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Independent Study and Mentorship

Research Assessment #2

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Subject: Early-life Influences on Obesity

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"Early-life Influences on Obesity." *The New York Academy of Sciences*. N.p., n.d. Web. 12 Sept. 2016. <http://www.nyas.org/Publications/Ebriefings/Detail.aspx?cid=e7004c1a-6f40-4e45-a6c7-6970e8a83936>.

Analysis:

Recently, the epidemic of obesity has taken the world by storm. There are many different aspects that can affect obesity, including genetics and the environment. Too much stress and sedentary activity along with calorie-rich diets have been linked to higher rates of obesity. However, one of the most important factors is timing. In the years between conception to adolescence, risks of obesity are especially sensitive. Maternal fitness and childhood physical activity and diet are influential in the chances of an individual becoming obese.

This study focuses on developmental effects on obesity during childhood. There are three contributors with different facets of the topic to discuss that stood out to me. One of the most intriguing to me was Dr. Wahlqvist's idea that the geographical area in which a child grows up in can affect the risks of obesity. He stated that areas with greater rates of financial insecurity were linked to higher rates of obesity. Economic factors affect the risks because they bring added stress to individuals, as well as the more frequent availability and consumption of fast food in certain geographical areas. This concept was interesting to me because it went against the common misconception that those with lower incomes are left without food. Instead, it reveals the lesser-known truth that those in worse financial situations are forced to resort to unhealthy, inexpensive fast food and convenience store options. This leads to higher percentages of obesity in geographical areas like these, as opposed to more wealthy areas, where residents can afford healthy lifestyles with diets of organic, whole foods and nutritious options.

Dr. Lawrence Finer talked about the effects of unintended pregnancies on the rate of obesity in these children. He stated that mothers who did not intend to become pregnant generally sought less prenatal care throughout the process. However, Dr. Finer also remarked that the rates of unintended pregnancies are hopeful to decline, with more forms of contraception available for women of all demographics across the world. I had never considered this idea, but reading about it created a sense of clarity and realization of the effects of an unintended pregnancy on the subsequent care and upbringing of a child.

Another extremely interesting and more involved aspect of obesity risk increase was implemented by Dr. Stephen Krawetz. He delved into the cellular processes that may affect risks of obesity prior to conception of the child. Through his research in male

gametes, he uncovered that sperm RNA from a male that binds to the oocyte from the mother can leave a significant impact on the child. Factors including stress and smoking can alter the miRNA content of the sperm from the father, which then go on to affect how the male gamete impacts the offspring as it grows up in any environment. Understanding the intercellular processes within the body and how they affect a child's upbringing and risks of obesity is eye-opening to me because it intertwines real life with the biological processes inside a person's organs.

Ultimately, this study has brought to light for me the different effects that an individual's childhood can have on the rest of his or her life regarding weight and obesity risks. From varying topics ranging from the geographical area of upbringing, to the intentions of the mother's pregnancy, to the intracellular biological processes that affect the fetus's composition, the factors of childhood leave great influences on the risks of obesity in an individual's life. Through this research assessment, I now have a greater understanding of the importance of the time period from conception to adolescence, which just so happens to coincide with the ages of children that are cared for by pediatricians. The field of pediatrics is vital to the health and well-being of children, and I now know that the impact of a pediatrician's guidance can change the course of a person's life through their weight and risks of obesity.

Early-life Influences on Obesity, Pre-conception to Adolescence

Rates of overweight and obesity have skyrocketed in the past three decades in many parts of the world and in all age groups. These chronic conditions increase risk of death as well as diabetes, heart disease, and certain cancers. According to the World Health Organization, 35% of adults were overweight in 2008 and another 11% were obese. There were 40 million overweight or obese children under age 5 in 2012.

Our modern environment plays a clear role in the increasing prevalence of obesity, as do genetic and epigenetic influences transmitted from parent to child. The conference explored numerous etiological factors predisposing to obesity and related chronic metabolic diseases. Such factors include the stress of living in transitional economies or diverse societies and the obesifying effects of antibiotic use, which reduces microbial diversity.

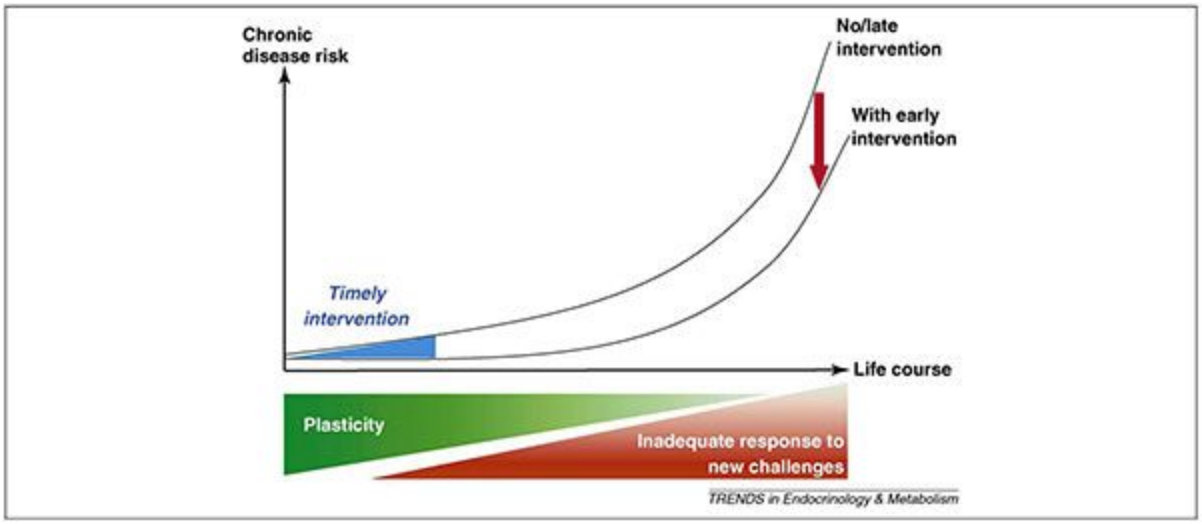
The conference focused on environmental exposures that occur in the earliest stages of life. The period from gestation through age 3 is regarded as a critical time for determining obesity outcomes. After birth, neurons involved in appetite and satiety continue to develop, representing a window when interventions could be particularly effective.

It is also important to study maternal fitness before and during pregnancy. Yet the speakers emphasized that mothers must not be blamed for childhood obesity. Several talks explored how the nutritional status of mothers and fathers before conception, the stress they experience, and even the experiences of their parents, could influence a child's obesity risk. Researchers think these effects are mediated through epigenetics, which are modifications to gene expression that do not affect the DNA sequence and can be heritable.

In the session devoted to pre-conception and generational effects of nutrition, Mark L. Wahlqvist made the case that where we live affects obesity risk and Maria Gloria Dominguez-Bello discussed the impact of urbanization on obesity rates. Lawrence B. Finer discussed the impact of unintended pregnancy. Stephen A. Krawetz explored paternal influences on obesity, particularly through RNA delivered to the oocyte at fertilization. A panel discussion moderated by John G. Kral further explored harmful early-life exposures and looked at efforts to reverse obesity trends. Linda M. Szymanski described how physical activity could reduce the adverse pregnancy outcomes of gestational weight gain, gestational diabetes, and preeclampsia.

In the session on intrauterine environment and programming, Shari Barkin described an upcoming IOM conference that will look at external environment, nutrition, and development in early life. Robert A. Waterland explained an epigenetic effect called metastable epialleles, and Michael G. Ross and Mina Desai discussed rat models that support the importance of the intrauterine environment in childhood obesity. Julie A. Mennella discussed the impact of eating habits established early in life, followed by Nancy F. Krebs, who described the importance of infant diet in the 6 months after birth.

In the final session, which explored interventions, Christiane Wrann talked about the potential for exercise to act as a mechanism for resetting brain function, and Susanne Stormer described some of the efforts underway at Novo Nordisk, a Copenhagen-based company, to combat the diabetes epidemic. Finally, Nico S. Rizzo presented discouraging data on physical fitness in children and adolescents in view of the known benefits of physical activity in reducing obesity among adolescents.



Speakers:

Mark L. Wahlqvist, Zhejiang University, China

Lawrence B. Finer, Guttmacher Institute

Stephen A. Krawetz, Wayne State University School of Medicine

Highlights

- Built environments can be designed to facilitate walking and to promote safety and dietary diversity.
- Women who have unintended pregnancies are less likely to obtain adequate prenatal care or to breastfeed.
- Sperm cells deliver many types of RNA to the oocyte during fertilization, some of which may be involved in metabolism.
- Changes in nutritional status during critical periods before puberty could affect health and longevity in subsequent generations.

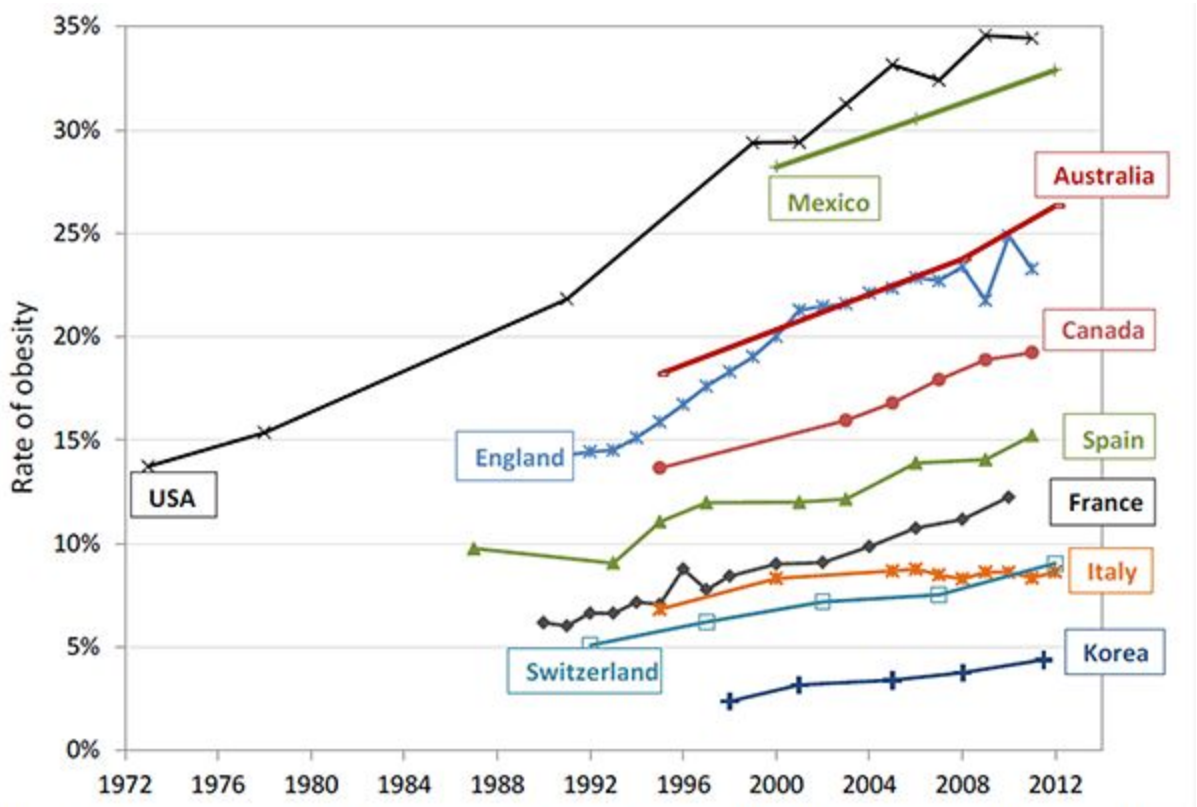
Weight management in transitional economies

Mark L. Wahlqvist of Zhejiang University, China, began by making the case that where we live affects obesity risk. As is well known, high agricultural productivity tends to correlate with high rates of obesity. Financial insecurity can also affect obesity rates; an Australian study, for example, associated stress during the global financial crisis of 2008 with increased obesity risk. But economic factors cannot fully explain obesity trends. For example, obesity has increased more in the past several decades in the U.S. and Mexico than in other countries with similar levels of economic development, such as France, Italy, and Korea.

The built environment also plays a role in obesity rates, and Wahlqvist argued we should change the way we interact with it. A cohort study by his colleague found a reduced risk of death among adults in Taiwan who walked for 15 minutes every day (about half the amount of exercise currently recommend by the World Health Organization). Jogging or running lowered the risk further. However, built areas that offer the option to walk are becoming less common, especially in areas that are under economic pressure to expand urban development,

Wahlqvist explained. It is also important to consider how cities are developed. Wahlqvist and colleagues found an association between a high density of fast-food stores and higher BMI among boys in Taiwan aged 6–13 years old.

Some countries have made progress in reducing obesity among children through efforts including changing the environment and increasing awareness of healthy diets and lifestyles. One example is the EPODE European Network, a community-based intervention program that targets children aged up to 12 years old. The program began in France and is now operating in many countries. Among the study's goals is to encourage families and children to exercise and follow healthy diets. The program relies on the participation of politicians, town planners, health groups, teachers, journalists, and sociologists. Wahlqvist stressed the importance of community support for EPODE and similar programs. In France, obesity rates among children aged 3–17 years old have stabilized in the past 30 years. Wahlqvist attributed part of this success to the EPODE program.



Note: Age- and gender-adjusted rates of obesity and overweight, 2005 OECD standard population.

Intended and unintended pregnancies

Lawrence B. Finer of the Guttmacher Institute talked about the impact of unintended pregnancies on the health of mothers and infants. Mothers who have unintended pregnancies are less likely to obtain adequate prenatal care or to breastfeed their babies. Finer presented recent U.S. data showing 14% of births were from pregnancies that women did not want and 26% were from mistimed pregnancies (women wanted to get pregnant at a different time). The rate of unintended pregnancy in the U.S. increased between 1994 and 2008.

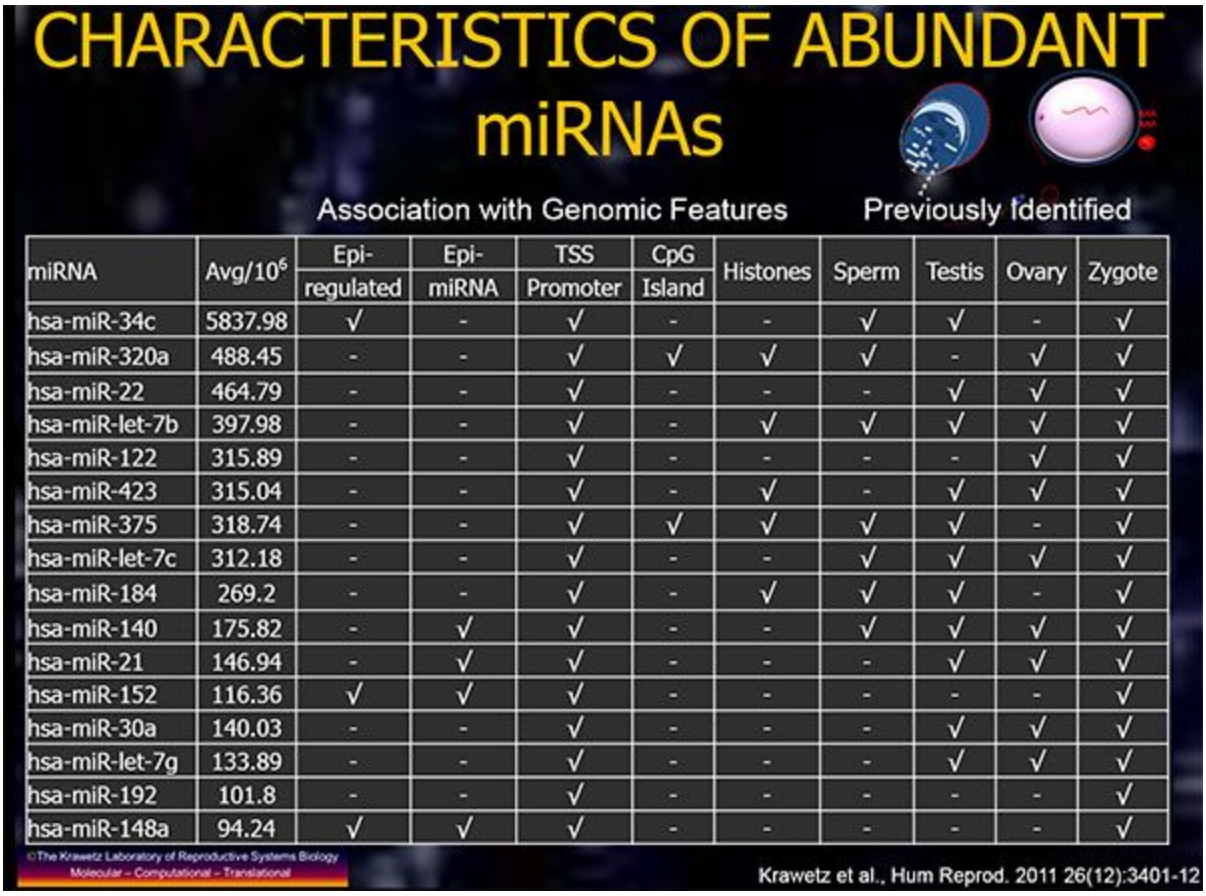
Finer suggested this trend could be due in part to shifting demographics, with higher representation of groups that tend to have more unintended pregnancies, such as women living with a partner, Hispanic women, and women with low income or education levels. Among low-income and less educated women, who have historically carried a disproportionate burden of unintended pregnancies, the rates are increasing. However, Finer is hopeful that data from recent years (which will soon be available) will show unintended pregnancy declining as more women start using highly effective contraceptive methods, such as intrauterine devices (IUDs).

Paternal contributions: the role of sperm RNA

Stephen A. Krawetz of Wayne State University School of Medicine explored paternal influence on early embryonic metabolism, particularly through RNA delivered to the oocyte from the sperm. His team has identified many classes of RNA molecules in sperm cells. Although sperm RNA has generally been assumed to be less important than oocyte RNA because it is much less abundant, these RNA molecules have begun to be recognized in the past 10 years for their many possible roles in embryogenesis.

Similar to somatic cell RNA, about 89% of sperm cell RNA is ribosomal. Another 5% is mitochondrial and the remaining 6% comprises coding RNAs, long and short noncoding RNAs, repetitive sequences, and intronic, exonic, and intergenic elements. Many of the coding RNAs, or transcripts, are thought to code for proteins involved in male fertility, such as integrator complex subunit 1 (INTS1). Krawetz and his team have focused on a class of small noncoding RNAs called microRNAs, or miRNAs. The sperm delivers many miRNAs to the oocyte. The most abundant, miR-34c, is required for cell division. Several others are involved in establishing early metabolism. Two, miR-375 and miR-192, are involved in insulin sensitivity and resistance, respectively.

Recent studies suggest that factors such as stress, obesity, and smoking alter the miRNA content of sperm. These findings raise the possibility that environmental cues leave marks on the male gamete that may affect how the offspring responds to its environment.



miRNA	Avg/10^6	Epi-regulated	Epi-miRNA	TSS Promoter	CpG Island	Histones	Sperm	Testis	Ovary	Zygote
hsa-miR-34c	5837.98	√	-	√	-	-	√	√	-	√
hsa-miR-320a	488.45	-	-	√	√	√	√	-	√	√
hsa-miR-22	464.79	-	-	√	-	-	-	√	√	√
hsa-miR-let-7b	397.98	-	-	√	-	√	√	√	√	√
hsa-miR-122	315.89	-	-	√	-	-	-	-	√	√
hsa-miR-423	315.04	-	-	√	-	√	-	√	√	√
hsa-miR-375	318.74	-	-	√	√	√	√	√	-	√
hsa-miR-let-7c	312.18	-	-	√	-	-	√	√	√	√
hsa-miR-184	269.2	-	-	√	-	√	√	√	-	√
hsa-miR-140	175.82	-	√	√	-	-	√	√	√	√
hsa-miR-21	146.94	-	√	√	-	-	-	√	√	√
hsa-miR-152	116.36	√	√	√	-	-	-	-	-	√
hsa-miR-30a	140.03	-	-	√	-	-	-	√	√	√
hsa-miR-let-7g	133.89	-	-	√	-	-	-	√	√	√
hsa-miR-192	101.8	-	-	√	-	-	-	-	-	√
hsa-miR-148a	94.24	√	√	√	-	-	-	-	-	√