

Experiences for the DAISY/TEDDY/ASK Cohorts

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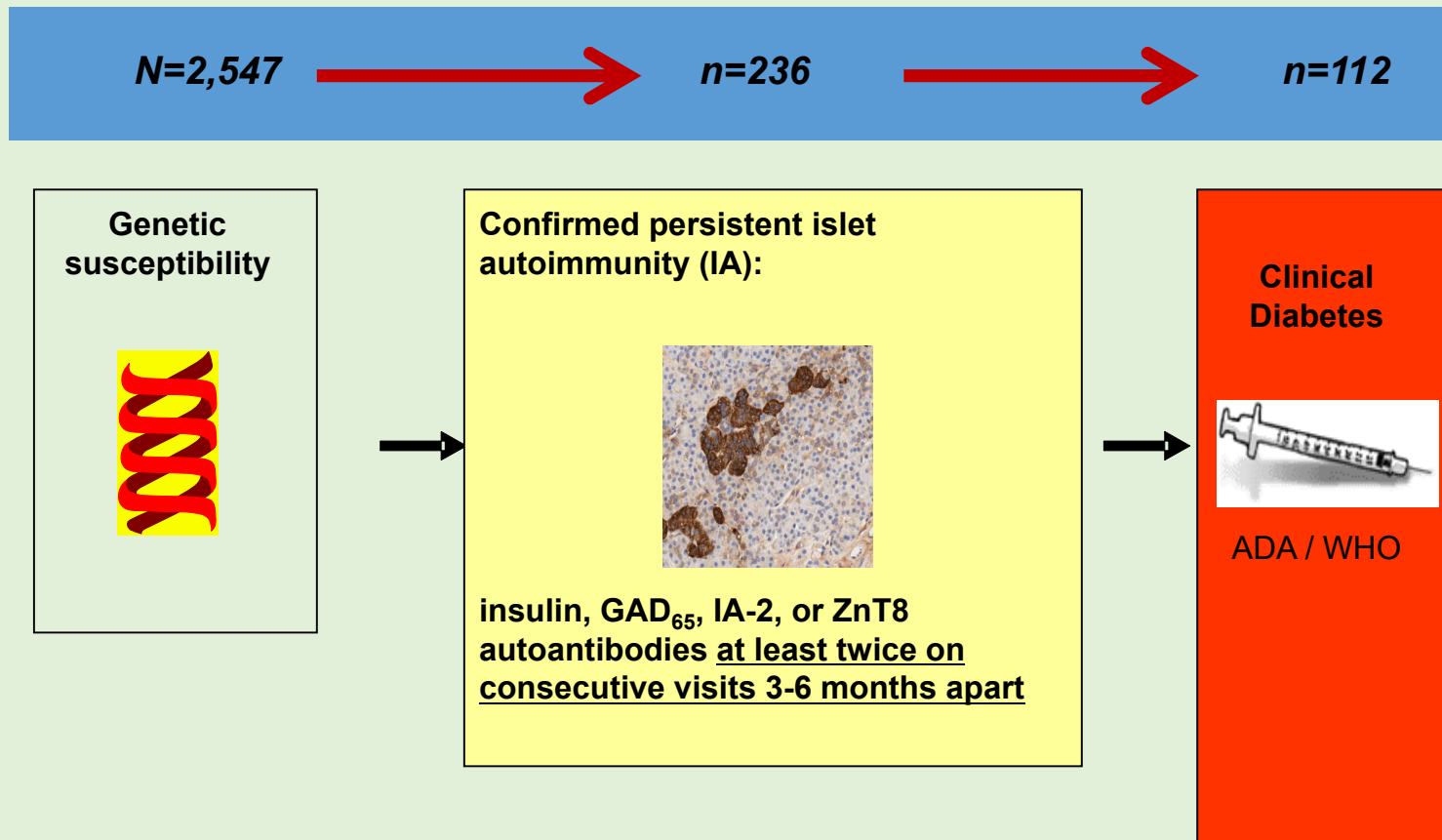
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Research Instructor

Experiences from Follow-Up

- Study Overview
- Case Review
- Challenges and Successes
 - DAISY: Michelle Hoffman
 - TEDDY: Tricia Gesualdo
 - ASK: Kim Bautista
- Lessons Learned

Development of islet autoimmunity and T1D

DAISY 1993-2022



Case Review #1: FDR, MAB+

- Male enrolled at birth
- Non-Hispanic White ^{RMJ0}
- HLA DR X/X (low risk)
- Dual participant DAISY/ TrialNet (Oral Insulin arm) ^{RMJ2}

Diagnosis:

- Age 20.5
- In Clinic RG 167 asymptomatic
- A1c 6.9

Referred to BDC Adolescent Clinic

- Home glucose testing (HGT) X 1 week
- Random glucoses ≥ 200
- Developed decreased energy, increased thirst



Slide 4

RMJ0 Enrolled at birth

Rewers, Marian J, 2022-11-06T14:33:32.139

RMJ1 Unclear which clinic - BDC? Primary care?

Rewers, Marian J, 2022-11-06T14:34:31.185

RMJ2 Please emphasize that while the two cases may not be typical of "childhood diabetes" you picked them to illustrate that:

1) islet autoantibodies can develop after 15

2) T1D diagnosed in young adults starts as islet autoimmunity in childhood

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DATE	GAD	IAA	IA-2	ZnT8	RG	A1C	RMJO
12/18/96	-1.017	30	-0.002				
5/21/97	0.026	37	0.001				
9/3/97	-0.014	24	-1.012				
9/9/98	-0.035	12	-0.002				
Yearly	Neg	Neg	Neg				
10/28/11	0	0.007	0	-0.009			
12/27/12	483	0.004	416	-0.004			
5/31/13	609	0.006	357	-0.001	95	5.6	
9/20/13	356	0.003	296	-0.001	77	5.5	
12/20/13	197	0.004	320	0.006	96	5.8	
3/14/14	214	0.007	353	-0.004	99	5.9	
7/22/14	168	0.015	324	0.017	81	5.5	
10/20/14	207	0.014	339	0.031	104	5.9	
2/6/15	217	0.011	396	0.014	72	5.5	
6/12/15	175	0.016	295	0.086	97	5.9	
10/13/15	165	0.021	393	0.13	80	5.7	
12/22/15	126	0.002	376	0.032	102	5.8	
3/21/16	219	0.004	645	0.054	89	6.0	
6/20/16	105	0.007	255	0.089	94	6.1	
9/8/16	104	0.007	315	0.021	167	6.9 *	

Slide 5

RMJO

Nobody is using term BDC512

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OGTT results CGM results

DATE	-10	0	Average -10/0	30	60	90	120	A1c	Status	RMJO
12/20/13	95	96	96	142	139	136	110	5.4	Normal	
7/22/14	93	88	91	162	160	132	112	5.6	Normal	
CGM 2/6/15	84	84	84	138	170	162	111	5.5	Normal	
6/12/15	94	90	92	146	114	133	139	5.6	Normal	
12/22/15		102					119	5.8	Stage 2	
6/20/16		92					128	6.1	Stage 2	

DATE 2/6/15 CGM

% in Target (140): **96**

% in Hyperglycemia (140): **1**

2 Peaks > 200: **0**

Slide 6

RMJO

Lower table reformatted;

Age , -10/0 rounded

Stage 2 added

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Challenges

- Protocol: CGM difficulties, dual participation
- Life Complexity: busy life, scheduling difficulty
- Avoidance: Home glucose testing

Successes

- Staff Support/Trust in Research: Persistence in contact attempts, clinician consistency
- Knowledge: Accurate risk perception, fam hx T1D
- Access to study: Lived locally throughout study
- Tools to Monitor: HGT supplies

Case Review #2: FDR, MAB+

- Female
- HLA DR 4/4 (moderate risk)
- Non-Hispanic White
- Refused dual participation DAISY/TrialNet

Diagnosis:

- Age 22.3 y
- Moved home post-graduation
- Parent noted symptoms immediately
 - Weight loss, polydipsia, polyuria, lack of energy
 - Home glucose 460
- ER glucose 485, A1c 12.2
- No DKA

DATE	GAD	IAA	BDC512	ZnT8	RG	A1C
8/18/00	-0.008	-0.003	0.004	-0.002		
8/10/01	-0.012	-0.01	-0.003	0		
8/22/02	-0.035	-0.005	-0.009	-0.001		
10/3/03	0.062	-0.015	0.005	0.001		
12/13/03	0.026	-0.007	-0.003	0.001	78	5.2
6/25/04	-0.048	0.001	-0.002	0.02	86	5.5
6/17/05	0.091	-0.005	-0.036	-0.002	101	5.2
9/9/05	0.299	0.001	-0.002	-0.002	107	4.9
4/21/06	0.477	0.001	-0.015		56	5.3
12/1/06	0.224	0.002	-0.013	-0.005	99	5.4
6/13/07	0.579	0.001	0.001	0.005	105	5.7
1/18/08	0.543	-0.003	0.019		89	5.2
12/1/08	0.234	0.004	-0.002		100	5.7
9/2/09	0.25	0.003	0.006		127	5.6
8/4/10	343	0.002	175	0.001	115	5.7
12/20/10	360	-0.005	228		92	5.6
3/17/11	376	0.001	145		90	5.4
7/29/11	292	0.001	206	0.006	98	5.3
11/4/11	310	0.003	200	-0.007	81	5.7
4/24/12	256	-1.001	235	-0.005	92	5.7
8/3/12	250	-0.002	174	-0.006	108	5.6
2/15/13	376	0.004	385	0.002	72	5.6
7/19/13	226	-0.002	353	-0.002	112	5.6
3/30/15	127	0.001	209	-0.003	102	5.6
8/7/15	121	0.001	165	0.004	99	5.7
4/29/16	155	-0.003	195	-0.007	115	6.0
12/20/16	78	-0.004	148	0.002	99	6.1

Challenges

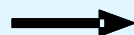
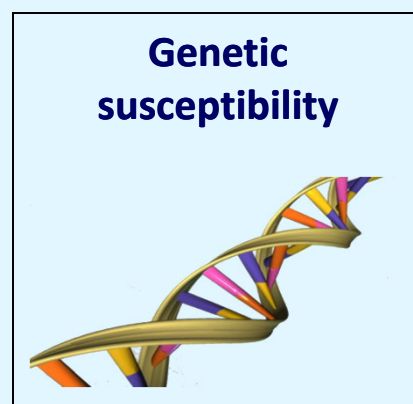
- Family Dynamics:
 - Difficult relationship with diabetic parent, Transition from parent-directed participation to independent
- Personal:
 - Body image disturbance
 - Denial/invincibility
- Protocol Adherence: Refused OGTTs/CGMs, home glucose testing
- Life change: Move out of state, refused long distance participation

Successes

- Family Dynamics: Maternal Involvement
- Staff Support/Trust in Research: Relationship with staff, social Work and dietician involvement
- Tools to Monitor: Provided testing supplies, frequent reminders to test



The Environmental Determinants
of Diabetes in the Young



Primary endpoint

Confirmed persistent islet autoimmunity:

GADA, IA-2A or IAA (+ZnT8A)
at least twice 3 months apart & confirmed in the
second laboratory



Primary endpoint

**Clinical
diabetes**

ADA / WHO



8676 enrolled

n=858

n=438

1368 enrolled (Colorado)

n=130

n=79

Case Review #1

- 8yo FDR female
- IAA+ at 21months
- 6-12 month gap between visits
- No OGTTs; home glucose unknown
- At Dx: HbA1c 7, no symptoms/No DKA



Visit Type	Visit Date	GAD	IA-2	IAA	RBG	A1C
3 month	8/10/2007	0.013	-0	0		
6 month		0.001	-0	-0		
9 month	2/23/2008	0.003	-0.01	0		
18 month	1/5/2009	-0	0.006	0.003		
21 month	3/6/2009	-0	0	0.017		
30 month	12/7/2009	0.114	0.046	0.05	101	5.1
33 month	2/23/2010	204	25	0.039	103	4.9
36 month	5/17/2010	402	53	0.057	98	5.1
39 month	9/13/2010	302	54	-0	105	5
42 month	12/6/2010				90	4.9
4.25 year	9/12/2011	296	166	0.057	86	5
5 year	5/21/2012	283	288	0.015	82	4.9
6 year	7/2/2013	194	422	0.02	90	5.1
7 year	4/24/2014	100	220	0.011	82	5.3
7.25 year	Did not complete					
7.5 year	Did not complete					
7.75 year	Did not complete					
8 year	7/6/2015	45	280	0.013	136	7
Post dx	9/14/2015	71	236	0.035	319	7.8

Case Review #1

Challenges

Behavioral:

- Needle phobia
- Generalized anxiety disorder/OCD

Family:

- 2 young children in TEDDY
- Parents work full-time

Study protocol:

- Infrequent TEDDY visits
- Travel to BDC

Successes

Staff Support:

consistency/persistence

Family: Probable intuition at dx

Tools to Monitor:

- Pediatrician involvement

TEDDY Case Review #2

- 16 yo male: GP
- Long distance protocol
- Withdrew at 3 years
- Re-enroll at 14.5 years
 - GAD and IAA +
- Completed TEDDY at 15 years
- Enrolled in TEDDY Grad
- Current HbA1C 5.7



<u>Visit Date</u>	<u>Visit Type</u>	<u>GAD Result</u>	<u>IA-2 Result</u>	<u>IAA Result</u>	<u>ZnT8 Result</u>	<u>RBG</u>	<u>A1C</u>
12/27/2006	3 month	0.015	-0.005	-0.003			
3/7/2007	6 month	0.004	0	0.004			
6/8/2007	9 month	0.003	-0.001	-0.002			
9/8/2007	12 month	0.011	-0.001	0.001			
12/15/2007	15 month	-0.001	-0.002	-0.002			
3/3/2008	18 month	-0.002	-0.001	0.001			
6/9/2008	21 month	0.004	-0.002	0.001			
9/6/2008	24 month	0.006	-0.002	0.002			
12/6/2008	27 month	-0.003	-0.002	-0.001			
2/28/2009	30 month	-0.001	-0.001	0.001			
6/13/2009	33 month	0	0	0			
9/19/2009	36 month	-0.007	-0.001	0.002			
3/18/2021	14.5 year	490	0	0.012	0.001		5.4
6/16/2021	14.75 year	613	0	0.013	-0.003	69	5.4
10/22/2021	15 year	372	0	0.012	0		5.6

<u>Visit Date</u>	<u>Age</u>	<u>GAD</u>	<u>IAA</u>	<u>ZnT8</u>	<u>A1c</u>
3/30/2022	15.56	591	0.01	-0.002	5.7
8/2/2022	15.90	591	0.007	-0.001	5.7

<u>Visit Date</u>	<u>Visit Type</u>	<u>Age</u>	<u>GAD</u>	<u>ECL GAD</u>
3/30/2022	Every 3 mo	15.56	591	0.655
8/2/2022	Every 3 mo	15.90	591	0.874

Slide 16

RMJO Split in 2 slides and follow DAISY template
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Case Review #2

Challenges

Location: Lives in Michigan: LDP lab

Study protocol:

- 11 year gap in participation
- Underestimation of risk
- Minimal connection to TEDDY Staff
- “I've never met anybody from the TEDDY program”
- No interest in TrialNet

Family:

- Teenager
- Sibling now AB+

Successes

Study protocol:

- Ab testing before the 15 year visit

Family:

- Involved parents
- Sibling tested in ASK and AB+; referred to ASK the Experts

Autoimmunity Screening for Kids (ASK) Education and Monitoring Denver, Colorado

303-724-1ASK | ASKhealth.org
1 2 7 5

Autoimmunity Screening for Kids
ask 
FREE
A SIMPLE TEST TO DETECT
Childhood Diabetes + Celiac

Approved by the Colorado Multiple IRB #14-0553 Marion J Rovers, MD, PhD



Sponsors:

JDRF IMPROVING
LIVES.
CURING
TYPE 1
DIABETES.

THE LEONA M. AND HARRY B.
HELMSLEY
CHARITABLE TRUST

janssen  PHARMACEUTICAL COMPANIES
OF **Johnson & Johnson**

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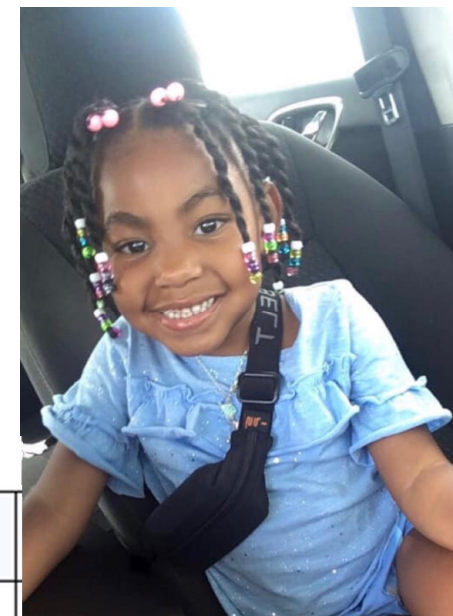


Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Case Review #1

GP, MAB+

- Demographics
 - African American, female, screened at DH East Side clinic
- Screened at the age of 2y9m and DX at 6y3m
- DX Info: 4/2021, HbA1c 7.0%, home BG 319, no sx, no DKA



T1D Antibodies

Date	Visit	GAD	GAD ECL	IA-2	IA-2 ECL	IAA	IAA ECL	ZnT8	ZnT8 ECL	RBG	A1C
10/13/2018	Screening	395	0.649	273	0.118	0.151	0.228	-0.005			
11/7/2018	Confirmation	322	0.207	447	0.231	0.218	0.157	0.01		120	5.2
2/15/2019	Baseline	234	0.101	193	0.097	0.231	0.114	-0.002		106	5.1
4/29/2019	Follow-up 2 <i>OGTT CGM</i>	262	0.035	248	0.026	0.209	0.106	-0.005		102	5.4
9/10/2019	Follow-up 3 <i>CGM</i>	195	0.051	275	0.038	0.273	0.14	0.001		112	5.3
1/10/2020	Follow-up 4	122	0.081	382	0.18	0.228	0.087	0.005		104	5.3
9/16/2020	Follow-up 5 <i>CGM</i>	124	0.1	337	0.657	0.187	0.421	0.018	0	100	5.5
4/13/2021	Follow-up 6 <i>CGM</i>	135	0.092	376	0.259	0.263	0.058	0	0.009	90	7

OGTT, CGM & A1c Results

Date	Protocol	Result	Fasting BG	2h BG	Time >140	Peaks ≥200	Average glucose	A1c
Apr 2019	OGTT clinic		93	Failed				
May 2019	CGM	Normal			0.8%	no	100	5.4%
Sept 2019	OGTT home		Failed	Failed				
Sept 2019	CGM	Normal			1.9%	no	99	5.3%
Sept 2020	CGM	Impaired			14.1 %	no	120	5.5%
Apr 2021	CGM placed, started insulin	Dx Stage 3						7.0%



Challenges

- Behavioral: Blood draw anxiety/needle phobia
- COVID: Unresponsive
- Life Change: New baby=non-adherence to HGT

Successes

- Staff Support/Trust in Research: Persistence in contact attempts, clinician consistency
- Knowledge: Accurate risk perception
- Action: Response to contacts/timing



Case Review #2

GP, MAB+

- Demographics
 - Hispanic, male, screened at CHC South
- Screened at the age of 8y10m and DX at 10y5m
- DX Info: 4/2021, HbA1c 5.7%, home BGs 229 & 277, polyuria and polydipsia , no DKA, COVID at time of dx so dx completed via telemed



T1D Antibodies

Date	Visit	GAD	GAD ECL	IA-2	IA-2 ECL	IAA	IAA ECL	ZnT8	ZnT8 ECL	RBG	A1C
8/4/2017	Screening	195	0.077	0	-0.002	0.009	0.003	-0.003			
9/5/2017	Confirmation	273	0.082	0	0	0.011	0.004	-0.003		96	5.5
10/2/2017	Baseline	261		0		0.011		-0.002		109	5.5
3/12/2018	Follow-up 2	261	0.148	0	0.003	0.012	0.003	-0.004		100	5.2
6/18/2018	Follow-up 3	246	0.081	11	0.098	0.011	0.004	-0.005		110	5.3
10/30/2018	Follow-up 4	267	0.161	311	0.195	0.02	0.009	-0.002		102	5.1
12/3/2020	Follow-up 6	135	0.12	227	0.297	0.027	0.039	0.002	0.008	93	5.7
3/18/2021	Follow-up 7 OGTT CGM	104	0.105	248	0.046	0.036	0.009	0.004	0.001	109	5.7

*Came in for a clinic visit Jan/2019, refused bd, but wore CGM

OGTT, CGM & A1c Results

Date	Protocol	Result	Fasting BG	2h BG	Time >140	Peaks ≥200	Average glucose	A1c
Jan 2019	CGM	Normal			10%	No	116	BD skipped, no A1c
March 2021	OGTT	Impaired	106	152				5.7
March 2021	CGM	Impaired			33.9%	Yes	137	5.7

Challenges

- Behavioral: Blood draw anxiety/needle phobia
- Family Dynamics: Parental substance abuse and domestic violence
- Life Change: Parent incarcerated

Successes

- Staff Support: Persistence in contact attempts/Clinician Consistency
- Family: Mat GMA became guardian
- Tools to Monitor: Home glucose teaching
- Knowledge: Accurate risk perception
- Action: HGT adherence

Lessons Learned

- Each study has informed the next
- Guided development of large-scale screening and monitoring efforts
- Important to keep reaching out using various methods
- Meet families where they are, to discover what monitoring activities are most feasible for them.
- Even when we think families aren't "hearing" us, they are...
- Staff trained and experienced in early T1D monitoring