# Eversense® Continuous Glucose Monitoring (CGM) System

**March 29, 2018**

Senseonics, Inc.

Clinical Chemistry and Clinical Toxicology Device Panel

# Introduction

**Mukul Jain, PhD**

Chief Operating Officer

Senseonics, Inc.

# Eversense Continuous Glucose Monitoring (CGM) System

**90-day Implantable Sensor**
subcutaneous

**Removable Transmitter**
worn over skin

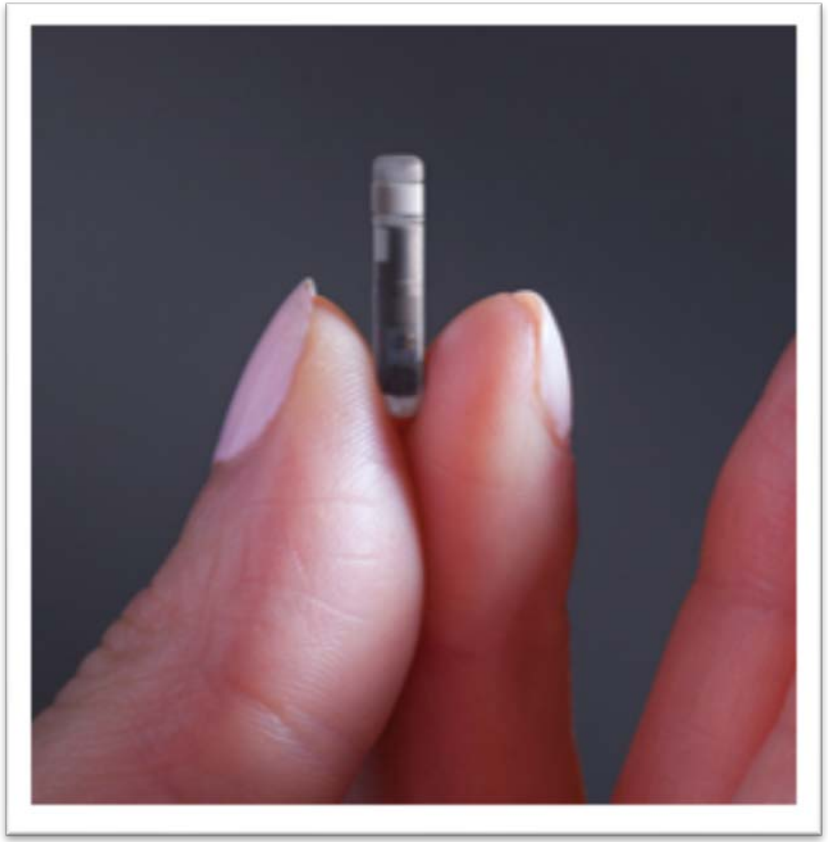
**Mobile Application**
handheld device

# Proposed Indication for Use

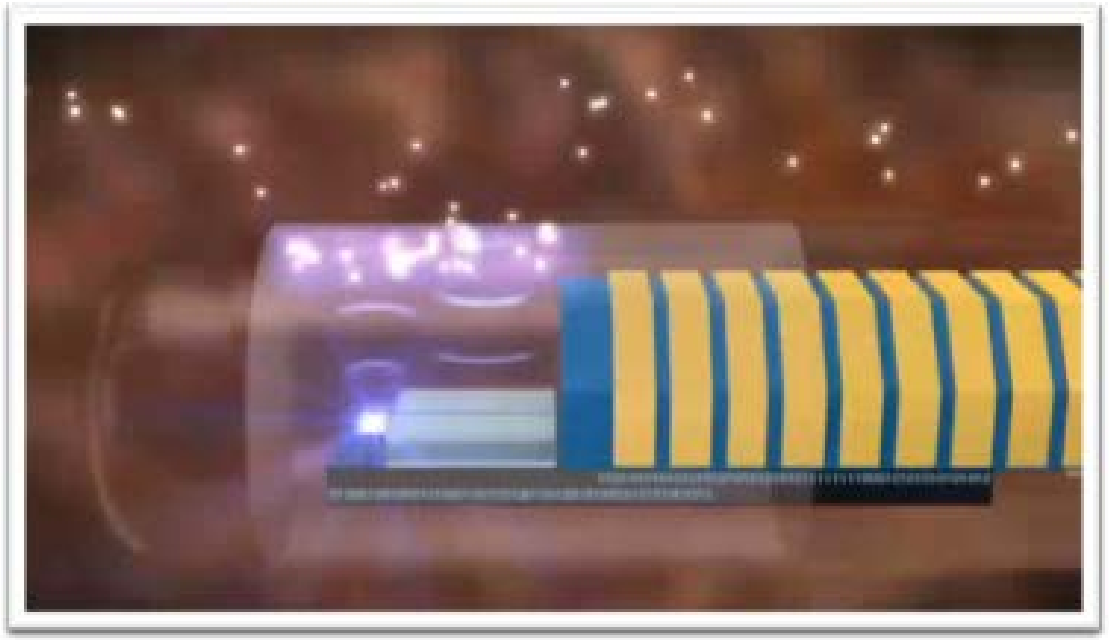
- For continually measuring glucose levels in adults (age ≥ 18) with diabetes for operating life of sensor
- System provides:
  - Real-time glucose readings
  - Glucose trend information
  - Alerts for detection and prediction of episodes of low blood glucose (hypoglycemia) and high blood glucose (hyperglycemia)
- Adjunctive device to complement, not replace, information obtained from standard home blood glucose monitoring devices

# System Components: Sensor

- Inserted into upper arm
- Lasts up to 90 days
- Measures glucose every 5 min
- Silicone collar containing 1.75 mg dexamethasone acetate (DXA)
  - Reduce inflammation around sensor



# Sensor Technology Based on Fluorescence



# System Components: Transmitter

- Calculates glucose values and trends
- Worn externally over inserted sensor
- Secured with adhesive patch
- Vibrates for alerts and notifications
- Rechargeable

# System Components: Mobile Medical Application


- Displays glucose information from transmitter
  - Values and trends
  - Alerts and notifications
- Runs on smartphone
- Reminds user to calibrate (2x/day)
- Option to upload data to Senseonics' Data Management System

# Multiple Alert Types to Ensure Safety

- **Threshold**
  - Identify glucose levels below or above pre-set values
- **Predictive**
  - Signal when alert level is expected to be crossed in immediate future (e.g. 10 minutes prior)
- **Rate of change**
  - Identify rising or falling glucose exceeding pre-set rate of change

# Vibratory, Visual, and Audio Alerts

- Transmitter vibrates whether mobile app is active or in vicinity
- Unique vibration patterns
- Audible alert AND visual message on handheld device

# Sensor Inserted in Upper Arm During Simple, Office-Based Procedure

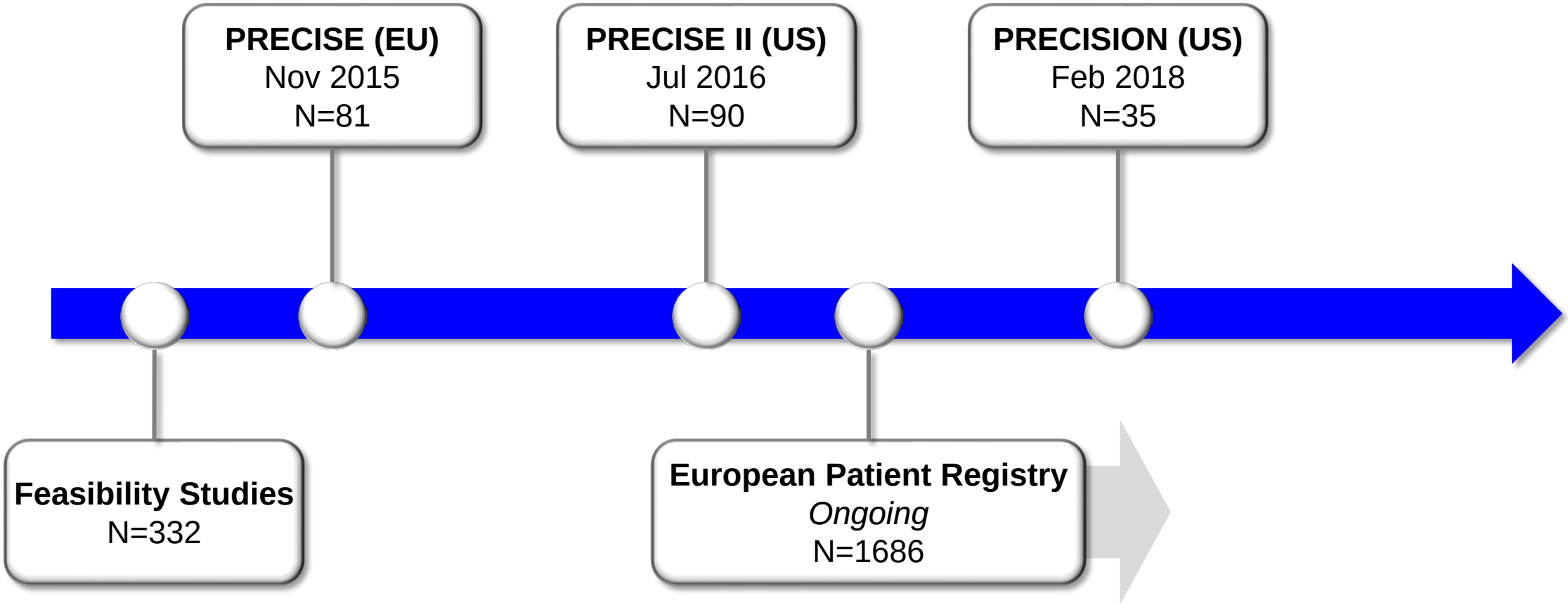
- Sensor inserted/removed by HCP
- Brief, office-based procedure
- Custom insertion tools
- Procedure:
  - Skin anesthetized and disinfected
  - Small incision in upper arm
  - Blunt dissector creates subcutaneous pocket
  - Sensor transferred to pocket
  - Similar removal procedure

# Eversense System Regulatory Status

- CE Mark received May 2016
- Available in 14 countries
- 1686 patients commercially
  - 2386 insertions
  - Up to 7 sequential sensors
- PMA submitted to FDA in October 2016

As of February 2, 2018

# Clinical Program: 2224 Patients




= Ongoing study

# FDA Discussion Topics: Design Changes

- Design changes since PRECISE II
  - Transmitter
  - Glucose algorithm
  - Sensor end cap
  - Blunt dissector tool
- Study results establish Eversense is safe and effective
- Changes are incremental in nature
  - Continuous improvement in design

# Design Changes: Transmitter

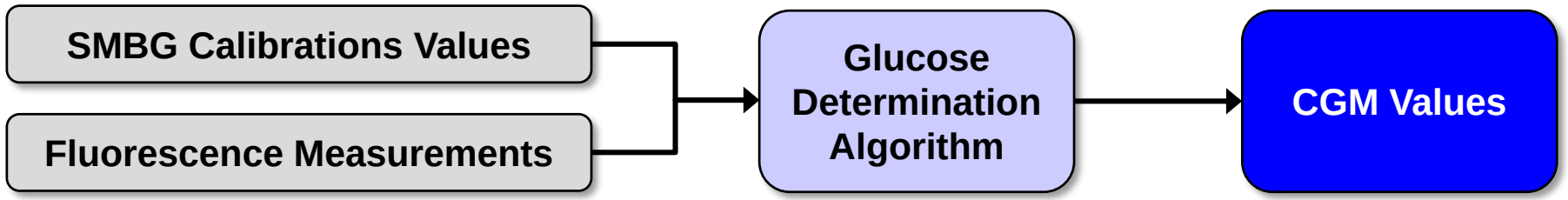
**Generation 2**
**PRECISION**

**Generation 1**
**PRECISE II + PRECISION**

- More ergonomic design
  - Thinner
  - Lighter
  - Less obtrusive
- Water-resistant
- Passed verification and validation testing
- Extensive EU commercial experience

# Design Changes: Glucose Algorithm

- Glucose algorithm updated to improve performance in
  - Early sensor wear
  - Hypoglycemic range
- Raw sensor data independent of algorithm in transmitter




- Algorithm developed with data from EU pivotal study (PRECISE)
- Post hoc processing of US data collected with SW 602
- Eversense performance accurate and reliable with Study SW and SW 602

# FDA Discussion Topics: Sensor Accuracy

- Amount of data relative to sensor life (90 days)
- Accuracy in early wear period

# PRECISE II: Eversense System is Highly Accurate

- Demonstrated accuracy
  - 8.5% mean absolute relative difference (MARD)
  - 87% of readings within 15 mg/dL or 15% of reference
- Excursions consistently detected
  - 96% of hypoglycemic excursions*
  - 98% of hyperglycemic excursions*
- Duration of use
  - 91% of sensors functioned for 90 days

*Includes 70 mg/dL and 180 mg/dL thresholds and 10-minute predictive alerts

# Eversense System is Safe

- No device-related SAEs
  - 1 procedure-related SAE through 90 days post-insertion
- No unanticipated AEs
- Low rate of infections and adhesive patch skin reactions
- AEs consistent with other CGMs and subcutaneous implants

# Repeat Sensor Use is Safe

- Risk analysis
  - Risks are consistent, predictable, can be mitigated
  - Single insertion characterizes impact, 90-day use, removal, and healing
- Clinical study results
  - Device and insertion/removal procedure are safe
  - Nominal/complete healing following sensor removal
- Post-marketing studies of repeat use
  - EU Registry (1686 patients, up to 7 sequential sensors)
  - Repeat sensor not associated with increased AEs

# Agenda

| | |
|---|---|
| **Unmet Need** | **Jeremy H. Pettus, MD**<br>**University of California at San Diego** |
| **Study Design** | **Tim Goodnow, PhD**<br>**Senseonics, Inc.** |
| **Effectiveness** | |
| **Safety** | **Lynne Kelley, MD, FACS**<br>**Senseonics, Inc.** |
| **Post-approval / Training** | |
| **Clinical Perspective** | **Steven J. Russell, MD, PhD**<br>**Harvard Medical School** |

# Additional Experts

- *Clinical Pharmacology*
  **Nicholas Fleischer, RPh PhD**
  Vice President
  Clinical Pharmacology and Biopharmaceutics
  The Weinberg Group

- *Statistics*
  **Richard Holcomb, PhD**
  Consultant

- *Study Conduct*
  **Katherine Tweden, PhD**
  Senseonics, Inc.

- *Dermatology*
  **Howard I. Maibach, MD**
  Dermatologist
  Professor of Dermatology
  University of California, San Francisco

- *Pathology*
  **Renu Virmani, MD FACC**
  President
  CVPath Institute

# Unmet Need

**Jeremy H. Pettus, MD**

Assistant Professor of Medicine

Endocrinology, Diabetes and Metabolism

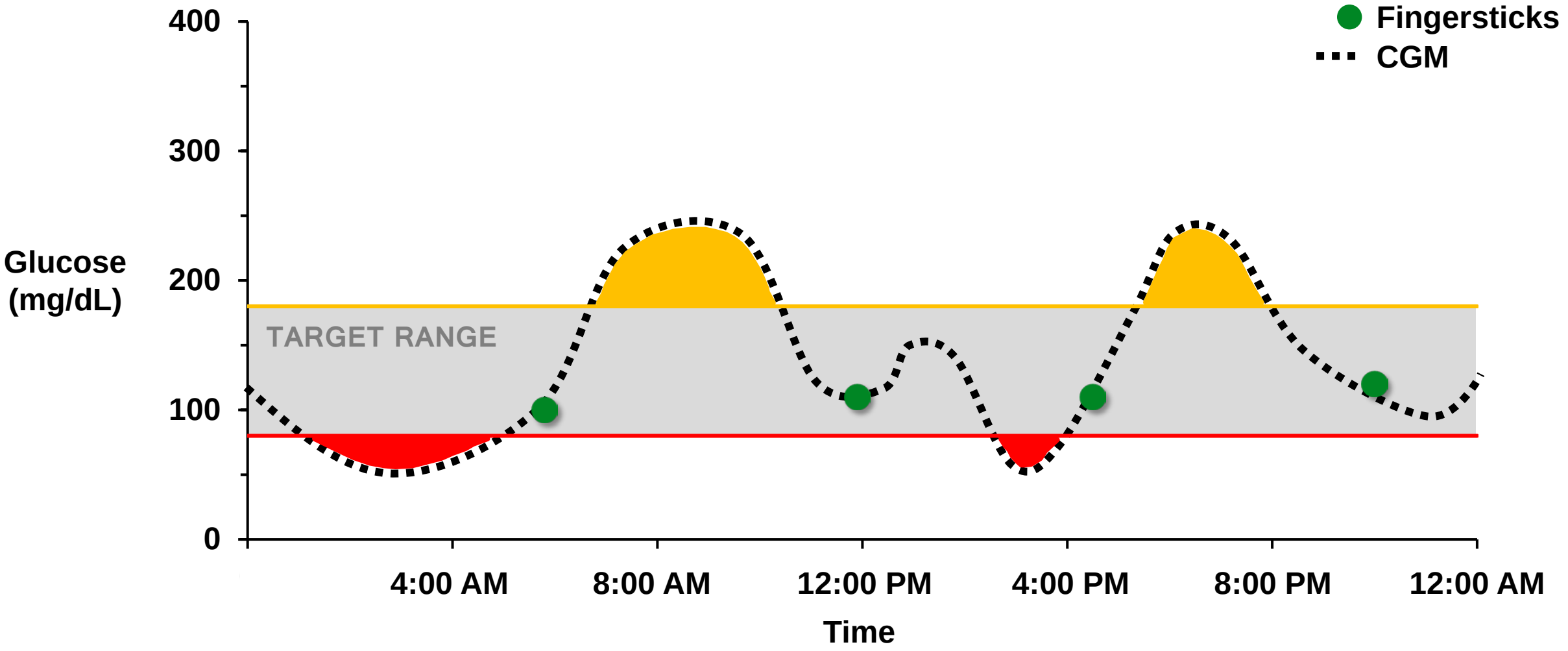
University of California, San Diego (UCSD)

# CGM Overview

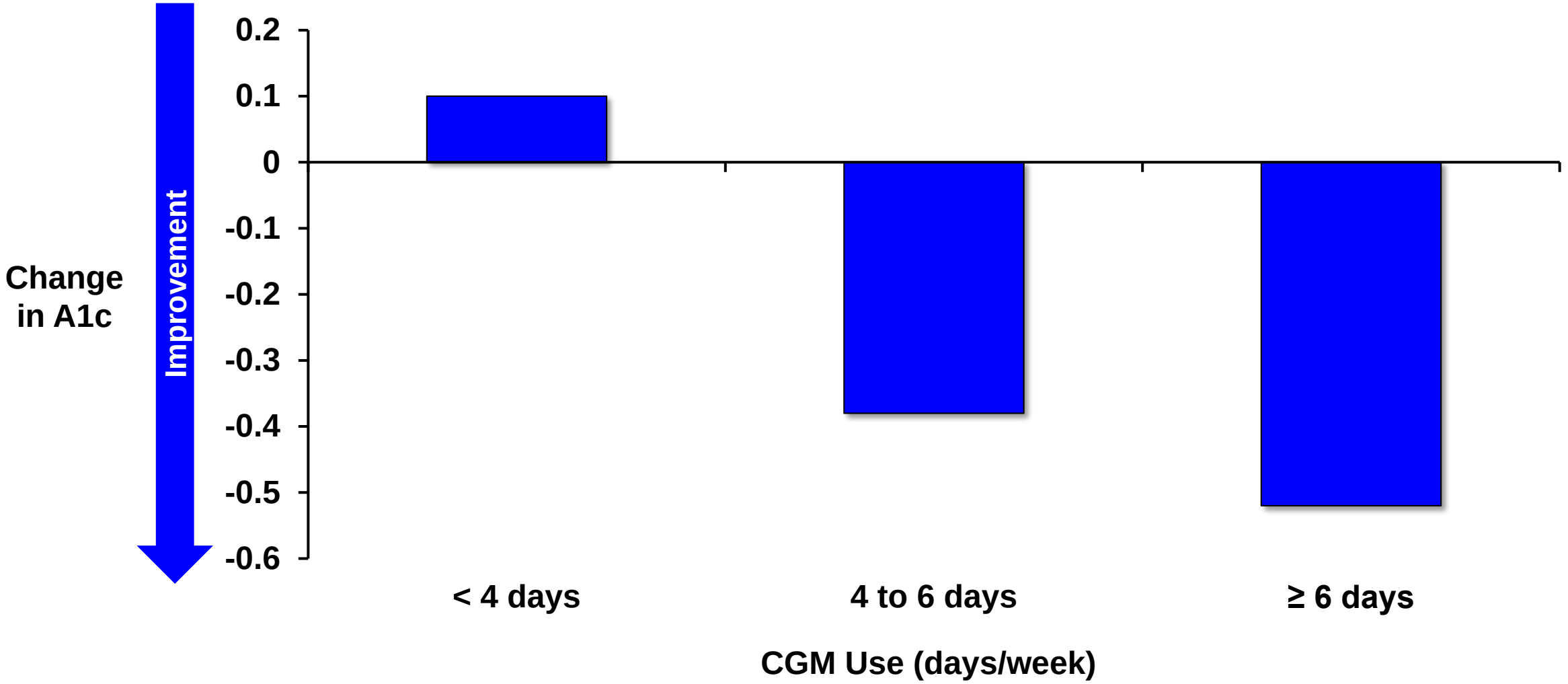
- CGM benefits
  - Improved overall glucose control → lower HbA1c levels
  - Increased time spent within normal glucose range
  - Improved quality of life
- CGM use supported by society guidelines*
- Greatly underutilized

**Polonsky et al. (2017)**
***American Diabetes Association, Endocrine Society, and American Association of Clinical Endocrinologists**

# Intermittent Monitoring with Home Blood Glucose Meter Leads to Unnoticed Highs and Lows

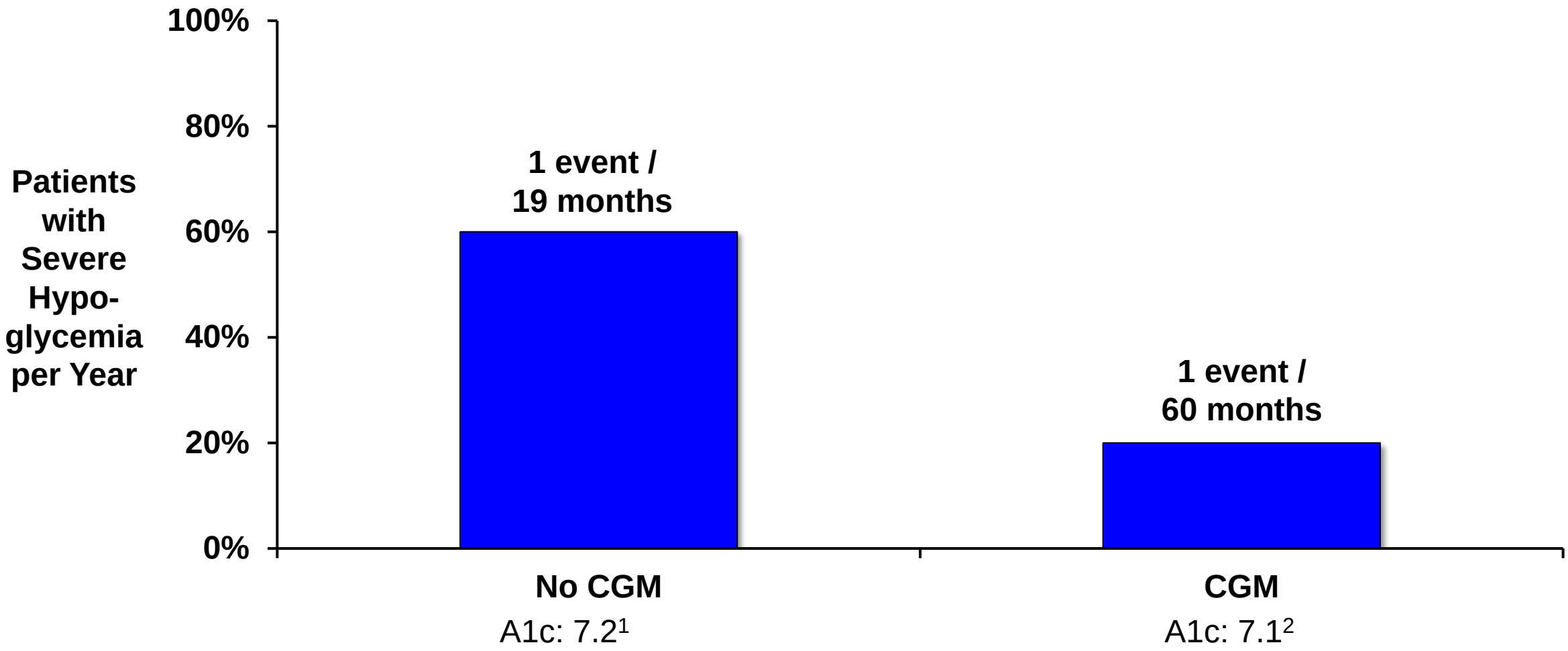


# Maximum A1c Improvement with Regular CGM Use



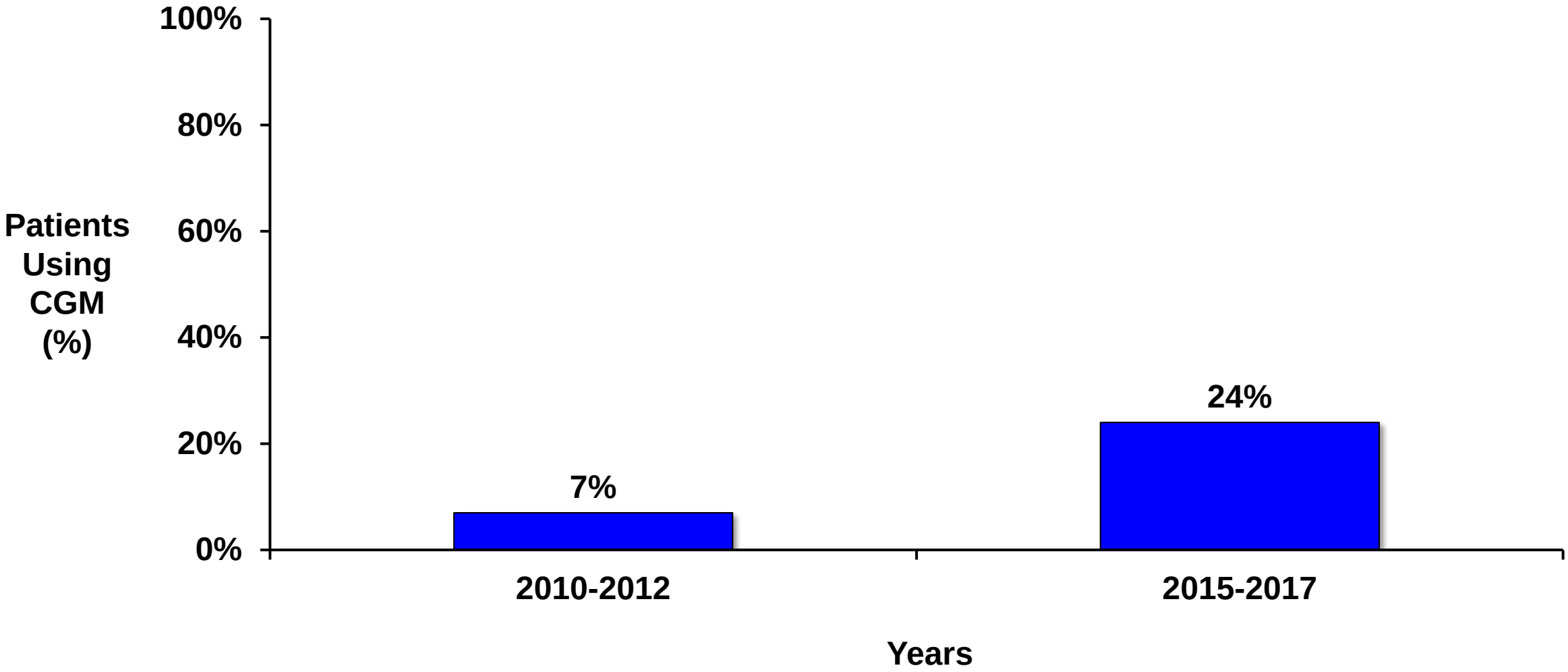

JDRF CGM Study Group (2008)

# CGM Protects Against Severe Hypoglycemia




1. DCCT Research Group (1993); 2. JDRF CGM Study Group (2008)

# CGM Systems Are Underutilized: 76% of Patients Do Not Use CGM




Type 1 Diabetes (T1D) Exchange registry

# 27% of Patients Discontinue CGM Use Within 1 Year

| Reason | N=262 |
|---|---|
| CGM not working properly / accurate enough | 71% |
| Problems with adhesive/insertion | 61% |
| Too expensive / not covered by insurance | 58% |
| Uncomfortable to wear | 41% |
| Using pump / don’t want two sites on body | 33% |
| CGM too big | 28% |

Type 1 Diabetes (T1D) Exchange Registry (2016)

# Advancements Needed in CGM Systems

- Longer sensor life
- Less frequent sensor insertions
  - Current systems require 25–50 replacements/year
- Easy to wear and easily removed
  - For physical activities or discretion

# Natural Evolution of Sensor Technology: Longer-Lasting, Less Intrusive

- Proven clinical benefit
- Many patients have not adopted CGM technology or quickly abandon it
- Patients missing opportunity to improve diabetes status and quality of life
- Need more CGM options to increase patient access

# Study Design and Effectiveness

**Tim Goodnow, PhD**

Chief Executive Officer

Senseonics, Inc.

# Eversense Clinical Program

| Study | Duration | Patients | Sites | Role |
|---|---|---|---|---|
| PRECISE II | 90 days | 90 | 8 US | Pivotal |
| PRECISION | 90 days | 35 | 3 US | Supportive |
| PRECISE | 180 days | 81 | 7 EU | Supportive |
| | | | | |
| European Patient Registry *(ongoing)* | 2 years | 1686 | 350 EU | Post-market |
| Feasibility Studies | Varied | 332 | 10 | Pilot |
| Total | | 2224 | | |

# PRECISE II: Pivotal Study Design

- Non-randomized, single-arm, multi-center study
- N=90 patients
  - n=75 one sensor inserted
  - n=15 two sensors inserted (one in each arm)
- Sensors calibrated 2x/day using home glucose meter
- Glucose readings and high/low alerts were blinded during study

# PRECISE II: Pivotal Study Schedule

| Clinic Visit | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Day | -30 | 0 | 1 | 30 | 60 | 90 | 100 |
| Screening / Follow-up | ✓ | Insertion | | | | Removal | ✓ |
| Accuracy (in-clinic) | | | ✓ | ✓ | ✓ | ✓ | |
| Challenges* | | | | ✓ | ✓ | ✓ | |

At-home wear for 90 days

*Meal, exercise, compression challenges

# PRECISE II: Primary Endpoint Based on MARD

- Mean absolute relative difference (MARD)
  - Compares sensor reading with reference glucose
  - Smaller MARD = higher accuracy
- Percent of sensor values within 15 mg/dL or 15% of reference

# PRECISE II: Additional Effectiveness Characterization

- Sensor accuracy across 90 days of use
- Agreement of sensor readings within accuracy limits
- High and low glucose alert performance
- Impact of compression
- Paired precision
- Kaplan-Meier analysis of sensor life
- Method comparison, bias analysis, Clarke & Consensus Error Analysis

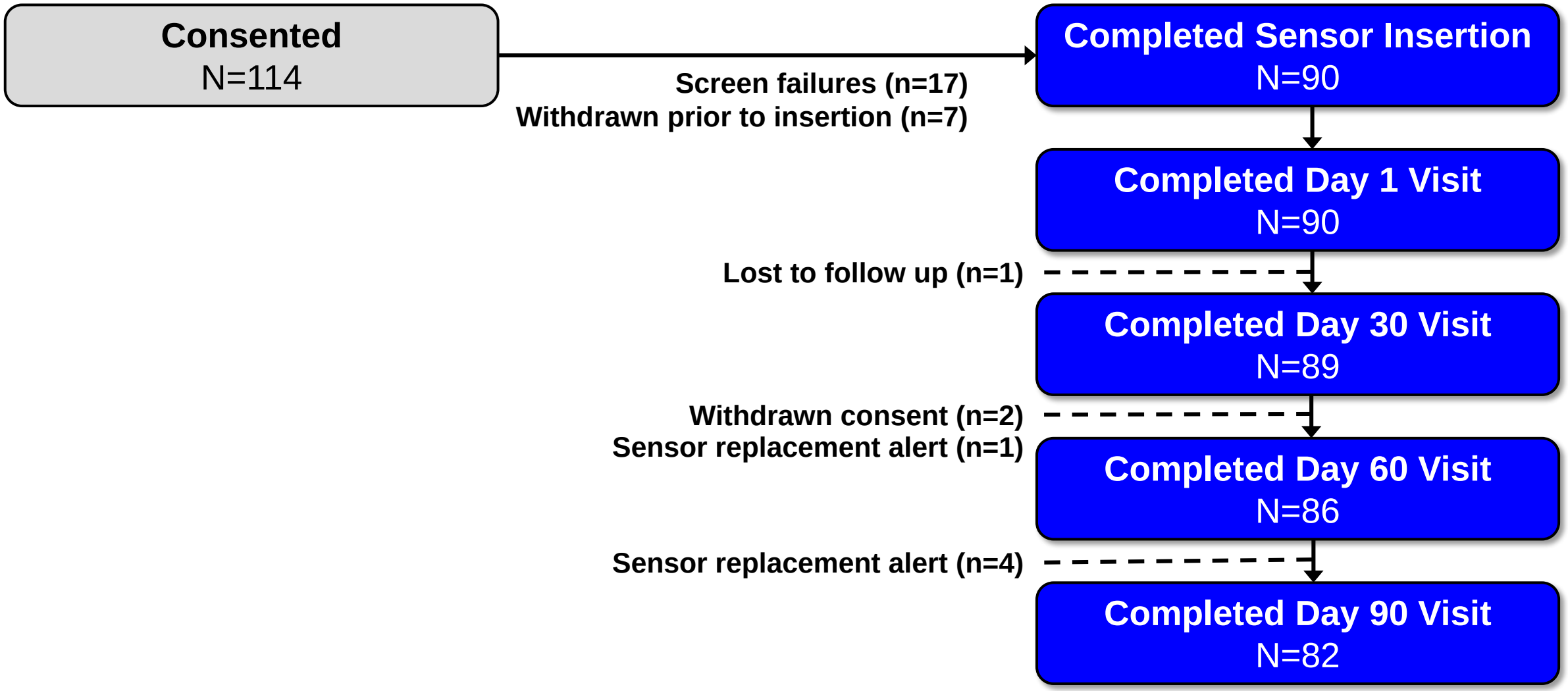
# PRECISE II: Key Enrollment Criteria

- Adults diagnosed with diabetes mellitus for at least 1 year
- No severe hypoglycemia within last 6 months
- No diabetic ketoacidosis requiring hospitalization within 6 months

# PRECISE II Demographics: Representative Study Sample

| Parameter | | N=90 |
|---|---|---|
| Sex | Male | 60% |
| Age | Mean | 45 years |
| Race | Caucasian | 86% |
| | Black or African American | 8% |
| | Asian | 3% |
| | Other | 3% |
| Body Mass Index | Mean | 29 kg/m$^2$ |
| Glycosylated Hemoglobin (HbA1c) | Mean | 7.6% |
| Time since diabetes diagnosis | Mean | 20 years |
| Diabetes type | Type 1 | 68% |
| | Type 2 | 32% |
| Type of insulin therapy | Continuous insulin infusion pump | 48% |
| | Multiple daily injections | 27% |
| | None (Type 2, not on insulin) | 22% |
| | Other (long-acting insulin only) | 3% |

# PRECISE II: Disposition



# PRECISE II: Primary Effectiveness Endpoint Met Using Study Software

| Software Version | Unique Patients N | Paired Values N | Mean Absolute Relative Difference (95% CI) | p-value |
|---|---|---|---|---|
| **Study SW** | **90** | **15,704** | **8.8%** (8.3%, 9.4%) | **< 0.0001** |

**Based on all evaluable data from all patients with at least one paired glucose reading between primary sensor and reference values**

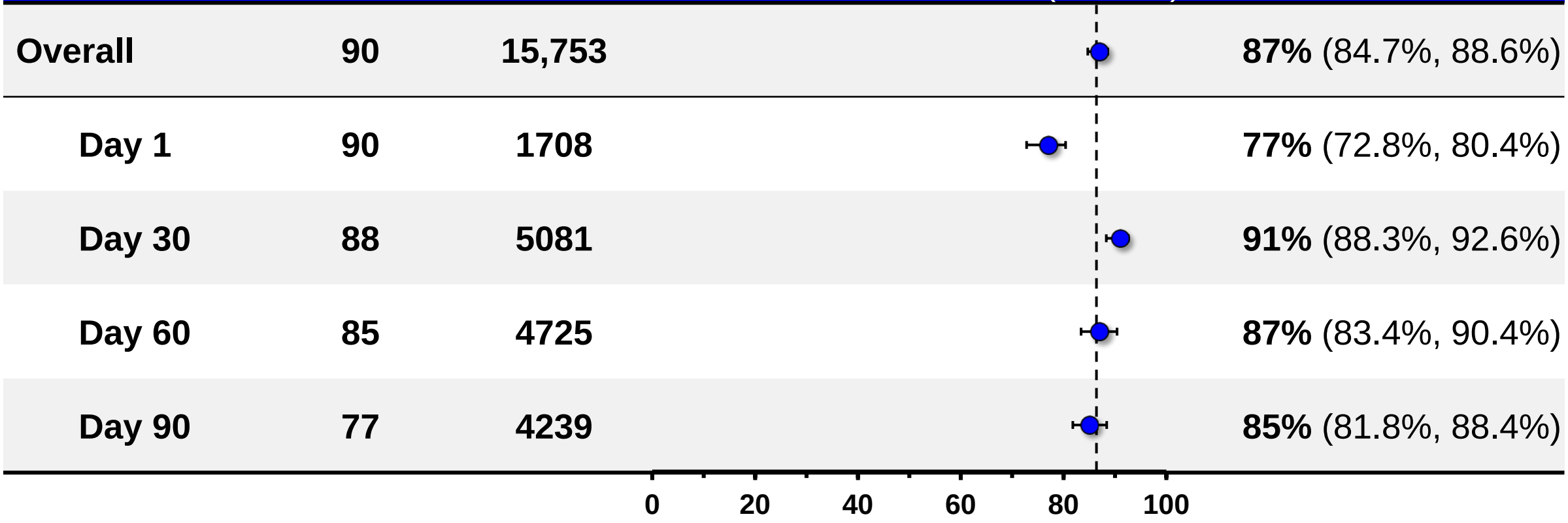
# PRECISE II: Primary Effectiveness Endpoint Met Using SW 602

| Software Version | Unique Patients N | Paired Values N | Mean Absolute Relative Difference (95% CI) | p-value |
|---|---|---|---|---|
| **SW 602** | **90** | **15,753** | **8.5%** (8.0%, 9.1%) | **< 0.0001** |

**Based on all evaluable data from all patients with at least one paired glucose reading between primary sensor and reference values**

# PRECISE II:
# Sensor Accurate through 90 Days of Use

| Study Time Point | Unique Patients N | Paired Values N | % of CGM Readings within 15/15% of Reference (95% CI) |
|---|---|---|---|
| **Overall** | **90** | **15,753** | **87%** (84.7%, 88.6%) |
| **Day 1** | **90** | **1708** | **77%** (72.8%, 80.4%) |
| **Day 30** | **88** | **5081** | **91%** (88.3%, 92.6%) |
| **Day 60** | **85** | **4725** | **87%** (83.4%, 90.4%) |
| **Day 90** | **77** | **4239** | **85%** (81.8%, 88.4%) |



# Eversense Clinical Program

| Study | Duration | Patients | Sites | Role |
|---|---|---|---|---|
| PRECISE II | 90 days | 90 | 8 US | Pivotal |
| PRECISION | 90 days | 35 | 3 US | Supportive |
| PRECISE | 180 days | 81 | 7 EU | Supportive |
| | | | | |
| European Patient Registry *(ongoing)* | 2 years | 1686 | 350 EU | Post-market |
| Feasibility Studies | Varied | 332 | 10 | Pilot |
| Total | | 2224 | | |

# PRECISION Study Design

| Clinic Visit | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| Day | -30 | 0 | 1 | 7 | 14 | 30 | 60 | 90 | 100 |
| Screening/Follow-up | ✓ | | | | | | | | ✓ |
| Accuracy (in-clinic) | | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Challenges* | | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |

Insertion

Removal

At-home wear
for 90 days

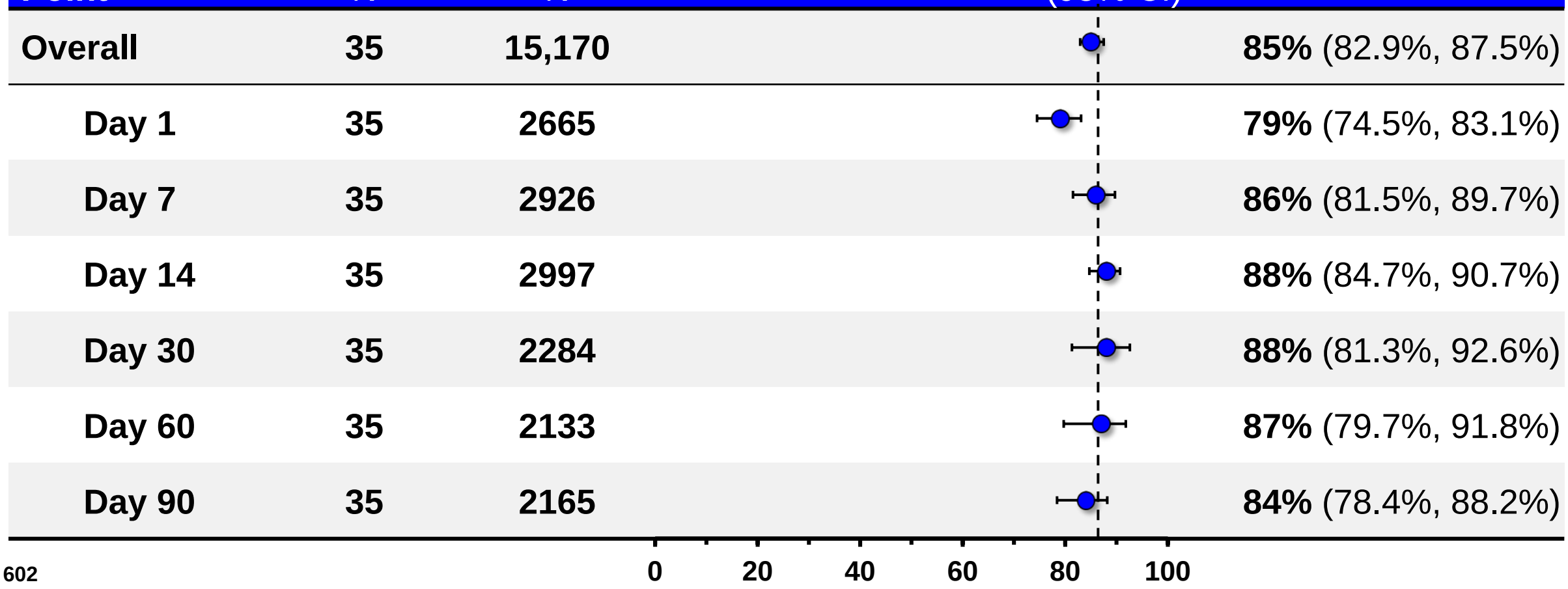
*Meal challenges; Overnight challenges were performed on Days 7 and 14

# PRECISION Differences from PRECISE II

- 3 US sites
- 35 patients with sensors inserted
  - 27 patients had 2 sensors inserted
- Unblinded sensor glucose values and active high/low alerts

# PRECISION:
# Sensor Accurate over 90 Days of Use

| Study Time Point | Unique Patients N | Paired Values N | % of CGM Readings within 15/15% of Reference (95% CI) |
|---|---|---|---|
| **Overall** | **35** | **15,170** | **85%** (82.9%, 87.5%) |
| **Day 1** | **35** | **2665** | **79%** (74.5%, 83.1%) |
| **Day 7** | **35** | **2926** | **86%** (81.5%, 89.7%) |
| **Day 14** | **35** | **2997** | **88%** (84.7%, 90.7%) |
| **Day 30** | **35** | **2284** | **88%** (81.3%, 92.6%) |
| **Day 60** | **35** | **2133** | **87%** (79.7%, 91.8%) |
| **Day 90** | **35** | **2165** | **84%** (78.4%, 88.2%) |



# Accuracy Comparison with Approved CGMs through Sensor Life

| Device | Data Source | Percent of System Readings Within 15/15% of Reference | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Day 1 | Day 3-4 | Day 7 | Day 10 | Day 14 | Day 30 | Day 60 | Day 90 |
| Eversense (SW 602) | PRECISE II | 77% | -- | -- | -- | -- | 91% | 87% | 85% |
| | PRECISION | 79% | -- | 86% | -- | 88% | 88% | 87% | 84% |
| Dexcom G5* | -- | 77% | 89% | 90% | -- | -- | -- | -- | -- |
| Medtronic Guardian (3)*‡ | -- | 68% | 87% | 82% | -- | -- | -- | -- | -- |
| FreeStyle Libre* | -- | 76% | 82% | 85% | 85% | -- | -- | -- | -- |

* Summary of Safety and Effectiveness Data (SSED) - Medical Device Databases - http://www.fda.gov
‡ Results based on calibration every 12 hours

# Accurate Detection of Glucose Excursions

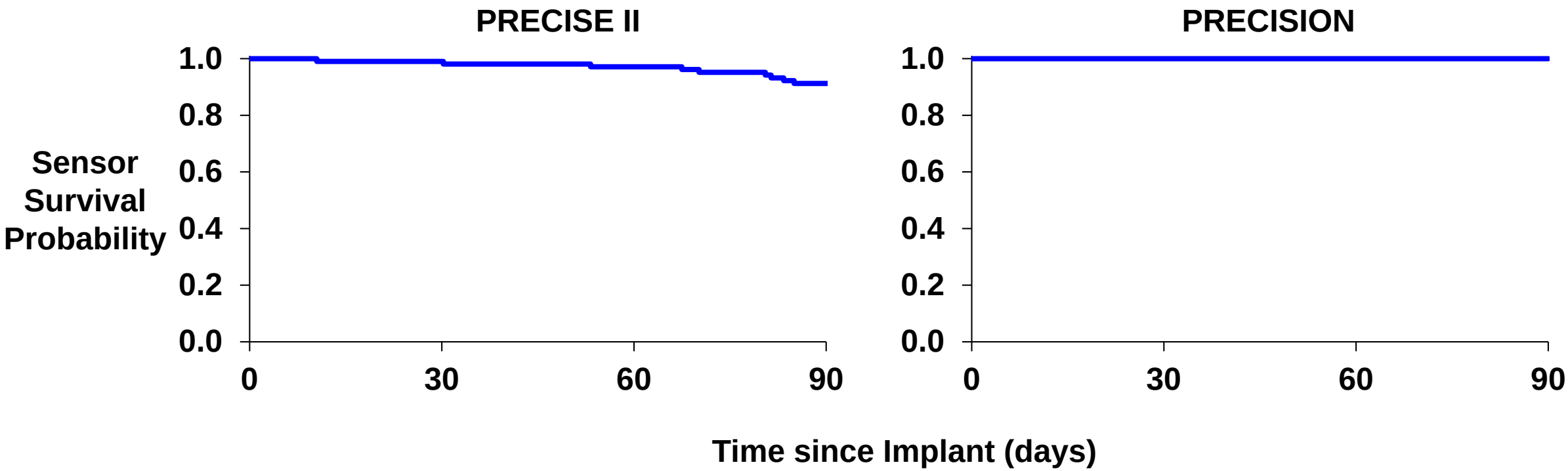
| Alert Setting | PRECISE II | | PRECISION | |
|---|---|---|---|---|
| | Detection Rate | False Alert Rate | Detection Rate | False Alert Rate |
| Low Glucose Alert at 70 mg/dL* | 96% | 16% | 95% | 8% |
| High Glucose Alert at 180 mg/dL* | 98% | 7% | 99% | 7% |

SW 602

*Includes threshold and 10-minute predictive alerts

# PRECISE II and PRECISION: Eversense Sensor Longevity

- PRECISE II: KM survival probability of 91% at Day 90
- PRECISION: All sensors functioned 90 days



# PRECISE II and PRECISION: System Adherence

| | PRECISE II | PRECISION |
|---|---|---|
| Median wear time | 23.4 hours | 23.4 hours |
| % transmitters worn > 20 hours/day | 87% | 91% |

# Effectiveness Summary: Eversense is Accurate for 90 Days

- PRECISE II: 87% of sensor readings with 15/15% of reference
- PRECISION: 85% of sensor readings with 15/15% of reference
- Accurate at each measured time point
- No degradation of sensor performance
  - 91% of sensors function through 90 days
  - “Sensor Replacement” alert appropriately produced
- Over 95% detection rates for glycemic excursions
  - High (180 mg/dL) and low (70 mg/dL) glucose

# Clinical Safety

**Lynne Kelley, MD, FACS**
Chief Medical Officer
Senseonics, Inc.

# Overview of Safety Profile

- Eversense system has acceptable safety profile
  - Similar to other marketed CGM systems
- Procedural risks of implantable sensor mitigated
  - Device design, training, and continued improvements based on post-market surveillance
- Eversense reduces some known risks associated with other CGM systems

# Eversense Clinical Program

| Study | Duration | Patients | Sites | Role |
|---|---|---|---|---|
| PRECISE II | 90 days | 90 | 8 US | Pivotal |
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# PRECISE II and PRECISION: Device Exposure

| | PRECISE II | PRECISION |
|---|---|---|
| **Sensors inserted and removed** | **106 sensors** (90 patients) | **62 sensors** (35 patients) |
| **Procedures performed** | **212 procedures** | **124 procedures** |
| **Sensor use (mean duration)** | **92.2 days** | **91 days** |
| **Sensor exposure** | **9,773 days** | **6,148 days** |

# PRECISE II and PRECISION: Primary Safety Endpoint

- Incidence of device-related or insertion/removal procedure-related serious adverse events (SAEs) at any point during sensor use

# PRECISE II and PRECISION: Additional Safety Analyses

- Non-serious related adverse events
- AEs of special interest
  - e.g. infection, adhesive reactions
- Dexamethasone exposure over time

# PRECISE II and PRECISION: Serious Adverse Events (SAEs)

**PRECISE II**

- No device-related SAEs
- One procedure-related SAE reported
  - Sensor removal sensor unsuccessful (with and without ultrasound)
  - Sensor successfully removed by surgeon under general anesthesia

**PRECISION**

- No device- or procedure-related SAEs
  - 3 unrelated SAEs
  - Gastroenteritis, hypoglycemic episode, cellulitis of left foot

# PRECISE II and PRECISION: Device- or Insertion/Removal-Related AEs

| Adverse Event | PRECISE II Events | PRECISE II Patients N=90 | PRECISION Events | PRECISION Patients N=35 |
|---|---|---|---|---|
| All Events | 14 | 7 | 8 | 5 |
| Pain/discomfort | 4 | 2 | 2 | 2 |
| Bruising | 2 | 2 | -- | -- |
| Erythema | 2 | 2 | -- | -- |
| Device fragment not recovered | 2 | 2 | -- | -- |
| Syncope | 1 | 1 | -- | -- |
| Tingling | 1 | 1 | -- | -- |
| Delayed report of pain | 1 | 1 | -- | -- |
| Secondary procedure to remove sensor | 1 | 1 | 2 | 1 |
| Dermatitis at patch location | -- | -- | 2 | 1 |
| Skin hyperpigmentation | -- | -- | 2 | 1 |

# PRECISE II:
# Two Events Related to Device Fragment

- All removed sensors returned to sponsor for inspection
- 2 devices did not have cap upon return
- Corrective and preventative action plan implemented
  - Implementing enhanced quality procedures (cap adhesion)
- Cap material: PMMA highly biocompatible, permanent implant
  - Orthopedic, dental, and ophthalmologic
- Cap size: 3.2 mm x 0.8 mm

# PRECISE II and PRECISION: Additional Safety Outcomes

- No infections
- All related AEs considered expected and common for subcutaneous implant
- All related AEs resolved fully

# Role of Dexamethasone-Eluting Silicone Collar

- Contains 1.75 mg dexamethasone acetate (DXA)
  - Water-insoluble corticosteroid
  - Reduces local inflammatory response
  - Extends sensor life
- Controlled and slow DXA release
  - < 3 µg/day to local tissue
  - < 300 µg delivered over entire 90 days

# Impact of Dexamethasone Exposure

- Blood assayed for DXA to 50 pg/mL level
  - No detectable plasma levels of DXA observed
  - No systemic effects
- DXA collars examined after removal
  - Minimal DXA exposure confirmed 3 µg/day
- 2 events of transient hyperpigmentation
  - Resolved upon sensor removal

# Eversense Clinical Program

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# Integrated Device Exposure

- Three multi-center studies
  - PRECISE II, PRECISION, and PRECISE
- 206 subjects
- 335 sensors
- 670 insertion/removal procedures
- 22,529 patient-days of sensor wear

# Integrated Summary of Related Adverse Events

| Adverse Event | Events | Patients N=206 |
|---|---|---|
| All Events | 41 | 26 (13%) |
| Pain/discomfort | 10 | 8 (4%) |
| Redness/erythema | 6 | 6 (3%) |
| Secondary procedure to remove sensor | 4 | 3 (1%) |
| Infection | 3 | 3 (1%) |
| Bruising/hematoma | 3 | 3 (1%) |
| Device fragment not recovered | 2 | 2 (1%) |
| Dermatitis at patch location | 3 | 2 (1%) |
| Skin hyperpigmentation | 2 | 1 (< 1%) |

Events occurring once: neuropathy, vertigo, disturbed sleep, headache, paresthesia, syncope, hypertension, and nausea

# Low Rate of Infections Observed in Studies

- Aggregate infection rate 1%
- Improved incision care instructions
  - PRECISE: leave bandage for 24 hours
  - PRECISE II: leave bandage for 48 hours
- Infection rate observed is below literature reports for similar implants and minor procedures:  2–4%*

*Buprenorphine, Braeburn Pharmaceuticals, Inc.
*http://www.worldwidewounds.com/2005/september/Gottrup/Surgical-Site-Infections-Overview.html

# Eversense Clinical Program

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|---|---|---|---|---|
| PRECISE II | 90 days | 90 | 8 US | Pivotal |
| PRECISION | 90 days | 35 | 3 US | Supportive |
| PRECISE | 180 days | 81 | 7 EU | Supportive |
| | | | | |
| European Patient Registry *(ongoing)* | 2 years | 1686 | 350 EU | Post-market |
| Feasibility Studies | Varied | 332 | 10 | Pilot |
| Total | | 2224 | | |

# European Patient Registry

- All patients inserted commercially enrolled in registry
  - Enrollment completed when 100 patients reach 4 insertions
- All patients enrolled to be followed through 8 insertions and removals

# Low Rate of AEs with Repeat Insertions

| Events, n (%) | Post Insertion # 1 N=1686 | 2 N=443 | 3 N=143 | 4 N=58 | 5 N=39 | 6 N=14 | 7 N=3 |
|---|---|---|---|---|---|---|---|
| **SAEs** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| **Device-, procedure-related AEs** | | | | | | | |
| Infection (at sensor site) | **8 (0.5%)** | **4 (1%)** | **2 (1%)** | **-** | **-** | **-** | **-** |
| Secondary procedure to remove sensor | **7** | **2** | **-** | **-** | **-** | **-** | **-** |
| Adhesive patch site irritation | **5** | **-** | **2** | **-** | **-** | **-** | **-** |
| Prolonged wound healing | **3** | **-** | **-** | **-** | **-** | **-** | **-** |
| Redness/reaction to dressing | **3** | **-** | **-** | **-** | **-** | **-** | **-** |
| Sensor broke during removal | **3** | **-** | **-** | **-** | **-** | **-** | **-** |
| Skin atrophy over sensor w/ skin discoloration | **2** | **1** | **-** | **-** | **-** | **-** | **-** |
| Skin atrophy over sensor | **1** | **-** | **-** | **-** | **-** | **-** | **-** |
| Skin discoloration | **1** | **2** | **-** | **-** | **-** | **-** | **-** |
| Sensor site pain/discomfort | **1** | **-** | **-** | **-** | **-** | **-** | **-** |
| Bruising | **1** | **1** | **-** | **1** | **-** | **-** | **-** |
| Patient fainted during procedure | **1** | **-** | **-** | **-** | **-** | **-** | **-** |
| Hematoma | **-** | **-** | **-** | **1** | **-** | **-** | **-** |

# Proposed Post-Approval Study

# Proposed U.S. Post Approval Study Design

- Serial sensor insertions and removals for 2 years
- 175 patients in up to 20 clinical sites
- **Primary safety endpoint**
  - Rate of device-related and insertion/removal procedure-related SAEs through 12 months ≤ 7%
- **Primary effectiveness endpoint**
  - Time in range (between 70 mg/dL and 180 mg/dL), 12 months vs. first month

# Proposed U.S. Post Approval Study: Other Outcome Measures

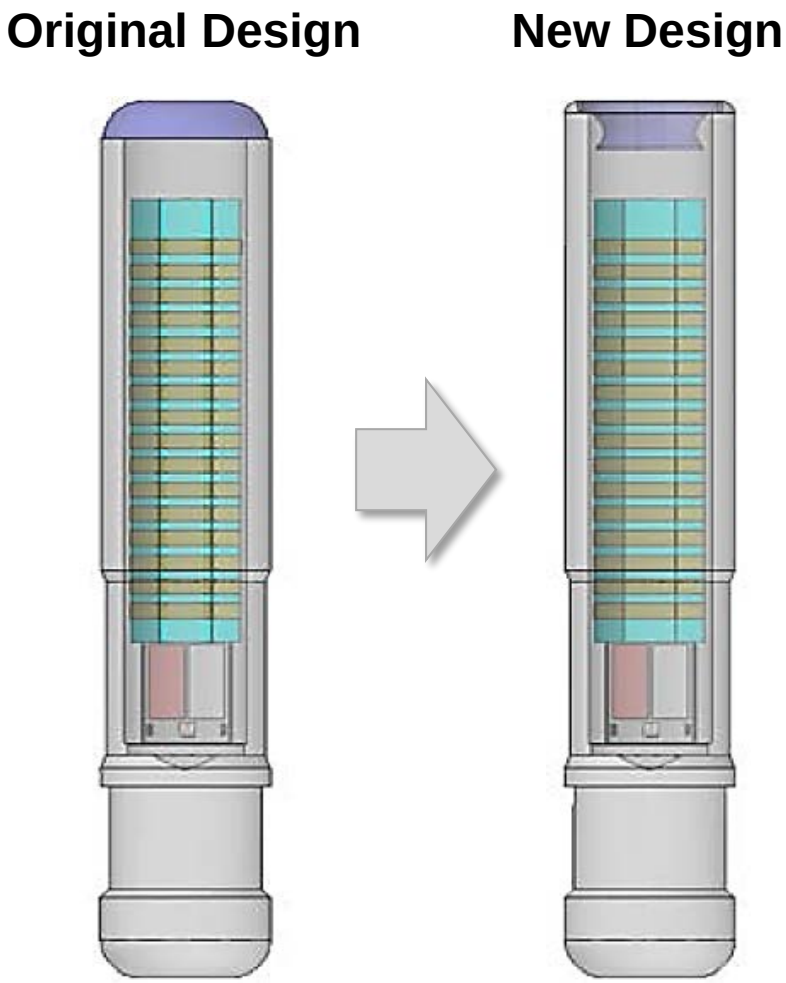
- All related AEs through 2 years
- Plasma dexamethasone levels every 6 months
- Effectiveness of training program
  - Success rate of insertions/removals
- Diabetes distress scale and CGM satisfaction scale
  - Baseline and annually

# Design Changes

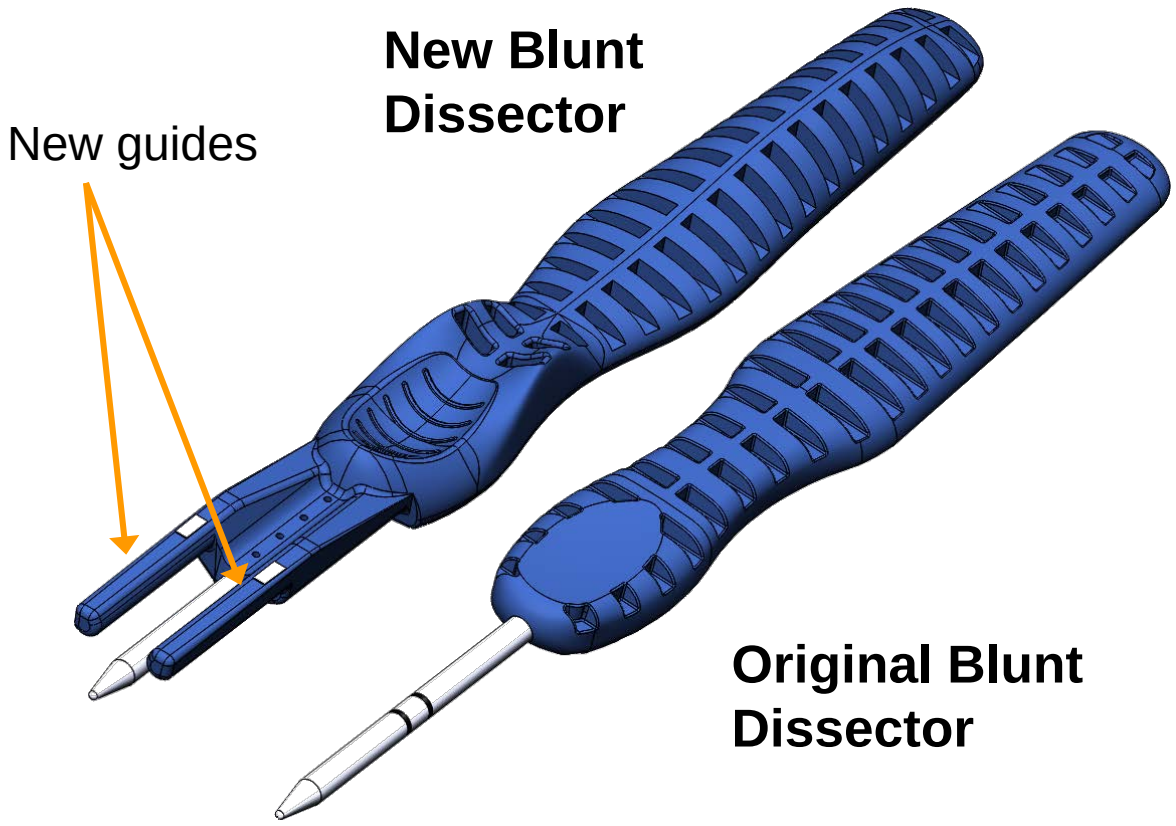
- Sensor end cap
- Blunt dissector tool

# Sensor End Cap Improvement

- End cap redesigned to be flush with end of sensor
- Design verification
  - Compressive forces
  - Torque
  - Maintains functional compatibility with insertion tool



# Blunt Dissector Design Improvement




- Same function
- Consistent placement facilitates removal
  - Proper entry angle
  - Pocket depth / length
  - Parallel to skin
- Validated with Human Factors testing

# Training for Clinicians

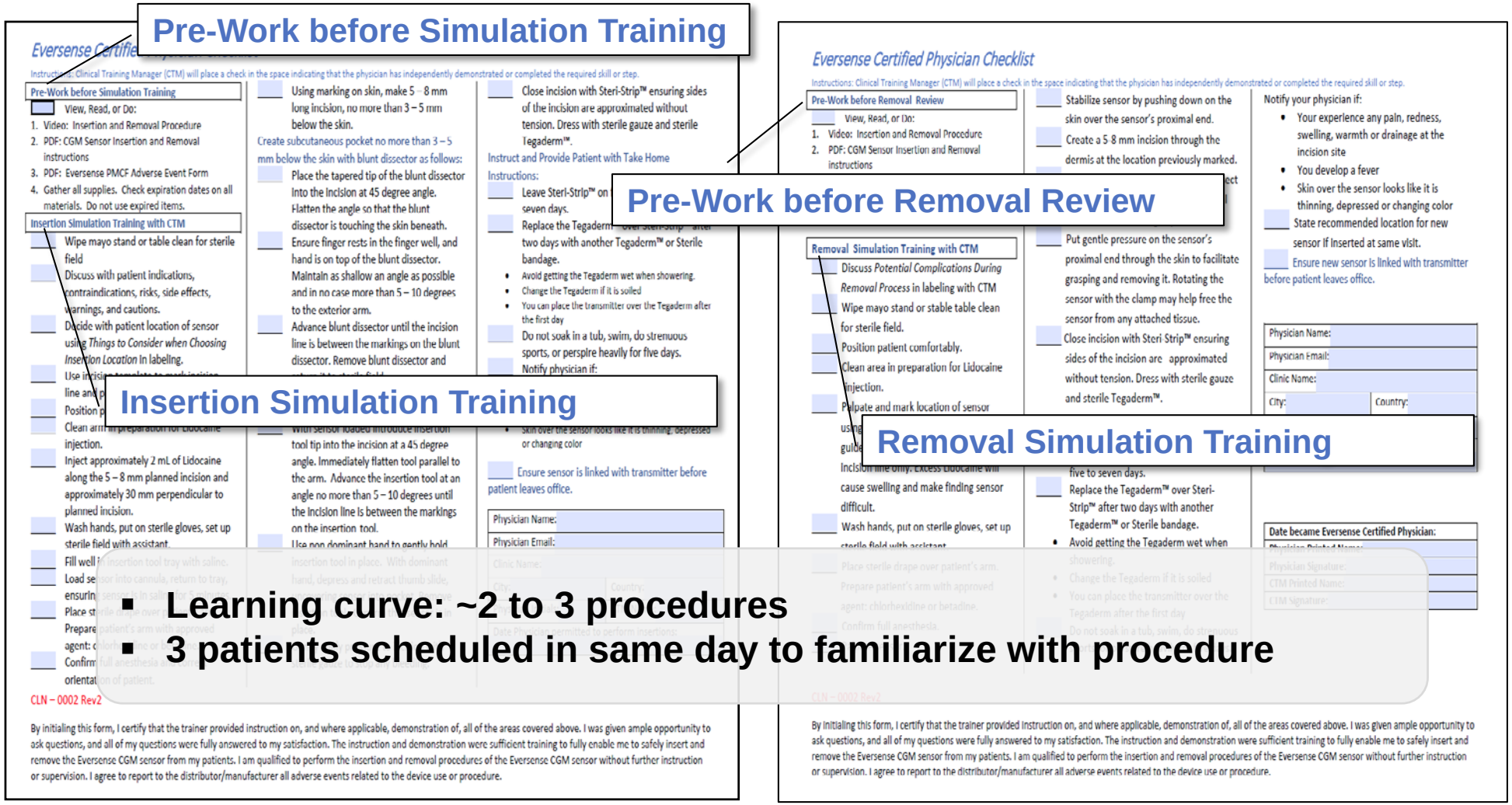
# Training Program Overview

- Mandatory comprehensive training
- Certification process led by Senseonics approved trainers
  - ✓ Didactic session
  - ✓ Practices with simulated skin
  - ✓ Initial insertions and removals are observed

**Training resources**:

- *CGM Sensor Insertion and Removal Instructions*
- Insertion videos
- Removal videos
- Simulation station
- Procedure poster
- Take-home instructions

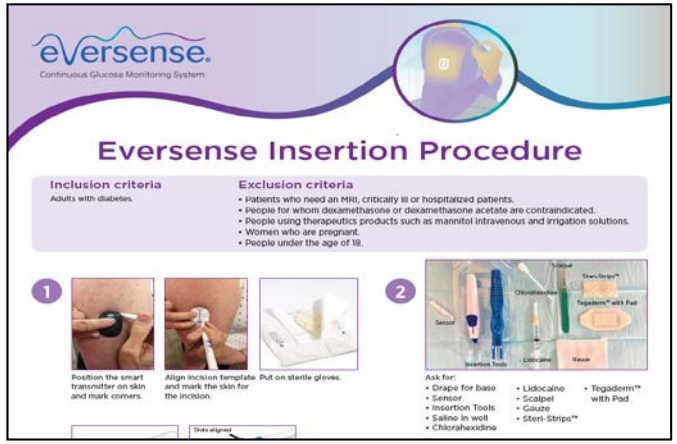
# Training Checklist for Certification

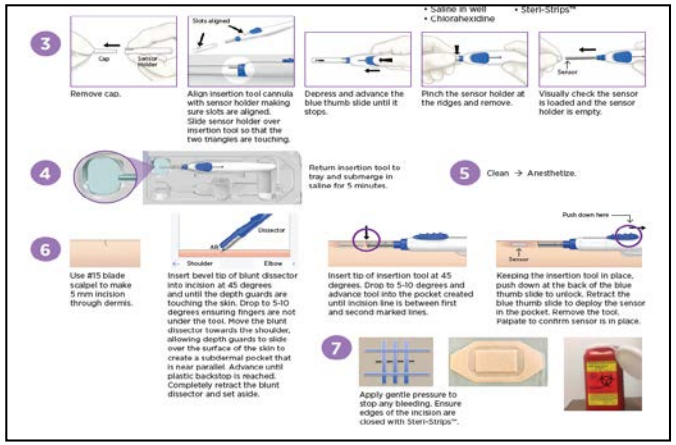


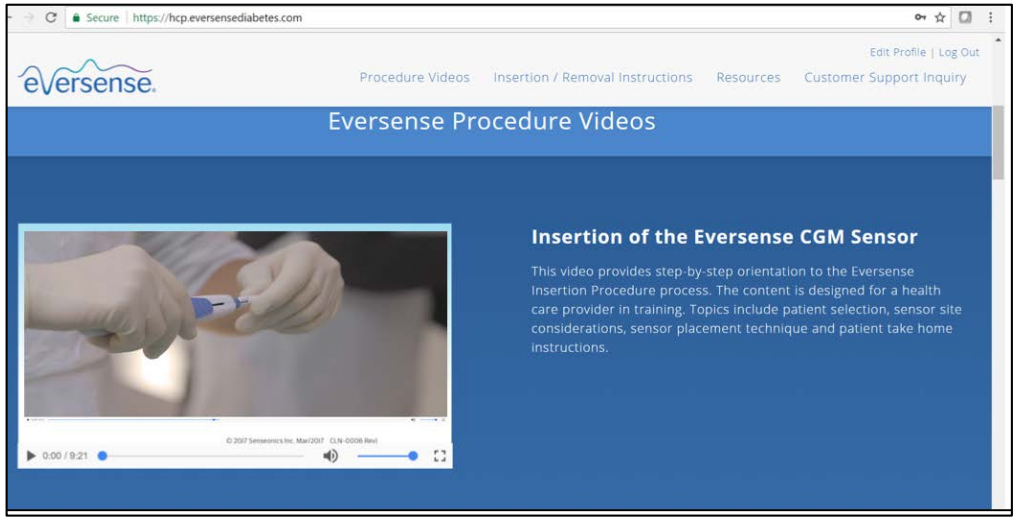

- **Learning curve: ~2 to 3 procedures**
- **3 patients scheduled in same day to familiarize with procedure**

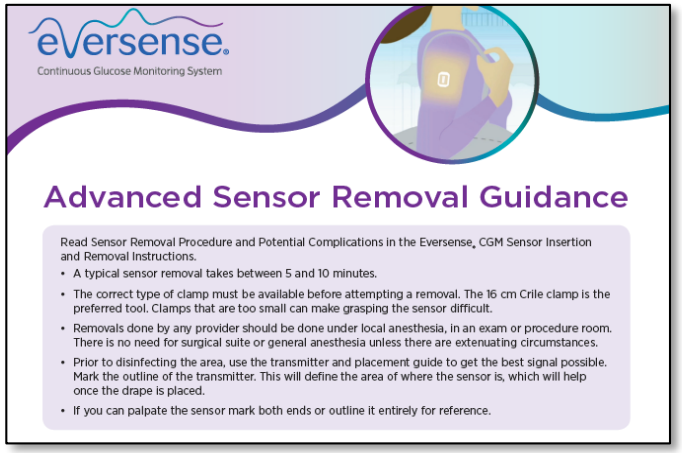
# Hands-On Practice Session with Simulated Skin, Sterile Field, and Required Supplies

# Examples of Training Materials



# Trained Providers Outside U.S.

- 461 clinicians trained on insertions
  - 94% certified to do insertions independently
- 258 clinicians trained on removals
  - 86% certified to do removals independently

# Europe:
# Successful Insertion and Removal Training

- Procedure easily learned by physicians with no prior Eversense experience
- 99% of removals successful on first attempt
- Low infection rate (0.5%)

# PRECISE II and PRECISION: Successful Insertion and Removal Training

- 100% of insertions and 99% of removals successful on first attempt
- 91% of insertions and 80% of removals completed in < 5 min

| | Insertion N=168 | Removal N=168 |
|---|---|---|
| **Mean time** | **2.3 min** | **4.5 min** |

# Eversense System Has Acceptable Safety Profile

- No unanticipated adverse events
- Limited AEs related to device or procedure
  - All AEs reported resolved fully
  - No Infections in US clinical trials
  - No detectable blood levels of dexamethasone
- One procedure-related SAE, resolved
- No device-related SAEs
- Eversense is safe for intended use

# Clinical Perspective / Benefit-Risk

**Steven J Russell, MD, PhD**

Associate Professor of Medicine

Harvard Medical School

# Relevant CGM Experience

- Experience with all currently approved CGMs (since 2004)
  - Published accuracy comparison studies of CGMs
- Developing bionic pancreas
  - Depends on CGM accuracy and reliability
  - Motivates interest in new CGM technologies
- Clinical investigator in artificial pancreas trials
  - Used Eversense system
  - Inserted and removed sensors
  - Trained quickly

# Current Situation:
# Majority of Patients Do Not Meet Glycemic Goals

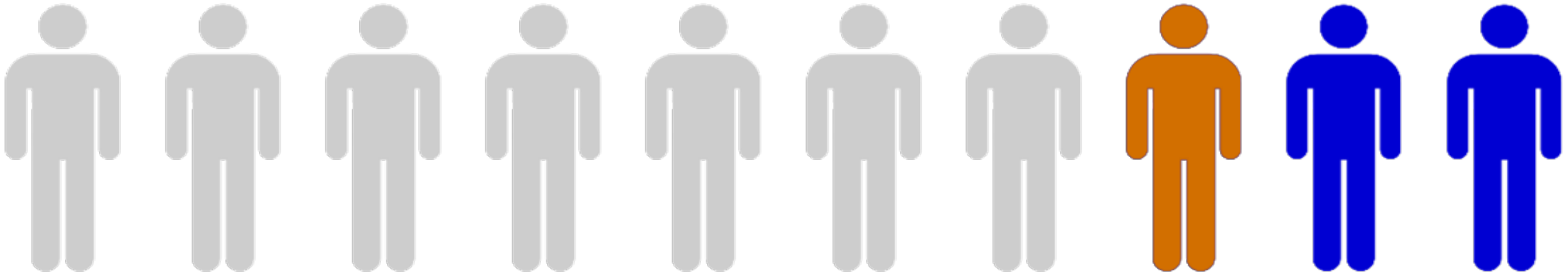
- 70% not at A1c targets*
  - Hypoglycemia still very common
- CGM systems are proven to help
  - Improve glucose control
  - Lower risk of hypoglycemia
  - Improve patients' lives

*Type 1 Diabetes Exchange

# The Current Situation:
# Only 3 Out of 10 Patients with T1D Use CGM

- **Perceived burden of repeat insertion**
- **Fear of pain**

# The Current Situation:
# 1 out of 3 CGM Users Discontinue within 1 Year



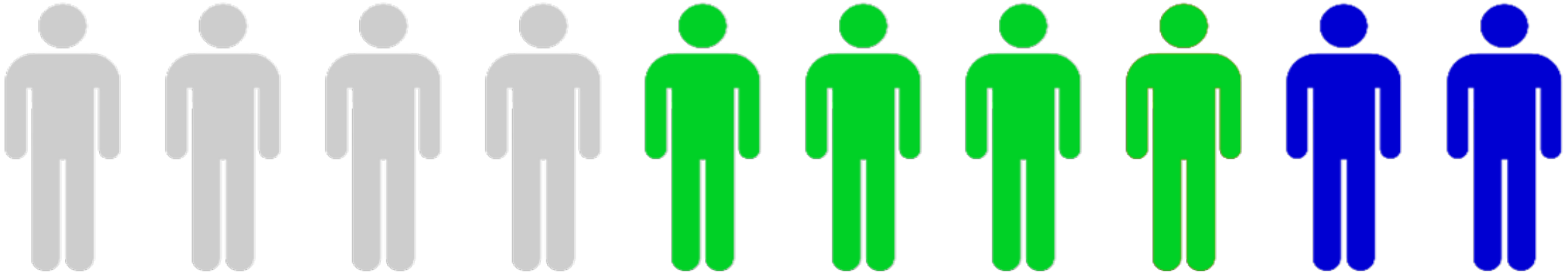
- Problems with adhesive / insertion
- Uncomfortable

# Eversense Addresses Many Barriers to CGM Use

- Longer sensor life (90 days)
- Less frequent sensor insertions
  - Eversense: 4 times per year
  - Current systems:  25–50 times per year
- Easy to wear and easily removed
  - For physical activities or discretion
- On-body vibration from transmitter provides extra safety measure

# The Goal: Increase Use of CGM

- Improve glucose control
- Lower risk of hypoglycemia



# Eversense® Continuous Glucose Monitoring (CGM) System

**March 29, 2018**

Senseonics, Inc.

Clinical Chemistry and Clinical Toxicology Device Panel