Juvenile Diabetes Cure Research Tax Check-Off Program Annual Report


Tom Corbett, Governor
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Juvenile Diabetes Cure Research Tax Check-Off Program
Created in September 2004 with the passage of Act 133, Juvenile Diabetes Cure Research, the Juvenile Diabetes Cure Research Tax Check-Off Program provides a state income tax check-off option for individuals to contribute a portion of their state tax refund to support research for juvenile diabetes, more commonly known as type 1 diabetes. The program funds research grants focused on restoring normal blood levels, preventing and reversing complications of the disease, and/or prevention of juvenile diabetes.

Type 1 Diabetes Overview
Type 1 diabetes (T1D), previously known as insulin-dependent diabetes mellitus (IDDM), or juvenile-onset diabetes, is an auto-immune disease in which the immune system destroys the insulin-producing beta cells of the pancreas that regulate blood glucose. As a result, the pancreas no longer produces insulin, the hormone needed to convert sugar (glucose), starches and other foods into energy needed for living. This form of diabetes usually strikes children and young adults, although disease onset can occur at any age. In adults, type 1 diabetes accounts for approximately 5 percent of all diagnosed cases of diabetes. Risk factors may be autoimmune, genetic or environmental, but the exact cause of type 1 diabetes is unknown, with no known way to prevent it. In addition, there is no cure.

Type 1 diabetes comes on suddenly, causes dependence on injected or pumped insulin for life, and carries the constant threat of devastating complications. While insulin injections or infusions allow a person with type 1 diabetes to stay alive, they do not cure diabetes, nor do they necessarily prevent the possibility of the disease’s devastating effects, which may include kidney failure, blindness, nerve damage, heart attack, stroke and amputations. Research focused on type 1 diabetes provides hope to detect its causes and to find a cure.

Diabetes Statistics
In 2011, the World Health Organization reported that non-communicable diseases (NCDs) killed 63 percent of people who died worldwide in 2008. Cardiovascular diseases account for most NCD deaths, or 17 million people annually, followed by cancer (7.6 million), respiratory disease (4.2 million) and diabetes (1.3 million). These four groups of diseases account for about 80 percent of all NCD deaths and share four common risk factors: tobacco use, physical inactivity, the harmful use of alcohol and poor diets.3

- According to the Centers for Disease Control and Prevention (CDC), it is estimated that 25.8 million people of all ages in the United States have diabetes (with 18.8 million diagnosed and seven million undiagnosed).1
- In adults, type 1 diabetes accounts for approximately 5 percent of all diagnosed cases of diabetes.1
- After adjusting for population age and sex differences, average medical expenditures among people with diagnosed diabetes were 2.3 times higher than expenditures would be in the absence of diabetes.1
Diabetes was the seventh leading cause of death based on U.S. death certificates in 2007.\(^1\)
Diabetes and its complications are the seventh leading cause of death in Pennsylvania, responsible for 3,415 Pennsylvania deaths in 2011 – which could be expressed as an average of nine deaths per day.\(^4\)
Between 1,000,000 and 1,100,000 adults age 18+ in Pennsylvania (10-11 percent of the target population) are estimated to have been diagnosed with diabetes.\(^5\)
It is important to note that diabetes can go undetected for quite some time. Therefore, the percentage of Pennsylvania adults with diabetes was likely higher than 10 percent in 2012.

**Type 1 Diabetes Statistics**
- The rate of T1D incidence among children under age 14 is estimated to increase by three percent annually worldwide.\(^11\)
- As many as three million Americans may have T1D.\(^8\)
- T1D accounts for $14.9 billion in healthcare costs in the U.S. each year.\(^12\)
- Each year, more than 15,000 children and 15,000 adults—approximately 80 people per day—are diagnosed with T1D in the U.S.\(^9\)
- Approximately 85 percent of people living with T1D are adults, and 15 percent of people living with T1D are children.\(^8\)
- The prevalence of T1D in Americans under age 20 rose by 23 percent between 2001 and 2009.\(^10\)
- An estimated 14 percent (95% confidence interval: 10-20) of Pennsylvania adults age 18+ ever told they have had diabetes have Type 1 diabetes.\(^13\)
- Diagnoses of T1D in Philadelphia children younger than 5 jumped 70 percent between 1985 and 2004.\(^7\)

**Diabetes Costs Overview**
Diabetes is one of the costliest chronic diseases. Medical expenses for people with diabetes are more than two times higher than for people without diabetes.\(^1\)

- National Estimated Diabetes Costs for 2007\(^1\)
  - Total (direct and indirect): $174 billion
  - Direct medical costs: $116 billion
  - Indirect costs: $58 billion (disability, work loss, premature mortality)

- Pennsylvania Estimated Diabetes Costs for 2007\(^6\)
  - Hospitalizations for which diabetes was the principal diagnosis incurred over $833 million in hospital charges and accounted for over 132,200 hospital days.
  - From 2003 to 2007, total costs for diabetes-related hospital charges in Pennsylvania have reached more than $3.6 billion and accounted for over 663,000 days in the hospital.
Administration of the Program
The Pennsylvania Department of Health Diabetes Prevention and Control Program is responsible for the administration of the Juvenile Diabetes Cure Research Tax Check-Off Program. A $100,000 two-year grant was awarded to The Pennsylvania State University College of Medicine to conduct research to understand the molecular basis for vision impairment in diabetic retinopathy for patients with type 1 diabetes. Research began Jan. 1, 2009, and ended on Dec. 31, 2010. A second two-year grant for $150,000 was awarded to The Pennsylvania State University Department of Pharmacology to conduct vision impairment diabetic retinopathy research. Research began July 1, 2012, and will end on June 30, 2014.

Significant progress has been made using these funds, and the eventual significance of this research on public health outcomes could be enormous. The results of these studies have led to published manuscripts that describe roles for altered lipids and enzyme inhibition in diabetic retinopathy and complications. A list of these manuscripts is found on page 7.

In the first grant, The Pennsylvania State University College of Medicine has leveraged their findings for additional extramural funding as a bridge to national research funding from the National Institutes of Health (NIH) and American Diabetes Association (ADA):
   1) National Institutes of Health National Eye Institute – The Role of Glycosphingolipids in Diabetic Retinopathy
   2) American Diabetes Association – Therapeutically modulating glycosphingolipid metabolism in a model of type 1 diabetes

PSU Department of Pharmacology has incorporated further exploration of the role of diminished caveolin-1 in ocular inflammation and vascular leakage in the present grant and is attempting to leverage these funds.

Research Results from the Program
PSU College of Medicine Grant:
Results from the first grant indicated that too much of a type of glycolipid in the type 1 diabetic retinas of both rat and mouse models causes insulin to fail to be processed properly, as well as causing detrimental effects of inflammation, vascular dysfunction and neuronal cell death. An enzyme called glucosylceramide synthase (GCS) catalyzes the reaction that creates glucosylceramide in the retina. Juvenile Diabetes Cure Research Tax Check-Off Program grant funds were successfully used to identify and validate GCS as a target in reducing or eliminating diabetic complications.

PSU Department of Pharmacology Grant:
The title of the new grant is “Studies to Verify Dysfunctional Toll-like Receptor Signaling and Diabetic Retinopathy.” Studies were initiated in July 2012 to quantify the expression, cell-type and lipid microdomain localization of Toll-Like Receptors (TLRs) in the diabetic retina. The grantee reports significant progress in establishing the models and validating the tools necessary to accomplish the task. The major goals of this grant are to A) identify the major alterations of inflammatory TLRs in the diabetic retina and B) to validate that TLRs contribute to diabetic retinopathy.
In May 2014 the grantee reported the following progress:

Diabetic retinopathy is the leading cause of vision loss among working age adults. While several underlying factors have been identified, none have accounted for the full spectrum of changes that occur or have led to effective new therapies. The “microbiome” consists of microorganisms, such as bacteria, that live inside the human body. This population of microorganisms can be beneficial as well as detrimental. We are investigating how this microbiome may contribute to complications of diabetes with an emphasis on diabetic retinopathy. One mechanism by which the human body recognizes microorganism is a group of proteins, called Toll-Like Receptors (TLRs). Upon binding of microorganism components to these TLRs, several signaling events can occur that may contribute to pathology of diabetic retinopathy.

We have found that within models of type 1 diabetes, there is an elevation in endotoxins. Endotoxins are a component of certain types of bacteria and can initiate inflammation through the binding and subsequent activation of TLR4. We are currently investigating how endotoxins may contribute to retinal pathology in diabetes through increasing white blood cell (leukocyte) adhesion to the retina vasculature. More specifically, we are examining the underlying changes to lipids that endotoxins have on the retina. We have noted significant alterations of retinal lipids comprised of the omega-3 polyunsaturated fatty acid, docosahexaenoic acid (DHA). DHA is very abundant in the retina and is very important for visual function. We’ve also observed changes in lipids comprised of arachidonic acid, an omega-6 fatty acid that can have inflammatory properties. Most recently, we have started work with a new investigational drug to inhibit retinal inflammation. In vitro work has shown this inhibitor to suppress inflammation-induced leukocyte adhesion molecules. We are hoping to begin testing this compound in vivo soon.

**Plans for Fiscal Year 2014-2015**

The Diabetes Prevention and Control Program (DPCP) will issue a request for application (RFA) in 2014. Proposed projects must have been subject to an established peer and scientific review process identical or similar to the National Institutes of Health review system. The purpose of the resulting grant will be to conduct research that focuses on juvenile diabetes as it relates to restoring normal blood levels, preventing and reversing complications from the disease, and/or preventing juvenile diabetes. Research funds from the program are restricted to institutions of higher education and independent research institutes of the Commonwealth of Pennsylvania.
Tax Check-Off/Private Contributions
Tax Year 2012 (Calendar Year 2013) was the eighth year in which contributions were collected for this fund. Contributions to the fund in 2013 totaled $43,079.06. These annual contributions are displayed below in Figure 1. Total revenue through December 31, 2013 was $462,681.16 and the cumulative balance was $216,751.16.

How to Contribute to the Program Fund
Individuals may indicate the amount of their state tax refund they wish to contribute to the Juvenile (Type 1) Diabetes Cure Research Fund. Contributions may be made payable to the Juvenile Diabetes Cure Research Fund and sent to:

Pennsylvania Department of Health
Bureau of Administrative and Financial Services
Division of Budget
625 Forster St.
Health and Welfare Building
Harrisburg, PA 17120
For Additional Information

This report was prepared by the Diabetes Prevention and Control Program, Division of Nutrition and Physical Activity, Bureau of Health Promotion and Risk Reduction, Pennsylvania Department of Health. For additional information, contact:

Pennsylvania Department of Health
Diabetes Prevention and Control Program
625 Forster St., Room 1000, Health and Welfare Building
Harrisburg, PA, 17120
717-787-5876
www.health.state.pa.us/diabetes

For additional information regarding type 1 diabetes, including managing the disease and current research being conducted, please visit the following:

- Centers for Disease Control and Prevention, http://www.cdc.gov/diabetes;
- Juvenile Diabetes Research Foundation, http://www.jdrf.org; and

References


8. Type 1 Diabetes, 2010; Prime Group for JDRF, Mar. 2011.


10. SEARCH for Diabetes in Youth data by the Centers for Disease Control and Prevention and the National Institutes of Health.


13. 2009 Pennsylvania Behavioral Risk Factor Surveillance System. These data were provided by the Bureau of Health Statistics and Research, Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analysis, interpretations or conclusions.

**Manuscript List**

1. Fox TE, Han X, Kelly S, Merrill AH 2nd, Martin RE, Anderson RE, Gardner TW, Kester M. “Diabetes alters sphingolipid metabolism in the retina: a potential mechanism of cell death in diabetic retinopathy” (DIABETES is the publication that contains the original article that provided initial data for this grant). Accepted Aug. 24, 2006.


5. Fox TE, Young MM, Pedersen MM, Han X, Gardner TW, Kester M. “Diabetes diminishes phosphatidic acid in the retina: implications for reduced mTOR signaling and increased
neuronal cell death in diabetic retinopathy” (under peer review at Investigative Ophthalmology and Visual Science).


Pennsylvania Health Care Cost Containment Council (PHC4) Disclaimer
The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency responsible for addressing the problem of escalating health costs, ensuring the quality of health care and increasing access to health care for all citizens regardless of ability to pay. PHC4 has provided data to the Pennsylvania Department of Health in an effort to further PHC4’s mission of educating the public and containing health care costs in Pennsylvania. PHC4, its agents, and staff, have made no representation, guarantee or warranty, express or implied, that the data -- financial, patient, payor and physician specific information -- provided to this entity, are error-free, or that the use of the data will avoid differences of opinion or interpretation. This analysis was not prepared by PHC4. This analysis was done by the Pennsylvania Department of Health. PHC4, its agents and staff, bear no responsibility or liability for the results of the analysis, which are solely the opinion of this entity.