (2).

Battle of the Atlantic and food rationing

These still-living elderly might also remember the food shortage during the war, especially food rationing. Britain was very much dependent on fuel, but especially on food delivered from the British Empire and other world regions. The Battle of the Atlantic War severely disrupted the supply routes (3). Even after the war, the rationing of certain food items still continued in Britain, whereas, especially in West Germany (where the areas under military rule from England, the USA, and France were joined into the Federal Republic of Germany in 1949 (2492) under the legendary canceler Adenauer and the Minister for Economy, Ludwig Ehrhardt) the economy improved before Britain. West Germans will not recall rationing even after 1950 (2493), while sugar rationing in the UK ended three years later.

Singular sudden increase in sugar consumption

Britain, where the national drink is tea, sugar, and sweets, was rationed for almost a decade for about 40 g for adults and 15 g for children. Rationing was abolished in September. The sugar intake, relative to rationing, from the first quarter of 1953 to the first quarter of the following year increased by more than 30%, with an additional sharp increase throughout 1954 (see Fig. 1A (4)). Almost 70% of an increase in calories was accounted to sugar, while the consumption of fats, protein, fruits, and vegetables in 1953 didn't change very much. The unique situation triggered the interest in the aftereffects of a sudden high sugar intake in the first 1.000 days after conception, almost without confounder effects of other nutrients. Preceding investigations in human and animal studies indicated long aftereffects on health, resulting in obesity, hypertension, and insulin resistance in adults (5, 6). Truly convincing evidence about the harmful effects of sugar was still missing. The UK Biobank opened the opportunity to conduct an event study on how dietary sugar reduction prevents non-communicable diseases in later life.

UK Biobank

The UK Biobank originates from a large prospective cohort study with 500.000 participants aged 40 to 69 recruited from England, Wales, and Scotland from 2006 (5042) to 2010 (2553). The information contains sociodemographic-, physical-, lifestyle-, and health-related variables. With ongoing enhanced data collection, genotyping and biochemical assays are included. The health condition is followed up through links to national health-related data sets (7, 8).

Increase in the risk of T2DM and hypertension in adults born after releasing food rationing

Using the UK Biobank, groups of adults exposed and not exposed to food rationing during pregnancy and a specific period in infancy were selected. Lifting rationing, sugar consumption increased from 41 g in the first quarter in 1953 to 80 g by the third quarter in 1954. From the data set, 60.183 persons aged 51 to 66 and born between October 1951 and March 1956 were studied. Five 'rationed' age cohorts were singled out, starting from conception throughout pregnancy and continuing for 24 months throughout the food rationed period; another age group was under the same condition throughout 18 months and 12 months. The fourth group was those born close to uplifting food rationing so that only the fetus experienced food rationing through their mothers. These age groups were compared with those never exposed to rationing (4). (Table 2 within the publication skipped the second group).

The two diseases of interest were type 2 diabetes mellitus (T2DM) and hypertension. With increasing age, all the participants increased the risk for both diseases but at an earlier age than those exposed to rationing. Verification is demonstrated by calculating the Hazard ratio through the Gompertz distribution relative to the duration of exposure to rationing. The increase in risk over time could not explained by distribution functions like the Weibull one (see Table 2 (4) (9).

Regarding T2DM, the hazard ratio (against no rationing) for those exposed to rationing through their mother and up to two years after birth had the lowest ratio of 0.64, gradually increasing to 0.87, in that only the mother experienced rationing up to the birth of the child. The highest hazard ratio in the delay of onset of T2DM amounted to 4.17 by exposure in utero and two years after birth. At the same time, the opportunity to avoid diabetes was lower, with a hazard ratio of 1.46. The hazard ratio to be spared from hypertension according to the different categories of exposure to rationing ranged from 0.81 to 0.92, and the delay of onset of hypertension, according to age, decreased from 2.12 to 0.53.

Interpreting the unadjusted Kaplan-Meier survival curves makes the beneficial reduction in sugar intake during rationing easier to understand. Compared to those not exposed to rationing in utero and postnatally, those exposed to rationing in utero and postnatally had a higher chance of not suffering from T2DM as adults, from 65.5% to 92.2% up to age 60, and from hypertension, from 61.4% to 89.1% (see Fig. 2 (4)).

In summary, the message of the most recent 'event study approach' hints at the apparent benefit of strictly reducing sugar during the first 1000 days after gestation. Of the 60,000 people born between 1951 and 1956, 4,000 developed diabetes type 2 (T2DM) and 20,000 hypertension. Those adults who were conceived and born within an 18-month age range before the restriction was removed had a 40% lower risk for T2DM and a 20% lower risk for hypertension (10).

Conclusion and outlook

The implications are that the information achieved is based on well-thought-out epidemiologic and statistical tools. The results further support the 'fetal origins hypothesis' (11, 12). They give weight to the recommendations of pediatricians and those in mother and child health care to

observe, especially during pregnancy and after the first 1.000 days after birth, to significantly limit the intake of sweet drinks and sugary feedings, such as condensed milk and other sugary food (13).

Health authorities might consider increasing the price of sugar through taxes to decrease intake. This would stimulate the commercial sector's opposition. A similar attempt to regulate alcohol consumption resulted in less convincing regulations.

Of scientific interest is the metabolic and genetic background of events affecting pregnant women and infants, giving rise to unhealthy conditions and diseases in later life, now identified as epigenetic mechanisms.

The World Wars, particularly the Second World War, gave ample opportunity to study epigenetic outcomes of much more devasting events than food rationing. The next entry in this blog will review some of those historical events and will comprehend epigenetics in more detail.

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Frank P. Schelp is responsible for the manuscript's content, and the points of view expressed might not reflect the stance and policy of the Faculty of Public Health, Khon Kaen University, Thailand.

For comments and questions, please contact <awuso11@gmail.com.