3.10  No Mother Should Bury Their Child

Sponsored by the 501(c) (3) nonprofit Institute for Education, Research, and Scholarships (IFERS), EASE T1D (Education, Awareness, Support, Empowerment for Type 1 Diabetes) is the joint effort of two mothers—Debbie George and Michelle Thornburg—who have children with Type 1 diabetes [105]. EASE T1D addresses the misconceptions of Type 1 diabetes and the lack of knowledge on the differences between Type 1 (little to no insulin) and Type 2 (insulin resistance, too little insulin). Type 1 diabetes is a chronic, life-threatening autoimmune disease for which there is currently no cure. Contrary to popular belief, diet and lifestyle are not causes of the disease.

Undiagnosed Type 1 diabetes can result in Diabetic Ketoacidosis (DKA) which can lead to serious conditions including coma, brain damage, and even death. With the slogan “No parent should bury their child,” EASE T1D started a petition in May 2015 to encourage physicians, physician assistants, and nurses in California to educate parents on the signs and symptoms of Type 1 diabetes as well as to check blood glucose levels of children and adults who present flu-like symptoms in an effort to prevent a misdiagnosis and to save lives. This legislation is modeled after Reegan’s Rule.

Reegan’s Rule was started in North Carolina by a mother whose 16-month-old baby girl, Reegan Oxendine, passed away from undiagnosed Type 1 diabetes. Little Reegan had been misdiagnosed several times over a 3-month period before her death. Reegan’s mother, Darice Oxendine, created a legislation to encourage parent education on Type 1 diabetes during well-child care visits from birth to age 5 years old. The first-of-its-kind legislation was signed into North Carolina Law in October 2015 [106].

Advocacy efforts for similar legislation have been happening nationwide. In November 2015, House Resolution No. 569 passed in Pennsylvania due to the efforts of Debbie Healy and her State Representative, Ryan MacKenzie. The resolution encourages physicians to educate and discuss the warning signs and symptoms of Type 1 diabetes with parents or guardians [107].

In March 2016, California Senator Richard D. Roth’s measure to raise awareness of Type 1 diabetes passed the State Senate on a bipartisan, unanimous vote of 38-0 (see Fig. 3.21). “I am proud to have authored Senate Resolution 63 and thank my colleagues in the State Senate for joining me in raising awareness of this life threatening disease,” said Senator Roth. “Educating parents regarding Type 1 diabetes is critical to diagnosing and treating this condition early and effectively, helping ensure children and adolescents learn to manage their condition and live long, healthy lives” [108].

With all the grassroots awareness campaigns spearheaded by concerned parents, some promising solutions are on the horizon. Partnering with Dr. Jane Buckner of Benaroya Research Institute (BRI) at Virginia Mason, Dr. David Rawlings and his team at the Seattle Children’s Research Institute have been studying an immunotherapy approach. “In Type 1 diabetes, a type of immune system cell, called
WHEREAS, Diabetes is a chronic disease that affects an estimated 29.1 million Americans, or 9.3 percent of the population, on a daily basis; and

WHEREAS, Approximately 3.8 million people in California are living with diabetes, and it is estimated that over one million Californians are undiagnosed; and

WHEREAS, Diabetes costs an estimated $37.1 billion in California each year; and

WHEREAS, Type 1 diabetes accounts for $4.9 billion in health care costs in the United States each year; and

WHEREAS, Type 1 diabetes, previously called juvenile-onset diabetes, occurs when the body does not produce insulin, a hormone that is necessary to convert sugar, or glucose, into energy; and

WHEREAS, Type 1 diabetes is the third most common autoimmune disease among children; and

WHEREAS, Between 2001 and 2009, there was a 21 percent increase in the prevalence of Type 1 diabetes in people under 20 years of age; and

WHEREAS, Only 5 percent of diabetics have Type 1 diabetes, and it is typically diagnosed in children and young adults; and

WHEREAS, Early diagnosis of Type 1 diabetes can help prevent diabetic ketoacidosis, a potentially fatal condition that develops from high blood glucose levels; and

WHEREAS, In 2009, among hospital discharges of children and young people 0 to 17 years of age, about 74 percent had diabetes as the first-listed diagnosis, and of these patients, 64 percent of the diagnoses were for diabetic ketoacidosis; and

WHEREAS, Education concerning Type 1 diabetes is critical to raising awareness and diagnosing and treating this condition effectively; and

WHEREAS, With the help of insulin therapy and other treatments, young children and adolescents can learn to manage their condition and live long, healthy lives; and

WHEREAS, Since early diagnosis is the key to successful treatment of Type 1 diabetes, health care practitioners can increase the likelihood of early diagnoses by discussing warning signs and symptoms of Type 1 diabetes with parents or guardians at least once a year during well child visits for infants and children from birth to five years of age; now, therefore, be it

RESOLVED BY SENATOR RICHARD D. ROTH, That he calls the attention of the public to the importance of raising awareness about Type 1 diabetes through education and learning to recognize the warning signs and symptoms of this chronic disease so that it may be diagnosed early in its course and treated effectively.

Member Resolution No. 202
Dated this 14th day of March, 2016.

Honorable Richard D. Roth
31st Senatorial District

Fig. 3.21 California Senate Resolution 63 “Type 1 Diabetes Awareness” signed by the Honorable Richard D. Roth, 31st Senatorial District, on March 14, 2016
an effector T cell, malfunctions and attacks pancreas cells that create insulin,” Rawlings explained. “Normally, effector T cells attack foreign viruses, not the body’s own cells. With this research, we will edit genes in these cells and change these ‘dangerous’ cells into regulatory T cells, another type of immune cell that regulates an immune system’s response and keeps it from going into overdrive. We expect these gene-edited regulatory T cells, when returned to a diabetic’s body, will stop effector T cells from destroying the body’s insulin-producing cells” [109].

Clinical trials for new treatments have already begun. In June 2015, Massachusetts General Hospital launched phase II trial of vaccine bacillus Calmette-Guérin (BCG) to reverse advanced Type 1 diabetes [110]. In March 2016, Professor Mark Peakman at King’s College London started testing MultiPepT1De (Multiple beta cell Peptides in Type 1 diabetes) injections on trial participants. The peptides are protein molecules found in the insulin-producing beta cells of the pancreas (see Fig. 3.22). Researchers hope that the peptides will re-train the patient’s immune system to get rid of its autoimmune disorder.

Although researchers have been making steady progress, fundraising to support them is not easy. Once in a blue moon there are successful campaigns like the Ice Bucket Challenge by the ALS Association to fight Lou Gehrig’s disease (see Fig. 3.23). However, the majority of people in the world could care less about diabetes, cancer, or any incurable disease unless they are inflicted by it or they have to take care of a family member who is suffering from it. The public generally relies on deep-pocketed pharmaceutical companies to fund expensive research which

![Google search on “peptides” returns a Knowledge Graph of a definition from Wikipedia about biologically occurring short chains of amino acid monomers linked by peptide (amide) bonds](image)

**Fig. 3.22** Google search on “peptides” returns a Knowledge Graph of a definition from Wikipedia about biologically occurring short chains of amino acid monomers linked by peptide (amide) bonds
Fig. 3.23 Google search on “Lou Gehrig’s disease” returns a Knowledge Graph of information, symptoms, and treatments from Mayo Clinic and other sources.
often results in high drug prices. *The Wall Street Journal* reported that in 2014 the U.S. Food and Drug Administration (FDA) approved 41 new drugs, the most in nearly two decades, but the catch is their cost [111]:

Recent treatments for hepatitis C, cancer and multiple sclerosis that cost from $50,000 annually to well over $100,000 helped drive up total U.S. prescription-drug spending 12.2% in 2014, five times the prior year’s growth rate… Out-of-pocket prescription-drug costs rose 2.7% in 2014. … Even patients with insurance and comfortable incomes are sometimes forced to make hard choices—tapping savings, taking on new debt or even forgoing treatment. … Patients on Medicare are starting to feel some relief from out-of-pocket expenses through a provision in the Affordable Care Act that requires a gradual lowering of patient contributions.

In 2015, the U.S. government spent 28.7% of taxpayer’s money on health programs (see Fig. 3.24) [112]. The second largest spending was 25.4% on the Pentagon and the military. A healthy population is vital to a country’s economy and national security.
3.11 Big Data for “Nowcasting” of Epidemics

“One in 20 Google searches are for health-related information,” wrote Google product manager Prem Ramaswami in the Google official blog in February 2015 [113]. Instead of calling doctors at the first sign of symptoms, people turn to Google search for help. So much so that Google can predict where and when an epidemic will occur based on geographical data and search queries.

In 2008, Google engineers started working on Flu Trends. It turned out to be a big data success story of “nowcasting” which aims to offer near-term forecast with a high degree of detail and accuracy. During the 2012–2013 season in the United States, Google Flu Trends correctly estimated the start and duration of the season, but overestimated the severity of the flu [114]. Then Google software engineer Jeremy Ginsberg and his research team cautioned that “this system is not designed to be a replacement for traditional surveillance networks or supplant the need for laboratory-based diagnoses and surveillance” [115].

In 2015, Google Flu Trends and Google Dengue Trends stopped publishing estimates of flu and dengue fever based on search patterns. Instead, Google began to provide flu and dengue signal data directly to Columbia University’s Mailman School of Public Health, Boston Children’s Hospital/Harvard, Centers for Disease Control and Prevention (CDC) Influenza Division, and other institutions that specialize in infectious disease research [116].

3.12 Top 10 Lists of Health-Related Search Queries

According to Simon Rogers, a data editor for Google’s News Lab, the top 9 health-related questions on Google search in the United States from January to November 2015 were [117]:

1. Is bronchitis contagious?
2. Is pneumonia contagious?
3. How much water should I drink?
4. How many calories should I eat?
5. What is lupus?
6. How far along am I?
7. When do you ovulate?
8. What is gluten?
9. How long does the flu last?

Megan Ranney, Content Marketing Manager at Mashable, reported on countries using Google search to eat and live healthier in 2015. She summarized in her article that “how to eat healthy, healthy body mass index parameters, how to lose weight and how to eat healthy on a budget all ranked among the world’s top 10 search
queries, as well as questions about whether specific foods were healthy” [118]. The worldwide top 10 health-related queries in 2015 were:

1. How to eat healthy
2. What is health?
3. Is [food] healthy? (Some foods listed were sushi, hummus, and popcorn)
4. How can I be healthy?
5. What is a healthy BMI?
6. How to stay healthy
7. How to lose weight
8. How to eat healthy on a budget
9. What is a healthy blood pressure?
10. What is a healthy heart rate?

3.13 Knowledge Graph of Health Information

Knowledge Graph is Google’s “first step towards building the next generation of search, which taps into the collective intelligence of the web and understands the world a bit more like people do” [119]. In February 2015, Google product manager Prem Ramaswami announced the expansion of Knowledge Graph to cover health-related search queries [120]:

One in 20 Google searches are for health-related information. And you should find the health information you need more quickly and easily. … When you ask Google about common health conditions, you’ll start getting relevant medical facts right up front from the Knowledge Graph. We’ll show you typical symptoms and treatments, as well as details on how common the condition is—whether it’s critical, if it’s contagious, what ages it affects, and more. For some conditions you’ll also see high-quality illustrations from licensed medical illustrators. Once you get this basic info from Google, you should find it easier to do more research on other sites around the web, or know what questions to ask your doctor.

Larry Page and Sergey Brin wrote in the August 2004 Google IPO letter that Google users trust the search engine to help them with important decisions including medical advice and that Google search results are unbiased and objective [121]. Google relies on its team of medical doctors and the Mayo Clinic to ensure the quality of medical information:

We worked with a team of medical doctors (led by our own Dr. Kapil Parakh, M.D., MPH, Ph.D.) to carefully compile, curate, and review this information. All of the gathered facts represent real-life clinical knowledge from these doctors and high-quality medical sources across the web, and the information has been checked by medical doctors at Google and the Mayo Clinic for accuracy.

For instance, when we Google “Type 1 diabetes” we get a Knowledge Graph of “About,” “Symptoms,” and “Treatments” from Mayo Clinic and other sources (see Figs. 3.25, 3.26, and 3.27). Although the Knowledge Graph is very useful, it is by no means comprehensive or inclusive of all types of treatment, new theories, and
Fig. 3.25 Knowledge Graph of “About” for “Type 1 diabetes”
Fig. 3.26 Knowledge Graph of “Symptoms” for “Type 1 diabetes”
Fig. 3.27  Knowledge Graph of “Treatments” for “Type 1 diabetes”
modern advances. Nevertheless, the Knowledge Graph provides adequate basic information and offers additional search queries such as “Carbohydrate counting” and “Diabetic diet” to help users explore related topics. To cure Type 1 diabetes and other serious hereditary diseases (see Fig. 3.28), advanced medical treatments such as gene therapy offer promising solutions.

**Fig. 3.28** Google search on “hereditary diseases” returns a Knowledge Graph of “genetic disorder” listing the most common types including down syndrome, cystic fibrosis, Huntington’s disease, Duchene muscular dystrophy, sickle cell anemia, hemophilia, thalassemia, and fragile X syndrome.
3.14 CRISPR-Cas9 Gene Editing

In 2012, biochemist Jennifer Doudna, microbiologist Emmanuelle Charpentier, and their team of scientists published a seminal research paper on CRISPR-Cas9 (Clustered Regularly-Interspaced Short Palindromic Repeats—CRISPR associated protein 9) which allows scientists to edit genomes with precision, efficiency, and flexibility (see Fig. 3.29) [122].

In 2013, Chinese scientists Yuyu Niu, Bin Shen, Yiqiang Cui, Yongchang Chen, and others at Yunnan Key Laboratory of Primate Biomedical Research and Nanjing Medical University created the first-ever mutant twin cynomolgus monkeys by coinjection of one-cell-stage embryos with Cas9 mRNA and sgRNAs (see Fig. 3.30) [123].

In 2014, Temple University professor Wenhui Hu and his collaborators at Case Western Reserve University and Sichuan University successfully used RNA-directed gene editing to eradicate latently infected cells and to immunize uninfected cells against HIV-1 infection [124].

In 2015, Prof. Junjiu Huang and his research team at the Sun Yat-sen University in Guangzhou, China modified the DNA of human embryos in order to eliminate the inherited blood disease thalassemia [125]. “I believe this is the first report of CRISPR/Cas9 applied to human pre-implantation embryos and as such the study is a landmark, as well as a cautionary tale,” said George Daley, a stem-cell biologist at Harvard Medical School. “Their study should be a stern warning to any practitioner who thinks the technology is ready for testing to eradicate disease genes” [126].

**Fig. 3.29** Google search on “gene editing” returns a Knowledge Graph of definition from Wikipedia about a type of genetic engineering in which DNA is inserted, deleted or replaced in the genome of an organism using engineered nucleases, or molecular scissors
In 2016, the Human Fertilization and Embryology Authority (HFEA) regulator in the United Kingdom approved a license application by stem cell scientist Kathy Niakan at the Francis Crick Institute in London to perform gene editing on human embryos [127]. “This research will allow scientists to refine the techniques for creating GM (genetically modified) babies,” said Dr. David King, director of Human Genetics Alert. “Many of the government’s scientific advisers have already decided that they are in favor of allowing that. So this is the first step in a well mapped-out process leading to GM babies, and a future of consumer eugenics” [128].

It may come as a surprise to many people that the human genome (see Fig. 3.31) contains human endogenous retroviruses (HERVs) (see Fig. 3.32) that are linked to cancer [129], autoimmune diseases [130], multiple sclerosis [131], schizophrenia [132], and more. Gene editing offers a new hope to eradicating many deadly hereditary diseases. Christoph Lahtz, former cancer researcher at the City of Hope Beckman Research Institute, describes gene editing as a new hope for cancer treatment in Chap. 20 of this book.

**Fig. 3.30** First-ever mutant twin cynomolgus monkeys in China created by coinjection of one-cell-stage embryos with Cas9 mRNA and sgRNAs