THE SYNCOPE CHALLENGE IMPACT

35% of the population will have at least one syncopal event in their lifetime

Syncope accounts for 1-3% of emergency room visits

32% of those ER patients are hospitalized

HALF OF PATIENTS ADMITTED TO THE HOSPITAL AFTER A SYNCOPE EVENT LEAVE WITHOUT A DIAGNOSIS

SYNCOPE ETIOLOGY
A SYMPTOM WITH MANY POSSIBLE CAUSES

- Cardiac: 9.5%
- Orthostatic: 9.4%
- Vasovagal: 21.2%
- Unexplained: 36.6%
- Medication: 6.8%
- Other: 7.5%
- Non-syncopal TLOC: 9.0%

26.5% of which will receive a cardiac diagnosis with ICM monitoring*

*(Solbiati 2017 meta-analysis
THE CAUSE OF SYNCOPE MATTERS
CARDIAC CAUSE INCREASES
MORTALITY RATES

Overall Survival of Participants with Syncope According to Cause

Patients endure ongoing diagnostic testing and still come away with no answers.

Physician specialties consulted

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiologist</td>
<td>43%</td>
</tr>
<tr>
<td>Emergency Medicine</td>
<td>23%</td>
</tr>
<tr>
<td>Internal Diseases</td>
<td>36%</td>
</tr>
<tr>
<td>Neurologist</td>
<td>38%</td>
</tr>
<tr>
<td>General Practitioner</td>
<td>47%</td>
</tr>
</tbody>
</table>

Diagnostic tests performed

<table>
<thead>
<tr>
<th>Test</th>
<th>Total Recruitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard ECG</td>
<td>556 (98%)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>490 (86%)</td>
</tr>
<tr>
<td>Basic laboratory tests</td>
<td>488 (86%)</td>
</tr>
<tr>
<td>Ambulatory ECG monitoring</td>
<td>382 (67%)</td>
</tr>
<tr>
<td>In-house ECG monitoring</td>
<td>311 (55%)</td>
</tr>
<tr>
<td>Exercise testing</td>
<td>297 (52%)</td>
</tr>
<tr>
<td>Ortho static blood pressure measurements</td>
<td>275 (48%)</td>
</tr>
<tr>
<td>MRI/CT scan</td>
<td>267 (47%)</td>
</tr>
<tr>
<td>Neurological or psychiatric evaluation</td>
<td>270 (47%)</td>
</tr>
<tr>
<td>EEG</td>
<td>222 (39%)</td>
</tr>
<tr>
<td>Carotid sinus massage</td>
<td>205 (36%)</td>
</tr>
<tr>
<td>Tilt test</td>
<td>201 (35%)</td>
</tr>
<tr>
<td>Electrophysiology testing</td>
<td>144 (25%)</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>133 (23%)</td>
</tr>
<tr>
<td>External loop recording</td>
<td>67 (12%)</td>
</tr>
<tr>
<td>ATP test</td>
<td>15 (3%)</td>
</tr>
<tr>
<td>Other tests</td>
<td>52 (9%)</td>
</tr>
</tbody>
</table>

### SYNCOPE DIAGNOSIS
TESTING OPTIONS AND THEIR DIAGNOSTIC YIELD

<table>
<thead>
<tr>
<th>Test/Procedure</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>3-5%(^1)</td>
</tr>
<tr>
<td>Holter Monitoring</td>
<td>5-11%(^2,3)</td>
</tr>
<tr>
<td>External Loop Recorder</td>
<td>20%(^4)</td>
</tr>
<tr>
<td>Tilt Table</td>
<td>15-21%(^1)</td>
</tr>
<tr>
<td>EP Study without structural heart disease</td>
<td>10%(^5)</td>
</tr>
<tr>
<td>Neurological (CT scan, MRI, carotid doppler)</td>
<td>1-2%(^1)</td>
</tr>
<tr>
<td>Reveal™ ICM</td>
<td>43-59%(^2,4,6,7)</td>
</tr>
</tbody>
</table>

LIVING WITHOUT A DIAGNOSIS COMPROMISES QUALITY OF LIFE\textsuperscript{1-3}

\begin{itemize}
  \item 36\% suffer significant trauma\textsuperscript{4}
  \item 70\% hospitalized at least once for syncope\textsuperscript{4}
  \item 2x risk of loss of employment\textsuperscript{3}
  \item 1.4x higher risk of on-the-job accidents\textsuperscript{3}
\end{itemize}

Syncope compromises quality of life, affecting patients physically, economically, and psychologically.

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LIVING WITHOUT A DIAGNOSIS IS COSTLY TO THE PATIENT

$26,000 per hospitalization*¹

$12,988² cost of minor injury†

$29,886² cost of major injury†

$4,419 cost of conventional testing,²,³ which renders low diagnostic yield of 5-20% vs. 44% ICM yield

* Median cost
† Mean cost of injury alone, not including rehabilitation or long-term costs.
ICM MORE LIKELY TO DIAGNOSE INFREQUENT SYNCOPE THAN CONVENTIONAL TESTING
META-ANALYSIS: BRIGNOLE, EUROPEAN HEART J 2018

- Supported 2018 ESC Syncope Guidelines improved recommendation for ICM and published in guidelines supplement
- n = 657 patients
- Meta-analysis of 5 randomized clinical trials (published 2001-2016)
  - Comparing diagnostic yield of ICM monitoring to standard of care

![Table showing diagnostic yield with ICM and standard of care](image)

3.6X more likely to reach a diagnosis with ICM vs. standard of care

HIGH DIAGNOSTIC YIELD IN UNEXPLAINED SYNCOPE META-ANALYSIS: SOLBIATI, INT J CARDIOL 2017

- 49 studies (published 1998-2015), n = 4,381 patients
- 44% diagnostic yield at 1 year and 25% were diagnosed with an arrhythmia
  - Diagnosis = ICM recording during recurrent event OR automatic detection of significant arrhythmia
- Median time to diagnosis: 134 days (range 30-600)
- Median follow-up: 365 days (range 168-660)

ICMs ARE A COST-EFFECTIVE DIAGNOSTIC TOOL EARLIER UTILIZATION REDUCES COST

Multiple studies show ICM monitoring resulted in cost savings in syncope patients compared to conventional testing through fewer tests and hospital admissions.¹-⁴

88% of patients who are guideline-eligible for an ICM are over-tested with other modalities before being offered an ICM.⁵

At 3 years monitoring, hospitalizations reduced by 60%⁶

Over-testing increases cost with no improvement to diagnostic yield.⁵

67% cost reduction through fewer tests and hospital days⁷

⁵ Edvardsson N, Europace. 2015;17:1141-1148.
82% of Reveal ICM guided diagnoses led to treatment, with 57% receiving pacemaker or ICD

Note: Therapy percentages listed include patients who received more than one therapy.

THE LONGER YOU LOOK THE MORE YOU FIND VALUE OF SUPERIOR DIAGNOSTIC YIELD

- Accurate diagnosis of cardiac arrhythmia
- Timely and informed treatment decisions
- Reduced cost

ICM CAN RULE IN OR RULE OUT CARDIAC CAUSE OF SYNCOPE¹,²

<table>
<thead>
<tr>
<th>3.6x</th>
<th>44%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>more likely to reach a diagnosis with ICM vs. standard of care³</td>
<td>diagnostic yield of ICM &amp; increases over time at 52% in year 3²</td>
<td>of syncope diagnosed with ICMs occurred after 2 years⁸</td>
</tr>
</tbody>
</table>

| vs. standard of care | 5-20% ⁴⁷ |

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SUMMARY

✓ Syncope is prevalent and difficult to diagnose
✓ Patients suffer compromised quality of life and high costs
✓ ICM is more likely to provide a diagnosis than standard of care for unexplained syncope
✓ ICM is more cost-effective than standard of care
✓ ICM leads to treatment decisions
✓ Diagnostic yield increases over time
If initial evaluation is unclear and a cardiac cause is suspected, cardiac monitoring should be performed — Class I Recommendation

Patient selection is based on frequency of symptoms, likelihood of arrhythmic cause, and patient characteristics — ICMs should be placed in all patients with infrequent symptoms

Randomized clinical trials support the recommendation for ICM monitoring in syncope patients

Applies to patients after a normal initial evaluation without significant injury or cardiovascular morbidities; patients followed up by primary care physician as needed.

† In selected patients.

ICM is recommended for patients with symptoms > 30 days apart

<table>
<thead>
<tr>
<th>Symptom Frequency</th>
<th>More than 30 days apart$^{1,2}$</th>
<th>Weekly to monthly$^1$</th>
<th>Daily to several times a week$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Monitor</td>
<td>Insertable Cardiac Monitor</td>
<td>External Loop Recorder/Extended Holter</td>
<td>Holter Monitor</td>
</tr>
</tbody>
</table>

If initial monitoring is non-diagnostic, continue monitoring with ICM. Get to the answer.

Extensive changes from 2009 based on new evidence:

- Increased role of prolonged ECG monitoring with ICM
- Revised recommendation from Class I to Class II for Holter monitors and tilt tests
- Increased importance of risk stratification from ED and referral to syncope specialist

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A</td>
<td>UPGRADED: ICMs upgraded to Class I/Level A recommendation — the strongest level of clinical evidence — for early monitoring in low-risk patients and after workup of high-risk patients.</td>
</tr>
<tr>
<td>IIb</td>
<td>B</td>
<td>NEW: ICMs added as a Class II/Level B recommendation to diagnose unexplained falls and unconfirmed epilepsy</td>
</tr>
<tr>
<td>IIA</td>
<td>B</td>
<td>ICMs should be considered in patients with suspected or certain reflex syncope presenting with frequent or several syncopal episodes.</td>
</tr>
</tbody>
</table>

COR — Class of Recommendation
LOE — Level of Evidence

T-LOC suspected syncope

Certain diagnosis/mechanism
Treat appropriately

Syncope

High risk* arrhythmia likely
In-hospital (Class I)
IF NEGATIVE
ICM (Class I)

Low risk* arrhythmia likely and recurrent episodes
ICM (Class I)
ELR (Class IIa)
Holter (Class IIa)

Low risk* reflex likely and need specific therapy
ICM (Class IIa)

Low risk* and rare episodes
None indicated

Low risk*
arrhythmia likely

T-LOC Non-syncopal
Uncertain Diagnosis

Unconfirmed epilepsy or Unexplained falls

*High Risk & Low Risk Recommendations Summarized on Slides 18 – 19


Downgraded (from Class I in 2009) due to low diagnostic yield and lack of cost effectiveness
EXPERIENCE
THE REVEAL LINQ™
ADVANTAGE

REVEAL LINQ™
INSERTABLE CARDiac MONITOR
AN OVERVIEW
REVEAL LINQ™ SYSTEM ADVANTAGES
REVOLUTIONIZING CARDIAC MONITORING

The smallest, most powerful insertable cardiac monitor

**SMALL**
One-third the size of a AAA battery (1.2 cc)

**3 YEAR**
Up to a 3-year longevity for long-term monitoring

**MR**
MR Conditional at 1.5 and 3.0 Tesla

**EASY**
Minimally invasive, simplified insertion procedure

**96.7%**
of patients very satisfied or satisfied with Reveal LINQ ICM after insertion

---

1 Reference the Reveal LINQ ICM Clinician Manual for usage parameters.
REVEAL LINQ™ SYSTEM ADVANTAGES
SIMPLE INSERTION PROCEDURE

Best location:
45 degrees to sternum over 4th intercostal space,
2 cm from left edge of sternum

97%
of physicians found the insertion tool simple and intuitive.¹

Requires minimal procedure time and clinical resources

REVEAL LINQ™ SYSTEM ADVANTAGES
AN ADVANCED MONITORING SOLUTION

Solution Enablers

Insertion Tools
Patient Assistant
App-based Reveal LINQ Mobile Manager
Reveal LINQ Monitoring Service*

*The Reveal LINQ Monitoring Service is provided by Medtronic Monitoring Inc., a wholly owned subsidiary of Medtronic.
**Patient Assistant**

**THE REVEAL LINQ™ ADVANTAGE**

**SMART ECG DATA STORAGE**

ECG data storage: 59 minutes total

Patient-activated: up to 30 minutes

<table>
<thead>
<tr>
<th>Episodes</th>
<th>Duration</th>
<th>Prior Time</th>
<th>Patient-activated</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 episodes</td>
<td>@ 7.5 minutes each</td>
<td>6.5 min</td>
<td>1 min</td>
</tr>
<tr>
<td>3 episodes</td>
<td>@ 10 minutes each</td>
<td>9 min</td>
<td>1 min</td>
</tr>
<tr>
<td>2 episodes</td>
<td>@ 15 minutes each</td>
<td>14 min</td>
<td>1 min</td>
</tr>
</tbody>
</table>

Reference the Reveal LINQ ICM Clinician Manual for usage parameters.
ADVANCED MONITORING
INNOVATIVE SOLUTIONS. SIMPLIFIED EXPERIENCE.

STREAMLINED INSERTION WORKFLOW

Simple, minimally invasive outpatient insertion procedure

App-based device management with the Reveal LINQ™ Mobile Manager

ACTIONABLE REPORTS

- Supported by an enhanced Medtronic CareLink™ network
- Industry’s highest diagnostic yields, with actionable reports.¹-⁴

SIMPLIFIED PATIENT MANAGEMENT

Resources to support clinic efficiency and data review

- Medtronic Academy Learning Plan
- Patient Education Resources
- Reveal LINQ Monitoring Service

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EXPERIENCE THE REVEAL LINQ ADVANTAGE

Unmatched Accuracy\(^1\)

Superior Evidence
500+ Reveal™ ICM Publications\(^2\)

MRI Conditional
Same Day at 1.5 and 3.0 Tesla.*

*Reveal LINQ ICM has been demonstrated to pose no known hazards in a specified MRI environment with specified conditions of use. Please see the Reveal LINQ ICM clinician manual or MRI technical manual for more details.

LEADING INNOVATION

1998
Reveal™ ICM
World’s First ICM

2000
Reveal™ Plus ICM
World’s Second ICM
MRI Conditional 1.5 T

2007
Reveal™ DX ICM
Three-year battery life
MRI Conditional 1.5 or 3.0 T

2009
Reveal™ XT ICM
World’s First AF Algorithm

2011
Reveal™ XT ICM Pause Algorithm with diminishing R-wave analysis

2014
Reveal LINQ™ ICM
World’s Smallest ICM

2017
TruRhythm™ Detection
- Third-generation algorithms for Brady and Pause
- Smart filtering technology

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ADVANCED MONITORING
SYNCOPE PATIENT IMPACT

William’s story
Reveal LINQ™ ICM used to discover non-sustained SVT event

William remembered his fainting spells seemed to come out of nowhere. The first time it happened was just after he stood up to get a second cup of coffee. He was unconscious for 30 seconds while his parents and wife feared he was dead. Another time, he was having dinner while on a cruise ship when, without warning, his head fell forward and he lost consciousness.

William experienced an ambulance trip, multiple visits to the hospital and appointments with various physician specialties. Multiple tests showed nothing.

Years went by without incident until he was on another family vacation — this time to Paris. As he walked along a cobblestone street with his family, William collapsed.

“My face slammed into a cobblestone curb and knocked out my four front teeth. I had a cut under my chin, my mouth was gushing blood, I had a gash over my right eye, and I’d fractured my upper mandible on the left- side of my jaw. I also had hairline fractures of the orbital bones under my eyes.”

William returned to the U.S. for reparative surgery, and to meet with an Electrophysiologist who recommended the Reveal LINQ™ ICM. The device was inserted in February, 2016 and the following August, Dr. Sanchez called William to tell him that an episode was detected. The data showed that, while William slept, he experienced a non-sustained SVT event: 20 heartbeats in a 5-seconds span.

Today, following a successful ablation procedure, William is back to enjoying life. He works out multiple times a week and enjoys traveling with his family, playing basketball, tennis and golf.
ADVANCED MONITORING
SYNCOPE PATIENT IMPACT

Kymberli’s story
Reveal LINQ™ ICM used to discover malignant vasovagal syncope

On a February morning in 2015, Kymberli, the busy mother of four young children prepared for her triplets’ first birthday party. Suddenly, she felt queasy, confused, and clammy. She passed out before she could say anything.

Kymberli was taken by ambulance to the emergency room. After a CT scan and a 2D echo, she was discharged and sent to a cardiologist. She was given a 30-day event monitor that showed nothing of concern related to her heart. The doctors thought it was possible that stress, dehydration, or lack of sleep had triggered the event.

Kymberli wasn’t convinced. She made an appointment with an electrophysiologist specializing in the diagnosis and treatment of abnormal heart rhythms. He ordered a cardiac MRI and a stress test, both of which came back normal. Aside from a low heart rate and hypotension she’d had her entire life, Kymberli appeared healthy.

Her doctor recommended Reveal LINQ™ ICM. The device was inserted in June 2015 and the following November Kymberli blacked out while home alone with the children. The data from Kymberli’s device was transmitted to her doctor’s office. Just minutes after receiving it, they contacted Kymberli and told her to call 911. The data showed Kymberli’s heart had stopped for 19 seconds.

Kymberli was diagnosed with malignant vasovagal syncope and sick sinus syndrome. A pacemaker was implanted to regulate Kymberli’s heart.

“The Reveal LINQ is the reason I’m here today,” says Kymberli. “Without it, my doctor wouldn’t have detected my heart’s 19-second pause. With that information, he could diagnose the malignant form of vasovagal syncope and prevent syncope with a pacemaker. Now I have comfort in knowing I’m OK and that my heart will keep beating.”

This story reflects one person’s experience. Not every person will receive the same results.
Debbie’s story
Reveal™ ICM used to discover a rare form of AT

After Debbie fainted the first time, she didn’t think much about it. As a cardiac nurse, she knew there were many reasons people faint. But the fainting continued, and within a couple of months she was passing out three times a day. Her cardiologist decided to give Debbie a Medtronic Reveal insertable cardiac monitor (ICM).

Based on the information from the Reveal ICM, her doctors determined Debbie had a rare, aggressive form of atrial tachycardia (AT) that was very resistant to treatment. She tried new medications. Debbie’s doctors also relied on the Reveal ICM to monitor how her heart responds to the therapy.

With her fainting under better control, Debbie got back to practicing ballet.

She encourages people who experience fainting episodes to make a doctor appointment right away.
INDICATIONS, SAFETY, AND WARNINGS

If you are located in the United States, please refer to the brief statement below to review applicable indications, safety, and warning information. See the device manual for detailed information regarding the implant procedure, indications, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please call Medtronic at 763-514-4000 and/or consult the Medtronic website at medtronic.com.

If you are located outside the United States, see the device manual for detailed information regarding the implant procedure, indications, contraindications, warnings, precautions, and potential adverse events. For further information, contact your local Medtronic representative and/or consult the Medtronic website at medtronic.com.

www.medtronic.com/manuals

Consult instructions for use at this website. Manuals can be viewed using a current version of any major Internet browser. For best results, use Adobe Acrobat Reader® with the browser.

Important Reminder: This information is intended only for users in markets where Medtronic products and therapies are approved or available for use as indicated within the respective product manuals. Content on specific Medtronic products and therapies is not intended for users in markets that do not have authorization for use.

Reveal LINQ™ LNQ11 Insertable Cardiac Monitor and Patient Assistant

Indications
Reveal LINQ™ LNQ11 Insertable Cardiac Monitor
The Reveal LINQ insertable cardiac monitor is an implantable patient-activated and automatically-activated monitoring system that records subcutaneous ECG and is indicated in the following cases:
• Patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
• Patients who experience transient symptoms such as dizziness, palpitation, syncope, and chest pain, that may suggest a cardiac arrhythmia
This device has not been specifically tested for pediatric use.

Patient Assistant
The Patient Assistant is intended for unsupervised patient use away from a hospital or clinic. The Patient Assistant activates the data management feature in the Reveal™ insertable cardiac monitor to initiate recording of cardiac event data in the implanted device memory.

Contraindications
There are no known contraindications for the implant of the Reveal LINQ insertable cardiac monitor. However, the patient’s particular medical condition may dictate whether or not a subcutaneous, chronically implanted device can be tolerated.

Warnings/Precautions
Reveal LINQ™ LNQ11 Insertable Cardiac Monitor
Patients with the Reveal LINQ insertable cardiac monitor should avoid sources of diathermy, high sources of radiation, electrosurgical cautery, external defibrillation, lithotripsy, therapeutic ultrasound, and radiofrequency ablation to avoid electrical reset of the device, and/or inappropriate sensing as described in the Medical procedure and EMI precautions manual. MRI scans should be performed only in a specified MR environment under specified conditions as described in the Reveal LINQ MRI Technical Manual.
INDICATIONS, SAFETY, AND WARNINGS, CONT'D.

Patient Assistant
Operation of the Patient Assistant near sources of electromagnetic interference, such as cellular phones, computer monitors, etc., may adversely affect the performance of this device.

Potential Complications
Potential complications include, but are not limited to, device rejection phenomena (including local tissue reaction), device migration, infection, and erosion through the skin. Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

Medtronic MyCareLink™ Patient Monitor, Medtronic CareLink™ Network, and CareLink™ Mobile Application

Intended Use
The Medtronic MyCareLink™ patient monitor and CareLink™ network are indicated for use in the transfer of patient data from some Medtronic implantable cardiac devices based on physician instructions and as described in the product manual. The CareLink™ mobile application is intended to provide current CareLink network customers access to CareLink network data via a mobile device for their convenience. The CareLink mobile application is not replacing the full workstation, but can be used to review patient data when a physician does not have access to a workstation. These products are not a substitute for appropriate medical attention in the event of an emergency and should only be used as directed by a physician. CareLink network availability and mobile device accessibility may be unavailable at times due to maintenance or updates, or due to coverage being unavailable in your area. Mobile device access to the Internet is required and subject to coverage availability. Standard text message rates apply.

Contraindications
There are no known contraindications.

Warnings and Precautions
The MyCareLink patient monitor must only be used for interrogating compatible Medtronic implantable devices.

See the device manual for detailed information regarding the implant procedure, indications, contraindications, warnings, precautions, and potential implications/adverse events. For further information, please call Medtronic at 1-800-328-2518 and/or consult the Medtronic website at medtronic.com.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.