Washington State Health Care Authority

Health Technology Assessment Clinical Committee Meeting Program Update

Leah Hole-Curry, JD

Health Technology Assessment

March 18, 2011

Presentation Overview

- **HTA Program Overview**

- **HTA Program Updates**
  - Topics

Today's Topic

- Glucose Monitoring for insulin dependent individuals under 19
- Spinal Injections

Governor Gregoire's strategy : Improve quality in health care

- **Governor Gregoire's five point plan to improve health care (2005)**
  - *Emphasize evidence based health care*
    - Create more transparency in the health care system
    - Promote prevention, healthy lifestyles, and healthy choices
    - Better managed chronic care
    - Make better use of information technology
- **WA State Legislature and Blue Ribbon Commission (2006)**
  - Goals set for 2012 including use of evidence based medicine
- **Collaboration of Programs across State purchasing –**
  - Total of about 450,000 beneficiaries and 3.5 billion purchased
  - Health Care Authority – Public Employees and subsidized low income (Basic Health, **Uniform Medical Plan**, PEBB)
  - **Medicaid** Purchasing Agency – federal/state low income health care program with **fee for service** and managed care plans
  - Labor and Industries – **Worker's compensation** program
  - Department of Corrections – Correctional health care

Why Health Technology Assessment?

- **Part of an overall strategy**
- **Medical technology is a primary driver of cost**
  - The development and diffusion of medical technology are primary factors in explaining the persistent difference between health spending and overall economic growth.
  - Some health experts arguing that new medical technology may account for about one-half or more of real long-term spending growth.

    Kaiser Family Foundation, March 2007: **How Changes in Medical Technology Affect Health Care Costs**
- **Medical Technology has quality gaps**
  - Medical technology diffusing without evidence of improving quality Highly correlated with misuses, overutilization, underutilization.

    Cathy Schoen, Karen Davis, Sabrina K.H. How, and Stephen C. Schoenbaum, "U.S. Health System Performance: A National Scorecard," *Health Affairs*, Web Exclusive (September 20, 2006): w459

KEY HTA Products

Pay for What Works: Better Information is Better health

- **<u>Transparency:</u> Publish topics, criteria, reports, open meeting**
- **<u>Technology Assessment Report</u>: Formal, systematic process to review appropriate healthcare technologies.**
- **<u>Independent Coverage decision</u>: Committee of practicing clinicians make decisions that are scientifically based, transparent, and consistent across state health care purchasing agencies.**

Key focus questions:

- Is it safe?
- Is it effective?
- Does it provide value (improve health outcomes)?

HTA Program Elements

1. **HCA Administrator Selects Technology**

Nominate, Review, Public Input, Prioritize

↓ *Semi-annual*

2. **Vendor Produce Technology Assessment Report**

Key Questions and Work Plan, Draft, Comments, Finalize

2-8 Months ↓

3. **Clinical Committee makes Coverage Determination**

Review report, Public hearing

↓ *Meet Quarterly*

4. **Agencies Implement Decision**

Implements within current process unless statutory conflict

Evidence for use in Policy Decisions

Different Data Sources

- **Efficacy**
  - How technology functions in “best environments”
    - Randomized trials-distinguish technology from other variables
    - Meta-analysis
- **Effectiveness**
  - How technology functions in “real world”
    - Population level analyses
    - Large, multicenter, rigorous observational cohorts (consecutive pts/objective observers)
- **Safety**
  - Variant of effectiveness
    - Population level analyses
    - Case reports/series, FDA reports
- **Cost**
  - Direct and modeled analysis
    - Administrative/billing data (charge vs cost)
- **Context**
  - Mix of historic trend, utilization data, beneficiary status, expert opinion

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HTCC Decision Basis

- **Clinical Committee Decision must give greatest weight to most valid and reliable evidence**
  - Objective Factors for evidence consideration
    - Nature and Source of evidence
    - Empirical characteristics of the studies or trials upon which evidence is based
    - Consistency of outcomes with comparable studies
  - Additional evaluation factors
    - Recency (date of information)
    - Relevance (applicability of the information to the key questions presented or participating agency programs and clients)
    - Bias (presence of conflict of interest or political considerations)

WAC 182-55-030: Committee coverage determination process

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Technology Topics Underway

- ABA Therapy for Autism
- Sleep Apnea Diagnosis and Treatment
- CT/MR for Pelvic and Abdomen
- Elective Cesarean Section
- Stereotactic radiosurgery
- Femoro-acetabular surgery for hip impingement syndrome
- Positron Emission Tomography (PET) scans for Lymphoma
- Microprocessor controlled Prosthetics – lower limb
- Bone graft products (autograft, allograft and synthetic)
- Osteoarticular Transfer System Cartilage Surgery (OATS)
- Robotic assisted surgical devices (e.g. Davinci, Zeus)
- Upper Endoscopy for GERD

Washington State Health Care Authority, HTA Program
FINAL Key Questions and Background
Glucose Monitoring

Introduction

HTA has selected Glucose Monitoring to undergo a health technology assessment where an independent vendor will systematically review the evidence available on the safety, efficacy, and cost-effectiveness. HTA posted the topic and gathered public input about available evidence. Key questions guide the development of the evidence report. They are posted for public review and comment. HTA seeks to identify the appropriate topics (e.g. population, indications, comparators, outcomes, policy considerations) to address the statutory elements of evidence on safety, efficacy, and cost effectiveness relevant to coverage determinations.

There are concerns about efficacy, safety, cost, and health impact of glucose monitoring on clinical outcomes among patients with diabetes (and/or subgroups). The role of glucose monitoring is unclear. Intermittent glucose monitoring employs a small quantity of capillary blood obtained by pinprick and placed on a reactive test strip that is read by an electronic meter. Continuous glucose monitoring employs a probe placed under the skin, connected to a monitor that reads glucose levels at frequent intervals, virtually continuously. Important questions remain about its effect on patient outcomes, education regimens, titration schemes, and determining adequacy of an overall treatment plan.

Key Questions

For patients 18 years of age or under with insulin requiring diabetes mellitus:

1. What is the evidence of efficacy and effectiveness of glucose monitoring? Including consideration of:
    a. Achieving target A1c levels
    b. Maintaining target A1c levels
    c. In conjunction with provider specific report cards for target (e.g. under 7/over 9)
    d. Reduce hospitalizations or acute episodes of diabetic ketoacidosis, hyperglycemia and hypoglycemia
    e. Reduce microvascular complications (retinopathy, nephropathy, neuropathy)
    f. Reduce Mortality
    g. Effect on medication or nutritional management
    h. Quality of life
2. What is the evidence on optimal or improved efficacy or effectiveness of glucose monitoring based on frequency or mode (continuous versus self monitoring) of testing?
3. What is the evidence of the safety of glucose monitoring? Including consideration of:
    a. Adverse events type and frequency (mortality, major morbidity, other)
4. What is the evidence that glucose monitoring has differential efficacy or safety issues in sub populations? Including consideration of:
    a. Gender
    b. Age (differential within the 18 and under population)
    c. Psychological or psychosocial co-morbidities

d. Other patient characteristics or evidence based patient selection criteria
e. Provider type, setting or other provider characteristics
f. Health care system type, including worker's compensation, Medicaid, state employees

5. What is the evidence of cost implications and cost-effectiveness of glucose monitoring? Including consideration of:

   a. Costs (direct and indirect) in short term and over expected duration of use
   b. Estimates of costs saved by preventing morbid events

Technology Background

Disease: Diabetes mellitus, or diabetes, is a serious chronic disease without a definitive cure and associated with significant acute and chronic morbidity and mortality. Diabetes is a metabolic disorder caused by defects in insulin secretion, insulin action or both. Type 1, insulin requiring diabetes, refers to cell-mediated autoimmune destruction of the pancreatic beta islet cells, which leads to absolute insulin deficiency.

Technology: Glucose monitoring is a process to assist in managing diabetes by measuring and controlling blood glucose (often measured by HBA1c levels). Monitoring glycemic status is used as a way to evaluate sufficiency of treatment and guide selection of appropriate interventions. Traditionally, glucose monitoring occurs through a combination of testing during office visits and self-monitoring by patients. Self monitoring in patients with diabetes who use insulin may contribute to improved glycemic control and reduced hypoglycemia by allowing for self-adjustments in insulin does to be made based on meter readings and may also allow for appropriate changes in diet and physical activity to be made.

Although organizations make recommendations and guidelines exist on use of blood glucose monitoring, the effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial. Several lines of evidence suggest an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test. On the other hand, children and adolescents can be especially at risk for some diabetes related complications (e.g. hypoglycemia, ketoacidosis). Information about the best management strategies for diabetics under 18, including evidence of efficacy and safety and cost; and correlation of frequency (including strip frequency and continuous monitoring) to improved outcomes is needed.

Public Comment and Response

HTA received ten timely public comments, most of which cited evidence supporting the efficacy, effectiveness, safety and cost effectiveness of glucose monitoring. This information will be relayed to the evidence vendor for review. Comments that addressed the key questions and their relevance to guide the development of the evidence report were evaluated along with input from the technology assessment center. HTA reviewed the public comments, consulted clinical committee members and the technology assessment centers, and gathered follow up information from the nominating agencies. A summary of the input and modification to key questions is below.

Overall topic/other information: Several commenters questioned the appropriateness of the topic and population in general and assert that glucose monitoring is a long-standing practice with clear clinical evidence and guidelines.

This topic was prioritized based on agency prioritizing the encouragement of the best chronic care management possible, especially with high impact condition such as diabetes. Concerns initially centered primarily on two areas: the frequency and method of glucose monitoring. The goal is to gather and summarize the current evidence around the safety, efficacy and effectiveness and cost of glucose monitoring so that we can ensure payment policies are aligned to support appropriate utilization of diabetic management technologies.

The key questions reflect our statutory criteria and standard HTA methodology about population, intervention, comparators, and outcomes. Specific to this topic, the core of the glucose monitoring concerns are reflected in key question #2 around evidence about when, what type, and how much. The subpopulation of focus (insulin requiring patients 18 and under) was chosen because there is currently several well conducted and recent publications to help glucose monitoring policies for adults with non-insulin requiring diabetes, but not for youth with insulin requiring diabetes. Summary of additional comments by question follows.

Question 1: Three commenters felt the subcategories in question 1 should be modified based on the population to better illustrate potential complications.

The subcategories are updated.

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Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000		X
2.	Equity interests such as stocks, stock options or other ownership interests		X
3.	Status or position as an officer, board member, trustee, owner		X
4.	Loan or intellectual property rights		X
5.	Research funding	X	
6.	Any other relationship, including travel arrangements	X	

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

1) Research funding: Ipsen, Lilly, NovoNordisk, Pfizer, Genentech; growth hormone & IGF-1 research. Medtronic: Donation of glucose sensors for research study.

2) Travel for meetings: Ipsen, Lilly, NovoNordisk, Pfizer, Genentech

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

7. If yes, Provide Name and Funding Sources: _____

_____

_____

_____

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X Patricia Y. Fechner, MD — *Signature*

Date

Patricia Y. Fechner, MD — *Print Name*

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742, PO Box 42712, Olympia, WA 98504-2712

February 11, 2011

CURRICULUM VITAE

PATRICIA YVONNE FECHNER, M.D.

Place of Birth: United States

Office Address: Division of Pediatric Endocrinology
Seattle Children's Hospital
University of Washington
4800 Sand Point Way, M/S A5902
Seattle, WA 98105-0371

Telephone Number: 206-987-5037
Email Address: Patricia.Fechner@seattlechildrens.org

Education

1977-1981 B.S. in Life Sciences with minor in Electrical Engineering
Massachusetts Institute of Technology
Cambridge, Massachusetts

1981-1986 M.D.
Northwestern University School of Medicine
Chicago, Illinois

1984-1985 Special Graduate Student
Massachusetts Institute of Technology
Cambridge, Massachusetts

Postgraduate Training

1986-1989 Pediatric Internship and Residency
University of California, Irvine
Orange, California

1989-1993 Post-doctoral Fellow in Pediatric Endocrinology
Division of Pediatric Endocrinology
Johns Hopkins University School of Medicine
Baltimore, Maryland

Faculty Positions

11/1/06-present Associate Professor, Pediatrics
Division of Pediatric Endocrinology
Seattle Children's Hospital
University of Washington
Seattle, Washington

9/1/01-10/31/06 Clinical Assistant Professor of Pediatrics
Division of Pediatric Endocrinology
Stanford University School of Medicine
Stanford, California

9/1/98-8/31/01 Assistant Professor of Pediatrics (Research)
Division of Pediatric Endocrinology
Stanford University School of Medicine
Stanford, California

4/1/97-8/31/98 Acting Assistant Professor of Pediatrics
Division of Pediatric Endocrinology

	Stanford University School of Medicine Stanford, California
7/1/93-3/15/97	Assistant Professor of Pediatrics Division of Pediatric Endocrinology Johns Hopkins University School of Medicine Baltimore, Maryland

Hospital Positions

2/1/10-7/11/2010	Interim Division Chief Division of Endocrinology Seattle Children's Hospital Seattle, Washington
2006-present	Staff Physician Division of Endocrinology Seattle Children's Hospital Seattle, Washington
1997-2006	Staff Physician Division of Pediatric Endocrinology Lucile Packard Children's Hospital Palo Alto, California
2006	Staff Physician Santa Clara Valley Medical Center Santa Clara, California
1993-1997	Staff Physician Division of Pediatric Endocrinology Johns Hopkins Hospital Baltimore, Maryland

Honors and Awards

1991	Stetler Fellowship
1993-1995	Pfizer Clinical Scholar Award for New Faculty
1993	Richard S. Ross Clinician Scientist Award
1993-1995	Lawson Wilkins Pediatric Endocrine Society Genentech Clinical Scholar Award
1993-1998	NIH Clinical Investigator Award
1999	Katherine Dexter McCormick Travel Award
2001-2003	GlaxoSmithKline Junior Faculty Award

Board Certification

1987	Diplomate, National Board of Medical Examiners
1989, 1998, 2008	Pediatrics
1992, 1998, 2007	Pediatric Endocrinology

Current License to Practice	Washington 2006-present California 1988-present

Professional Organizations

1991-present	Endocrine Society
1993-present	Lawson Wilkins Pediatric Endocrine Society
	1998-2000 Nominations Committee
	2000 Chair, Nominations Committee
1996-present	Association of Clinical Endocrinologists

Glucose Monitoring Scheduled Public Comments (4 minutes per presenter)				
#	**Name**	**Representing**	**COI**	**PPT**
1	Joan Sanders	Juvenile Diabetes Research Foundation (JDRF)	Yes	No
2	Melinda Woods	Parent	Yes	No
3	Lynn Kern	Parent		No
4	Dr. Irl B. Hirsch	WA Diabetes Care Center	Yes	Yes
5	Catherine Pihoker, MD	Seattle Children's Hospital	Yes	Yes
6	Kathleen Schneider, RN	Seattle Children's Hospital	Yes	Yes
7	Lori Laffel, MD	ADA	Yes	Yes
8	Bruder Stapleton, MD	Seattle Children's Hospital	Yes	Yes

Joan Sanders -GM

Washington State Health Care Authority

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000		✓
2.	Equity interests such as stocks, stock options or other ownership interests		✓
3.	Status or position as an officer, board member, trustee, owner		✓
4.	Loan or intellectual property rights		✓
5	Research funding		✓
6	Any other relationship, including travel arrangements		✓

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship

	Potential Conflict Type	Yes	No
7	Representation: If representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		✓

7 If yes, Provide Name and Funding Sources:

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may *attach additional sheets* explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X [signature] 2.17.11 JOAN SANDERS

Signature Date Print Name

FOR QUESTIONS: Denise Sampyo, Health Care Authority, 360-923-2742,

Irl B. Hirsch, MD-GM

Washington State Health Care Authority

Disclosure

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	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000		XX
2.	Equity interests such as stocks, stock options or other ownership interests		XX
3.	Status or position as an officer, board member, trustee, owner		XX
4.	Loan or intellectual property rights		XX
5.	Research funding	XX	
6.	Any other relationship, including travel arrangements		XX

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

I am the principle investigator for several industry-sponsored research studies, all of which are funded through the University of Washington. Although these trials are not funded by glucose meter companies, to be fully transparent I am happy to list them: 1. Novo-Nordisk, 2. Mannkind Corp, 3. Halozyme.

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		xx

7. If yes, Provide Name and Funding Sources: I am representing myself and my views should not be considered approved by the University of Washington

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

Catherine Piholer, MD - 6M

Washington State Health Care Authority

Disclosure

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	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000		X
2.	Equity interests such as stocks, stock options or other ownership interests		X
3.	Status or position as an officer, board member, trustee, owner		X
4.	Loan or intellectual property rights		X
5.	Research funding		X
6.	Any other relationship, including travel arrangements		X

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

_____

_____

_____

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		X

7. If yes, Provide Name and Funding Sources: _____

_____

_____

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X Catherine Piholer 02/18/2011 Catherine Piholer MD

Signature *Date* *Print Name*

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712

Washington State Health Care Authority

Kathleen Schneidea, RN – GM

Disclosure

Any unmarked topic will be considered a "Yes"

	Potential Conflict Type	Yes	No
1.	Salary or payments such as consulting fees or honoraria in excess of $10,000		✓
2.	Equity interests such as stocks, stock options or other ownership interests	✓	✓
3.	Status or position as an officer, board member, trustee, owner		✓
4.	Loan or intellectual property rights		✓
5.	Research funding		✓
6.	Any other relationship, including travel arrangements		✓

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

I own Johnson & Johnson stock

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).		✓

7. If yes, Provide Name and Funding Sources:

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I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X Kathleen Schneider 3/1/11 Kathleen Schneider

Signature *Date* *Print Name*

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742, PO Box 42712, Olympia, WA 98504-2712

Loki Laffel, MD - 6M

Washington State Health Care Authority

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2.	Equity interests such as stocks, stock options or other ownership interests		X
3.	Status or position as an officer, board member, trustee, owner		X
4.	Loan or intellectual property rights		X
5.	Research funding	X	
6.	Any other relationship, including travel arrangements		X

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

- Bayer Diabetes - Educational Grant
- Medtronic - Research Grant

	Potential Conflict Type	Yes	No
7.	Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).	X	

7. If yes, Provide Name and Funding Sources:

Representing American Diabetes Association;
- Chair Youth Strategies Committee, previous Board member-Nat'l, grant support

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X [signature] 3/2/11 Loki Laffel

Signature *Date* *Print Name*

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742,

Bruder Stapleton, MD - 6M

Washington State Health Care Authority

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2.	Equity interests such as stocks, stock options or other ownership interests		✓
3.	Status or position as an officer, board member, trustee, owner		✓
4.	Loan or intellectual property rights		✓
5.	Research funding		✓
6.	Any other relationship, including travel arrangements		✓

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	Potential Conflict Type	Yes	No
7.	Representation: If representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).	✓	

7. If yes, Provide Name and Funding Sources: Seattle Children's Hospital; Chief Academic Officer, Sr V.P.

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.

X _____ 3/8/11 F. Bruder Stapleton MD

Signature *Date* *Print Name*

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742, PO Box 42712, Olympia, WA 98504-2712

Understanding Type 1 Diabetes in 2011

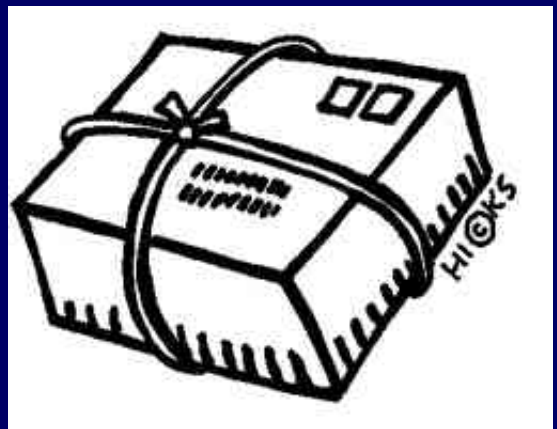
Irl B. Hirsch, M.D.

Professor of Medicine

University of Washington School of Medicine

The Issue: What Exactly is "Intensive Insulin Therapy"?

- A PACKAGE
  - Insulin replacement (multiple injections or insulin pump therapy), to match food with insulin, frequent home blood glucose testing, psycho-social support, objective assessment with A1C



The Evolution of Eye and Kidney Disease in Childhood Type 1 diabetes

	1940s-1970s	Conventional N=730	Intensive N=711
Sight-threatening eye-disease	50%	25%	10%
Kidney Disease	35%	16%	6%

Conventional: once or twice daily insulin, no home glucose testing

Intensive: multiple injections, home glucose testing 4-5 times daily

Arch Intern Med 169:1307, 2009

Beneficial effects of intensive therapy of diabetes during adolescence: Outcomes after the conclusion of the Diabetes Control and Complications Trial (DCCT)

Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group[a]

(J Pediatr 2001;139:804–12) (J PEDIATR 1994;125:177-88)

- Intensive insulin therapy:
  - improved A1c compared with conventional insulin therapy
  - reduced the risk of diabetic eye disease by 53-70% ($P<.05$)
  - reduced the risk of diabetic kidney disease by 55% ($P<.05$)
- Blood glucose monitoring played a major role in intensive insulin therapy, allowing for optimal insulin dosing
- There were no reported safety issues related to BG monitoring

What Makes Insulin Therapy So Difficult?

- Hypoglycemia (low blood sugar)-the rate-limiting factor in type 1 diabetes therapy
- Young children-cannot express symptoms-may only present as altered behavior, but could progress to seizures or coma
- All-lose normal ability for body to combat hypoglycemia
- Despite overall lower glucose levels with today's therapies, hypoglycemia rates have been dramatically reduced

Why?

- It is clear home blood glucose monitoring is one of the most if not *the* most important reason

Let Me Clear So There is NO Misunderstanding

- Home blood glucose monitoring is not a cure, but it has dramatically improved both the quality of life and the risk for long-term complications in children with diabetes

What I Don't Want To Hear a Decade From Now (my world today with continuous glucose monitoring)

- "The JDRF and ADA found a cure for type 1 diabetes but my insurance won't pay for it"

Glucose monitoring in children with Type 1 Diabetes

Catherine Pihoker, M.D.
Professor of Pediatrics
University of Washington School of Medicine
Seattle Children's Hospital

Key Points

- Intensive diabetes management improves outcomes; glucose monitoring is an integral part of management
- More frequent glucose monitoring is associated with better outcomes
- Guidelines recommend ***individualized*** frequency of monitoring (at least 4-6 tests/day)
- Special considerations for children
- Need to improve overall care, including effectiveness of glucose monitoring

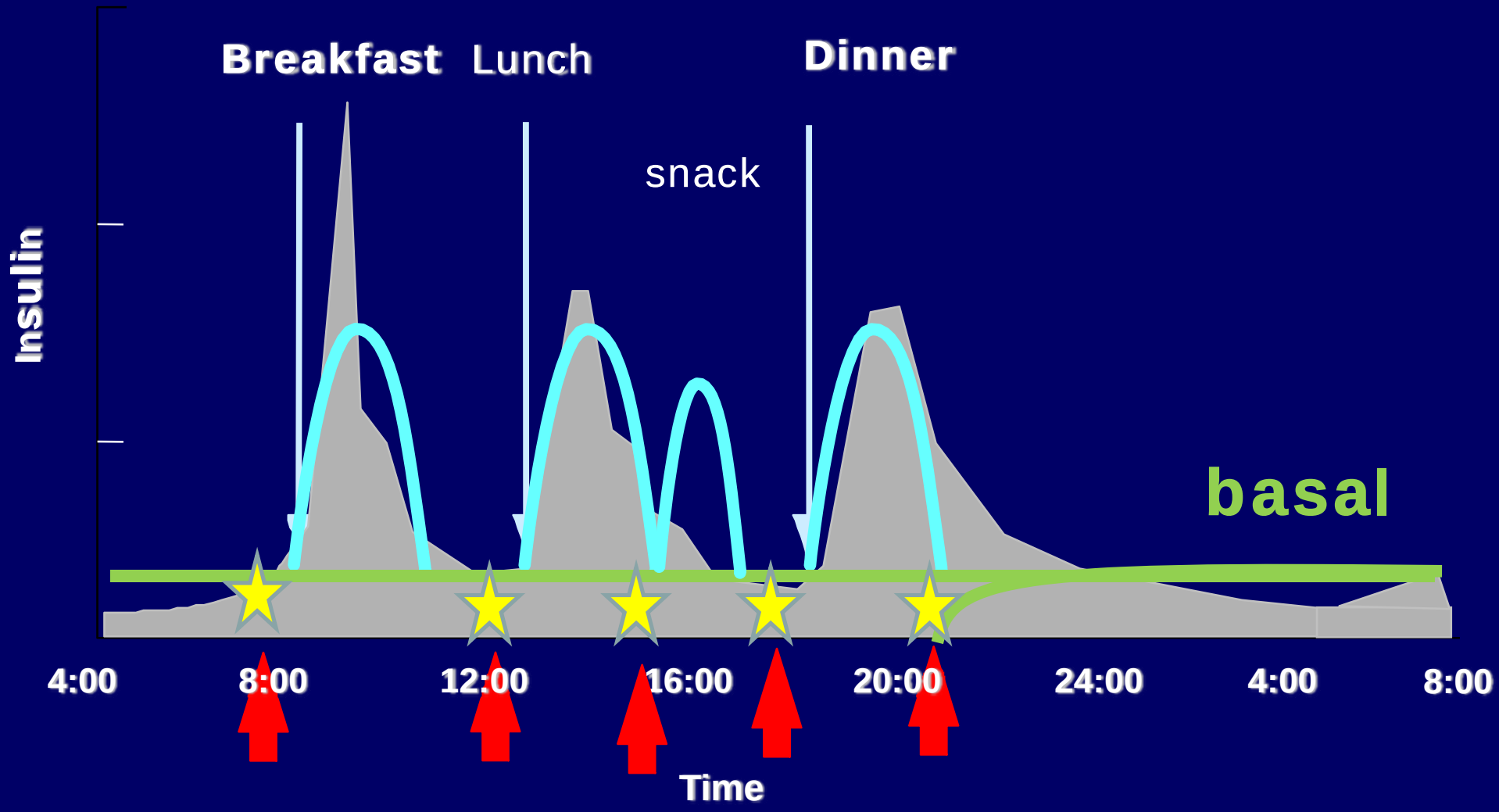
Usual treatment regimens

- All children with type 1 diabetes are on insulin
- Most children with type 1 diabetes are on multiple daily injections or insulin pumps
- Over half are on “basal-bolus” therapy (insulin pumps or long/rapid-acting insulin analogs)
  - Receive insulin before each meal (snack)
  - Dose is based on food to be consumed and blood glucose
    - Insulin is given 4+ times/day

Usual glucose monitoring regimen

- Before each meal/snack
- Before bed
- During the night (2-3 am)
- 2 hours after meals
- Additional checks for illness, hypoglycemia, change in regimen, activity, driving, etc.
- National and international guidelines recommend individualized testing, at least 4-6 tests/day

Basal-Bolus Treatment with Rapid & Long Acting Insulin Analogs



Calculation of bolus/meal doses

Insulin/Carbohydrate Ratio (or Carb Bolus)

1	units Humalog/Novolog	per	10	g of carb

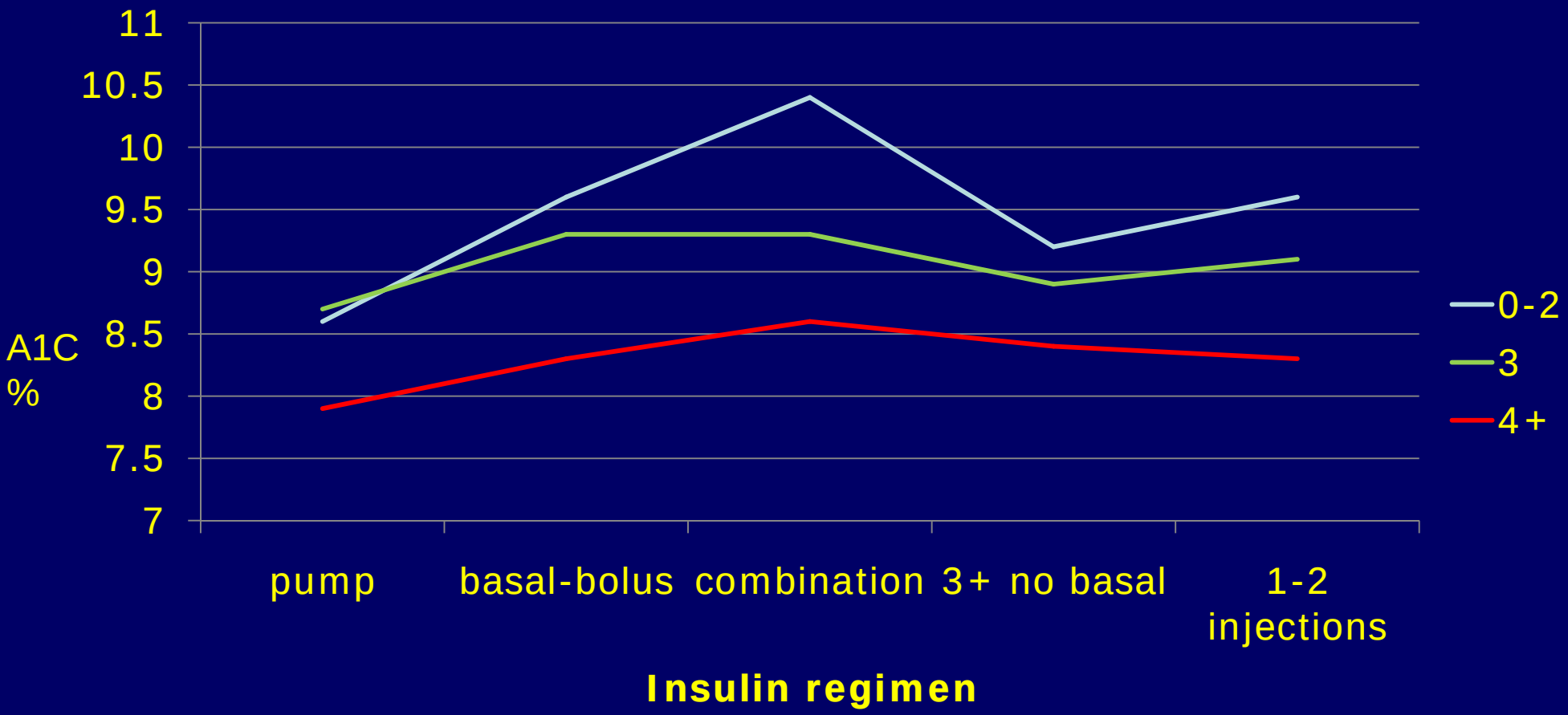
Correction Ratio for High Blood Sugars (AKA - Correction Bolus)

1	units Humalog/Novolog	per	30 (SENSITIVITY)	mg/dl >	120 (TARGET)	mg/dl

Use for: Breakfast/Lunch/Dinner/ALL MEALS

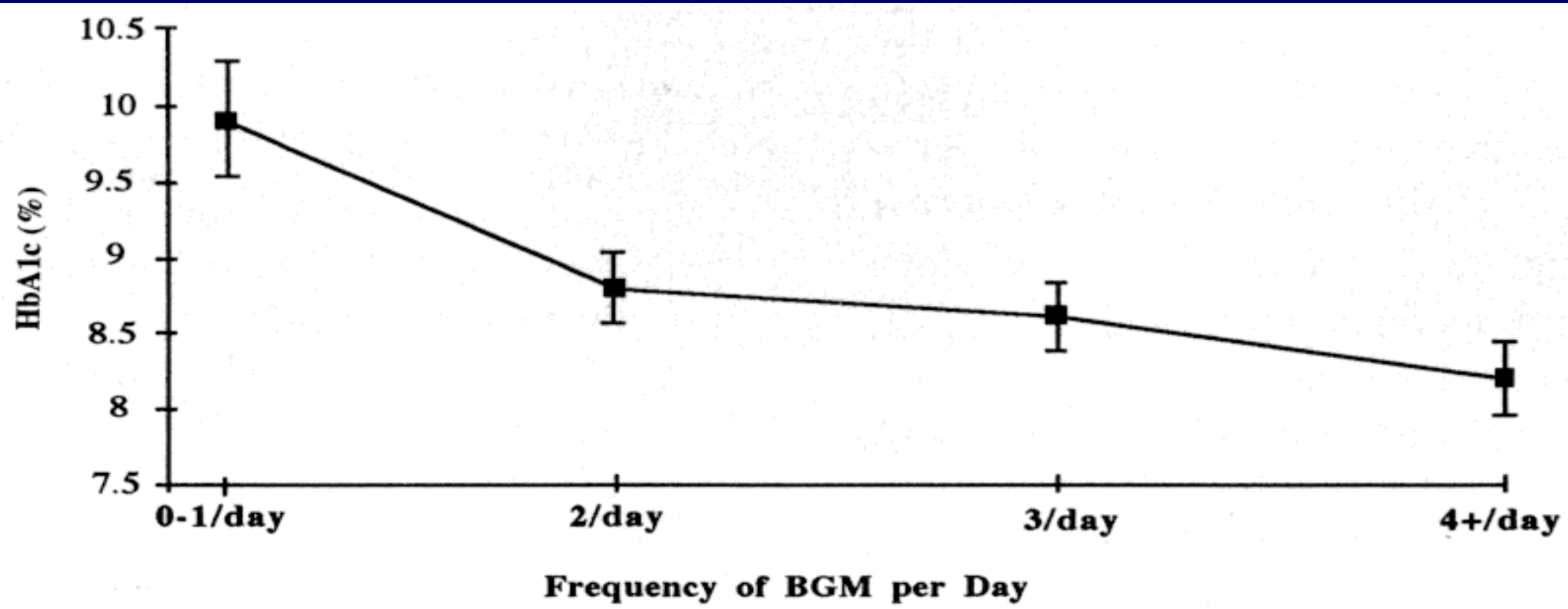
Grams of Carb	Blood Sugar value in mg/dl							
	< 150	150 - 179	180 - 209	210 - 239	240 - 269	270 - 299	300 - 329	330 - 359
0	0	1	2	3	4	5	6	7
10	1	2	3	4	5	6	7	8
20	2	3	4	5	6	7	8	9
30	3	4	5	6	7	8	9	10
40	4	5	6	7	8	9	10	11
50	5	6	7	8	9	10	11	12
60	6	7	8	9	10	11	12	13
70	7	8	9	10	11	12	13	14
80	8	9	10	11	12	13	14	15
90	9	10	11	12	13	14	15	16
100	10	11	12	13	14	15	16	17

Insulin regimen, glucose monitoring, and A1C



SEARCH for Diabetes in Youth Study
Paris et al, J Peds 2009 155:183-9

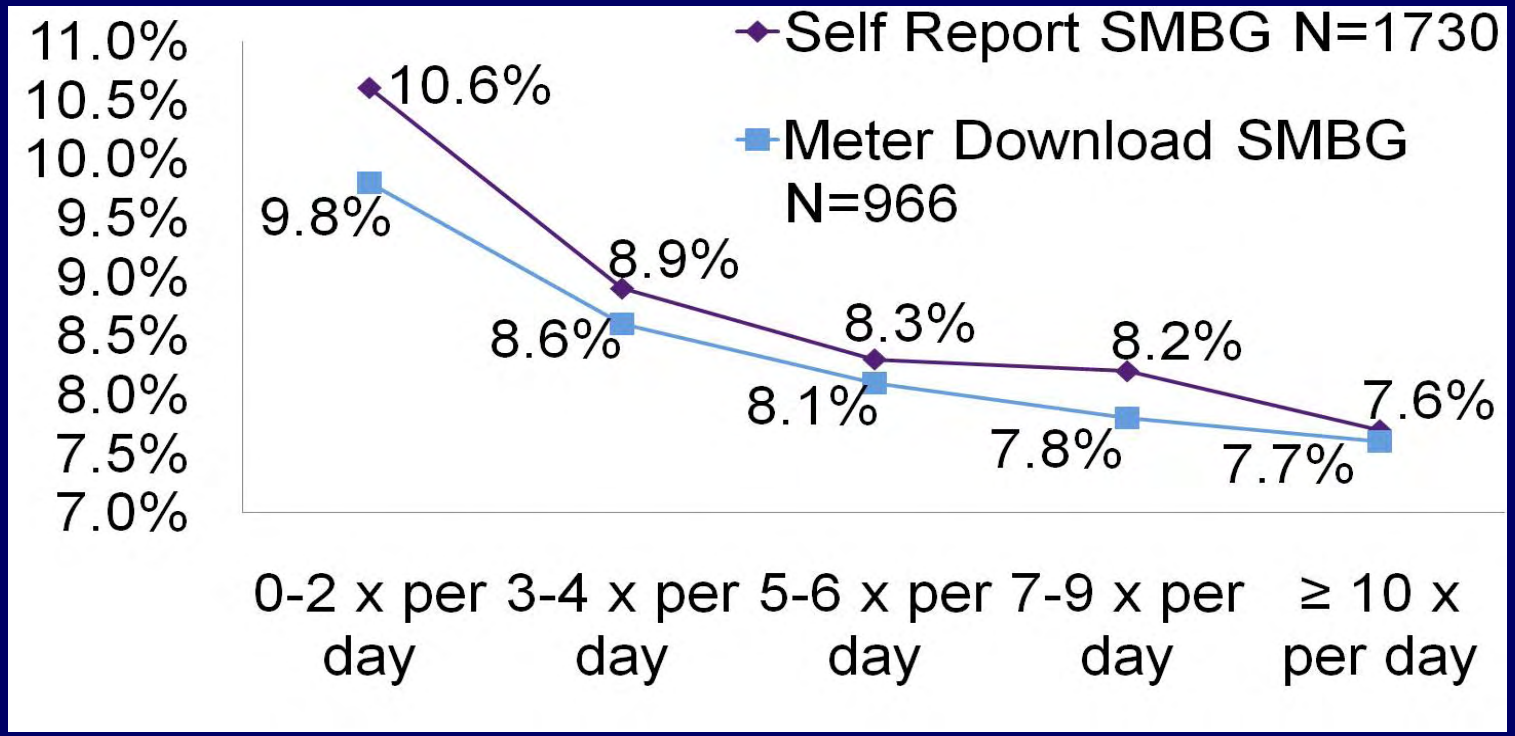
Glucose monitoring improves A1c



P<0.02

Anderson et al. J Peds, 1997
Laffel et al. J Peds, 2003
Levine et al. J Peds, 2001
Haller et al. J Peds, 2004

Glucose monitoring improves A1C



T1 Diabetes Exchange, 2011

Summary: glucose monitoring is effective

- Intensive management is associated with better outcomes
- Glucose monitoring is associated with better outcomes
- Many children have poor outcomes
  - Address frequency of monitoring in children doing poorly
  - Improve effectiveness of glucose monitoring
  - Identify other strategies, resources needed to improve outcomes

Glucose monitoring as part of self-management of diabetes

Kathleen Schneider, RN, CDE
Seattle Children's Hospital

Routine glucose monitoring

- Children and their caregivers are taught to monitor glucose, adjust insulin accounting for
  - Food
  - Glucose readings
  - Activity
  - Stress/illness
  - Other

Routine glucose monitoring

- Very young children need more frequent monitoring (more susceptible to hypoglycemia, unable to express symptoms)
- Growth, pubertal changes affect insulin needs
- Adolescents taught to check glucose before driving

Times requiring frequent monitoring

- Sick day management: check glucose and ketones often every 1-2 hours
- Treatment of Hypoglycemia: recheck until it has resolved, every 15+ minutes
- Hypoglycemic unawareness
- Adjustments in insulin regimen/doses
- Insulin pumps: fasts/adjusting basal rates
- New activity/change in schedule
- Menstrual periods, pregnancy

Times requiring frequent monitoring

- Caregivers outside home assist in monitoring glucose
  - School—pre/post lunch, recess, bus ride, field trips
  - Sports
  - Camps

- Testing is operator (and glucose meter) dependent
  - “wasted” test strips, errors
  - More common with less experience
  - Estimate 10% of test strips do not produce valid result

Special considerations for children

- Young children can’t recognize symptoms of hypoglycemia
- Both low and high blood glucoses can potentially affect developing central nervous system
- Children often have glucose tested 1-3 times/day at school
- Not all test strips produce a valid result
- Insulin requirements change as children grow, develop, live… and need to monitor glucose to safely administer insulin

Challenges and Opportunities in Childhood Type 1Diabetes

Impact of Glucose Monitoring

Lori Laffel MD MPH
Chair, Youth Strategies Committee
American Diabetes Association

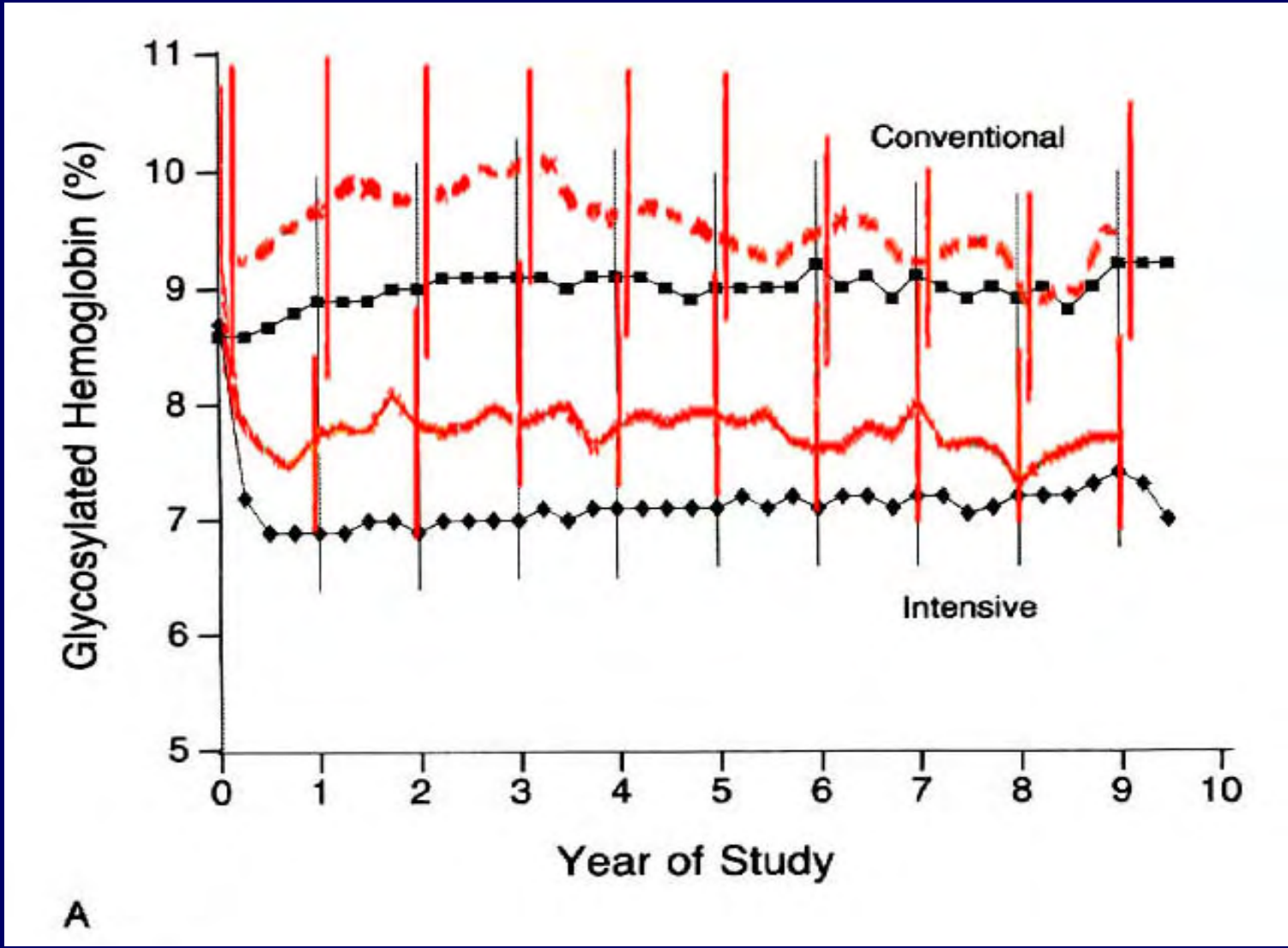
Chief, Pediatric, Adolescent & Young Adult Section
Joslin Diabetes Center
Harvard Medical School
Boston, MA

Key Points

- Challenges
  - Link between glycemic control measured as A1c and complications
    - Data from the DCCT and EDIC
      - Intensive insulin therapy reduces A1c
      - Lower A1c reduces diabetes complications

- Opportunities
  - Link between BG monitoring and A1c outcomes
  - Link between CGM use and A1c outcomes

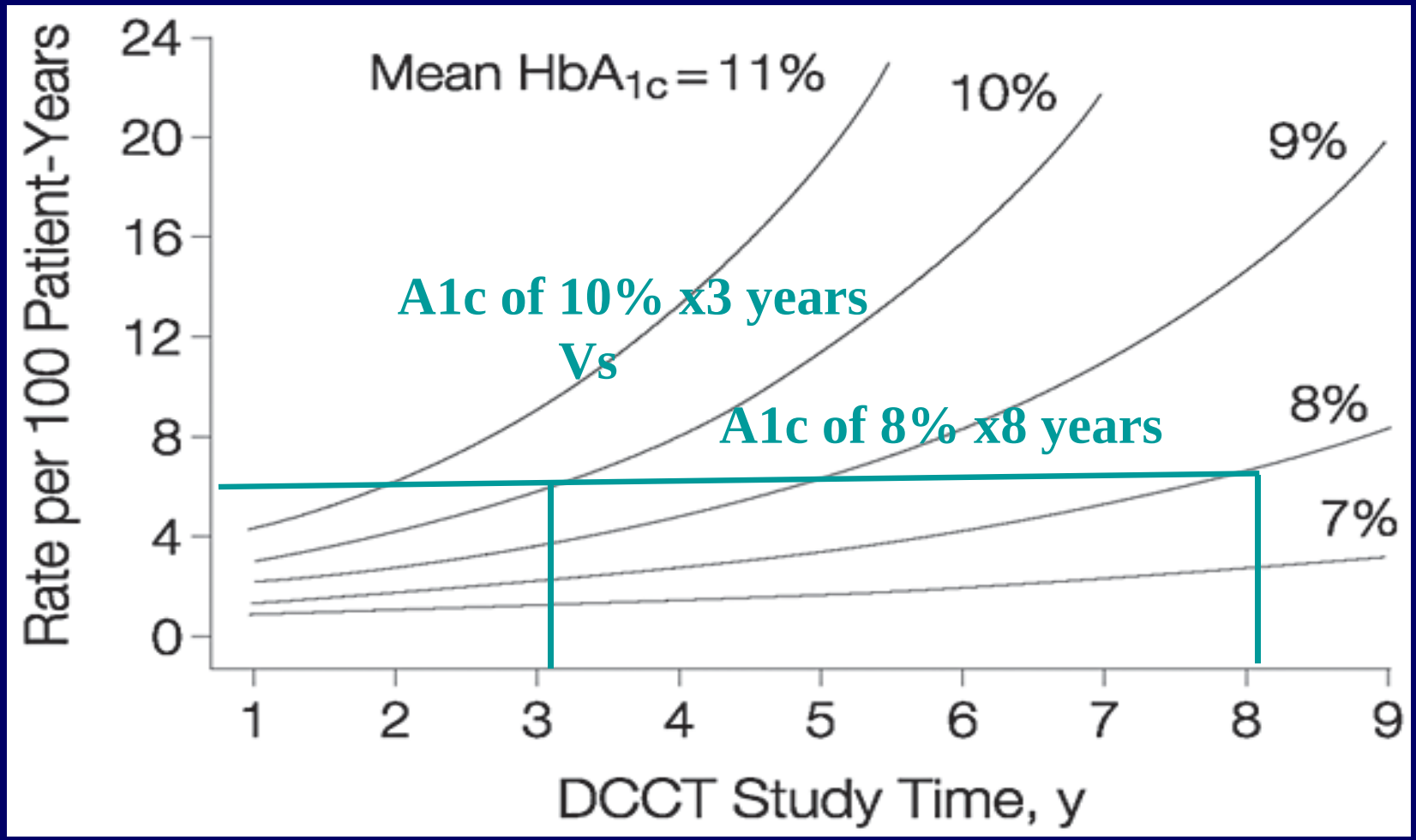
DCCT – Adult & Adolescent Cohorts



Adults
Adolescents

DCCT:
N Engl J Med. 1993
J Peds, 1994

Risk of Retinopathy Progression According to A1c



JAMA 2002:287

ADA Standards of Diabetes Medical Care

January 2011

Table 10—*Summary of glycemic recommendations for many nonpregnant adults with diabetes*

A1C	<7.0%*
Preprandial capillary plasma glucose	70–130 mg/dl* (3.9–7.2 mmol/l)
Peak postprandial capillary plasma glucose†	<180 mg/dl* (<10.0 mmol/l)

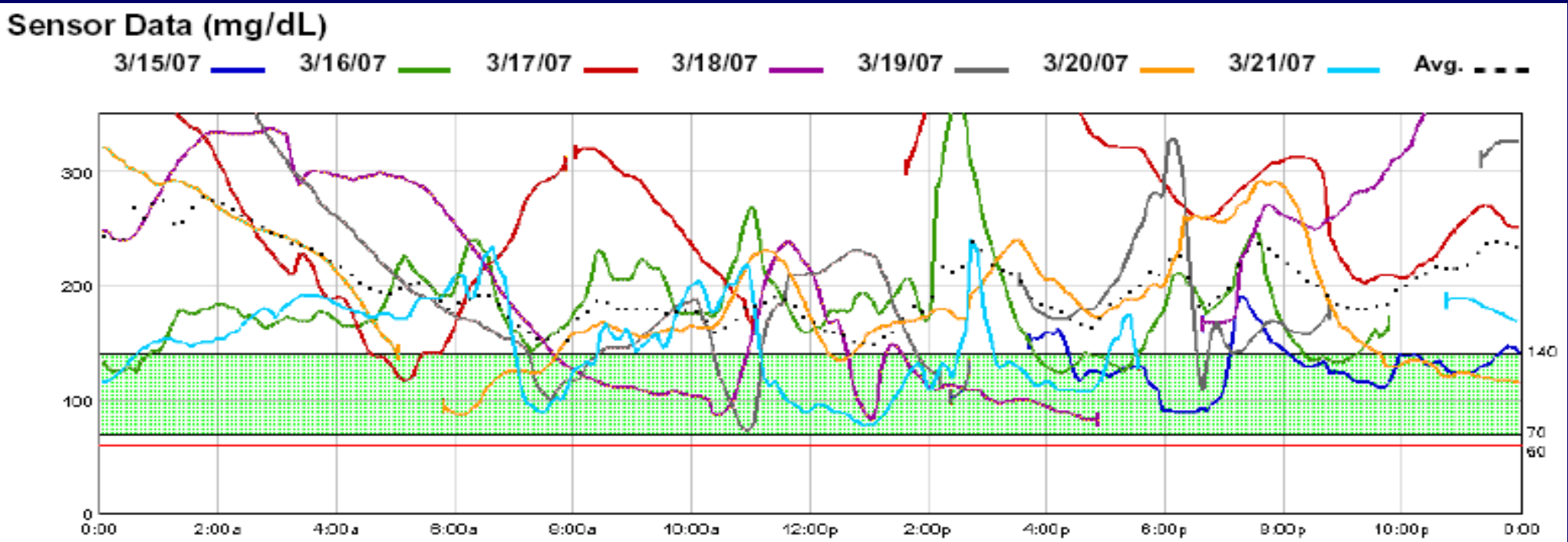
Glycemic Goals

	Plasma blood glucose goal range (mg/dl)			
	Before meals	Bedtime/overnight	A1C (%)	Rationale
Toddlers and preschoolers (0–6 years)	100–180	110–200	<8.5	• Vulnerability to hypoglycemia • Insulin sensitivity • Unpredictability in dietary intake and physical activity • A lower goal (<8.0%) is reasonable if it can be achieved without excessive hypoglycemia
School age (6–12 years)	90–180	100–180	<8	• Vulnerability to hypoglycemia • A lower goal (<7.5%) is reasonable if it can be achieved without excessive hypoglycemia
ISPAD Guidelines	90-145	80-180	<7.5%	
Adolescents and young adults (13–19 years)	90–130	90–150	<7.5	• A lower goal (<7.0%) is reasonable if it can be achieved without excessive hypoglycemia

Key concepts in setting glycemic goals

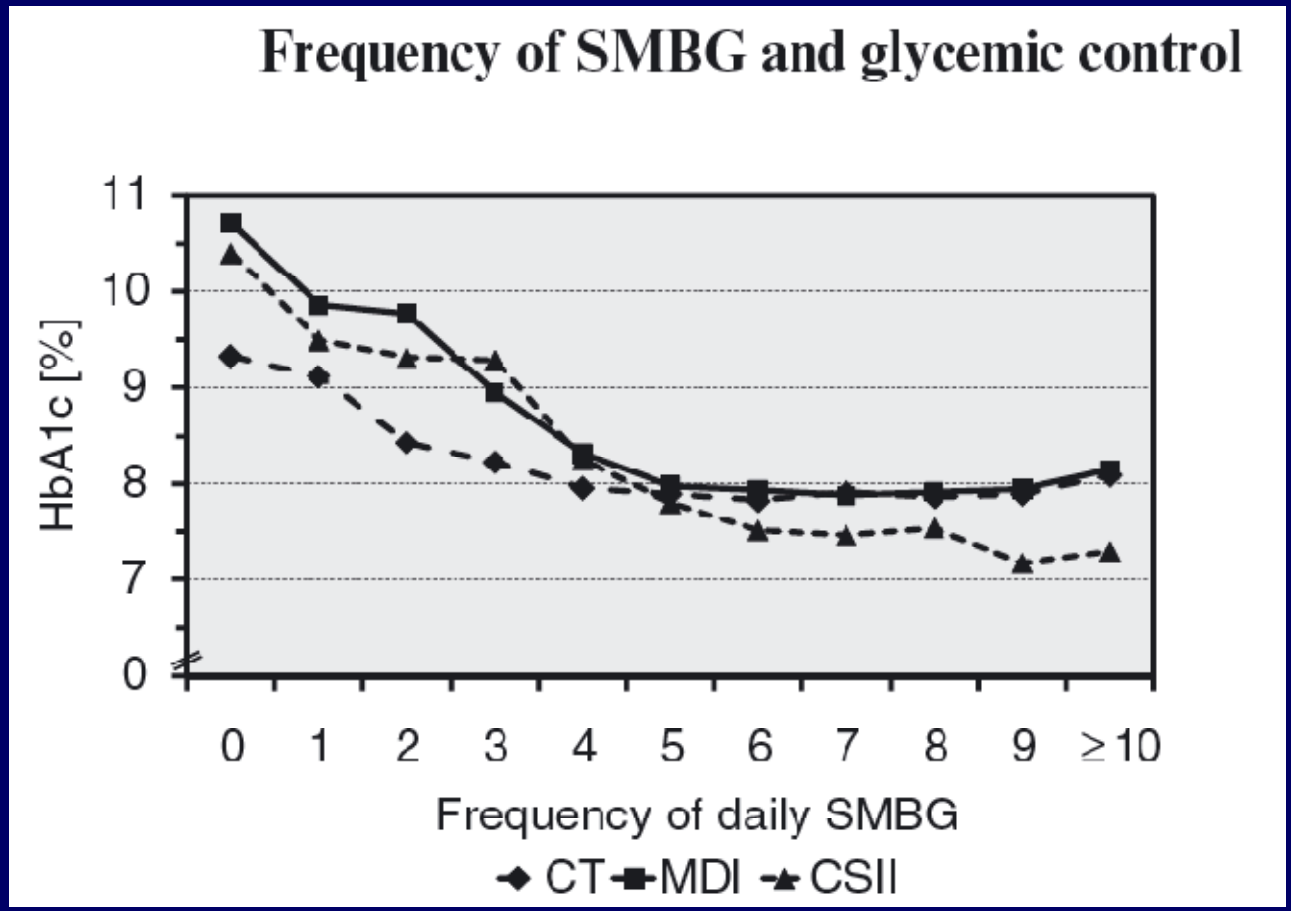
- Goals should be individualized and lower goals may be reasonable based on benefit-risk assessment.
- Blood glucose goals should be modified in children with frequent hypoglycemia or hypoglycemia unawareness.
- Postprandial blood glucose values should be measured when there is a discrepancy between pre-prandial blood glucose values and A1C levels and to help assess glycemia in those on basal/bolus regimens.

Young Boy using CSII
HbA1c: 8.1%, 3/06/07



	Average / Total
# Sensor Values	1,630
High SG (mg/dL)	400
Low SG (mg/dL)	72
Average SG (mg/dL)	200
Standard Dev.	78
MAD %	25.3
# Valid Calibrations	31

12 8/12 y/o boy with T1D of 11+ years duration
DOB 7/24/94
T1D diagnosed 1/96 at age 18 months



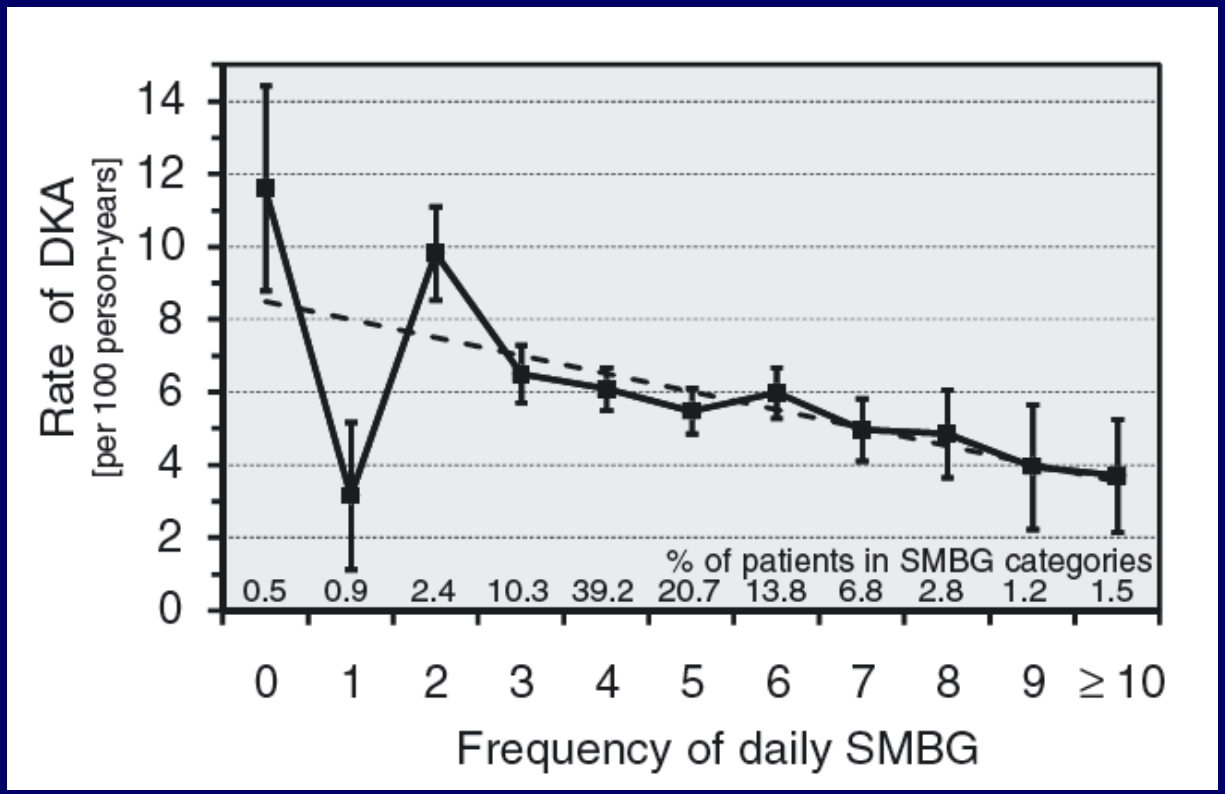
N=26,179

- **A1c was 0.5% lower per each additional BG check per day from 0-5 checks per day.**
- **A1c was 0.2% lower per each additional BG check per day across the range of BG checks.**

Ped Diabetes 2011 12:11-17

Frequency of SMBG correlates with HbA1c and acute complications in children and adolescents with type 1 diabetes

Pediatric Diabetes 2011: 12: 11–17



N=26,002

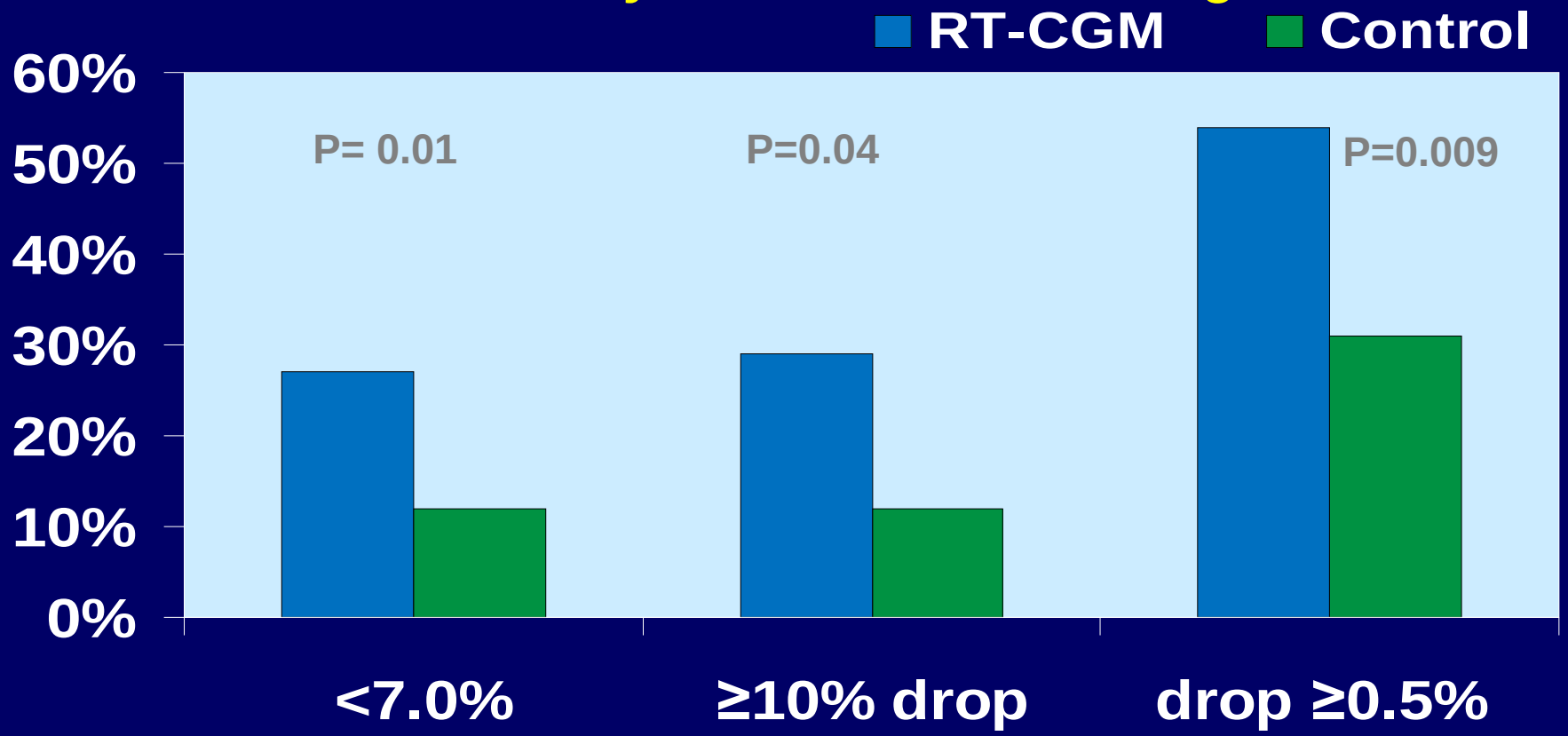
- **The frequency of diabetic ketoacidosis (DKA) was inversely related to the frequency of BG monitoring.**
- **The rate of DKA decreased by 0.4 events/100 person-years per 1 additional BG check/day (p=.006)**
- **This association was similar for all youth age groups 0-18).**

Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes

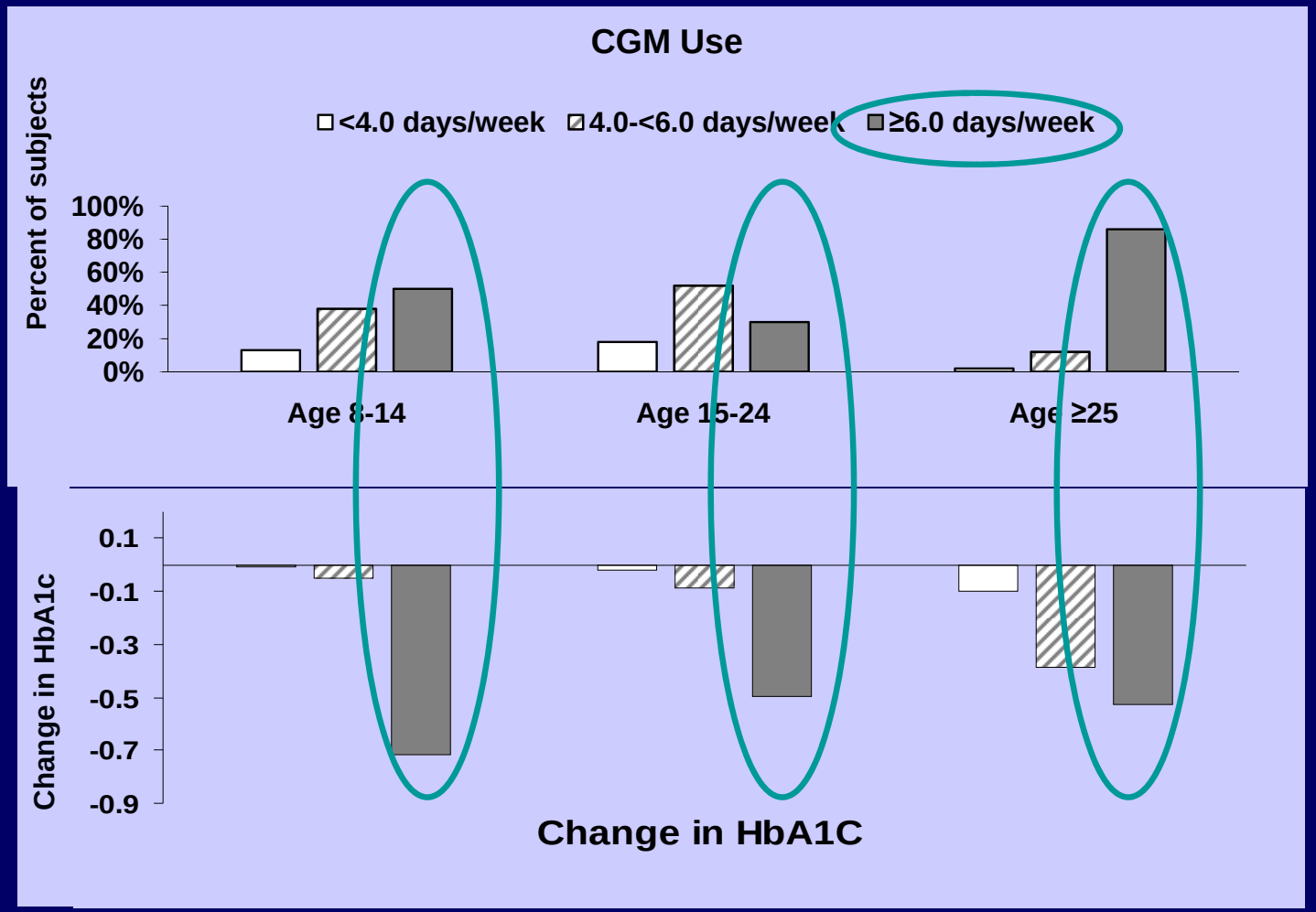
The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group*

NEJM 2008; 359

In 8-14 year olds, CGM Group was significantly more likely to reduce A1c by 10% & reach A1c target

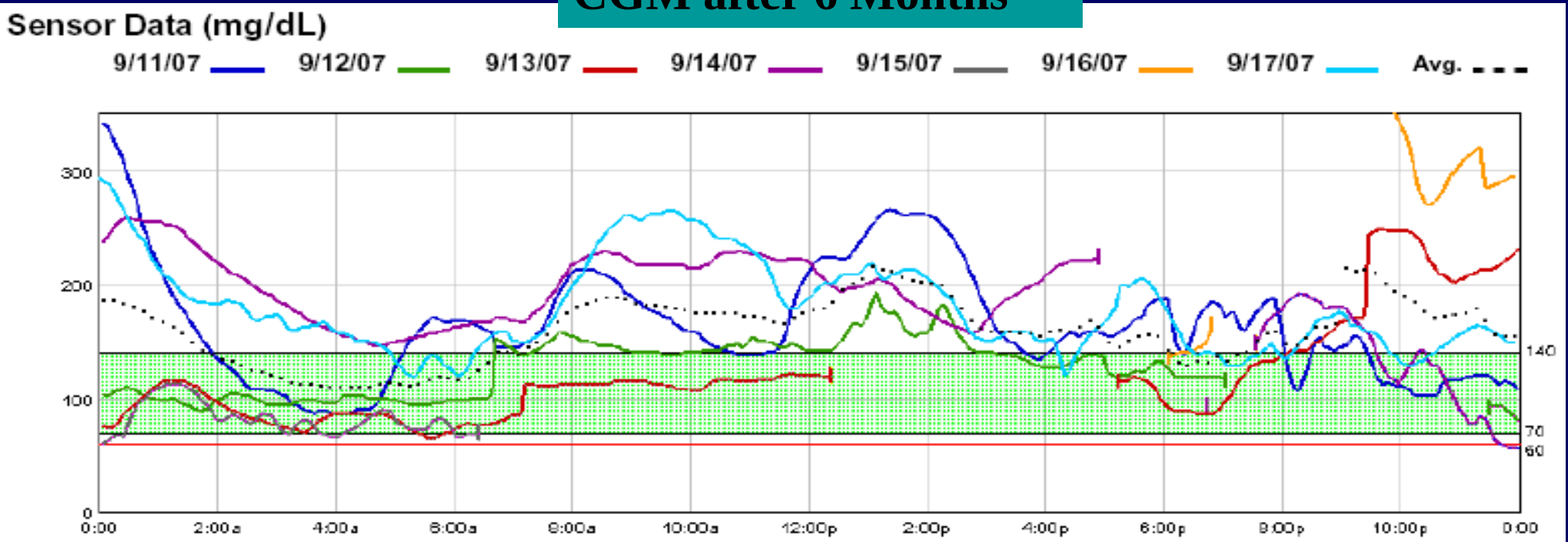


Relationship Between Change in HbA1c and Frequency of CGM Use



Sustained Benefit with CGM
HbA1c: 6.9%, 9/18/07

CGM after 6 Months



	Average / Total
# Sensor Values	1,424
High SG (mg/dL)	400
Low SG (mg/dL)	56
Average SG (mg/dL)	157
Standard Dev.	58
MAD %	19.8
# Valid Calibrations	24

12 8/12 y/o boy with T1D of 11+ years duration
DOB 7/24/94
T1D diagnosed 1/96 at age 18 months

Summary

- Type 1 diabetes is difficult to manage in youth who experience frequent, wide glycemic excursions
- Intensive insulin therapy leads to more optimal glycemic control (measured as A1c)
- Lower A1c levels are significantly associated with reduced risk of acute and chronic complications
- BG monitoring leads to lower A1c levels and reduced risk of complications
- There are no reported safety concerns with BG monitoring
- Continuous glucose monitoring can lead to lower A1c levels without an increase in the risk of severe low BG levels (hypoglycemia)

Delivering the Best Care for Children with Type 1 Diabetes

F. Bruder Stapleton, M.D.

Professor of Pediatrics

Chair, Department of Pediatrics

University of Washington School of Medicine

Seattle Children's Hospital

Decrease in complications with intensive management

- Experience as a pediatric nephrologist, witnessed marked decline in complications including diabetic nephropathy
  - better insulins, technologies, more intensive treatment

- Intensive diabetes management clearly improves outcomes—DCCT, EDIC
  - DCCT was stopped early because intensive management was better

Standard of care is intensive management

- Current management of diabetes is intensive, and that necessarily includes frequent glucose monitoring
- More frequent glucose monitoring is associated with better outcomes
- Glucose monitoring is safe and effective
- Patients admitted for severe acute complications are usually those who DO NOT monitor glucose

Delivering best care to children with diabetes

- Children are not small adults--special considerations
- How we manage children affects their life today and their future
- How do we best deliver care to children with diabetes?
  - Improve effectiveness of glucose monitoring
  - Identify additional resources needed
- Seattle Children's, Department of Pediatrics, is committed to delivering best care, partner effectively with state, to address these questions

Dear Commenter's,

I want to thank you all for taking the time to provide me with feedback. Many of you are busy parents of a child with a serious chronic condition, so I know that you have multiple priorities and it underscores how important this is.

I'd like to give you a brief background of our program to help with the context of this glucose monitoring review. But first, I wanted to assure you that the **rumor that Washington has proposed a 1 strip per day limit for type 1 diabetics is false**. This widely circulated statement is part of a scary mis-information campaign. Many advocates and others are monitoring this program directly know that no such limit has been suggested or proposed.

The HTA program is a commitment by the state to use tax-payer dollars wisely and to purchase medical care (for employees, Medicaid recipients, and injured workers) that works: to base decisions neither on short term budget issues nor slick marketing campaigns. The program selects about 10 medical tests and treatments per year where there are concerns about the safety, effectiveness, or cost-effectiveness to go through a specialized, open review that uses a report that summarizes the medical evidence and an independent group of local, practicing clinicians (not state employees). You can read about each of the steps in the glucose monitoring review here: http://www.hta.hca.wa.gov/glucose.html.

State agencies that pay for medical services agree that Glucose Monitoring is an important component of diabetes management; however there are important questions about optimization, frequency, outcomes, and methods for SMBG and those questions bear directly on how to create a policy that best supports diabetic beneficiaries total needs while being the highest and most efficient use of our shared state resources. Because the agencies share your concern and commitment to encouraging the best management of chronic conditions, especially one as impactful as diabetes, they asked that Glucose Monitoring policy go through this review. The program is here to serve the agencies when difficult and important topics require additional process and input. The HTA review process is the most open to public comment, with seven comment periods, it also commissions an external entity to review the scientific evidence, and finally the coverage policy is crafted by a group of 11 practicing clinicians, not the state agency. In having practicing clinicians weighing evidence to make the coverage decision, we can ensure that an open, rigorous, and clinician centric process is used to ensure that agency payment policies are supporting the most appropriate utilization.

Here's an excerpt from our glucose monitoring key questions about why this topic was selected. Although organizations make recommendations and guidelines exist on use of blood glucose monitoring, the effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial. Several lines of evidence suggest an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test. On the other hand, children and adolescents can be

especially at risk for some diabetes related complications (e.g. hypoglycemia, ketoacidosis). Information about the best management strategies for diabetics under 18, including evidence of efficacy and safety and cost; and correlation of frequency (including strip frequency and continuous monitoring) to improved outcomes is needed.

Status: The evidence report that summarizes the clinical information about Glucose Monitoring is finalized. The topic is scheduled to be heard by our independent clinical committee at their March 18th meeting, where a draft decision is made (that decision is then posted for public comment before finalizing). The committee (in addition to being practicing clinicians) will have the assistance of a pediatric endocrinologist at the meeting if they have additional clinical or technical questions. The meeting is open to the public. We have numerous clinicians, parents, and representatives from associations like the Juvenile Diabetes Association that have indicated they will attend and comment.

Again, I appreciate your comments and I hope that this information provides you with some assurance that we agree about the importance of this issue, which is why we are using this open, public process, a scientific report, and independent clinicians. Your comment will be forwarded to the clinical committee as part of their meeting package. Please feel free to contact me if you have additional questions. You can also use the link above to follow the outcome of the March meeting.

Regards,

Leah Hole-Curry, JD

Leah Hole-Curry, JD | WA Health Technology Assessment Program

Program Director | 360.923.2748 | HTA Website

"The most common way people give up their power is by thinking they don't have any" ***Alice Walker***

Abbott Diabetes Care, Inc.
1420 Harbor Bay Parkway
Alameda, CA 94502

Hon. Leah Hole-Curry
Health Technology Assessment program
Washington State Health care Authority

Re: Comments on Final Report "Glucose Self-monitoring in insulin-dependent patients under the age of 18"

Dear Ms. Hole-Curry:

We appreciate this opportunity to comment on the Final Report and overall process of health technology assessment.

Evidence-based medicine (EBM) is an important approach to formulating health policy that is grounded in high quality research. The "glucose self-monitoring" project is instructive as an example of the strengths and weaknesses of systematic literature review, one of the foundations of EBM methodology. Systematic literature review begins with the formulation of specific questions that guide the specification and scope of the literature search strategy. Studies identified with these criteria are then categorized according to "strength of evidence" criteria. Only studies achieving a specified level of quality are included in the final synthesis of evidence.

In the case of the glucose monitoring technology assessment, the "key questions" focused on the very narrow issue of the efficacy, appropriate frequency, and safety of self-monitored blood glucose (SMBG) for persons with insulin-dependent diabetes age 18 and below. The literature review and synthesis that was designed and executed with the same narrow focus. Overall, the result was essentially a finding of "lack of evidence to substantiate the efficacy and appropriate frequency of SMBG" for children with insulin-dependent diabetes.

While "correct" in the strictest sense of the project design, the report does not explore the reason for this seeming gap in the literature. The importance of SMBG as the foundation of a comprehensive treatment program was demonstrated by the landmark Diabetes Control and Complications Trial (DCCT), a trial that was stopped early due to the substantial benefit of the intervention

relative to usual care. People with insulin-dependent diabetes typically require injections of insulin several times a day. Dose calibration is critical to avoid hypoglycemia or hyperglycemia, and patients are advised to measure their glucose level prior to each dose. Thus, frequency of SMBG has a clear physiological rationale. Absence of recent reports of clinical trials testing the value of SMBG for insulin-dependent diabetes is no surprise given that conducting such trials is not necessary. As a practical matter, conducting such a study would be difficult due to ethical concerns as well as strict regulations governing trials involving children.

In addition to the changes mentioned previously, we urgently and respectfully request a further change to the report.

The Executive Summary of the Final Report (as well as the body of the report, p.24) contains the following statement:

> *"The effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial. Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test."*

It appears as though this language is drawn from the introduction of Gomes 2010, which references several studies on the adult type 2 diabetes population which does not require insulin (Faas 1997, Davidson 2005, Farmer 2007, Guerci 2003, O'Kane 2010, Kennedy 2001, Canadian 2009, Davis 2007). This population is drastically different from the population of study: pediatric type 1 diabetes patients who require insulin. This very strong statement casting self-monitored blood glucose in a negative light is subject to misinterpretation by persons lacking extensive knowledge of the field.

As described in the evaluation prepared for us by United BioSource Corporation which accompanies this letter, the body of the technology assessment report does not present evidence to substantiate any element of these assertions. For example, the statement that, "The effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial…" (for persons with insulin dependent diabetes age 18 and below) is refuted by the universal support of this practice in the many clinical practice guidelines cited in the report.

In summary, we again commend the State of Washington for its efforts to ensure that people with diabetes receive high quality and cost-effective care. We endorse and support the application of "evidence based medicine" in the form of literature review and synthesis. EBM is a vital part of healthcare evaluation, and diabetes is an important indication to study and monitor. We encourage the State of Washington to carefully review the process and application that was followed in this particular project, including the framing of key questions.

Sincerely,

Jared L Watkin
Divisional Vice President
Technical Operations

Eileen Bockoff (by Allison Wallace)
Eileen M. Bockoff
Director
Corporate Reimbursement

Canadian Optimal Medication Prescribing and Utilization Service. Systematic review of use of blood glucose test strips for the management of diabetes mellitus.
Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2009. Available: www.cadth.ca/media/pdf/compus_Draft_BGTS_SR_report_of_clinical_outcome.pdf (accessed 2009 Oct. 20).

Davidson MB, Castellanos M, Kain D, et al. The effect of self-monitoring of blood glucose concentrations on glycated hemoglobin levels in diabetic patients not taking insulin: a blinded, randomized trial. *Am J Med.* 2005;118:422-5.

Davis WA, Bruce DG, Davis TM. Does self-monitoring of blood glucose improve outcome in type 2 diabetes? The Fremantle Diabetes Study. *Diabetologia.* 2007;50:510-5.

Faas A, Schellevis FG, Van Eijk JT. The efficacy of self-monitoring of blood glucose in NIDDM subjects. A criteria-based literature review. *Diabetes Care.* 1997;20:1482-6.

Farmer A, Wade A, Goyder E, et al. Impact of self-monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group
randomised trial. *BMJ.* 2007;335:132.

Gomes T, Juurlink DN, Shah BR, Paterson JM, Mamdani MM. Blood glucose test strips: options to reduce usage. *CMAJ.* 2010 Jan 12; 182(1):35-8.

Guerci B, Drouin P, Grange V, et al. Self-monitoring of blood glucose significantly improves metabolic control in patients with type 2 diabetes mellitus: the Auto-Surveillance Intervention Active (ASIA) study. *Diabetes Metab.* 2003; 29:587-94.

Kennedy L. Self-monitoring of blood glucose in type 2 diabetes: time for evidence of efficacy. *Diabetes Care.* 2001;24:977-8.

O'Kane MJ, Bunting B, Copeland M, Coates VE. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON) study: randomized controlled trial. *BMJ.* 2008; 336:1174.

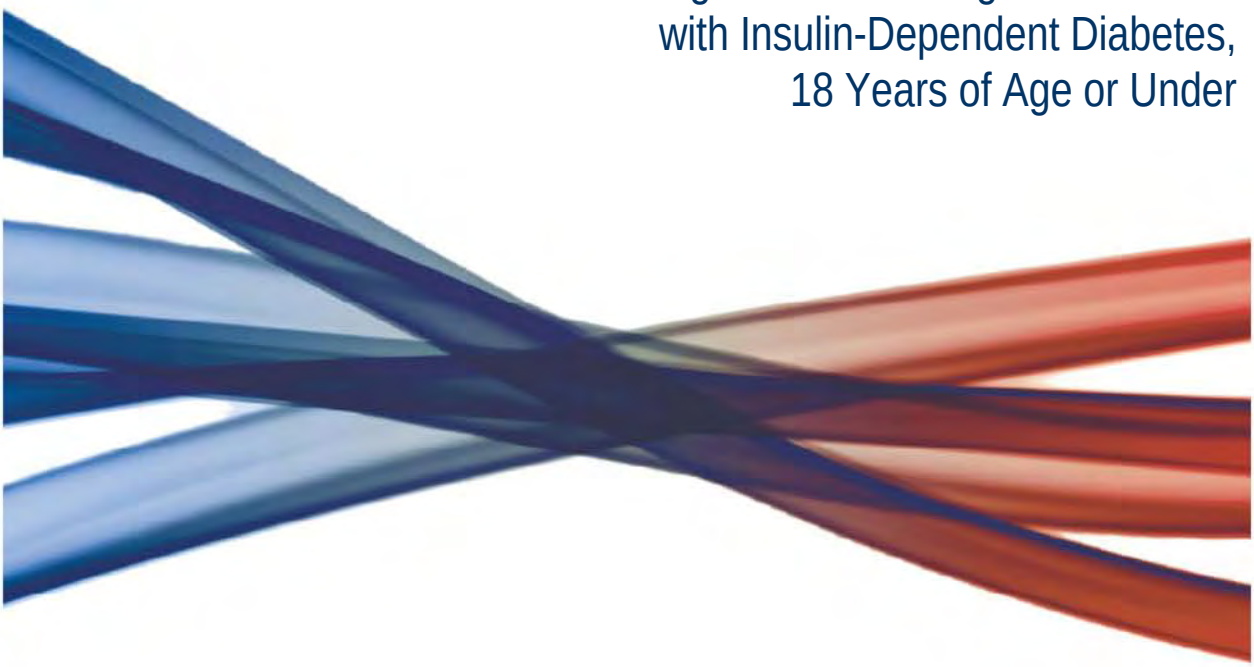
United BioSource Corporation
Evidence Matters®

Project Number | A-10918

Report prepared for:

Abbott Diabetes Care

Review of the State of Washington Health Technology Assessment: Glucose Monitoring: Self-monitoring in Individuals with Insulin-Dependent Diabetes, 18 Years of Age or Under



Prepared by
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Jill Bell, PhD
Elizabeth Wehler, BA
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March 4, 2011
Version: 1.0

Contact: Rachel Huelin
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EXECUTIVE SUMMARY

The Washington State Health Care Authority Health Technology Assessment Program (HTA) has now issued a final report entitled "Glucose Monitoring: Self-monitoring in Individuals with Insulin-Dependent Diabetes, 18 Years of Age or Under." Release of this report follows prior release of a Draft Final Report that was followed by a period of public comment.

HTA commissioned a private organization to perform a literature review and synthesis addressing four "key questions" relating to the effectiveness, safety, and costs of self-monitored blood glucose (SMBG) for persons with insulin-dependent diabetes age 18 years and under. Performance of the literature review was based on standard methods where strict criteria were established to assign "level of evidence" to published reports, resulting in exclusion of data labeled as low-quality of evidence.

The overall conclusion of the technology assessment report with respect to the Key Question 1 (efficacy) is that,

> *"No randomized controlled trials or observational studies which directly evaluated current methods of SMBG testing, as an independent component of management were found."* (p. 10).

Similarly, with respect to Key Question 2 (optimal test frequency), the conclusion is that,

> *"There were no randomized controlled trials (RCT) that directly evaluated the efficacy of SMBG frequency."* (p. 12)

In both cases the Diabetes Control and Complications Trial (DCCT) is described as providing indirect evidence for both the efficacy of glucose monitoring (Question 1) and the optimal frequency (Question 2). This landmark study is described as providing a low quality standard of evidence for both questions (pp. 16, 18) because glucose monitoring was not specifically addressed as "an independent component of management" (p. 10). The DCCT compared a strategy of measuring blood glucose four times daily and calibrating insulin dose accordingly with a strategy of insulin administration based on a single daily blood glucose measurement. To state that measurement of blood glucose was not evaluated as an "independent factor" misses the

point of the DCCT, which was to assess the relative benefit of tight glycemic control where every dose of insulin was titrated as a function of blood glucose level at that precise time. The DCCT provides strong evidence that, "… package of comprehensive, intensive diabetes care, which included SMBG four or more times a day and education on how to use the information to adjust insulin, diet, and exercise…" improves outcomes relative to standard care across a wide range of measures (p. 11).

The Executive Summary of the Final Report includes the following statement:

> *The effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial. Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test.*

None of these assertions are supported by "evidence" presented in the body of the report or evidence tables. It appears as though this language is drawn from the introduction of Gomes et al. 2010, which references several studies on the adult type 2 diabetes population which does not require insulin (Faas et al. 1997, Davidson et al. 2005, Farmer et al. 2007, Guerci et al. 2003, O'Kane et al. 2010, Kennedy et al. 2001, Canadian et al. 2009, Davis et al. 2007). This population is drastically different from the population of study: pediatric type 1 diabetes patients who require insulin. In fact, characterization of the effectiveness and optimal frequency of blood glucose monitoring for persons with insulin dependent diabetes as "controversial" is inappropriate and is countered by the numerous clinical practice guidelines listed in the report that specifically recommend the frequent self-monitoring of blood glucose. Inclusion of this statement in the final report demonstrates a lack of objectivity and the text should be deleted.

In summary, when reviewing and interpreting findings from the report, the State of Washington should give careful attention to a critical issue not addressed in the "key questions" – the long term financial and social consequences of inadequate glycemic control among children with insulin-dependent diabetes.

BACKGROUND

Project Objectives

The Washington State Health Care Authority Health Technology Assessment Program (HTA) issued a final report entitled "Glucose Monitoring: Self-monitoring in Individuals with Insulin-Dependent Diabetes, 18 Years of Age or Under." Public comments on the initial draft report were accepted until December 10, 2010. At that time, Abbott Diabetes Care (Abbott), along with support from United BioSource Corporation (UBC), provided comments in response to the report.

The Washington State Health Care Authority Health Technology Assessment Program reviewed and addressed the public comments in a final report issued on January 14, 2011. Abbott has again engaged UBC to perform a review and critique of the final report. In addition, the UBC review examines the State of Washington response to the Abbott /UBC submitted comments, in addition to other public comments submitted by Clinician Professional Organizations and Industry.

UBC Review Procedure

We begin by responding to the "frequently submitted comments" from the many organizations that submitted public comments on the Draft Final Report. We then respond to the comments from the State of Washington response to the Abbott/UBC comments on the Draft Final Report, including the overall appropriateness of the key questions given the complete lack of clinical community doubt of the critical nature of self-monitoring of blood glucose in patients under 18 years old. Finally, we present a summary assessment and critique of the Glucose Monitoring HTA Final Report.

Organization of Report

1. Observations on "Frequently Submitted Comments" on the Draft Final Report
2. State of Washington Response to Abbott/UBC Comments on the Draft Final Report
3. Summary Assessment and Comments on the Final Report

OBSERVATIONS ON "FREQUENTLY SUBMITTED COMMENTS" ON THE DRAFT FINAL REPORT

In the section below we provide our observations on the response by the State of Washington to the "frequently submitted comments" from the many organizations that submitted public comments on the Draft Final Report.

Strength of Evidence

While the report asserts that there is lack of evidence to make a causal claim for the impact of self-monitoring on HbA1c levels, this is still the best established standard of care of insulin dependent children. The report offers no alternative for maintaining glycemic control without frequent self-monitoring. The lack of more recent randomized clinical trials evaluating the efficacy, effectiveness, and safety of SMBG is likely not due to the lack of importance, but instead the fact that the standard of care is already well established. Moreover, the lack of evidence from RCTs does not indicate that there is no evidence, as suggested in the report by the State of Washington. It is unnecessary to study an area of care and treatment which is considered well-accepted. Further, because the DCCT has previously established intensive insulin therapy (IIT) as the goal for the majority of adolescents, additional randomized trials would be unethical. Importantly, growing evidence in the literature supports a positive relationship between glucose control and more frequent monitoring of blood glucose (Karter et al. 2001; Evans et al. 1999; Haller et al. 2004), providing further evidence of the importance of SMBG in the management of children and adolescents with insulin requiring diabetes.

The article by Haller and colleagues (2004) was not captured in the HTA literature search; however, it does provide critical evidence for frequent self-monitoring as a predictor of control of diabetes. The omission of these sources draws into question the thoroughness of the review and completeness of the HTA findings and conclusions. Overall, findings published in the literature indicate that frequent blood glucose monitoring may promote better metabolic control, potentially reducing the risk of diabetic complications.

Evidence and Ethics of RCTs

Several sections within the findings of the report note that no randomized controlled trials (RCTs) were found on the topic of self-glucose monitoring. Moreover, the conclusions made by

the State of Washington—that there is little to no evidence that glucose monitoring produces favorable outcomes in children with type 1 diabetes—is based on the available evidence from RCTs. Because of the ethical standards in place for the treatment of human subjects in RCTs, and the clinically accepted practice of SMBG, it is not surprising that few trials have been conducted in the pediatric population. SMBG has been established as an integral component of disease management for patients with type 1 diabetes. Although a well-designed large RCT would be an ideal study to determine the effectiveness for frequency of monitoring, such trials would be challenging in the given population, due to the ethical principles and guidelines for the protection of children in research. Thus, decisions made regarding standard of care should be considered based on the available evidence in the published literature (e.g., observational studies, non-randomized trials, etc.) and well established clinical practice guidelines.

In response to public comments, the State of Washington indicated that they are "fully aware of the ethical concerns, human subjects' issues, and regulations related to the use of children in research" and are not suggesting that such studies be conducted. However, there are fundamental issues with the appropriateness of the topics covered in the HTA. The standard practice for glucose monitoring to maintain good glycemic control is well established and documented, therefore, to assess the efficacy of this is not necessary. Additionally, there are few safety concerns with the monitoring practices themselves and instead far greater concern with the impact that lack of monitoring can have on glycemic control. Furthermore, the appropriateness of the questions in the context of a HTA may be problematic given the disease state that is being addressed. As discussed previously, current federal regulations as well as ethical conduct require that randomized control trials (RCTs) demonstrate clinical equipoise and also require special protection for children who are enrolled in clinical trials. For this reason published RCTs in insulin requiring diabetics in children and adolescents are rare and the appropriateness of drawing conclusions based on a lack of RCTs is questionable.

Glucose Monitoring as Part of a Package of Diabetes Care

Overwhelming evidence and an established standard of care in support of glucose monitoring to maintain glycemic control has been widely accepted and practiced for at least several decades. Further, it is also well-accepted that SMBG has been recommended as an integral component in

diabetes management for improving the control of blood glucose concentrations (ADA 1994). Moreover, evidence in the literature examining patterns of self monitoring and its effect on glycemic control showed that SMBG is associated with improved glycemic control in patients with type 1 diabetes, suggesting that self monitoring is critical for maintaining good diabetic control (Evans et al. 1999). The primary goal of treatment is to keep blood glucose levels in the normal to near-normal range and monitoring blood glucose levels is one of the best methods to understand how well your diabetes management plan is working. In accordance with regulatory guidelines and as evidenced in the existing published literature, it is critical to monitor blood glucose levels to determine the effectiveness of the management plan as quickly and conveniently as possible, and thus help to prevent hypoglycemia and extreme hyperglycemia and to avoid complications of diabetes.

Clinical Guidelines

Throughout the United States and worldwide, many respected organizations have issued clinical practice guidelines and recommendations for glucose monitoring in children and insulin-requiring diabetics. These guidelines were also presented in the HTA report. While it is recognized that different practice guidelines have different origins, it is clear that the clinical guidelines support the frequent monitoring of blood glucose for children (under age 18) who are insulin dependent to maintain glycemic control.

The current guidelines from the American Diabetes Association (ADA) Clinical Practice Recommendations (2010) provide evidence from published studies when possible, and expert opinion or consensus when necessary. Additionally, the guidelines also recommend more frequent self monitoring of blood glucose (SMBG) to achieve postprandial glucose targets. Although the most recent report does not specifically refer to the pediatric population, it is recommended that SMBG be performed three or more times daily for patients requiring insulin therapy and this most certainly applies to children. Guidelines published by the Diabetes Coalition of California (California Diabetes Program 2008), recommend SMBG testing in children and adolescents with type 1 diabetes a minimum of four times daily, consistent with recommendations published by the ADA. In addition, the International Society for Pediatric and Adolescent Diabetes (Rewers et al. 2009), states that “SMBG is an essential tool in the optimal

management of childhood and adolescent diabetes" and as such, recommend SMBG be performed at a frequency of 4-6 times daily to optimize diabetes control in children. The International Diabetes Federation (IDF 2007) recommends SMBG a minimum of three times per day in insulin requiring diabetics.

There is overwhelming agreement among clinical practice guidelines for the frequent monitoring of blood glucose for children (under age 18) who are insulin dependent to maintain glycemic control. Thus, clinical practice guidelines should be included as additional evidence on the frequency of glucose monitoring in children and any conclusions made in the final report should reflect current practice guidelines in addition to the published literature. The alternative of not monitoring would result in a larger proportion of children with dangerous hyperglycemia and hypoglycemia and overall poor glycemic control likely resulting in a lifetime of diabetes-related adverse events and significant mounting associated medical costs.

Safety

It is well recognized that there are few (if any) safety issues related to conventional self glucose monitoring, mainly due to improved blood drawing technology. However, Key Question 3 still fails to address what seems to be a critical safety issue: the risks and health consequences related to poor glycemic control due to inadequate blood glucose monitoring. It is well known that the long-term deleterious effects of poor glycemic control are separated into macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy). SMBG is essential for the prevention of hypoglycemia and additional long-term complications of unregulated diabetes, including heart disease, stroke, kidney failure, and nerve damage.

Additional References

There was additional published evidence available in the literature on the effectiveness of glucose monitoring in patients with diabetes requiring insulin therapy not included in the WA Health Technology Assessment draft report. As stated earlier, the omission of these sources draws into question the thoroughness of the review and completeness of the HTA findings and conclusions. We also note the use of language from Gomes et al. 2010, which was not cited in the report and was evaluating type 2 diabetes in adults who do not require insulin. Overall,

findings published in the literature indicate that frequent blood glucose monitoring may promote better metabolic control, potentially reducing the risk of diabetic complications.

STATE OF WASHINGTON RESPONSE TO ABBOTT/UBC COMMENTS ON THE DRAFT FINAL REPORT

In the section below we provide responses to the comments made by the State of Washington in response to the Abbott /UBC submitted comments.

Literature Search

Although the State of Washington acknowledged the limitations regarding the use of MeSH terms and indexing, they disagreed with UBC's assessment that their search algorithm was "very likely" to miss relevant studies and further stated that the use of unstructured key-word searches typically identify citations that are not pertinent. However, the search strategy undertaken by the State of Washington failed to capture all relevant articles. Six additional studies, which met all inclusion criteria and satisfied no exclusion criteria, identified by commentators were added to the final report. Furthermore, with a disease area like diabetes and glucose monitoring, it would be possible and more appropriate to create a structured search algorithm composed of keywords to identify relevant articles to further narrow the search and while limiting background "noise." Moreover, as evidenced in the response by the State of Washington, there were relevant articles identified by commentators that were "not captured" in their search "but were included in the final report for completeness." Even if the citations identified by commentators "added almost no substantive data" or substantially contributed to the final conclusions of the report, they still contribute to the body and strength of the evidence. Thus, to ensure that the original search was thorough, a supplemental keywords search with no limits should have been run to make sure all relevant citations were identified.

Grey Literature

Grey literature encompasses literature or information other than articles published in peer-reviewed journals. This type of literature can include HTA reports, clinical practice guidelines, conference/professional meeting abstracts or posters and professional association reports. We do understand that professional meeting abstracts, such as abstracts presented at the ADA annual meeting, are not critically reviewed; however, the reason to consider the inclusion of meeting

abstracts is that they typically highlight the latest thinking in the field and provide valuable insight on the future direction of research.

Contrary to the assumption made by the State of Washington, UBC did not miss the listings of clinical practice guidelines presented in the initial section of the report. As discussed in great detail in our earlier report, many respected organizations have issued clinical practice guidelines and recommendations for glucose monitoring in children and insulin requiring diabetics. As consistently stated by regulatory authorities, the self-monitoring of glucose is an essential component of management necessary to maintain glycemic control and has been widely accepted and practiced for at least decades. Given the substantial body of evidence in support of glucose self-monitoring, it is unclear what the State of Washington's objectives were in undertaking this topic for the HTA.

Finally, we are in agreement with the State of Washington that if the intention of the HTA was to focus on children and adolescents (under age 18 years) with insulin dependent diabetes, it is not necessary to include recommendations for type 2 diabetes; however, this was not clear in the draft report. General statements throughout the draft HTA such as the "primary focus is on evaluation of self-monitoring methods used to assess glucose levels at home for daily decision making regarding self-care," were suggestive of inclusion of both type 1 and 2 diabetes in children and adolescents.

Use of Non-Randomized, Observational Studies

The lack of more recent randomized clinical trials evaluating the efficacy, effectiveness, and safety of self-monitoring of blood glucose (SMBG) is likely not due to the lack of importance, but instead the fact that the standard of care is well established and the guidelines for treatment of human subjects, in particular, children are quite strict with regards to requirements for randomization. Given these regulatory guidelines, it would be highly unlikely a study would be conducted that would allow a group of children to be assigned to not monitor their glucose levels, therefore, increasing the risk of hypoglycemia and other safety events related to poor glycemic control. It would also seem unnecessary to study an area of care and treatment which is considered well-accepted. Furthermore, because the DCCT has previously established intensive

insulin therapy (IIT) as the goal for the majority of adolescents, additional randomized trials would be unnecessary and unethical.

Long Term Outcomes and Safety Related Risks and Consequences of Poor Control

SMBG is a fundamental component of comprehensive diabetes care in children and adolescents and achieving optimal glycemic control in adolescents with type 1 diabetes has been shown to delay the onset of microvascular complications. For instance, the relationship between metabolic control and the complications of type 1 diabetes has been previously established in several studies, including the DCCT, which has clearly demonstrated that intensive insulin therapy (IIT) reduces the risk of developing microvascular complications of type 1 diabetes, specifically retinopathy, nephropathy, and neuropathy (DCCT 1993 and 1995; Holman et al. 1983; Brinchmann-Hansen et al. 1992). More recently, the Epidemiology of Diabetes Interventions and Complications (EDIC) Study, an 8-year follow-up study among the DCCT cohort, demonstrated that the long-term effects of ITT in patients with type 1 diabetes had an extended beneficial effect in delaying the progression of diabetic nephropathy (EDIC 2003). Thus, improved metabolic control has unequivocally been demonstrated to delay the onset and slow the progression of microvascular complications in adolescents with insulin requiring diabetes, improving long-term outcomes and health related consequences of poor glycemic control.

SUMMARY ASSESSMENT AND COMMENTS ON THE FINAL REPORT

Study Key Questions

We recognize that the scope of this report is constrained by the framing of the key questions. Although the individual research questions outlined within the report address the areas of efficacy, effectiveness, and safety in self-glucose monitoring, there are fundamental issues with the questions in terms of their appropriateness for the topics covered in the HTA. The key questions in the context of a HTA may be problematic given the disease state that is being addressed. Thus, future studies should address the consequences of not achieving good glycemic control since health related consequences of poor glycemic control have been linked to both macrovascular and microvascular complications in insulin dependent diabetes.

Overall Findings as Reported for Key Questions

The overall conclusion of the technology assessment report with respect to the Key Question 1 is that,

> *"No randomized controlled trials or observational studies which directly evaluated current methods of SMBG testing, as an independent component of management were found."* (p. 10)

Similarly, with respect to Key Question 2, the conclusion is that,

> *"There were no randomized controlled trials (RCT) that directly evaluated the efficacy of SMBG frequency."* (p. 12)

In both cases the DCCT is described as providing indirect evidence for both the efficacy of glucose monitoring (Question 1) and the optimal frequency (Question 2). This landmark study is described as providing a low quality standard of evidence for both questions (pp. 16, 18) because glucose monitoring was not specifically addressed as "an independent component of management" (p. 10). Strictly speaking, this is correct. The DCCT compared a strategy of measuring blood glucose four times daily and calibrating insulin dose accordingly with a strategy of insulin administration based on a single daily blood glucose measurement. To state that measurement of blood glucose was not evaluated as an "independent factor" misses the point of the DCCT, which was to assess the relative benefit of tight glycemic control where every dose of insulin was titrated as a function of blood glucose level at that precise time. The DCCT provides strong evidence that, "… package of comprehensive, intensive diabetes care, which included SMBG four or more times a day and education on how to use the information to adjust insulin, diet, and exercise…" improves outcomes relative to standard care across a wide range of measures (p. 11).

According to the document *Peer Reviews, Public Comments & Responses* (January 14, 2011):

> *"The HTA evidence report is intended to summarize and critically appraise available literature, based on a systematic search and review of the literature with a focus on the highest quality evidence available."* (p. 3)

In accordance with this focus on "highest quality evidence available" the overall finding is a lack of evidence for the efficacy and effectiveness of blood glucose monitoring. The DCCT, widely viewed as a landmark study is categorized as a weak source of evidence. The absence of later trials and trials specifically addressing optimal frequency of SMBG is readily explained:

- Insulin cannot be safely administered without knowledge of blood glucose levels; dosing errors can lead to hypoglycemia or hyperglycemia, both of which can be life threatening in children.
- The rationale for frequent blood glucose measurement is directly linked to the frequency of insulin administration.
- The DCCT clearly demonstrated the benefit of tight glycemic control, primarily achieved by frequent blood glucose measurement with careful titration of insulin dose; benefit was so great that the study was stopped a year early.
- A subsequent study randomizing children to less frequent dosing would likely be seen as unethical and potentially harmful, and in violation of the Belmont principles.

In summary, rigid adherence to a very narrow definition of relevant literature results in findings that may be difficult to interpret and potentially misleading to the State of Washington health care policy-makers who will receive the report.

Misleading Statements in the Executive Summary

The Executive Summary of the Final Report (as well as the body of the report, p.24) contains the following statement:

> *"The effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial. Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring, along with a lack of clinically relevant improvement in diabetes-related outcomes in patients who self-test."*

It appears as though this language is drawn from the introduction of Gomes et al. 2010, which references several studies on the adult type 2 diabetes population which does not require insulin

(Faas et al. 1997, Davidson et al. 2005, Farmer et al. 2007, Guerci et al. 2003, O'Kane et al. 2010, Kennedy et al. 2001, Canadian et al. 2009, Davis et al. 2007). This population is drastically different from the population of study: pediatric type 1 diabetes patients who require insulin. This very strong statement casting self-monitored blood glucose in a negative light is subject to misinterpretation by persons lacking extensive knowledge of the field.

> *"The effectiveness and optimal frequency of self-monitoring of blood glucose in patients is controversial."*

This statement is not substantiated by information presented in any part of the report. Clinical practice guidelines as summarized in the report universally recommend frequent monitoring of blood glucose. The summary of clinical guidelines as presented in the report concludes that,

> *"Clinical guidelines specific to children or adolescents who require insulin recommend SMBG at least four times a day. They recommend CGM may be helpful to some patients and should be offered."* (p. 53)

Not surprisingly, the review of health insurance coverage policies for home blood glucose testing describes this procedure as "medically necessary." In summary, there is no controversy surrounding the necessity and frequency of SMBG for persons with insulin-dependent diabetes. However, the statement in the report is inaccurate and misleading and could easily be misinterpreted by readers who lack deep knowledge of diabetes.

> *"Several lines of evidence have suggested an association between glucose monitoring and increased discomfort, inconvenience and worsening of depression scores with regular self-monitoring."*

Here is another strong statement that casts blood glucose monitoring in a negative light. Describing these adverse consequences as emanating from "lines of evidence" suggests a basis in studies that would meet the criteria for "high strength of evidence."

- *Discomfort*. The only mentions of "discomfort" in the report pertain to the pain of finger sticks as associated with older technology (p. 43). Continuous glucose monitoring (CGM) is described as having the potential to reduce discomfort (p. 46).

- *Inconvenience*. The only mention of "inconvenience" in the report is in the background description of SMBG where "inconvenience" is cited as a barrier to testing (p. 44). No "evidence" is provided in the form of references to published studies.

- *Worsening of depression scores.* Evidence tables for the safety of SMBG and CGM (pp. 113–125) reveal no reports of depression. The summary of evidence for Key Question 3 (safety) makes no mention of depression (p. 134).

Clearly, frequent self-monitoring of blood glucose is uncomfortable and inconvenient if considered for a type 2 population not on insulin. For children especially, this frequent reminder that they have a chronic condition and are "different" from their peers could provoke anxiety and depression. But these are short-term issues. Parents and children need to understand the long-term consequences of lack of adherence, such as neuropathy or retinopathy, which can result in substantially more "discomfort, inconvenience, and depression" then blood glucose monitoring.

SUMMARY AND CONCLUSIONS

The stated focus of the HTA report is on the efficacy, safety and cost effectiveness related to SMBG in children and adolescents with type 1 diabetes; however, the report continues to neglect to address the indirect long-term impact of not maintaining glycemic control. Overwhelming evidence and an established standard of care in support of glucose monitoring to maintain glycemic control has been widely accepted and practiced for at least several decades. In accordance with regulatory guidelines and as evidenced in the existing published literature, it is critical to monitor blood glucose levels to determine the effectiveness of the management plan as quickly and conveniently as possible, and thus help to prevent hypoglycemia and extreme hyperglycemia and to avoid complications of diabetes.

The lack of more recent randomized clinical trials evaluating the efficacy, effectiveness, and safety of SMBG is likely not due to the lack of importance, but instead the fact that the standard of care is well established and the guidelines for treatment of human subjects, in particular, children are quite strict with regards to guidelines for randomization. Given these guidelines, it would be highly unlikely a study would be conducted that would allow a group of children to be assigned to not monitor their glucose levels, therefore, increasing the risk of hypoglycemia and

other safety events related to poor glycemic control. Further, it would seem unnecessary to study an area of care and treatment which is considered well-accepted.

Furthermore, the study questions and execution bring several factors into question. First and foremost, the defined research questions neglect to address some of the key factors related to SMBG such as long-term impact of poor glycemic control with regards to patient safety and associated cost. There are far more potential safety concerns related to poor glycemic control than concerns over the safety of performing SMBG which are addressed in this report. Also, while efficacy and effectiveness are evaluated for SMBG, there is substantial evidence to support the importance of frequent glucose monitoring which is established to be the best way to self-monitor.

Although the report asserts that there is a lack of evidence to make a causal claim for the impact of self-monitoring on HbA1c levels, this is still the best established standard of care for insulin dependent children. The report offers no alternative for maintaining glycemic control without frequent self-monitoring.

Clinical guidelines and well established clinical practice support the frequent monitoring of blood glucose for children (under age 18) who are insulin dependent to maintain glycemic control. The alternative of severely limiting monitoring or not monitoring would result in a larger proportion of children with poor glycemic control, likely resulting in a lifetime of diabetes-related adverse events and significant associated medical costs.

Finally, of critical concern, rigid adherence to a very narrow definition of relevant literature results in findings that may be difficult to interpret and potentially misleading to the State of Washington health care policy-makers who will receive the report.

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Dear Ms. Hope-Curry:

I was seriously considering moving to Washington from New York because of the excellent school system, etc.

However, I crossed Washington off my list as my 10 year old daughter has type 1 diabetes and needs to check her glucose 8 plus times per day and I find it completely unacceptable that you think she should only need to check her glucose 1 time per day! Are you serious???? Do you have any clue what type 1 diabetes is??? If my daughter were only permitted to check her glucose 1 time per day, she would die!!

I seriously wish people like you got this disease so you'd know exactly what people with type 1 diabetes go through 24 hours a day, 365 day a year. There are no breaks from this disease! My daughter will have this disease for the rest of her life!!!

Sincerely,

Allyson E. Kennedy

March 4, 2011

Leah Hole-Curry
Director
Health Technology Assessment Program
676 Woodland Square Loop SE
Lacey, WA 98503

RE: Glucose Monitoring: Self-monitoring in patients under 18 years old

Dear Ms. Hole-Curry:

The Washington Association of Diabetes Educators (WADE) is a not-for profit, all volunteer organization, made up of professional diabetes educators serving Washington State and surrounding areas. As diabetes educators, we strive each day to help our patients maintain and improve their health and quality of life, including instructing patients how and when to self monitor blood glucose (SMBG). WADE advocates for multiple blood glucose checks each day for people with diabetes. SMBG multiple times a day is especially important for people with Type 1 Diabetes utilizing a physiologic insulin replacement regimen to maintain and improve glycemic control.[1] Without the ability to check blood glucose levels when needed, severe hypoglycemia or hyperglycemia can occur.

In the State of Washington and elsewhere, babies and children diagnosed with Type 1 Diabetes are started on intensive "basal/bolus" insulin therapy. This therapy mimics the physiologic insulin of someone who does not have diabetes. In order for this therapy to be effective, however, it requires careful SMBG, with multiple blood glucose checks each day. Multiple checks allow glucose patterns to be more clearly followed which assists in insulin treatment design and modification. With instantaneous measurements, patients can self-adjust insulin doses based on actual, current glucose levels. It allows the practitioner, diabetes educator, and patient to assess the interaction of insulin with food, physical activity, stress, illness, and other physiological factors.

With any type of insulin therapy unexpected hypoglycemia and hyperglycemia are possible. The Type 1 Diabetes population that includes babies and children is one that can often not understand

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[1] *See* Mortensen HB, Hougaard P. Comparison of metabolic control in a cross-sectional study of 1,873 children and adolescents with IDDM from 18 countries. Diabetes Care, 1997l20:714-20; Anderson B, Ho J, Brackett J, Parental involvement in diabetes management tasks: relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus. J Pediatr. 1997;130:357-65; Levin BS, Anderson BJ, Butler DA, Predictors of glycemic control and short-term adverse outcomes in youth with type 1 diabetes. J Pediatr. 2001;139:197-203 (finding frequency of testing was the most important predictor of A1C levels in a study of 7 to 16 year olds). *See also* American Association of Diabetes Eductors. The Art and Science of Diabetes Self-Management Education, p. 192-94 (2006).

nor communicate symptoms of hypoglycemia or hyperglycemia. Furthermore, many of the symptoms of hypoglycemia and hyperglycemia are the same. Thus, the only way to know what treatment is needed is by SMBG on a regular basis throughout the day.

The development and improvement of SMBG combined with multiple blood glucose checks per day allows this more intensive "basal/bolus" insulin therapy to be effective at reducing acute complications (loss of consciousness, seizures, and even death) and chronic complications (kidney failure, blindness, and amputations). The DCCT[2] and the follow-up study Epidemiology of Diabetes Interventions and Complications (EDIC)[3] clearly showed that physiologic insulin replacement reduces microvascular and macrovascular complications of diabetes, but that multiple checks are necessary to provide the necessary feedback to adjust insulin doses in the optimum manner. What is standard insulin therapy today was brand new at the start of the DCCT. Much of the hypoglycemia during the trial occurred early in the study because the patients and the providers were learning how to manage the intensive insulin therapies[4]. During the course of the study, practitioners and patients became more skilled in recognizing the factors that led to hypoglycemia, in part because of SMBG multiple times per day. In the nearly 20 years that have passed since the time of the DCCT, intensive insulin therapy has become the standard and allowed for consistently better outcomes with less acute complications and less chronic complications.

As diabetes educators, we strive to give our patients the knowledge and skill to live their lives with diabetes as close to "normal" as possible. We believe that a reduction in coverage for SMBG could result in a change from intensive insulin therapy to less effective insulin therapies, as the intensive insulin therapy requires SMBG multiple times per day to reduce the risk of hypoglycemia and hyperglycemia which could lead to expensive emergency room and hospital visits. Adopting these less effective insulin therapies would be a step back in time and could have a long lasting negative impact on the patients and the State of Washington. It would take away the flexibility and the ability of Type 1 diabetics to live the normal lifestyle that the intensive insulin therapy provides and would restrict the critical amount of feedback that allows patients to self-regulate insulin dosing to feel and perform their very best.

We feel strongly as diabetes educators in the State of Washington that multiple blood glucose checks each day are necessary to optimize the quality of life and the longevity of life for people with diabetes and will significantly decrease acute complications leading to expensive emergency room visits and hospitalizations. Long-term we believe chronic complications from

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[2] DCCT Research Group (1993) The effect of intensive diabetes treatment on the development progression of long-term complications in insulin-dependent diabetes mellitus: The Diabetes Control and Complications Trial. New England Journal of Medicine 329:977-89.

[3] The Epidemiology of Diabetes Interventions and Complications (EDIC) Study. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy. JAMA. 2003;290:2159-67.

[4] Beaser, Richard. Joslin's Insulin Deskbook, Designing and Initiating Insulin Treatment Programs. Boston, MA. Joslin Diabetes Center, 2008.

diabetes can be significantly reduced with SMBG multiple times per day. We urge you to consider these factors when making your decision about limiting SMBG coverage.

Thank you.

Sincerely,

Caroline Hudders

Caroline Hudders RN, MS

Cindy Brinn

Cindy Brinn MPH, RD, CDE, BC-ADM

January 17, 2011

Leah Hole-Curry, JD, Program Director
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WA State Health Care Authority
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shtap@hca.wa.gov

Dear Ms. Hole-Curry,

I would like to have a final comment in addition to my first letter last month. I feel there are two major issues here as they pertain to home blood glucose monitoring. First is the concern about this technology requiring "evidence" in the current culture of "evidenced-based medicine". As reviewed previously, it is difficult if not impossible to incorporate the true definition into our current culture of diabetes management without returning to the era of more frequent severe hypoglycemia (well-documented there is less today for a variety of reasons), more frequent acute illness from hyperglycemia (including DKA), and perhaps most importantly, overall poorer blood glucose control for type 1 individuals. When HbA1c assays were first routinely used in type 1 diabetes, it was *extremely* rare to see a value under 10 or 11%. Again, one needed to understand the glucose values to know how much insulin to give.

I want to assume for a moment that we accept that home blood glucose monitoring is an accepted, important, and even critical aspect for the treatment of type 1 diabetes in children. What the real issue comes down to is how do we ensure the appropriate materials (and the quantity required) arrive to the patients intended? I appreciate that there can be "strip fraud" in that a physician writes for the glucose strips for one patient; yet another person actually uses the strips.

What some payers do (including Medicare) is they require a written log of blood glucose data from the patient (or family). Of course, I appreciate that these glucose results could be falsified if they are simply a written log. I'd suggest instead a meter download which I believe most pediatric endocrinologists do anyway. A meter (or meters) can be downloaded, the frequency of testing can be quickly noted, and the appropriate number of strips can be supplied to the patient. There are some problems with this that the system would need to address, including the fact that many meters lose their memory when the battery is changed, meters can be lost, etc. Nevertheless, there could be some initial flexibility in this policy and using a meter download would not add a huge burden to the majority of clinicians who care for these families, in addition to the fact the meters in many cases can be downloaded by the families themselves, thereby removing any burden from the provider if that is a problem.

I again applaud the committee in trying to find better more efficient ways to care for this population of patients. However, and as noted by Dr. Greenbaum in her letter, until one lives with a child with type 1 diabetes it is virtually impossible to appreciate the difficulty encountered by those families who need to live with this condition.

Sincerely,

Irl B. Hirsch, M.D.
Professor of Medicine
University of Washington School of Medicine

UNIVERSITY OF WASHINGTON
MEDICAL CENTER
UW Medicine

February 18, 2011

Dear Mr. Porter, Dr. Thompson, and Dr. Hayes,

I want to keep my letter brief, as there really isn't much more to say about self-monitoring of blood glucose (SMBG) in children under the age of 18 that hasn't been said by my colleagues or me. I grew up in the era prior to SMBG, diagnosed with diabetes at the age of 6 years old, which was 47 years ago. I am now a Professor of Medicine at the University of Washington and am the Medical Director of our diabetes clinic there, so I trust my credentials are not an issue.

My comments about our Health Technology Assessment for this topic are as follows:

1. SMBG efficacy in type 1 diabetes for children or adults can never be ethically tested. There are some areas of medicine where our push for "evidenced-based medicine" simply can't apply, and this is one of those cases.
2. Its value is self-evident. Injecting insulin into a 3 year-old four times daily, a 12 year-old before a football practice, or a 16 year-old driver without knowing the blood glucose level is absurd considering it is the standard of care around the world.
3. Limiting glucose test strip coverage increases the risk of short-and long-term complications, taking a human and economic toll. If we all agree that glucose control can retard or eliminate the chronic complications of diabetes, it would be impossible to treat childhood diabetes without SMBG. Indeed, we tried for the first 60 years after the discovery of insulin and we were unsuccessful. I should also point out that the acute complications from hypoglycemia and ketosis requiring ER visits would by necessity rise, especially the former as families attempt to keep glycemia well controlled will find it impossible without SMBG. My greatest concern is that we will see deaths due to the lack of SMBG in this population
4. Limiting coverage increases inequities in healthcare. Since SMBG is an international standard of care for any patient requiring insulin therapy, the impact of a negative decision for SMBG in children in our state is directly opposed to President Obama's goals for healthcare in our country.

My colleagues around the country and the world have some very concerning thoughts about the way we decide which healthcare services are worthy of coverage in our state. I can only hope that at some point common sense will prevail and children and their families will be able provided with the necessary supplies for diabetes management, including glucose test strips required to lead a healthy, successful life.

Sincerely,

Irl B. Hirsch, M.D.
Professor of Medicine
University of Washington

Diabetes Care Center
Box 354691 ▪ 4225 Roosevelt Way NE, Suite 101 ▪ Seattle, WA 98105 ▪ 206 – 598-4882 (Phone) ▪ 206 – 598-4976 (Fax)

My name is Jennifer and I am a type 1 diabetic, so is my 16 year old son. As type 1 diabetics we need to check our blood sugar anywhere from 4-8 times a day, and on days of illness or blood sugars that are not doing well it can be more. Type 1 diabetics, even on a controlled diet need to know what their blood sugar is before meals to properly administer medication as well as when they feel their sugar may be low or high. For the state of Washington to tell me that my son could test only once per day would be devastating and potentially life threatening. Imagine having a day of lows and you already used your allotted one strip. To use more strips to test means you would run short for the month, causing either further financial burden on the family already paying for multiple prescriptions per month and doctor bills, but also the hazard of needing to check and not being able to because you couldn't afford to go out and by more strips.

Please, before you consider such a hideous idea of limiting diabetics to 1 strip per day. Spend some time with diabetic children and adults. Talk to a diabetes educator or Endocrinologist. Educate yourself on Diabetes before you make such a harsh sentence.

Jennifer Reed
Type 1 Diabetic
12 years.

To Whom it May Concern,

I am the parent of a type 1 diabetic child. I am concerned that potential legislative changes will critically affect the life of my child. Children struggling with this disease do not have the ability to control their glucose by a simple set dosage of insulin. The disease is unpredictable. Glucose testing is the only way to properly dose insulin. By limiting the prescribed number of test strips to these individuals you would be endangering their lives each and every day.
Our current regimen includes a minimum of 6 glucose tests each day. Often times that number is insufficient. I cannot imagine sending a teen driver off without having her check her glucose level first. I cannot imagine her competing in a gymnastics meet without the knowledge that her glucose is at an acceptably safe level. I cannot imagine her menstrual cycle causing her blood sugars to spike and result in a hospital stay, simply because we were unable to properly monitor her glucose levels.

I understand that funding is an issue. I am well aware that diabetic supplies are expensive, and a tempting place to cut costs. As an independent sub-contractor and a stay at home mother we were greeted with this disease 4 years ago. It was necessary for me to go back to work to provide a better healthcare option for my family. My wages are insufficient to cover our family's insurance costs. We currently are paying $1,000.00 a month in medical expenses, in a time when we do not have $1,000.00 to spend. Add to that a $500 dollar deductible, which we meet each year, co-pay costs and prescriptions. As an insulin pump user, many of the supplies are not fully covered. You are proposing to cut our dosage from 10 strips down to 1 strip a day. This will exponentially increase our monthly costs and potentially increase the likelihood of future hospital stays. The long term complications of the disease include blindness, amputation, kidney failure, heart disease and more. This limited access to testing would be irresponsible and dangerous.

By limiting our ability to treat my daughter with the knowledge that a simple glucose test provides, her life is endangered. Excessively high blood sugars cause Diabetic Ketone Acidosis, with debilitating symptoms that would critically impair her ability behind the wheel of a car. A borderline low blood sugar at the onset of a gymnastics practice would cause her blood sugar to crash and cause a seizure, potentially endangering her life and limbs while in a compromised position on the vault or balance beam. A simple cold or even her normal menstrual cycle causes her to be more insulin resistant. Limited access to the information glucose testing provides, would mean that at minimum, every 28 days she would experience 5 days of unmanaged high blood sugars, putting her at risk of needing immediate hospitalization and chronic long term damage. While these thoughts are frightening to me, I can't imagine being the parent of a toddler or infant without access to blood glucose testing. Limited access to glucose testing will cost the lives of these children who don't have the ability to communicate or even understand what this disease is doing to their bodies.

I urge you and others to think through what your proposal would do to the thousands of children and adults suffering from type 1 diabetes. I urge you to think through the potential liabilities involved in changing the safety that multiple glucose tests provides.

Thank You,
Jill Delaurenti
Parent of Natalie Delaurenti
14 years old, Type 1 Diabetic
Diagnosed 2007

I understand that the State is considering covering only one test-strip for diabetic children per day. It is also my understanding that children may require from 1 to 12 per day, at a cost of ~$1 for each strip. Although many parents can afford the cost of the test strips, there are many who cannot. At for example 10 strips a day, a family might need to pay $300/month for them, which would be very difficult for a low-income family to afford for their diabetic child. I would hate to think that a child from a low-income family might die, merely because his mother could not afford to pay for the strips that might provide the vital information needed to save his life.

Thank you,
Judy Guitton

Program Director

Washington State Health Care Authority

Health Technology Assessment Program

676 Woodland Square, Loop SE

Lacey, WA 98503

Dear Leah Hope-Curry,

I was informed about the following information recently and am confused and alarmed:

The State of Washington is trying to limit the number of test strips used by diabetic children to one per day. A test strip is inserted into the blood sugar monitor each time the child needs to test his or her blood sugar. Michael tests 6 - 8 times per day - some kids test more, some kids test less. Some very young diabetics may test 15 times per day! Some children wear a CGM (continuous glucose monitor), but testing with a meter and strip is still the most common method.

Please understand the severity of this issue. I have two type 1 daughters who were diagnosed at ages 6 and 8. We had to constantly check their blood sugars to prevent them from going into shock if went to low. Please, please help insurance to understand why blood sugar control is so very important to our kids now and for the health of their future. Our insurance is already limiting the amount of test strips for my girls and we have to look for additional options and is very expensive.

Please help families dealing with Type 1 Diabetes! It can't be lumped in with Type 2 and is very different and much more dangerous if left unmonitored.

Sincerely,

Julie Edmark

Dear Leah Hope-Curry,

I was informed about the following information recently and am confused and alarmed:

The State of Washington is trying to limit the number of test strips used by diabetic children to one per day. A test strip is inserted into the blood sugar monitor each time the child needs to test his or her blood sugar. Michael tests 6 - 8 times per day - some kids test more, some kids test less. Some very young diabetics may test 15 times per day! Some children wear a CGM (continuous glucose monitor), but testing with a meter and strip is still the most common method.

Please understand the severity of this issue. My son is a type 1 diabetic diagnosed at age 2 1/2, he is now 11 . We have to constantly check his blood sugars to prevent him from going into shock from going too low or too high . Please, please help insurance to understand why blood sugar control is so very important to our kids now and for the health of their future. Our insurance is already limiting the amount of test strips for my son and we have to look for additional options and is very expensive.

Please help families dealing with Type 1 Diabetes! It can't be lumped in with Type 2 and is very different and much more dangerous if left unmonitored.

Sincerely,

Kim Miller

You people need to research type 1 diabetics and what they have to go through daily. How dare you try to put a limit on the number of test strips a t1 can use daily. Type 2 I understand. But come on these are children and there are major differences in the treatment of the two!! My 7 year old is completely dependent on insulin due to the fact her pancreas does not work! It is dead! Unlike in type 2 diabetics where it is a metabolic disease. Type 1 is an autoimmune disease in which the body sees the pancreas as an infection and KILLS it! Please for the sake of my youngest daughter don't put restrictions on this. She needs it to live a healthy life!!!!!!!

Kristina Earp

Sent from my U.S. Cellular BlackBerry® smartphone

Ms. Curry -

I am the mother of a child with type 1 diabetes. I have heard from several sources that the State of Washington is considering limiting the number of test strips used to monitor blood sugar to one per day. I am mortified and certainly hope this isn't true. Any parent of a child with type 1 diabetes can tell you that blood sugar levels are much easier to control with frequent testing. Any child with diabetes will tell you the same, despite the discomfort of testing! My son was diagnosed just a few weeks after his ninth birthday and is now fifteen. He checks his blood sugar an average of six times per day and has decent control. The teenage years are very challenging for a diabetic, and compliance can be an issue. When my son "forgets" to check his blood sugar, his numbers skyrocket! When is blood sugar is high, he is completely unable to focus in school and his grades suffer. There is ABSOLUTELY a HUGE correlation between the frequency of testing and the quality of blood sugar control! To even suggest otherwise is foolish, and potentially dangerous!

I realize times are tough and assume this strategy is yet another short-sighted attempt to save money. You are probably well aware of the long term complications of diabetes - these will end up costing our state much more than a reasonable amount of test strips could possibly cost! I am a life-long resident of this beautiful state; if this "threat" by our state is true, it will be an embarrassment to all that live here.

I look forward to your reply.

Sincerely,
Lynn Kern

Children and adults need to test every 2-4 hours. Anything else is un healthy, unsafe, and definitely NOT in the public interest. Do not make a policy of testing less than this.

Paul Richards
Edmonds Wa

To the Attention of Ms. Hope-Curry:

I have recently learned there is consideration being made to reducing test strips for type 1 diabetics.

My daughter, Rachel, age 12, has lived with this disease for five years now, not easy by any means. I wonder if you know any diabetics or have been personally touched by this chronic, relentless disease which robs children of their childhood and inviduals to go about their daily routing without another set of concerns for their health and wellbeing?

I know I knew nothing until my daughter was diagnosed and it's turned our world literally UPSIDE DOWN. No two days are like and MANY factors can influence blood glucose readings. For example for us right now, puberty with hormones changing drastically, and the stress of middle school alone can throw a blood sugar. Without testing as needed to confirm what the blood sugar is, there is no other way to know how to treat it, being low or high.

Without testing, we would not have been able to confirm Rachel was approaching DKA (ketones, sugar in her urine, very deadly) and that she needed emergency treatment. Without testing, we would not have been able to treat a severe low blood sugar that was severely close to becoming a catastrophic seizure.

Test strips are simply the best measure of blood sugar. With fluctuations that the body and outside factors produce, and the need to have accurate blood sugar readings before each meal, the use of test strips is inevitable. How would we possibly know how much insulin to give a diabetic without having an accurate test reading? We would not.

I would greatly appreciate deep consideration and research into the significance of the 'tools' each diabetic needs. Frankly, the thought of limiting what my daughter needs (as well as millions of other type 1 diabetics) to survive, is distressing. One thing we don't need more of is stress in our lives. Just managing the disease is a part to full time job for us. Then, living with it, is no joy ride either.

Diabetes is not a black and white disease, so please don't treat it that way.

Sincerely,

Sandy Scribner
425.212.9520

Agency Medical Director Comments

Agency Experience:

Glucose Monitoring in Pediatric Patients

March, 2011

Self-Monitoring of Blood Glucose (SMBG) in Pediatric Patients: Background

- Routine SMBG is considered the standard of care among diabetic patients, particularly those treated with insulin.
  - The cost of SMBG has been estimated to be about 40-50% of the total cost of care for diabetes in children
- Despite widespread use, there is no high-grade evidence addressing optimal frequency and strategy of SMBG.
  - Continuous glucose monitoring (CGM) is a relatively resource-intensive technology for which even less evidence is available; CGM is not considered the standard of care in typical cases
- Utilization of SMBG among pediatric patients is highly variable.
  - Guidelines, based primarily on expert opinion, typically recommend frequency of SMBG of 4 or more times/day in children with type 1 DM

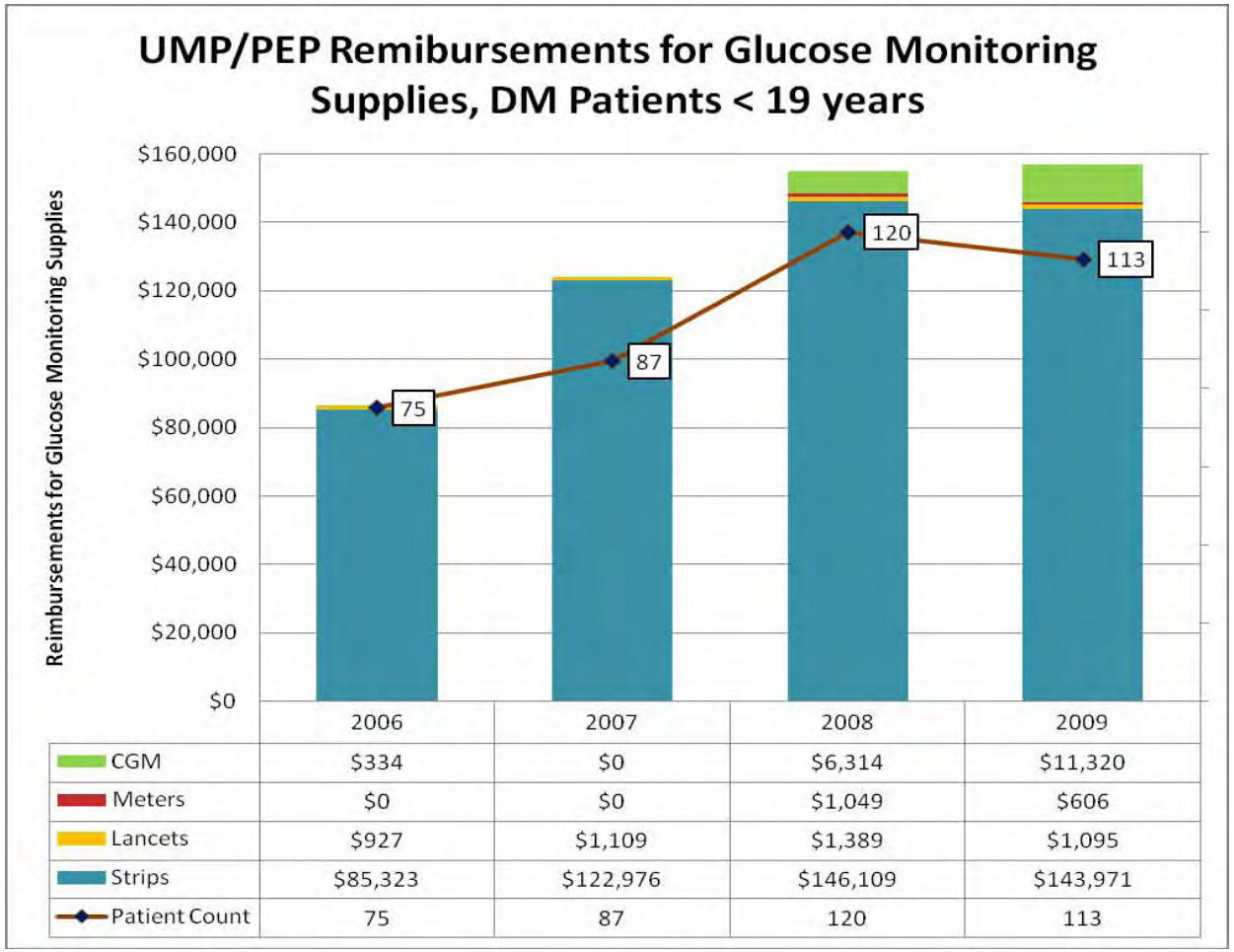
Agency Concerns-unrestricted use of SMBG

- Safety Concerns (Medium)
  - Excessive utilization of SMBG may reflect inadequate professional clinical supervision of diabetic care and/or ineffective glycemic management
- Efficacy Concerns (High)
  - Benefits of excessive SMBG (>4-5 times/day) in terms of improved clinical outcomes are unclear
- Cost Concerns (High)
  - The cost of SMBG is a major component of overall costs of diabetic care; unrestricted and excessive utilization carries potential for waste of limited healthcare resources (especially in the setting of inadequate professional clinical supervision and/or ineffective glycemic management)

Coverage Overview – SMBG in Pediatric Patients

- Currently covered without quantity restrictions by UMP
- Currently covered without quantity restrictions by Medicaid
- Only rare coverage at L&I

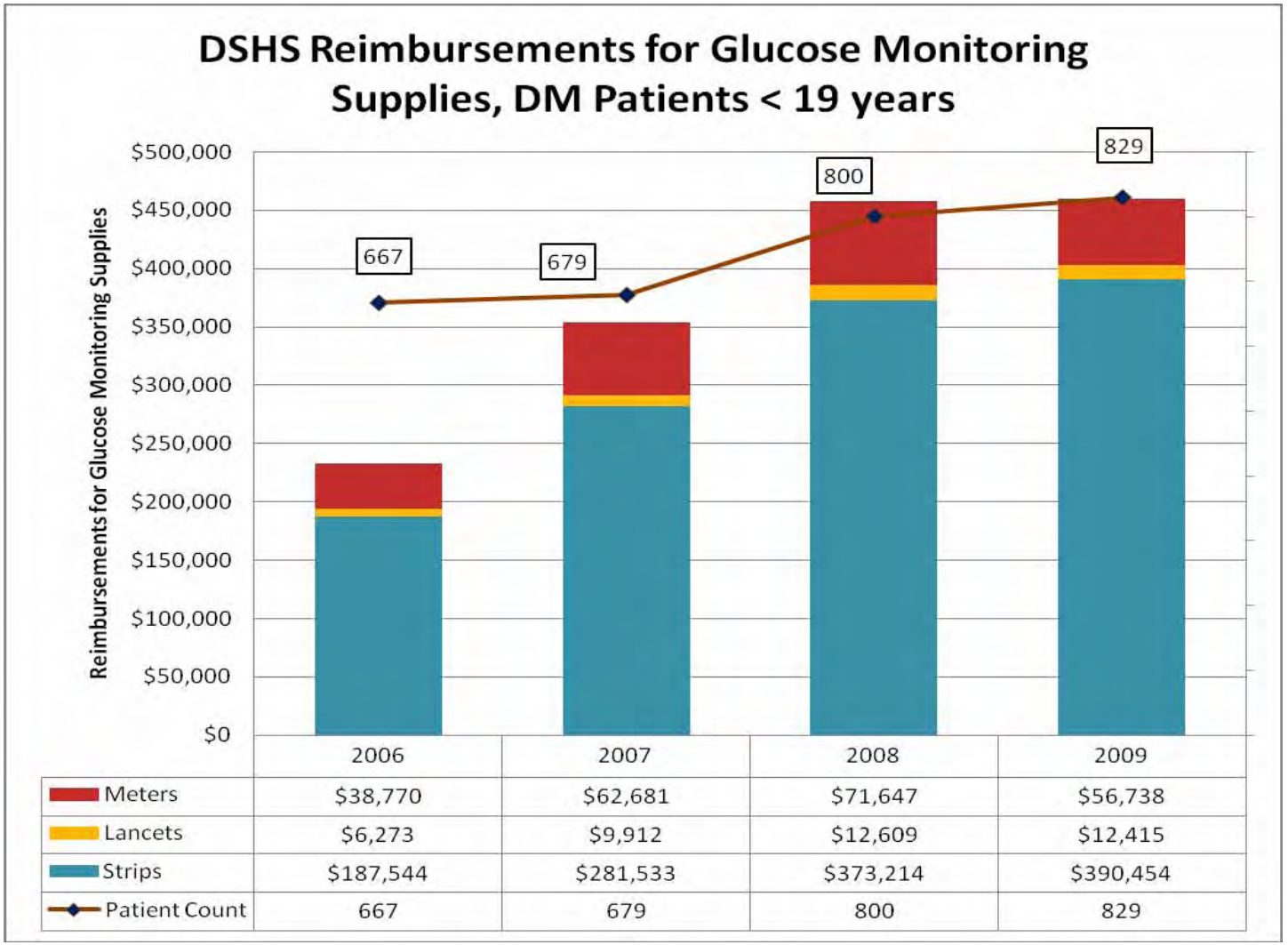
UMP Spends and Trends



	2006	2007	2008	2009
CGM	$334	$0	$6,314	$11,320
Meters	$0	$0	$1,049	$606
Lancets	$927	$1,109	$1,389	$1,095
Strips	$85,323	$122,976	$146,109	$143,971
Patient Count	75	87	120	113

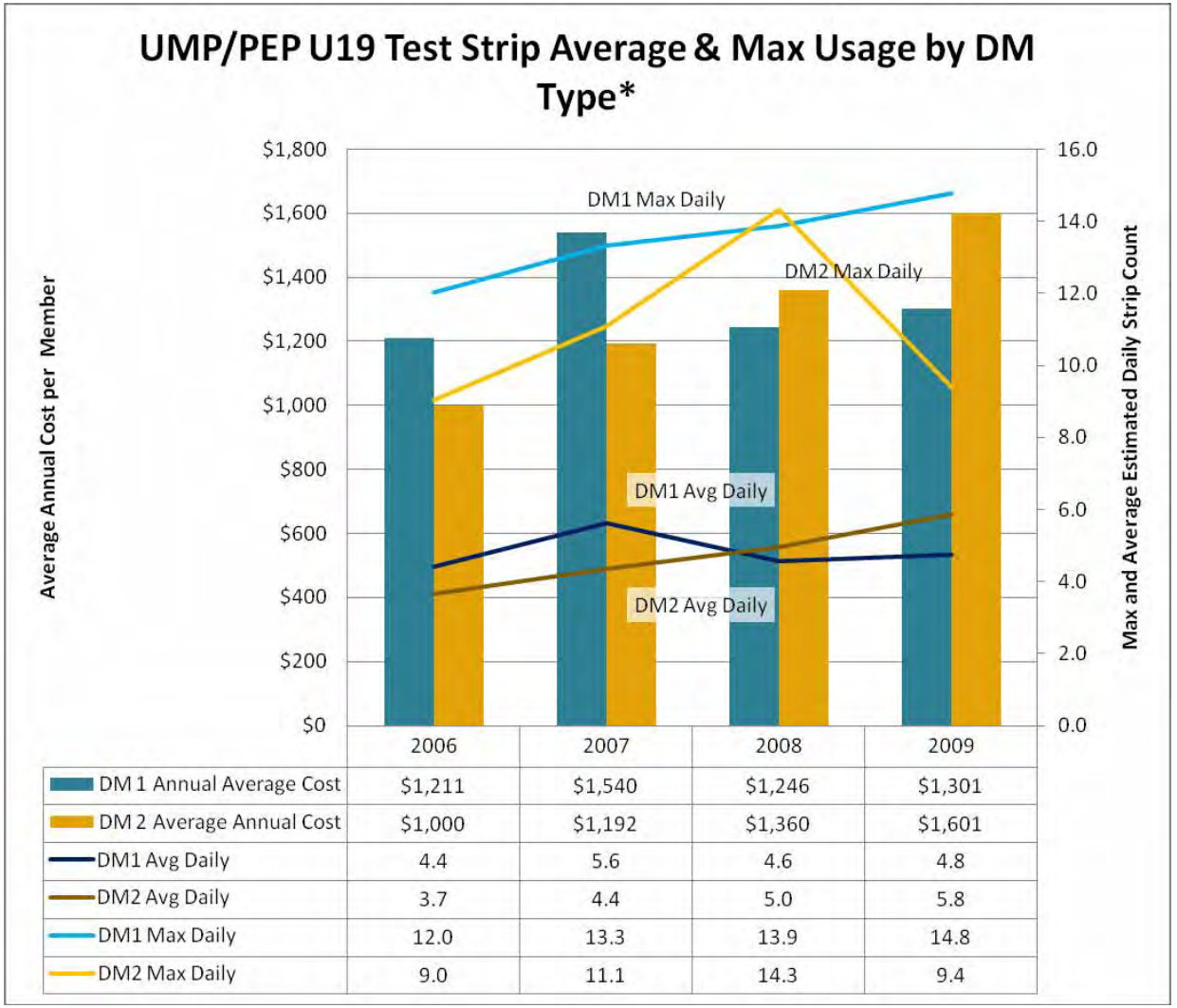
*CGM: Continuous Glucose Monitoring

Medicaid Spends and Trends



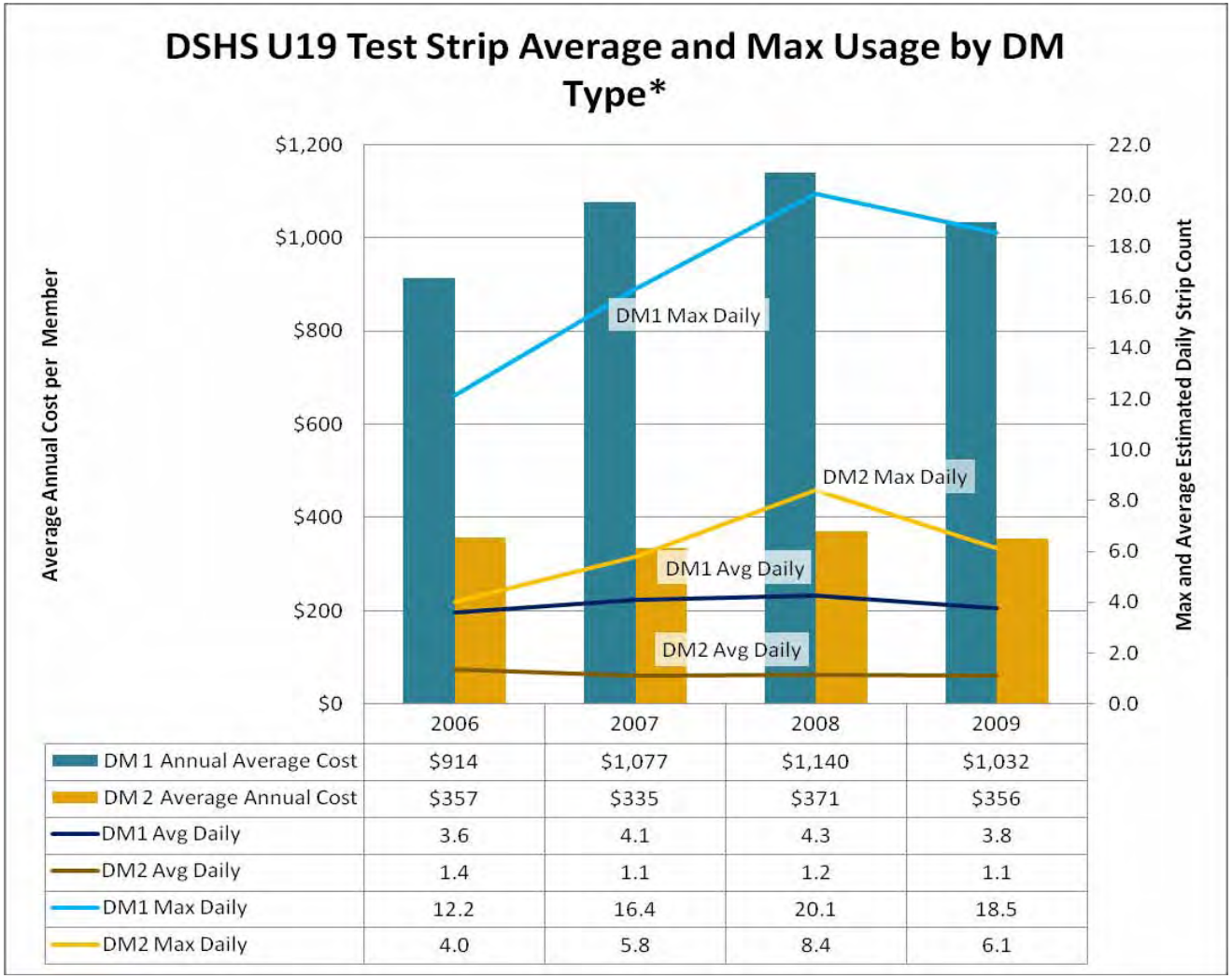
	2006	2007	2008	2009
Meters	$38,770	$62,681	$71,647	$56,738
Lancets	$6,273	$9,912	$12,609	$12,415
Strips	$187,544	$281,533	$373,214	$390,454
Patient Count	667	679	800	829

UMP Test Strip Utilization



	2006	2007	2008	2009
DM 1 Annual Average Cost	$1,211	$1,540	$1,246	$1,301
DM 2 Average Annual Cost	$1,000	$1,192	$1,360	$1,601
DM1 Avg Daily	4.4	5.6	4.6	4.8
DM2 Avg Daily	3.7	4.4	5.0	5.8
DM1 Max Daily	12.0	13.3	13.9	14.8
DM2 Max Daily	9.0	11.1	14.3	9.4

Medicaid Test Strip Utilization



	2006	2007	2008	2009
DM 1 Annual Average Cost	$914	$1,077	$1,140	$1,032
DM 2 Average Annual Cost	$357	$335	$371	$356
DM1 Avg Daily	3.6	4.1	4.3	3.8
DM2 Avg Daily	1.4	1.1	1.2	1.1
DM1 Max Daily	12.2	16.4	20.1	18.5
DM2 Max Daily	4.0	5.8	8.4	6.1

UMP/PEP U19 Diabetic Patients and Adverse Events

UMP/PEP U19 Diabetic Population	2006		2007		2008		2009	
	#	% mbrs	#	% mbrs	#	% mbrs	#	% mbrs
DM Type 1	71	83.5%	84	81.6%	118	89.4%	110	90.9%
DM Type 2	14	16.5%	19	18.4%	14	10.6%	11	9.1%
Adverse Events*								
ER visits	17	20.0%	14	13.6%	22	16.7%	15	12.4%
Critical Care	4	4.7%	2	1.9%	6	4.5%	3	2.5%
Ketoacidosis	13	15.3%	7	6.8%	5	3.8%	6	5.0%
Hyperglycemia	1	1.2%	2	1.9%	2	1.5%	4	3.3%
Diabetic coma	0	0.0%	0	0.0%	3	2.3%	2	1.7%

* Adverse event figures are member counts of those who experienced the event. Event counts (not shown) are higher, since members may experience multiple occurrences

DSHS U19 Diabetic Patients and Adverse Events

DSHS U19 Diabetic Population	2006		2007		2008		2009	
	#	% mbrs	#	% mbrs	#	% mbrs	#	% mbrs
DM Type 1	416	62.1%	452	66.6%	530	66.3%	547	65.9%
DM Type 2	241	36.1%	222	32.7%	255	31.9%	273	32.9%
Adverse Events*								
ER visits	229	34.3%	311	45.8%	352	44.0%	471	56.8%
Critical Care	42	6.3%	67	9.9%	59	7.4%	95	11.54
Ketoacidosis	75	11.2%	104	15.3%	106	13.3%	135	16.3%
Hyperglycemia	19	2.9%	33	4.9%	37	4.6%	34	4.1%
Diabetic coma	3	0.5%	2	0.3%	7	0.9%	4	0.5%

* Adverse event figures are member counts of those who experienced the event. Event counts (not shown) are higher, since members may experience multiple occurrences

AMDG: Concerns

- There is little evidence regarding optimum frequency of SMBG
- There is no evidence that >5 SMBG checks/day improves clinical outcomes
- There is concern that excessive use of SMBG may reflect ineffective clinical management
- There is evidence in the Washington State UMP and Medicaid fee-for-service populations of substantial morbidity among pediatric diabetic patients reflected in use of ER and critical care services and episodes of diabetic ketoacidosis
- Evidence for clinically significant improvement in outcomes resulting from CGM in pediatric diabetic patients is very weak

AMDG: Recommendations

- Optimal management of diabetes in pediatric patients should be multimodal, guided by qualified clinicians, to include:
  - Effective glycemic management through careful attention to diet, exercise, medication, and blood glucose levels
  - Consideration of intensive insulin therapy as appropriate
    - Intensive insulin therapy should be guided by regular SMBG, usually 4-5 times daily
    - Results of SMBG should be used appropriately to adjust diet, exercise, and insulin dosing to achieve appropriate glycemic control

AMDG: Recommendations

- Coverage of unrestricted quantities of SMBG test strips for all cases is not justified; cover with condition of up to 5 tests/day
- Coverage of >5 tests/day should require case review and justification as medically necessary
  - Could be made available as exception to rule in Medicaid
  - Consider requiring specialty consultation
- CGM should not be a covered benefit by Washington State purchased health plans (however, it could be provided in the setting of IRB-approved clinical trials)

Spectrum Research, Inc.

Bringing Evidence to Light

Health Technology Assessment:

Self-monitoring of individuals with insulin dependent diabetes 18 years of age or under

March 18, 2011

Andrea C. Skelly, PhD, MPH
Jeannette M. Schenk-Kisser, PhD, MS
Jennifer M. Mayfield, MD, MPH
Carin M. Olson, MD, MS
Erika D. Ecker, BS

Scope of Report

Critically summarize research on the efficacy, effectiveness and safety of self-monitoring of blood glucose (SMBG) and real-time continuous glucose monitoring (CGM) in those 18 years old or younger who require insulin

The report focuses on the highest quality evidence available based on systematic review of the literature

Background-Types of diabetes

- Diabetes mellitus (DM) is a serious chronic condition for which there is no definitive cure.
- DM is categorized into 3 major types, based on etiology
  - **Type 1 (T1DM):** is an autoimmune disorder that destroys pancreatic beta cells which make insulin. It is the most common form in persons ≤ 18 years old. Insulin therapy is required
  - **Type 2 (T2DM):** Is most common in adults and is caused by insulin resistance, disordered and inadequate insulin release and excessive glucose production by the liver. Diet, exercise and oral medications may be effective in the first years; however, it is progressive and insulin therapy may eventually be required.
  - **Gestational (GDM):** defined as glucose intolerance with pregnancy onset/first recognition of pregnancy.

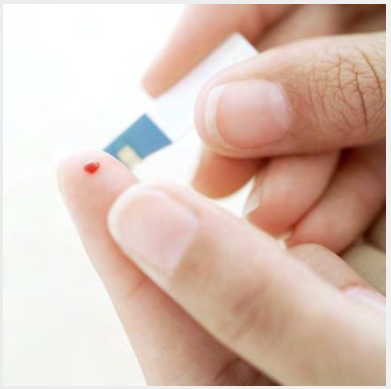
Background- Complications

- Chronic complications are strongly related to DM duration and glycemic control (T1 and T2DM):
  - Macrovasculsar complications (e.g. heart disease, stroke)
  - Microvascular complications (retinopathy, nephropathy, neuropathy)
  - Increased risk of infection, cancer, other autoimmune disorders (e.g. celiac sprue, thyroid disease)
- Diabetic ketoacidosis (DKA): severe hyperglycemia; leading cause of hospitalizations in children with T1DM nationally; can lead to coma, death
- Hypoglycemia: 3 X more common in children (vs. adults), may be difficult to detect (unawareness); can damage brain, lead to seizures, coma, death

Background

- DM duration is associated with chronic complications, thus, persons ≤ 18 years old may have the most to gain from maintaining good glycemic control yet have some of the greatest challenges in achieving and maintaining it.
- Goal: Achieve/maintain glucose and A1C levels as close to normal as possible while minimizing episodes of severe hypoglycemia
- Intensive management with tight control has become standard of care. Self-monitoring plays an integral part:
  - Provides data for decision making
  - Assists in identifying and preventing hypoglycemia
  - Provides “peace of mind” to care givers
  - Influences activities and quality of life

Self-monitoring of blood glucose (SMBG)
(intermittent monitoring)



- First FDA approval 1975
- Capillary blood drop placed on reagent-impregnated paper strips; monitor reads
- Provides “snap shot” of blood glucose levels
- Recommended: at least 4 times/day; individualized
- Barriers, adherence, use of data

SPECTRUM RESEARCH

Real-time Continuous Glucose Monitor (CGM)

Guardian REAL-Time System (Medtronic Mini-Med)

http://www.childrenwithdiabetes.com/continuous.htm

- FDA approval (7-17 years): Guardian and MiniMed Paradigm REAL-Time devices (later used w/pumps)
- Subcutaneously placed, enzyme-embedded sensor samples interstitial fluid glucose every 1-20 minutes
- Trend information; alarms for high and low levels
- *SMBG for verification and decision making per FDA*

Key Questions

1. What is the evidence of efficacy and effectiveness of self-glucose monitoring?
2. What is the evidence on optimal or improved efficacy or effectiveness of glucose monitoring based on frequency or mode (continuous versus self-monitoring) of testing?
3. What is the evidence of the safety of glucose monitoring?
4. What is the evidence that glucose monitoring has differential efficacy or safety issues in sub-populations?
5. What is the evidence of cost implications and cost-effectiveness of self-glucose monitoring?

Scope: Inclusion criteria

- **Population**
  - Persons ≤ 18 years old with insulin-requiring diabetes mellitus
- **Intervention**
  - Self-monitoring of blood glucose (SMBG) or currently available FDA-approved continuous glucose monitor (CGM) that allows for patient *real-time* use of data.
- **Comparator**
  - Frequency of SMBG or CGM use; conventional treatment; SMBG versus CGM
- **Study design**
  - Randomized controlled trials (RCTs),comparative studies with concurrent controls, studies describing associations between interventions and outcomes (prognostic studies)
- **Publication**
  - Full-length studies published in English in peer-reviewed journals, FDA reports (no meeting abstracts, proceedings)

SPECTRUM RESEARCH

Primary Outcomes
(based on available literature)

Efficacy and Effectiveness

- Mean A1C, Achieving, maintaining target A1C levels
  - ADA goals: <6 years old 7.5% -8.5%; age 6-12 <8.0%; adolescents <7.5%
  - Clinically meaningful change 0.5%
- Hypoglycemia, hyperglycemia, ketoacidosis
- Microvascular complications
- Quality of life

Safety

- Device-related
- Mortality

SPECTRUM RESEARCH

Literature search

- Electronic databases, HTA sites searched using a systematic approach; bibliographic review
- Literature search: 240 unique potentially relevant citations;
- Final number of included study reports: 49 and 3 FDA SSED; multiple studies contributed information to several key questions
- Primary evidence – efficacy and effectiveness
  - SMBG: 1RCT (DCCT) and 2 associated observational follow-up studies (EDIC) provide indirect evidence; 1 large registry study and 7 cross-sectional studies
  - CGM: 4 RCTS; JDRF trials' associated additional analyses; Data not uniformly available for those ≤ 18 years old
- No full economic studies were found

SPECTRUM RESEARCH

Key Question 1: Efficacy and Effectiveness of SMBG

1 RCT (LoE II) - Diabetes Complications and Control Trial (DCCT); N = 195 ages 13-17 years; 7.4 yrs f/u

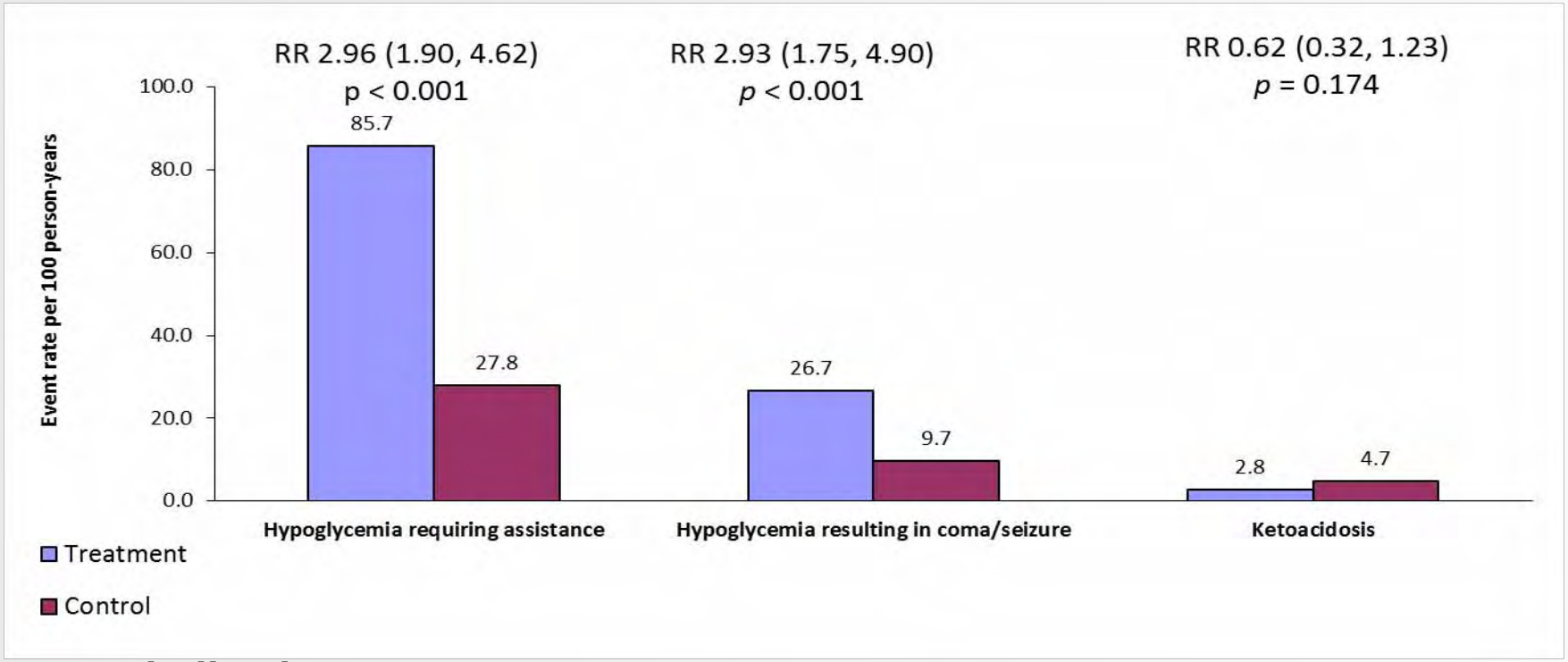
- SMBG ≥ 4/day *as part* of comprehensive, intensive care (insulin dose adjustment, diet, exercise) vs. SMBG or urine testing 1/day (insulin 1-2 injections/day; no daily changes of insulin or diet)
- Provides indirect evidence on efficacy of SMBG
- Primary prevention (PP) cohort (n = 125); participants with no retinopathy or nephropathy;
- Secondary intervention (SI) cohort (n = 70, 1-15 years); participants with mild to moderate non-proliferative retinopathy.

KQ 1: Efficacy of SMBG - DCCT results summary (N= 195)

	Intensive	Conventional	Effect size
Mean A1c (%)	8.06 ± 0.12	9.76 ± 0.12	1.70 ± 0.18 (p < 0.001*)

*authors appear to provide p-values for test of medians

Hypoglycemia and Ketoacidosis



Hospitalization

Severe hypoglycemia: IT n = 14, CT n = 5

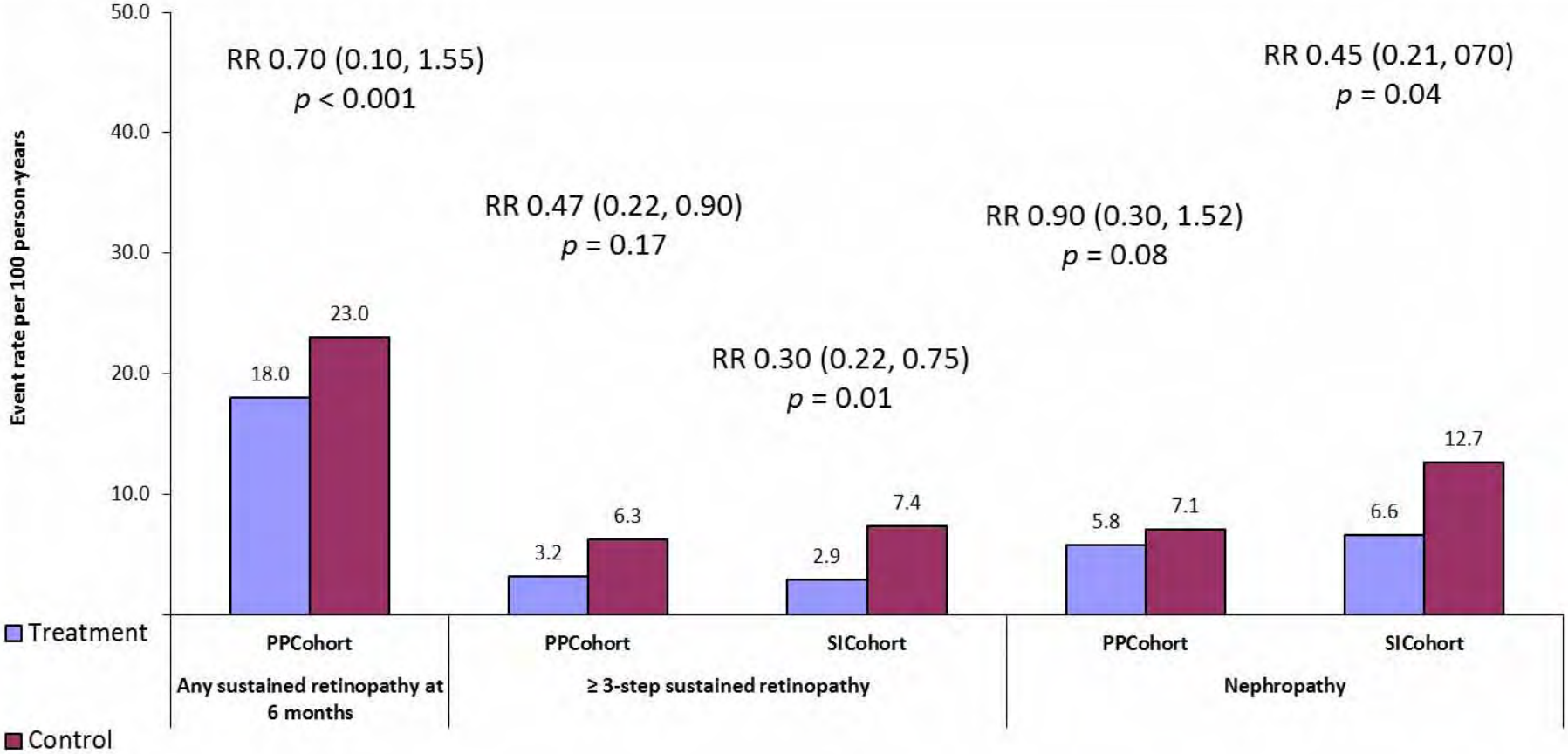
Major accidents (not specified): IT n = 4, CT n = 5, ns

SPECTRUM RESEARCH

Key Question 1: Efficacy of SMBG DCCT Summary

Neuropathy: IT group -significantly greater nerve transmission speed

Retinopathy and Nephropathy:



Key Question 1: Effectiveness of SMBG

- Epidemiology of Diabetes Interventions and Complications (EDIC) - 2 reports (LoE II)
  - Follow-up of DCCT participants 4 and 10 years after DCCT end;
  - Original IT group encouraged to continue regimens
  - Original CT group offered instruction on intensive therapy
- N =175 (91% of surviving DCCT adolescents) enrolled; 80% follow-up at year 10.
- Testing ≥ 4/day at 4 years: 24% IT, 29% CT and at 10 years and 64.5% IT 38.9% CT (means not provided)

SPECTRUM RESEARCH

Key Question 1: Effectiveness of SMBG
EDIC results summary

		Intensive	Conventional	Effect size
Mean A1c (%)				
	Year 4	**8.38 ± 1.7**	**8.45 ± 1.6**	**NS**
	Year 10	**8.2 ± 2.1**	**8.2± 1.3**	**NS**
Severe Hypoglycemia				
	Year 4	**51/100 p-y**	**57/100 p-y**	**RR 0.9, p = 0.749**
Retinopathy Progression				**Reduction in OR**
	Year 4	**7.1%**	**25.4%**	**77% (39, 92) p = 0.004**
	Year 10*	**50.9%**	**53.4%**	**10% (-104, 60) p = 0.8395**

*progression from DCCT baseline

SPECTRUM RESEARCH

Key Question 1: Effectiveness of SMBG
EDIC results summary

- Severe non-proliferative diabetic retinopathy (NPDR) or worse and proliferative retinopathy:
  - Year 4: Lower NPDR for IT 1.4% vs. CT 14.5%, p = 0.005; 1.4% IT vs. 8.7% for proliferative
  - Year 10: no significant differences between groups
  - NS differences: macular edema, laser therapy at both times
- Nephropathy (in those without microalbuminuria or albuminuria at DCCT baseline or close; page 95 of report)
  - Year 4: IT group rates were less, but NS; no one on dialysis or with renal transplant
  - Year 10 rates were similar

SPECTRUM RESEARCH

Summary and Overall Strength of Evidence: **KQ1**

Efficacy of SMBG (1 RCT) – SoE is low

- Indirect evidence from DCCT: SMBG ≥ 4/day as part of intensive, tight control program:
  - Short term (6-12 months): Lower A1C and daily blood glucose;
  - Longer (mean 7.4 years): sustained lower A1C, daily blood glucose; retinopathy and microalbuminuria risk reduction and; faster nerve conduction velocities
  - Higher rate of hypoglycemic events with intensive treatment

•Effectiveness (Observational) SMBG–SoE low

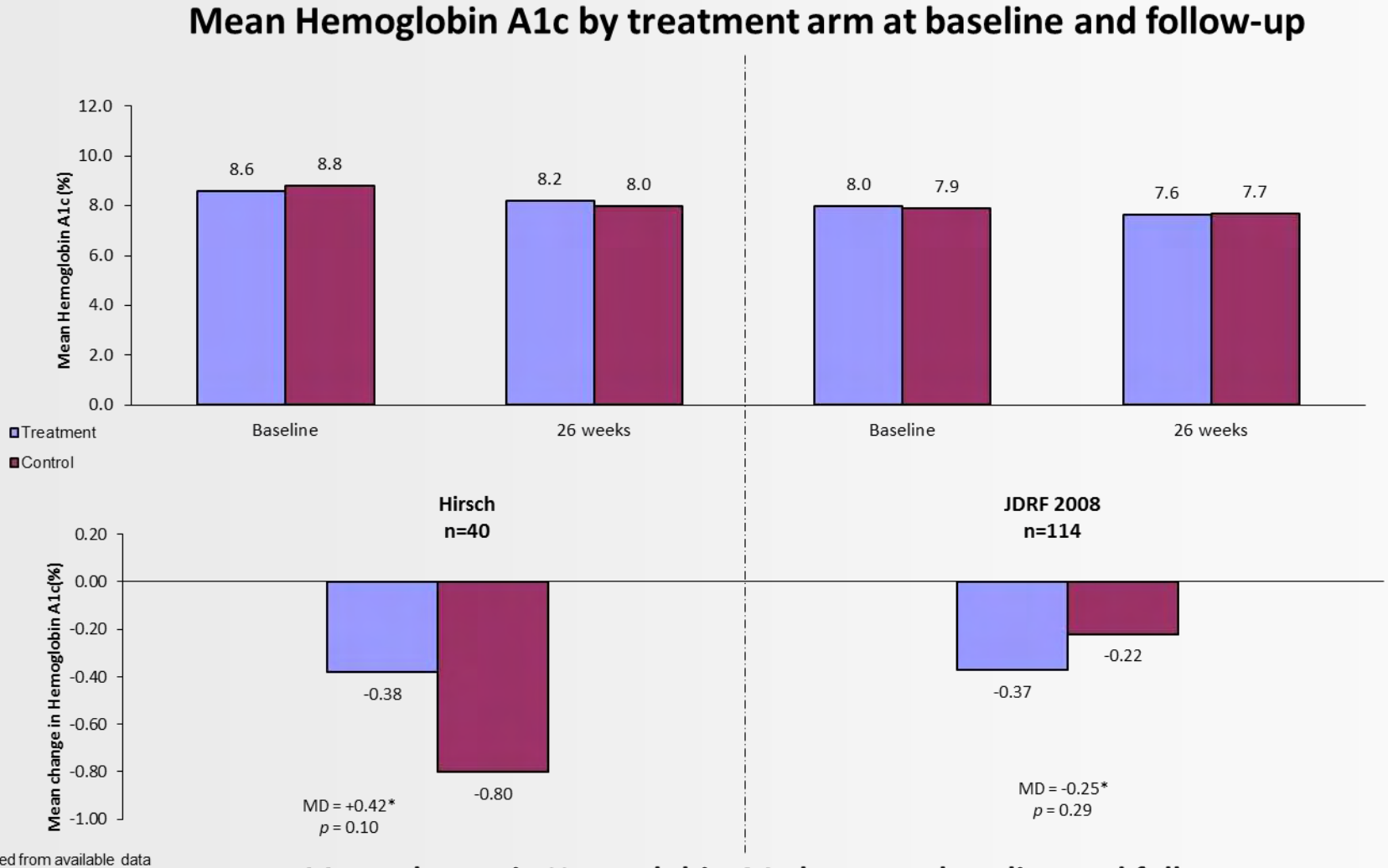
- EDIC -2 follow-up reports 4 and 10 years post DCCT:
  - 4 years: No differences in mean A1c between groups; IT group- lower rates of retinopathy progression, lower but NS difference in microalbuminuria or albuminuria prevalence
  - 10 years: No differences in mean A1C, retinopathy progression or microalbuminuria or albuminuria

SPECTRUM RESEARCH

KQ 2: Efficacy by frequency or mode

- **SMBG**: DCCT results (indirect evidence, ≥ 4/day)
- **Continuous Glucose Monitoring (CGM)**
  - 5 reports from 4 RCTS of real-time CGM; bulk of evidence comes from two RCTs
    - Limited data; stratified by age in 2 studies
    - One RCT compared CGM/pump vs. SMBG/MDI
  - CGM (+ SMBG for calibration and decision making) versus SMBG alone
  - Participants educated on data use for management decisions

RCTs: rt-CGM (+ SMBG) vs. SMGB alone



KQ 2: Efficacy of CGM (+ SMBG) vs. SMBG alone

Participants achieving A1C targets

A1C levels (26 weeks)	CGM	SMBG	Effect Size
JDRF 2008 (n = 114)			
<7.0%	27% (15)	12% (7)	RD 15%; p = 0.01
<7.0% with no severe hypoglycemic events	25% (14)	10% (6)	RD 15%; p = 0.02
≥ 10% relative ↓	29% (16)	12% (7)	RD 17%; p = 0.04
≥ 0.5% absolute ↓	54% (30)	31% (18)	RD 23%; p = 0.009
Hirsch 2008 (n = 40)	% NR	% NR	P = 0.052

KQ 2: Efficacy of CGM (+ SMBG) vs. SMBG alone

Hypoglycemia –JDRF 2008 (N = 114)

- ≥ 1 severe event: CGM 4 (7%), SMBG 6 (10%)
- Rates of severe hypoglycemia: p = 0.06
  - CGM 17.9/100,000 p-y; SMBG 24.4/100,000 p-y
- Min/day ≤ 50 mg/dl: CGM 10, SMBG 13; p = 0.50
- Min/day ≤ 70 mg/dl: CGM 47, SMBG 59: p = 0.29

Hyperglycemia –JDRF 2008 (N = 114)

- Min/day ≥ 180 mg/dl: CGM 643, SMBG 635; p = 0.58
- Min/day ≥ 250 mg/dl: CGM 242, SMBG 268: p = 0.18

SPECTRUM RESEARCH

KQ 2: Efficacy of CGM (+ SMBG) vs. SMBG alone

Quality of Life (26 weeks)

Combined populations of JDRF 2008 (>7.0% A1C at baseline) and JDRF 2009 (<7.0% A1C) (report page 104)

- Participants and parents completed diabetes-specific and general assessments of QOL
- Measures: Hypoglycemia Fear Survey subscale (HFS), Pediatric Quality of Life Inventory (PDsQL) generic and diabetes specific editions; Problem areas in Diabetes (PAID; parents only completed)
- No differences by treatment in mean values for any measure for either participants or parents

SPECTRUM RESEARCH

Summary and Overall Strength of Evidence: **KQ2**

Efficacy: CGM (+SMBG) vs. SMBG alone

SoE is low

- JDRF 2008 (N =114) and Hirsch 2008 (n = 40):
  - Short term (26 weeks): No differences in mean A1C; JDRF – CGM participants twice as likely to achieve A1C targets
  - JDRF: Lower rate of hypoglycemic events with CGM (but NS); % of participants achieving targets w/o such events significantly greater for CGM
  - Longer term: no studies found
- Combined JDRF 2008 and 2009 data
  - No differences in quality of life measures at 26 weeks for either participants or parents

SPECTRUM RESEARCH

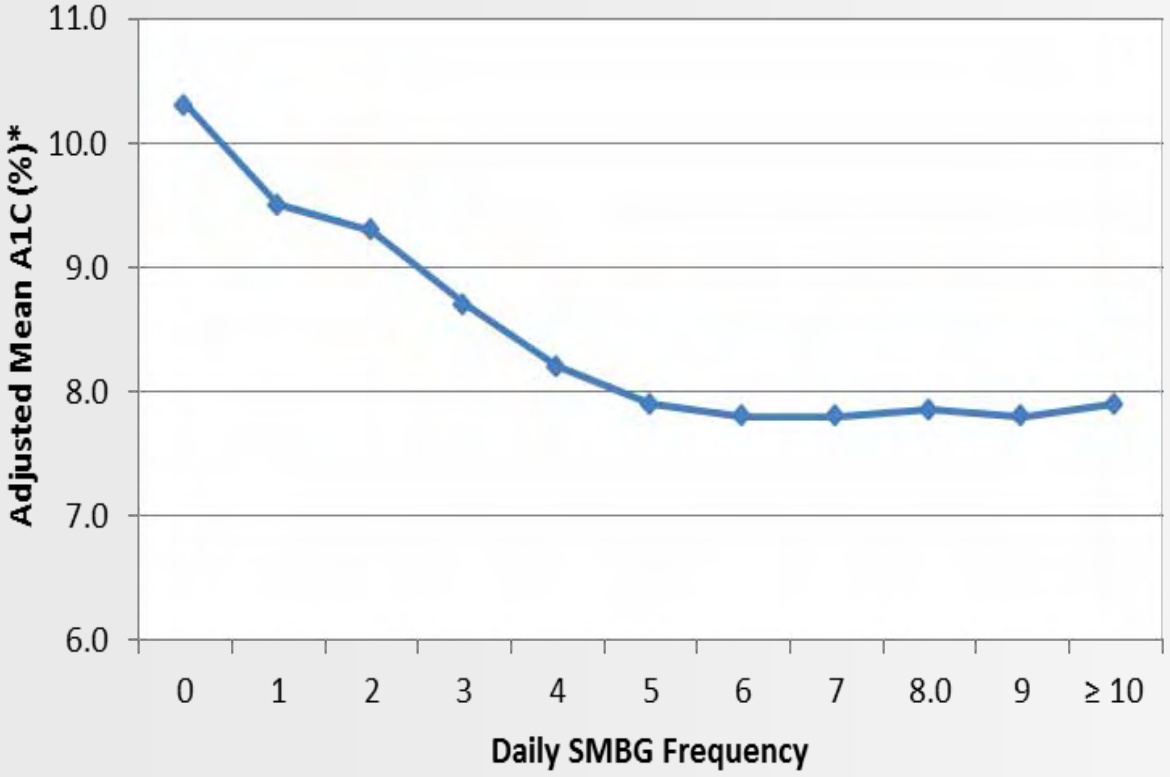
Effectiveness of CGM (+ SMBG) – Frequency of use

Extension studies JDRF 2008 and subanalysis of JDRF 2009

- Observational studies (LoE II and III)
  - JDRF 2008 extension studies (page 107)
    - Original CGM cohort (n = 80): Lower mean A1C (maintained by 12 months) and larger percentage of participants meeting targets with use ≥ 6 days/week
    - Original SMBG cohort offered CGM (with less intensive training; n = 47): no consistent pattern of improvement in A1C or for meeting target levels based on use. Lower hypoglycemia rates reported following 6 month CGM use (p not reported).
  - JDRF 2009 subananalysis of those with baseline ≤ 7.0% A1C: mean change in A1C of −0.72% with ≥ 6 days/week

Effectiveness- Frequency of SMBG

General trend: relationship between SMBG frequency
(estimated from Ziegler, N = 26,723; 0-18 years LoE III)



- Mean A1C ↓ 0.20% (± 0.007%) per 1 additional SMBG/day up to 5/day
- For 0-5/day, mean A1C ↓ 0.46% (± 0.014) per 1 additional SMBG/day

*mean A1C (%) values adjusted for age, gender, diabetes duration, year of treatment, insulin dose, insulin regimen, BMI -standard deviation scores and clinical center.

SPECTRUM RESEARCH

Effectiveness- Frequency of SMBG

6 cross-sectional studies (LoE III) (page 111)

- N ranged from 89-2,743; 5 report statistically significant *associations* between number of SMBG per day and lower A1C in multivariate analyses
- Testing at least 4 - 5 times per day

Hypoglycemia and DKA (Ziegler)

	Hypoglycemic events	**Diabetic Ketoacidosis events**
SMBG 0-4/day	13-20 events/100 p-years	6-12 events/100 person-years (except for 1SMBG/day)
SMBG ≥ 5/day	20-37 events/100 p-years	4-6 events/100 person-years

SPECTRUM RESEARCH

Summary and Overall Strength of Evidence: **KQ2**

Effectiveness CGM Frequency – SoE low

- JDRF 2008 extensions
  - Original CGM cohort: use ≥ 6 days/week appears to have maintained lower A1C and more met age appropriate targets
  - Original SMBG cohort provided with CMG: no consistent pattern of benefit with frequency of use

Effectiveness SMBG Frequency – SoE low

- One large registry, six additional cross-sectional studies
  - SMBG 4-5 times/day associated with lower mean A1C
  - Causality cannot be inferred

SPECTRUM RESEARCH

Key Question 3: Safety

- SMBG: No data for current devices
- CMG: (7 RCTs, 7 observational, 3 FDA SSED) (page 114)
  - No mortality in ≤ 18 year olds reported
  - Insertion site problems: Redness/itching (16%-45%); dry skin (21%); mild, moderate skin changes (14% each); irritation, bruising or pain (0-53%)
  - Sensor/Device concerns: alarm interferes with daily routine (38%); alarm irritating (38%-50%); sensor too bulky (22%-75%); sensor pulled out (10%-13%)
  - Many studies had small sample sizes

Overall Strength of Evidence

KQ #3: Safety - SoE – Moderate

- CGM: RCTs, observational studies, SSED
  - Primary concerns reported: Insertion site problems, alarm related
  - No deaths in age group or major adverse events reported
- SMBG: No studies on current devices
  - Older reports: sore finger, difficulty obtaining samples

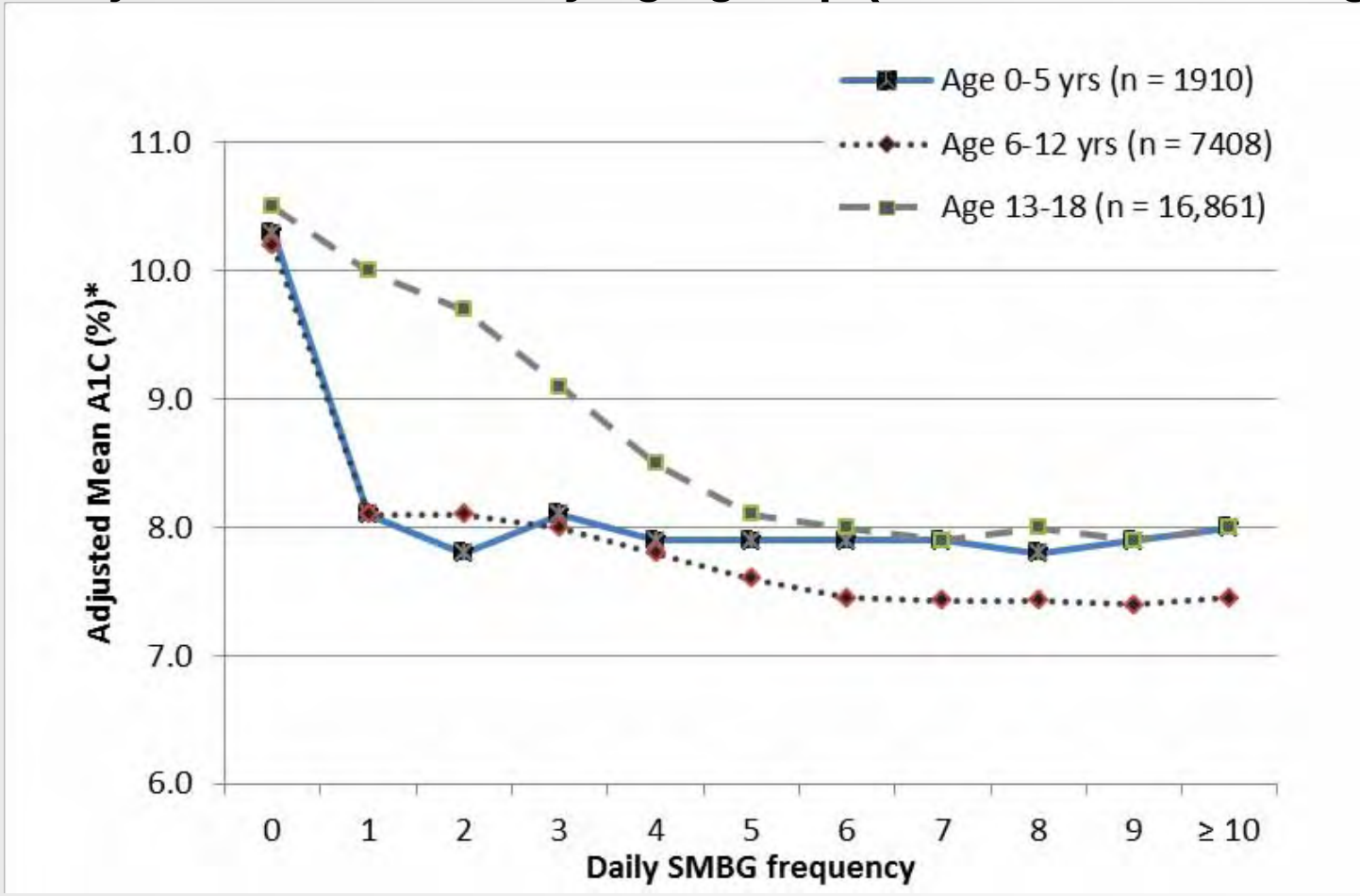
KQ 4: Differential outcomes for subpopulations

- CGM – JDRF 2008 RCT; Participants 8-14 years old and those 15-24 years old had similar results with regard to mean A1C, hypoglycemia;
- SMBG: Zeigler (LoE III) N = 26,723
  - Association between SMBG frequency and average improvement in A1C varied by age and insulin regimen

	0-5 years (n = 1989)	**6-12 years (n = 7568)**	**> 12 years (n = 17,166)**
Mean A1C	7.59% ± 1.34	7.61 ± 1.32	8.46 ± 1.85
SMBG frequency	6.0/day ±1.9	5.3/day ± 1.6	4.4/day ± 1.4
	CT (n = 5016)	**MDI (n = 18,565)**	**CSII (n = 3142)**
Mean A1C	7.64% ± 1.67	8.24% ± 1.75	8.01% ± 16.0
SMBG frequency	5.3/day ± 1.8	4.7/day ± 1.5	5.3day ±1.8

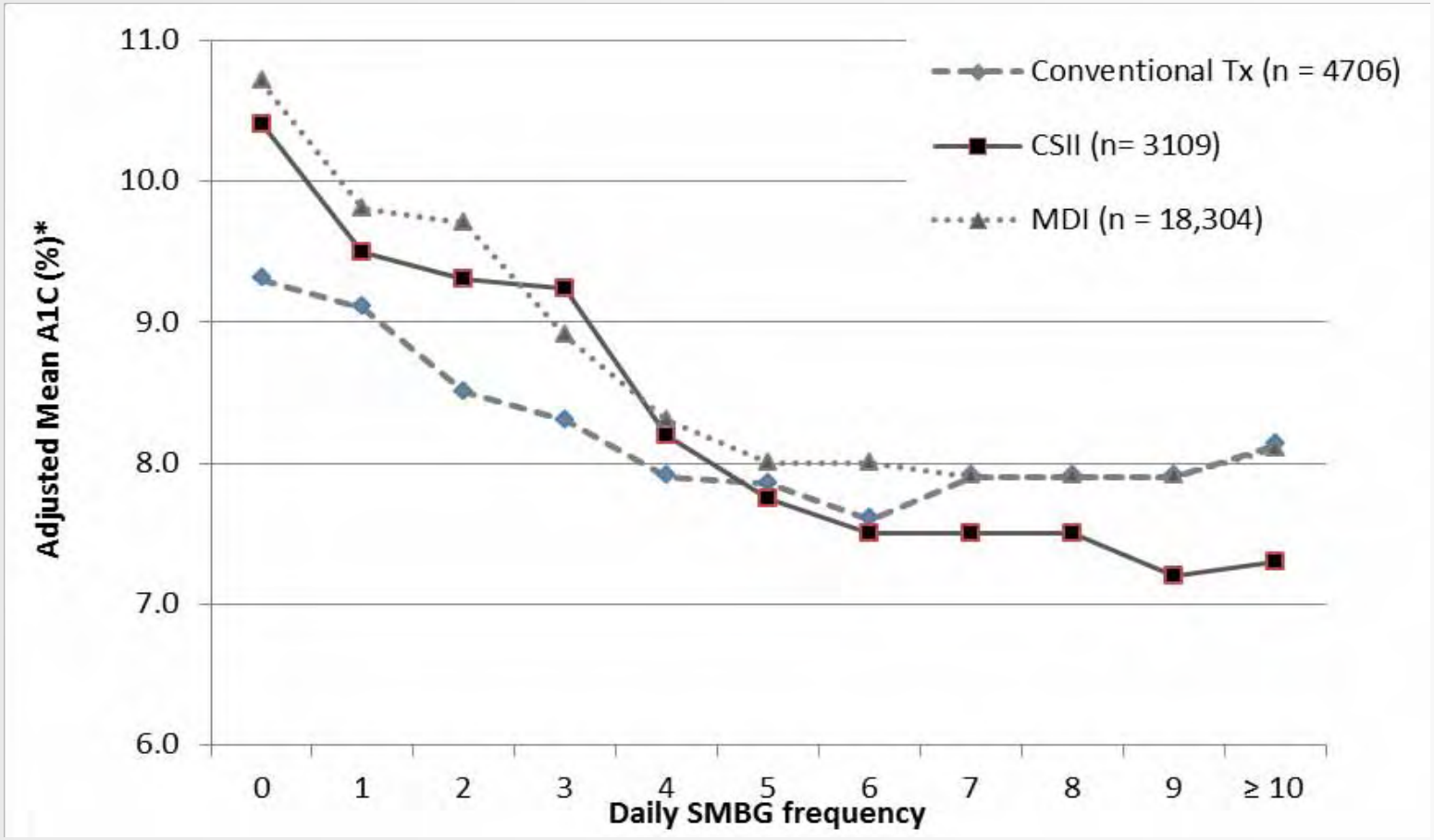
KQ 4: Differential outcomes for subpopulations

General trend for the relationship between frequency of SMBG and adjusted mean A1C by age group (estimated from Ziegler)



KQ 4: Differential outcomes for subpopulations

General trend for the relationship between frequency of SMBG and adjusted* mean A1C by insulin regimen (estimated from Ziegler)



Overall Strength of Evidence

KQ #4: Subpopulations – SoE Low

- **CGM**: 1 RCT; 8-14 year olds and 15-24 year olds had similar patterns for most results
- **SMBG**: Registry study

  Age
  - For 13-18 year olds, greater average improvement in A1C for each additional SMBG up to 5 per day
  - In 0-5 and 6-12 year olds, less improvement for each additional SMBG beyond the first.

  Insulin Regimen
  - CSII: tests up to 10 time/day closest to targets

KQ #5: Economic – no evidence, no full studies

SPECTRUM RESEARCH

Observations and Implications

- Diabetes management in children and adolescents presents a number of challenges and influences quality of life for the child and care givers.
- As DM duration contributes to development of complications, this younger age group may have the most to gain from good control.
- Self-monitoring is viewed as a critical component of management.
- Studies did not provide specifics regarding how data from self-monitoring (SMBG or CGM) are used to influence decisions on insulin dose/regimens, diet or exercise; thus it is not possible describe the independent influence of monitoring on outcomes.
- Adherence to monitoring and taking appropriate action based on the data are necessary to effect outcomes.
- SMBG is part of CGM use protocol. CGM's role for pediatric use is not yet defined in the literature. No long term studies in this population were found.

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective[1] as expressed by the following standards. [2]

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.[3]

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

[1] Based on Legislative mandate: See RCW 70.14.100(2).

[2] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

[3] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. Availability of Evidence:

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. Sufficiency of the Evidence:

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence[4] using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. Factors for Consideration - Importance

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

Medicare Coverage and Guidelines

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
CMS National Policy Decisions – WA HTA Centers for Medicare and Medicaid Services	2008	**No specific policy addressing children** To be eligible for coverage of home blood glucose monitors and related accessories and supplies, the patient (or patient's care-giver) must meet all the following criteria: ▪ Diagnosed with diabetes that is being treated by a physician ▪ Glucose monitor and related supplies ordered by the treating physician with documentation of medical necessity for the prescribed frequency of testing ▪ Successfully completed training or is scheduled to begin training in the use of these items ▪ Capable of using the test results to assure appropriate glycemic control ▪ Device is designed for home use Home blood glucose monitoring with special features are covered if the 5 above criteria are met and the treating physician verifies the patient has a visual impairment or other condition requiring this special device. Supplies covered: ▪ Up to 100 test strips and lancets every month for beneficiaries who are insulin dependent and every 3 months for those who are non-insulin dependent, and one lancet device every 6 months for both indications	▪ Rationale not reported Covered if selection criteria are met: ▪ CPT/HCPCS codes: E0607, E0620, E2100, E2101, A4233, A4234, A4235, A4236, A4244, A4245, A4246, A 4247, A4250, A4253, A4255, A4256, A4257, A4258, A4259, A9275, A9276, A9277, A9278 ▪ ICD-9 codes: 249.00–249.91, 250.00–250.93	N/A
Guidelines – WA HTA Page: 46 *American Diabetes Association (ADA)*	2010	The following guidelines are from the ADA publication "Standards of medical care in diabetes--2010." *Diabetes Care*33 Suppl 1: S11-61.[18] The information provided is based on evidence from published studies whenever possible and, when not, is supported by expert opinion or consensus. The level of evidence (A-E) supporting each guideline is provided when available. *Frequency of self-monitored blood glucose (SMBG)* SMBG in general has been extensively reviewed by the ADA and is recommended for patients of all ages with type 1 diabetes. The 2010 report did not specifically address frequency for children, however, in a statement published in 2005 by the ADA entitled Care of Children and Adolescents with Type 1 Diabetes[28] it is recommended		

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
		that SMBG be performed at least four times daily. *Continuous glucose monitoring (CGM)* "Continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens can be a useful tool to lower A1C in selected adults (age ≥ 25 years) with type 1 diabetes. (A) Although the evidence for A1C lowering is less strong in children, teens, and younger adults, CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device. (C) CGM may be a supplemental tool to SMBG in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes. (E)" *Glycemic goals (E)* "Consider age when setting glycemic goals in children and adolescents with type 1 diabetes, with less stringent goals for younger children." In this statement, age specific A1C values are listed with the caveat that goals should be individualized and lower goals may be reasonable based on benefit-risk assessment: • Toddler and preschoolers, 0–6 years: 7.5%–8.5% ○ Rationale: high risk and vulnerability to hypoglycemia • School age, 6–12 years: < 8% ○ Rationale: risks of hypoglycemia and relatively low risk of complications prior to puberty • Adolescents and young adults, 13–19 years: < 7.5% ▪ Rationale: risk of severe hypoglycemia; developmental and psychosocial issues; a lower goal (< 7.0%) is reasonable if it can be achieved without excessive hypoglycemia		
Guidelines – WA HTA Page: 47 *Diabetes Coalition of California, California Diabetes Program*	2008	"Basic guidelines for diabetes care." Sacramento (CA): Diabetes Coalition of California, California Diabetes Program; 2008.[42] Published evidence demonstrating efficacy or effectiveness and expert opinion were used in compiling this report and are consistent with the ADA's Clinical Practice Recommendations. This guideline addresses adults, children, and adolescents with type 1 and type 2 diabetes mellitus. Only information		

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
		specifically related to children/adolescents with type 1 diabetes is reported below: *SMBG testing* "Typically test at least 4x/daily." *Lab exams* "A1C should be checked 1–2/year if stable, quarterly if treatment changes or if not meeting goals. Target goal < 7.0% or < 1% above lab norms. For children, modify as necessary to prevent significant hypoglycemia." "Microalbuminuria should be checked beginning with puberty once the duration of diabetes is > 5 years unless proteinuria has been documented." *Self-care behaviors* ▪ "…as appropriate for child's developmental stage."		
Guidelines – WA HTA Page: 48 *International Society for Pediatric and Adolescent Diabetes (ISPAD)*	2009	ISPAD Clinical Practice Consensus Guidelines 2009 Compendium. "Assessment and monitoring of glycemic control in children and adolescents with diabetes." *Pediatr Diabetes*10 Suppl 12: 71-81.[43] The level of evidence (A-D) supporting each guideline is provided when available. In summary: "SMBG is an essential tool in the optimal management of childhood and adolescent diabetes and, when financially possible, should be made available for all children with diabetes. The cost of BG monitoring is very expensive and in many countries the cost relative to the cost of living may make this technology unavailable. However, all centers caring for young peoplewith diabetes should urge nations, states, and health care providers to ensure that children and adolescents with diabetes have adequate glucose monitoring supplies. It should be recognized that without accurate monitoring, the risks of acute crises and long-term vascular and other damaging complications are greatly increased leading to high levels of health care costs and personal disability." The specific recommendations are as follows: *Frequency of self-monitored blood glucose (SMBG)*		

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
		"SMBG should be prescribed at a frequency to optimize each child's diabetes control, usually 4–6 times a day, because frequency of SMBG correlates with glycemic control." (A, B) *Continuous glucose monitoring (CGM)* "Continuous monitoring devices are becoming available that may particularly benefit those with hypoglycemic unawareness, as the devices will alarm when glucose is below a specified range or with rapid rate of fall of glucose." (A, B) *Glycemic goals (A, B)* *"*The target HbA1C for all child age-groups is recommended to be < 7.5%." *"*Every child should have a minimum of one measurement of HbA1C per year. Ideally, there should be four to six measurements per year in younger children and three to four measurements per year in older children." "Targets for all age-groups include the requirement for minimal levels of severe hypoglycemia and absence of hypoglycemia unawareness." "When hypoglycemia unawareness is present, glycemic targets must be increased until hypoglycemia awareness is restored."		
Guidelines – WA HTA Page: 49 *National Institute for Health and Clinical Excellence (NICE)*	2004	*Summary of the findings from the following report commissioned by NICE:* National Collaborating Centre for Women's and Children's Health (NCC-WCH). "Type 1 diabetes: diagnosis and management of type 1 diabetes in children and young people." London (UK), Royal College of Obstetricians and Gynecologists. Sept 2004.[44] The guideline was developed by a multi-professional and lay working group (the Guideline Development Group, GDG) convened by the NCC-WCH that provided methodological support, undertook systematic searches, retrieval and appraisal of the evidence, and wrote successive drafts of the guideline. The level of evidence supporting each guideline is provided. *Frequency of self-monitored blood glucose (SMBG)* "…who are trying to optimise their glycaemic control and/or have		

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
		intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day." (GPP, Good practice point based on the view of the GDG) "…should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care team." (C) *Continuous glucose monitoring (CGM)* "…who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems." (B) *Glycemic goals* "…should be encouraged to use blood glucose measurements for short-term monitoring of glycemic control because this is associated with reduced levels of glycated haemoglobin." (A) "…the target for long-term glycaemic control is an HbA1C level of less than 7.5% without frequent disabling hypoglycaemia and [the child's] care package should be designed to attempt to achieve this." (A) "…the optimal targets for short-term glycaemic control are a preprandial blood glucose level of 4–8 mmol/l and a postprandial blood glucose level of less than 10 mmol/l." (D) "… using multiple daily injection regimens should be encouraged to adjust their insulin dose if appropriate after each preprandial, bedtimeand occasional night-time blood glucose measurement." (D) "… using twice-daily injection regimens should be encouraged to adjust their insulin dose according to the general trend in preprandial, bedtime and occasional night-time blood glucose measurements." (D) "…should be offered testing of their HbA1C levels two to four times per year (more frequent testing may be appropriate if there is concern about		

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
		poor glycemic control).” (D) “Current HbA1C measurements should be made available in outpatient clinics because their availability can lead to immediate changes in insulin therapy and/or diet and so reduce the need for follow-up appointments.” (D)		
Guidelines – WA HTA Page: 50 *American Association of Clinical Endocrinologists (AACE)*	2010	American Association of Clinical Endocrinologists (AACE) In 2010, the AACE published a Consensus Statement regarding CGM using evidence compiled by its Continuous Glucose Monitoring Task Force. Blevins TC, Bode BW, Garg SK, et al. “Statement by the American Association of Clinical Endocrinologists Consensus Panel on Continuous Glucose Monitoring” *Endocr Pract.* 2010; 16(No. 5): 730-745. Personal CGM is recommended for patients with type 1 DM and following characterisctics: “hypoglycemic unawareness or frequent hypoglycemia; HbA_{1c} over target, or with excess glycemic variability (eg, hypoglycemia judged to be excessive, potentially disabling, or life-threatening); requiring HbA_{1c} lowering without increased hypoglycemia; during preconception or pregnancy.” “Personal CGM use is recommended for children and adolescents with type 1 DM who have achieved HbA_{1c} levels less than 7.0% (these patients and their families are typically highly motivated); youth with type 1 DM who have HbA_{1c} levels of 7.0% or higher and are able to use the device on a near-daily basis.” “The following patients might be good candidates for personal CGM, and a trial of 2 to 4 weeks is recommended: youth who frequently monitor their blood glucose levels; committed families of young children (< 8 years old), especially if the patient is having problems with hypoglycemia.” “Intermittent use of profession CGM may be useful for youth with type 1 DM who are experiencing changes to their diabetes regimen or have problems with: nocturnal hypoglycemia/dawn phenomenon; hypoglycemia unawareness; postprandial hyperglycemis.”		

Organization	Date	Outcome	Evidence Cited?	Grade / Rating
Guidelines – WA HTA Page: 50 *British Society of Pediatric Endocrinology*	2009	Below is a summary of the findings from the following report: "Continuous glucose monitoring: consensus statement on the use of glucose sensing in outpatient clinical diabetes care-2009."[45] *Proven clinical indication*: "To lower HbA1C, when this remains above the individual's target despite optimized use of intensive insulin regimens (MDI or insulin pump therapy)". *Potential clinical indications*: *Diagnostic*: suspected nocturnal hypoglycemia and/or early morning hyperglycemia; suspected unrecognized hypoglycemia (e.g. exceptionally low HbA1C without reported hypoglycemia); HbA1C above individualized target despite intensified insulin therapy apparently optimized with self-monitoring; persistent disabling hypoglycemia despite conversion from MDI to CSII *Therapeutic*: Further optimization of pump therapy regimens when HbA1C cannot be consistently lowered below 7.5%; protection against recurrent disabling hypoglycemia, and for those with hypoglycemia unawareness or debilitating fear of hypoglycemia. "When continuous use does not result in any clinical improvement, either in terms of glycemic control or patient-related benefit, CGM should be discontinued."		

HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

	Glucose Monitoring: Self-monitoring in individuals with insulin dependent diabetes, 18 years of age or under
Safety Outcomes	**Safety Evidence**
Mortality	
Morbidity	
Insertion Site Problems	
Sensor / Device Related Concerns	
False Alerts	
Medically Related Complications	
Pregnancy Related Complications	
Device Recalls	
Other Adverse Events	
Efficacy – Effectiveness Outcomes	**Efficacy / Effectiveness Evidence**
Mode ▪ Continuous Glucose Monitoring (CGM) ▪ Self-monitoring of Blood Glucose (SMBG)	
Frequency ▪ Continuous Glucose Monitoring (CGM) ▪ Self-monitoring of Blood Glucose (SMBG)	
Insulin Administration ▪ Pump ▪ Multiple Daily Injections	
Pain Relief / Reduction	
Quality of Life	
Patient Satisfaction	

Other Patient Outcomes	
Special Population / Considerations Outcomes	**Special Population Evidence**
Gender	
Race	
BMI	
Hypoglycemia	
Hyperglycemia	
Clinical Neuropathy	
Patient Selection	
Payer or Beneficiary Type	
Cost	**Cost Evidence**
Cost Implications	
Direct and indirect - Short terms - Over expected duration of use	
Cost Effectiveness	

Clinical Committee Evidence Votes

First voting question
The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Is there sufficient evidence under some or all situations that the technology is:

	Unproven (no)	**Equivalent** (yes)	**Less** (yes)	**More** (yes)
Effective				
Safe				
Cost-effective				

Discussion
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second vote
Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

Discussion Item

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Clinical Committee Findings and Decisions

Next Step: Cover or No Cover
If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

Next Step: Cover with Conditions
If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
   - Refer to evidence identification document and discussion.
   - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
   - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
   - What are the known conditions/criteria and evidence state
   - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

Efficacy Considerations:

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
    - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
    - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

Cost Impact

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

Overall

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?