

STATE OF THE CURE FOR TYPE 1 DIABETES

2019

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1: Introduction

Welcome to the 8th annual edition of *The State of the Cure for Type 1 Diabetes*. In this report, we lay out progress during 2019 toward a Practical Cure and summarize the major trends in research and funding.

At some point in their life, almost everyone living with T1D has been assured that a cure is just around the corner. But for most, a T1D cure feels like a distant fantasy. The failure of the T1D research ecosystem to deliver any cure-related innovations since the discovery of insulin over 100 years ago continues to have massive ramifications across the economy. The absence of a cure also creates an enormous strain on the individuals who manage the disease every day, as the lifetime cost of care for an individual living with T1D amounts to \$11 million.

Furthermore, these costs do not account for the physical and emotional toll of the disease. Parents of children with T1D continue to live with the constant fear of an overnight episode of hypoglycemia or diabetic ketoacidosis and people living with the disease still battle life-threatening complications and restrictively high insulin prices.

The JDCA's annual *State of the Cure* report does not offer fantasy but a detailed overview of the progress made in the last year towards a Practical Cure. It also outlines the paradigm shift necessary for the T1D research and fundraising community to deliver a Practical Cure for you or your loved one.

Right now, out of almost 600 active type 1 diabetes research trials, only 14 are testing a Practical Cure and none have progressed beyond Phase-II clinical trials. Also, money for cure-focused research spending fell to historic lows at the three largest T1D funding organizations in 2019.

If you have one takeaway from this book it should be this: **without ongoing pressure for the major T1D nonprofits and government entities to adopt, institutionalize, fund and fully resource Practical Cure research, it is unlikely it will be achieved in time to impact people currently living with T1D.**

The time to act is now.

THE GLOBAL BURDEN OF TYPE 1 DIABETES



45 million

children and adults have type 1 diabetes

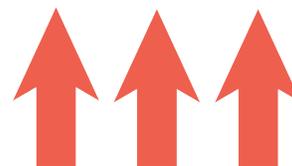
1,100,000

children have type 1 diabetes

45% of all newly diagnosed type 1 diabetes patients are children under 18



Type 1 diabetes in children is increasing by **3% annually**



\$76 BILLION

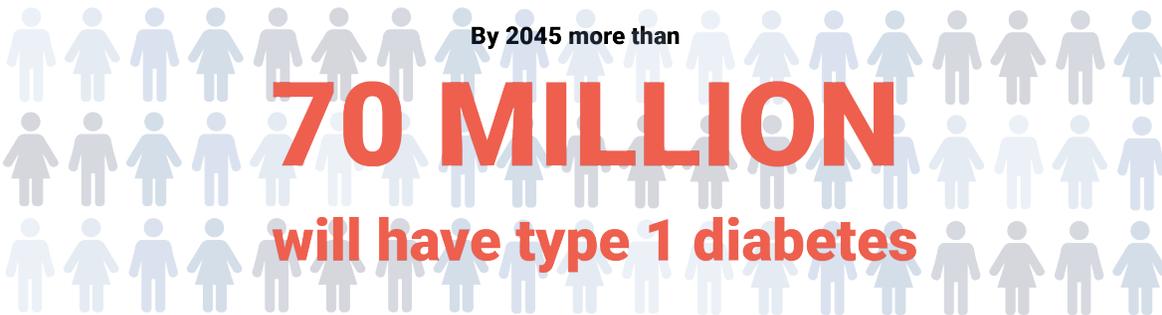
is spent on type 1 diabetes globally per year (3.5x more than 2008)

The cost of care has skyrocketed **+686%**



By 2045 more than

70 MILLION
will have type 1 diabetes



We Need a Cure NOW

Source: IDF Diabetes Atlas, 2019 and AJMC, 2019

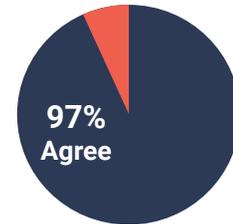
2: Donor Priorities

The vast majority of the donations that fuel the major type 1 diabetes charities come from people most directly connected to T1D— those living with type 1 as well as their family and friends. To gauge the attitudes and intentions of these T1D financial donors, the JDCA conducts and publishes annual surveys.

The key takeaways summarized below have remained consistent over the last seven years:

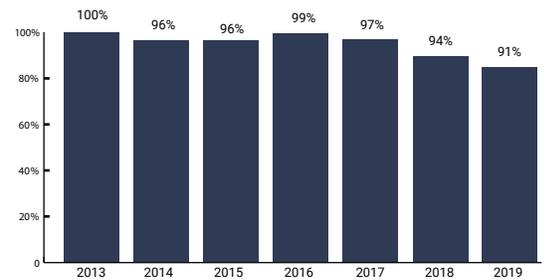
- **97%** of donors believe cure research should be the number one priority for charities. See **Chart 2a**.
- **78%** said ALL of the money raised at fundraising walks should be used for cure research. Said differently, four out of five walkers want 100% of the walk proceeds to be used for cure research.
- **91%** of donors would donate to support Practical Cure research if that option were made easily available to them. See **Chart 2b**.
- **85%** said the ADA and JDRF should seek direct donor input when making research funding decisions. Yet, few donors are represented in budget spending decisions at either organization.
- **58%** of respondents said "I will stop participating" or "I am less likely to participate" in future fundraising walks after learning how much of the ADA and JDRF income was actually used for research, indicating a potential risk for both organizations. See **Chart 2c**.

Chart 2a:
"Is cure research the primary reason you make a donation to a diabetes charity and/or participate in a fundraising activity?" Answer is percent who agree.



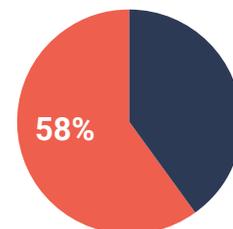
Source: JDCA Survey of Donor Sentiment, March 2019

Chart 2b:
"Would you donate to Practical Cure research projects if that option was made easily available to you?" Answer is percent who agree.



Source: JDCA Annual Surveys of Donor Sentiment, 2013-2019

Chart 2c:
Answer is percent of donors who will stop participating, or are less likely to participate, in future ADA/JDRF fundraising walks after learning JDRF spent only 37% of its annual income on T1D research and the ADA spent just 6%.



Source: JDCA Survey of Donor Sentiment, March 2019

HOW DO **T1D** DONORS WANT THEIR **MONEY** USED?



25 MILLION PEOPLE
have a family member or
a close relative with T1D
in the U.S.



Together they donate
\$450 MILLION
per year to type 1 diabetes



97%



**say they want their money
to be used for cure research**

Source: JDCA Survey of Donor Sentiment, March 2019 and JDRF and ADA Audited Financial Statements, 2018

3: Practical Cure Definition

A Practical Cure is defined as any solution which minimizes the disruptive aspects of T1D and delivers a near-normal quality of life.

A Practical Cure is different from a perfect or idealized cure in that it does not represent a reversal or complete elimination of the disease. This distinction is important. Scientists have been pursuing an idealized cure for almost 100 years but have made little to no progress. Alternatively, there are several projects in human trials that have the potential to become a Practical Cure, and there could be many more if resources and funding are significantly increased.

A PRACTICAL CURE IS OUTCOME FOCUSED

The infographic in the box on the right shows the various outcome criteria that a Practical Cure would fulfill. These include no dietary restrictions, minimal monitoring, insignificant side effects, elimination of hypos and HbA1C readings under seven percent with sustainability over time.

A PRACTICAL CURE IS TIME-BOUND

Any Practical Cure solution must have a reasonable chance of being available within the next 15 years— in time to transform the lives of people who are currently living with the disease. Considering that, on average, it requires 10-15 years from the beginning of human trials to receive FDA pre-market approval, research projects that are currently in human clinical trials have the best chance of meeting the timetable.

A time goal also provides an essential structure for prioritizing projects. Those that have already advanced into human trials should be given priority, fully funded and wholly resourced so they can move through human trials to conclusive results as quickly as possible, whether successful or not.

Clinical Requirements Needed to be a Practical Cure for T1D

- ✓ HBA1C <7%
- ✓ Minimal Monitoring
- ✓ Free Diet
- ✓ Eliminate Hypos
- ✓ Minimal Side Effects
- ✓ Less Than 10 Days in Hospital (if surgical)
- ✓ No More Than 5 Pills Per Day (if pharmacological)

4: Practical Cure Pathways

Four broad research pathways have the potential to result in a Practical Cure within the next 15 years. Certain solutions may require a combination of the pathways while others may stand on their own. All Practical Cure projects are listed and defined in full on page 9.

CELL TRANSPLANTION

Cell transplantation involves implanting islet cells, stem cells or precursor cells into a person with type 1 diabetes to achieve insulin independence. There are two main issues with cell transplantation which still need to be resolved: cell supply and cell survival. To date, the only proven source of cell supply is islet cells taken from cadavers, which have very limited availability. Research into deriving a sustainable cell supply from human stem cells has seen promising advances over the past decade and is currently being tested in humans. The remaining hurdle of increasing cell survival involves the development of an encapsulation device or sustainable long-term immune system modification to protect the cells from the body's immune response. **There are currently four active trials in human testing.**



IMMUNE SYSTEM MODIFICATION/ IMMUNOMODULATION

Immune system modification/ immunomodulation utilizes drugs or stem cell therapy to stop the body's immune system from attacking insulin-producing beta cells. Currently, immune system modification is being tested with the hope of regenerating existing beta cells remaining in the body. If regeneration proves ineffective, immune system modification would need to be combined with cell transplantation to be a Practical Cure. **There are currently ten active trials in human testing.**



GLUCOSE-RESPONSIVE INSULIN (GRI)

Glucose-responsive insulin, also known as "smart insulin," is chemically activated in response to changes in blood glucose. Smart insulin remains inactive until blood glucose rises above normal levels. At that point, the chemical component activates the insulin. Once blood glucose returns to normal, the insulin action ceases, avoiding low blood sugar. To be a Practical Cure, smart insulin would have to last long enough to eliminate the need for multiple daily injections. To date, Merck is the only company that has tested GRI in humans, and that trial failed. **There are currently no GRI trials in human testing.**



ADVANCED ARTIFICIAL PANCREAS

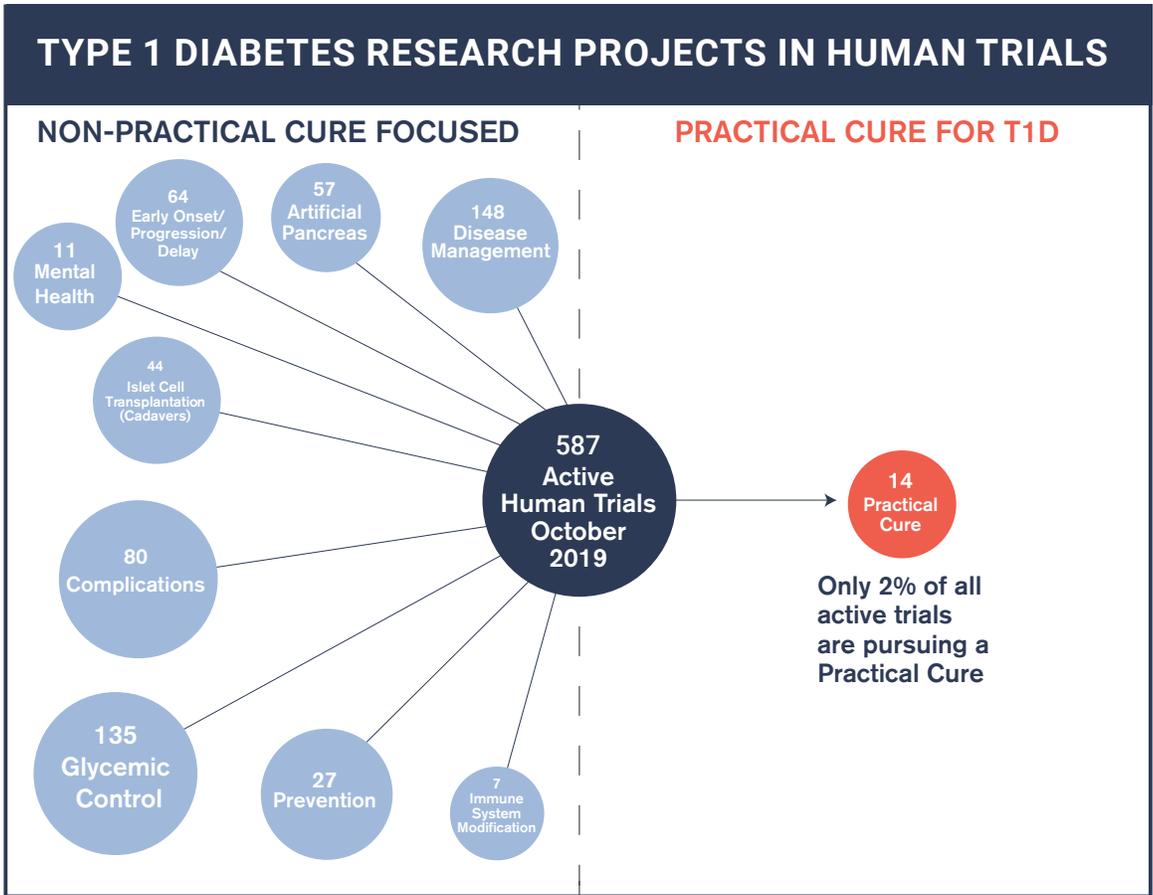
An advanced artificial pancreas is a device that mimics the glucose-regulating functions of a healthy pancreas, automatically controlling blood glucose levels and delivering insulin. In a JDCA survey of the T1D community, 88% of respondents said an artificial pancreas device would qualify as a Practical Cure if "it is small enough that you could generally forget that you are wearing it." **There are currently no trials testing an advanced artificial pancreas that meet the qualifications of a Practical Cure.**



5: Practical Cure Projects in Human Trials

There are 587 active T1D research trials in FDA-approved human trials (as of October 2019). These trials are researching a wide range of topics related to type 1 diabetes with the largest concentration working to improve glycemic control and disease management. As noted in the introduction and detailed on the following page, there are only nine Practical Cure projects currently in development. Those nine projects are being tested in 14 clinical trials (some projects are being tested in more than one trial). See **Chart 5a**.

Chart 5a:



Source: Clinicaltrials.gov

Each Practical Cure project is summarized in the charts on the following page and organized by project pathway. Please note that the JDCA presents these projects without any indication of preference or ranking. To qualify as a Practical Cure, all trials must target an increase in C-peptide production as a primary or secondary endpoint measure. C-peptide is commonly used as an indicator of insulin production. The trial must also be testing patients with fully established T1D (C-peptide \leq .5 ng/mL + one year past original diagnosis based on ADA diagnosis criteria— the point when the body is no longer able to produce its own insulin).

Two projects have been removed since the JDCA's last publication of Practical Cure projects: "T1D Immunotherapy" at UCSF and "Reversing Established Type 1 Diabetes" at University of Florida. Both projects completed and published unsuccessful results.

Active Practical Cure Projects by Pathway



CELL TRANSPLANT



Beta O2 BAir Bio-Artificial Pancreas
Uppsala University Hospital
Uppsala, Sweden

Phase: I/II

Active, Not Recruiting
Estimated Completion: May 2019

Description

Islet cells are encapsulated in a device the size of a hockey puck, which is implanted in the abdomen. Requires daily oxygen injections.



PEC-Encap
Viacyte
San Diego, CA

Phase: I/II (3 Trials)

Recruiting
Estimated Completion: March 2022

Description

Precursor cells, derived from an embryonic stem cell line, mature into functional beta cells when implanted under the skin. Cells are protected by an encapsulation device.



IMMUNE SYSTEM MODIFICATION / IMMUNOMODULATION



Stem Cell Educator
Tianhe Stem Cell Biotech
Hackensack, NJ

Phase: I

Recruiting
Estimated Completion: August 2022

Description

A patient's blood is passed through a machine which, through exposure to cord blood stem cells, re-trains the regular blood cells to cease the autoimmune attack.



Ustekinumab
Jewish General Hospital
Montreal, Canada

Phase: I

Completed March 2018
Results Not Yet Posted

Description

INGAP-P to induce beta cell regeneration combined with Ustekinumab for auto-immune modulation. Drug combination.



Monotherapy with Rapamycin
Fondazione Italiana Diabete Onlus, Italy

Phase: II

Recruiting
Estimated completion: March 2019

Description

Rapamycin to modulate immune system by reducing IL2. Vildagliptin to promote beta cell regeneration. Drug combination.



OMEGA-3 & Vitamin D in High Dose
DRI/ University of Miami
Miami, FL

Phase: I/II

Recruiting
Estimated completion: December 2023

Description

Combination of Omega-3 and Vitamin D is designed to halt immune system response and preserve residual B-cell function. Two oral drugs.



Umbilical Cord Blood Regulatory T Cells Plus Liraglutide
Second Xiangya Hospital
Hunan, China

Phase: I/II (4 trials)

Recruiting
Estimated Completion: November 2019

Description

Infusion of regulatory T cells grown from umbilical cord blood to control immune response. Liraglutide to stimulate beta cell growth.



TOL-3021
Tolerion
Portola Valley, CA

Phase: II

Recruiting
Estimated Completion: December 2023

Description

Vaccine designed to selectively repress T cells inappropriately activated in type 1 diabetes.



Liraglutide or Golimumab
Benaroya Research Institute
Seattle, Washington

Phase: I

Recruiting
Estimated completion: April 2020

Description

Liraglutide works to increase insulin release from the pancreas and decrease excessive glucagon release. Golimumab decreases inflammation caused by autoimmune attacks.

6: Cure Research Spending

The three organizations that fund most of the type 1 diabetes research conducted in the United States are JDRF, the American Diabetes Association (ADA), and the National Institutes of Health (NIH). JDRF and the ADA are non-profit organizations unaffiliated with the government, while the NIH is a US government agency.

The main takeaway from this section is T1D research spending has been cut dramatically over the past decade at JDRF as well as the NIH and has remained at immaterial levels at the ADA.

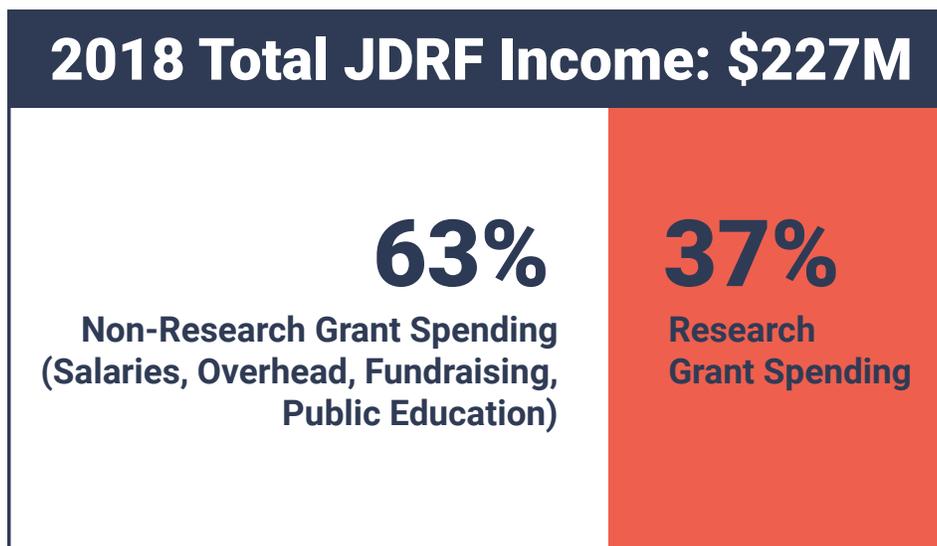
JDRF

Founded in 1970 with a mission of finding a cure for T1D, JDRF has grown to become one of the largest and most influential type 1 diabetes organizations in existence. *With chapters throughout the world and strong relationships with all the principal investigative research centers, JDRF is uniquely positioned to bring about a T1D research breakthrough.*

During 2018, JDRF only spent 37% of their total annual income on T1D research grants. The other 63% went to non-research grant expenses such as salaries, overhead, fundraising, administration and public education costs. See **Chart 6a**.

Chart 6a:

JDRF Research Grant Spending Vs. Non-Research Grant Spending

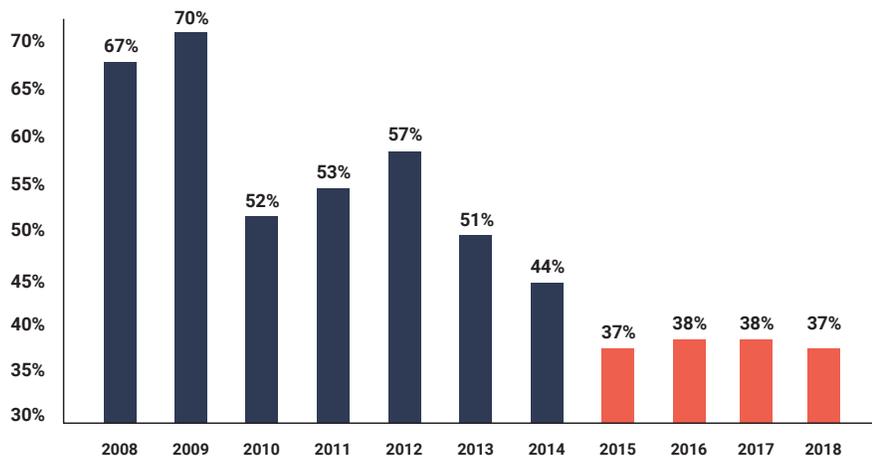


Source: JDRF Audited Financial Statements

JDRF Research Spending and Operating Costs

Up to 2009, research expenditures were consistent with the organization's mission where the majority of income was used to fund research grants. Since then, research spending has steadily declined to an all-time low. See **Chart 6b**.

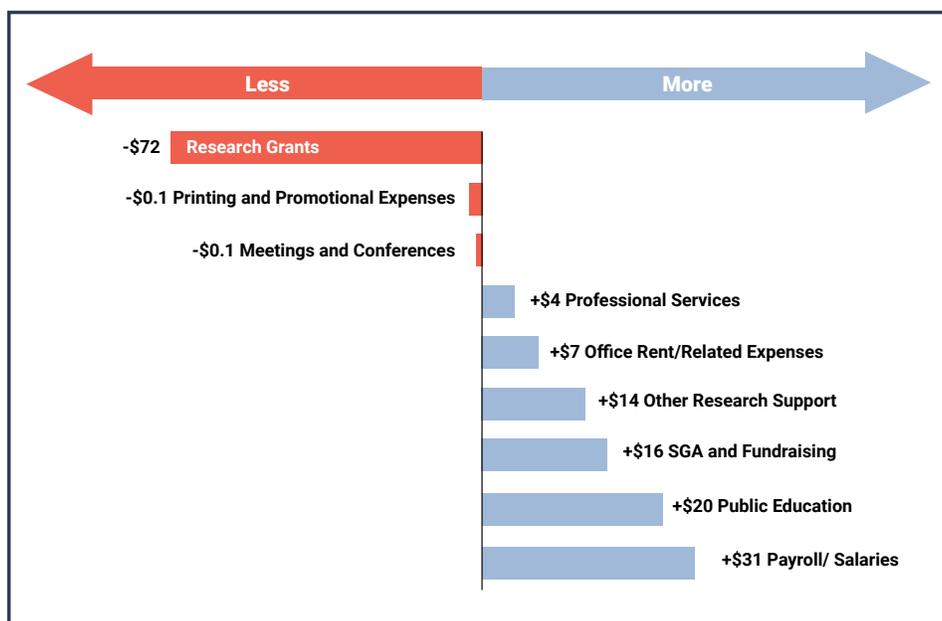
Chart 6b:
JDRF Research Grants as a Percent of Annual Income



Source: JDRF Audited Financial Statements

While research grant spending was cut in half, almost all other JDRF spending categories have increased, with salaries and payroll rising the most. Over the past ten years, JDRF payroll expenses have more than doubled. See **Chart 6c**.

Chart 6c:
2008 vs. 2018 JDRF Annual Spending Change (in millions)

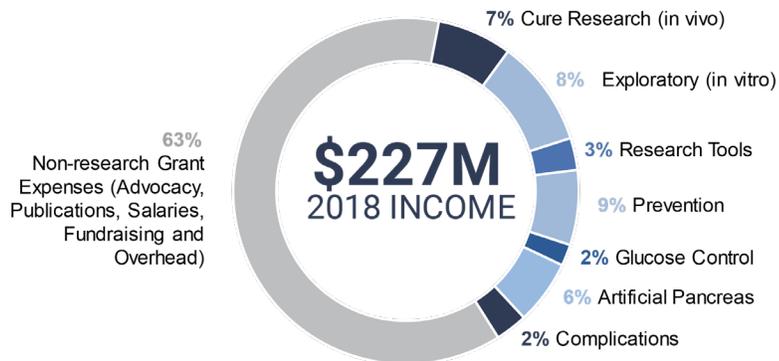


Source: JDRF Audited Financial Statements

JDRF Cure Research Spending

The JDCA reviewed every grant funded by JDRF during 2018, 451 projects in total. Of the \$85m JDRF used for research grants only 7% (\$6m) was spent on cure research in humans or animals in 2018. See **Chart 6d**.

Chart 6d:
JDRF Utilization of 2018 Annual Income Highlighting Research Grant Categories



Source: JDRF Audited Financial Statements and JDRF Grant Center

Furthermore, cure research spending declined 45% from 2014. Comparatively, prevention research has grown to be the biggest funding area of any research category, a concerning shift of focus away from people living with established T1D. See **Chart 6e**.

Chart 6e:
JDRF Research Grant Categories as % of Income by Year

Utilization % of JDRF Income by Year

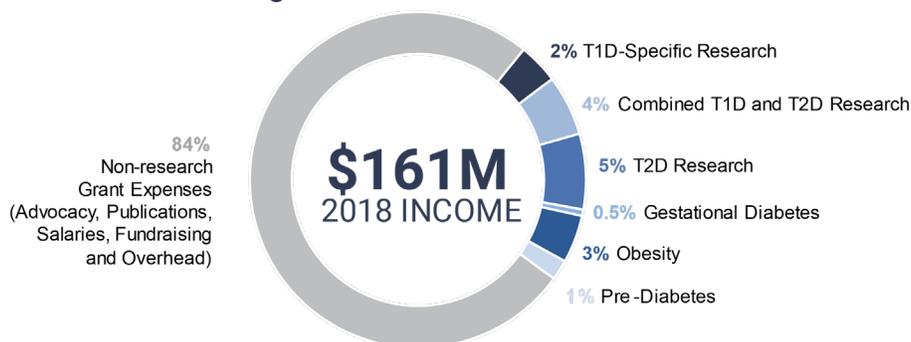
Research Categories	2014	2015	2016	2017	2018
Cure Research (in vivo)	12%	7%	7%	7%	7%
Basic and Exploratory (in silico/in vitro)	5%	10%	13%	10%	8%
Research Tools	6%	3%	4%	3%	3%
Prevention	4%	2%	6%	7%	9%
Glucose Control	4%	2%	1%	2%	2%
Artificial Pancreas	7%	7%	4%	6%	6%
Complications	5%	4%	3%	3%	2%
Unidentified	2%	2%	n.a.	n.a.	n.a.
Total	45%	37%	38%	38%	37%

The American Diabetes Association

The ADA was founded in 1940 with the mission of finding a cure for all types of diabetes. The ADA remains one of the largest and most powerful diabetes organizations in the world, but the organization almost exclusively dedicates its resources to type 2 diabetes and spends very little on type 1, despite claims of focusing on both equally.

In 2018, the ADA posted revenue of \$161 million, up from \$150m in 2017, raised primarily from donations and fundraising event proceeds.

Chart 6f:
ADA Utilization of 2018 Annual Income Highlighting Research Grant Categories



Source: ADA Audited Financial Statements

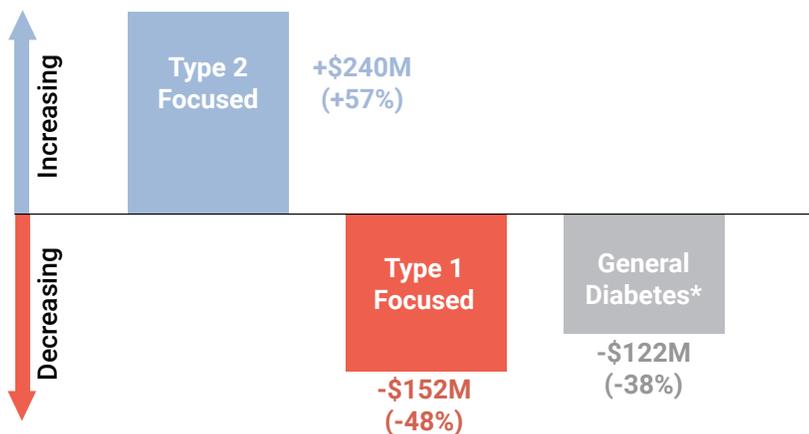
Despite the increase in total revenue, research grant spending dropped dramatically from \$37m (24% of total revenue) in 2017 to only \$27m (16%) in 2018, a historic ten-year low. Furthermore, only 2% of the ADA's 2018 income was allocated specifically to T1D research. This means for every dollar given to the ADA, only two cents were used for T1D research. See **Chart 6f**.

The ADA has an outstanding fundraising infrastructure, strong ties on Capitol Hill and access to researchers throughout the world. If the ADA were to commit to a substantial investment and increase their focus on type 1 diabetes, the impact would be monumental.

The National Institutes of Health

The JDCA categorized every grant awarded by the NIH over the past three years. In total, the NIH spent roughly \$1 billion on diabetes research in each year. However, funds allocated to type 1-focused research were cut in half from \$320 million in 2016 to \$168 million in 2018. At the same time, type 2-focused research increased from \$419m to \$659m. See **Chart 6g**.

Chart 6g:
NIH Diabetes Research Funding Change by Focus Area 2018 vs. 2016
(in millions)



*Projects which include non-specific diabetes research: complications, insulin, and base epidemiological research.

Source: NIH Research Grants: 2714 grants reviews individually

The decrease of T1D funding and reallocation of resources to T2D has become increasingly common across the diabetes research ecosystem, but it is still surprising to see how strong that trend was reflected at the NIH in 2018. The JDCA contacted the NIH in response to the decline and an official NIH representative responded the NIH does not track type 1 or type 2 funding, *“the NIH only reports ‘diabetes’ funding as a whole.”*

In 1998, the United States government created a program to ensure a certain amount of money is used for T1D yearly— the Special Statutory Funding Program for Type 1 Diabetes Research (SDP). The practical impact of the program is that it sets a bottom floor for the minimum amount of money the NIH must spend on T1D specific research. For the first time in 2018, SDP reached this \$150m bottom floor and nearly all the money used for T1D specific research was provided by SDP.

The fund has been approved for 2020 but will come up again for a vote next year. **Although there is no question the continuation of SDP funding is vital for T1D research, we must not overlook the fact that the level of T1D specific research funding at NIH was cut in half over the past two years.**

In order to restore NIH T1D research funding, we as a T1D community must speak loudly, clearly and above all as a unified voice. For donors, this means actively voicing a desire for an increase in T1D research funding directly to your state and federal representatives as well as advocates like the ADA and JDRF.

7: Fundraising for T1D

The ADA and JDRF are the two largest fundraisers for diabetes in the world. Each organization has built an extremely effective fundraising apparatus that combines professional staff with highly passionate volunteers. Both utilize campaigns that are executed on a national and local chapter level in cities throughout the United States.

Combined, the two organizations hosted 231 fundraising events in 2019, including walks, rides and galas, which generated over \$244 million in donations. These events are the primary source of funding for both organizations, delivering 3/4 of JDRF's annual income and 1/2 of the ADA's annual income.

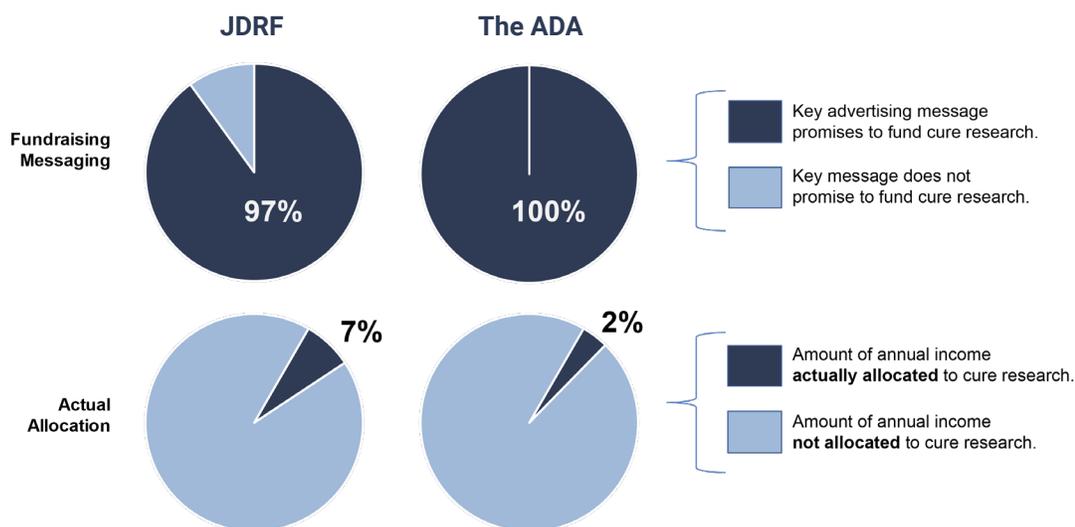
Most of these events either explicitly or implicitly communicate that the proceeds will be used for cure research. In fact, many familiar event names feature a cure message, including *JDRF One Walk for a World Without Type 1 Diabetes*, *Ride to Cure Diabetes*, *Team JDRF to Cure Diabetes*, *Tour de Cure* and the *Step Out Walk to Stop Diabetes*.

In 2019, 97% of all JDRF national fundraising events featured a cure message, a number consistent with prior years. Yet, only 7% of JDRF's annual income was utilized for cure research. The ADA featured a cure message in 100% of its 2019 events, but only an estimated 2% of annual income was used specifically for T1D research. See **Chart 7a**.

In summary, the fundraising promise remains unaligned with the way proceeds are actually used.

97% of all JDRF national fundraising events featured a cure message. Only 7% of JDRF's annual income was utilized for cure research.

Chart 7a:
2019 National Fundraising Messaging Compared to Actual Allocation



Source: JDRF and ADA websites and promotional materials. 282 national events reviewed individually.

8: Donating with Impact

When making an individual donation, the 4S's of Good Giving provides a powerful, straightforward and easy-to-implement approach that will help to ensure your generosity is used the way it is intended. See **Chart 8a**.

Chart 8a:

The 4S's of Good Giving



Strategy:

The first and most important step is to clearly state what impact you want your gift to deliver. If you are one of the 97% who want their gifts used to fund cure research, your objective is to give a gift that is actually used for cure research—any other application would be off strategy.

Select:

There are many fantastic organizations within the T1D community. These can be broken down into three basic groups: (1) major charities such as the ADA and JDRF; (2) medical research centers (either with a national presence or in your local area); (3) specific research projects. Choose the one that is most capable of delivering your strategy.

Specify:

When giving to a charity, the only way to ensure your money is used the way you want it to be used is to specify in writing.

Write a letter along with your gift specifically stating how the donation should be used. For example: "This donation in the amount of \$XX is to be fully used to fund cure research grants." If the recipient is not willing or able to use the money to fund cure research, they are obligated to return the money. The JDCA also provides cutout donation cards on the next page that you can use to specify that your gift should be used for T1D cure research.

Substantiate:

Every donor has the right to ask how a previous donation was used. This information can help you determine whether you want to continue or adjust your giving strategy. Asking how your gift is used also keeps the recipients on their toes and reminds them they are accountable and dependent upon you, the donor.



Juvenile Diabetes
Cure Alliance
The Voice of the Donor For a Cure