

THE LINQ BETWEEN CRYPTOGENIC STROKE AND AF

Atrial fibrillation detection and treatment matters for
improved stroke outcomes



Reveal LINQ™
Insertable Cardiac Monitoring System



Actual Size

Medtronic

CRYPTOGENIC STROKE IS A CHALLENGE



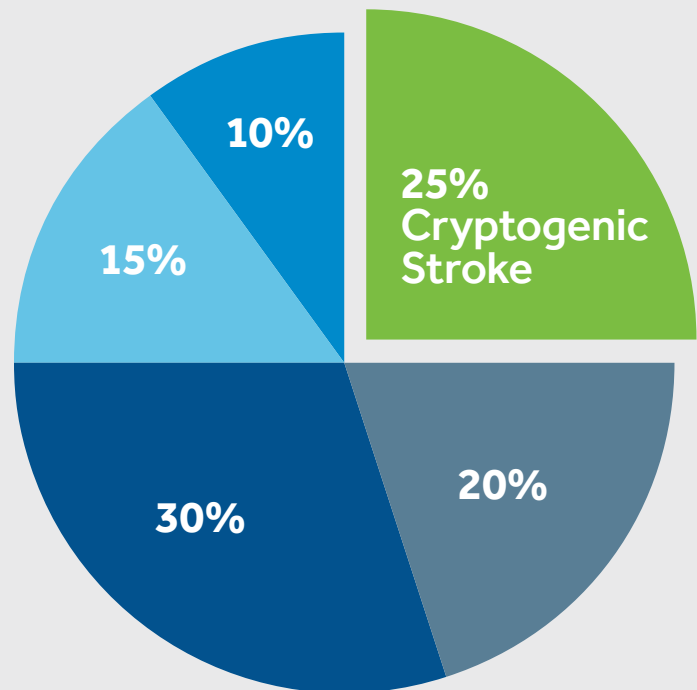
691,650

Americans experience ischemic strokes every year.¹

25%

Despite a comprehensive diagnostic workup, about **25% of ischemic stroke patients remain cryptogenic.**²

Up to 30% of patients with cryptogenic stroke may have previously undetected paroxysmal AF.³



■ Cryptogenic Stroke

■ Large Vessel

■ Other

■ Small Vessel

■ Cardioembolic

1 in 4

Stroke survivors will experience another stroke within 5 years.⁴

SECONDARY STROKE PREVENTION IS ESSENTIAL

AF Detection and Treatment Matters

Detection of AF in Cryptogenic Stroke Patients Changes Treatment



*If the patient is an appropriate candidate.

RE-SPECT ESUS and NAVIGATE ESUS trial results highlight the importance of detecting AF and tailoring treatment for cryptogenic stroke or ESUS patients.

	Study Outcome
NAVIGATE ESUS	NEGATIVE ⁸ Increase in bleeding in the rivaroxaban arm
RE-SPECT ESUS	FAILED PRIMARY OUTCOME ⁹ Dabigatran was not superior to ASA

5x

There is a 5-fold increase in ischemic stroke risk for AF patients.¹⁰

2x

more likely for AF-related ischemic stroke to be fatal than non-AF stroke.¹¹

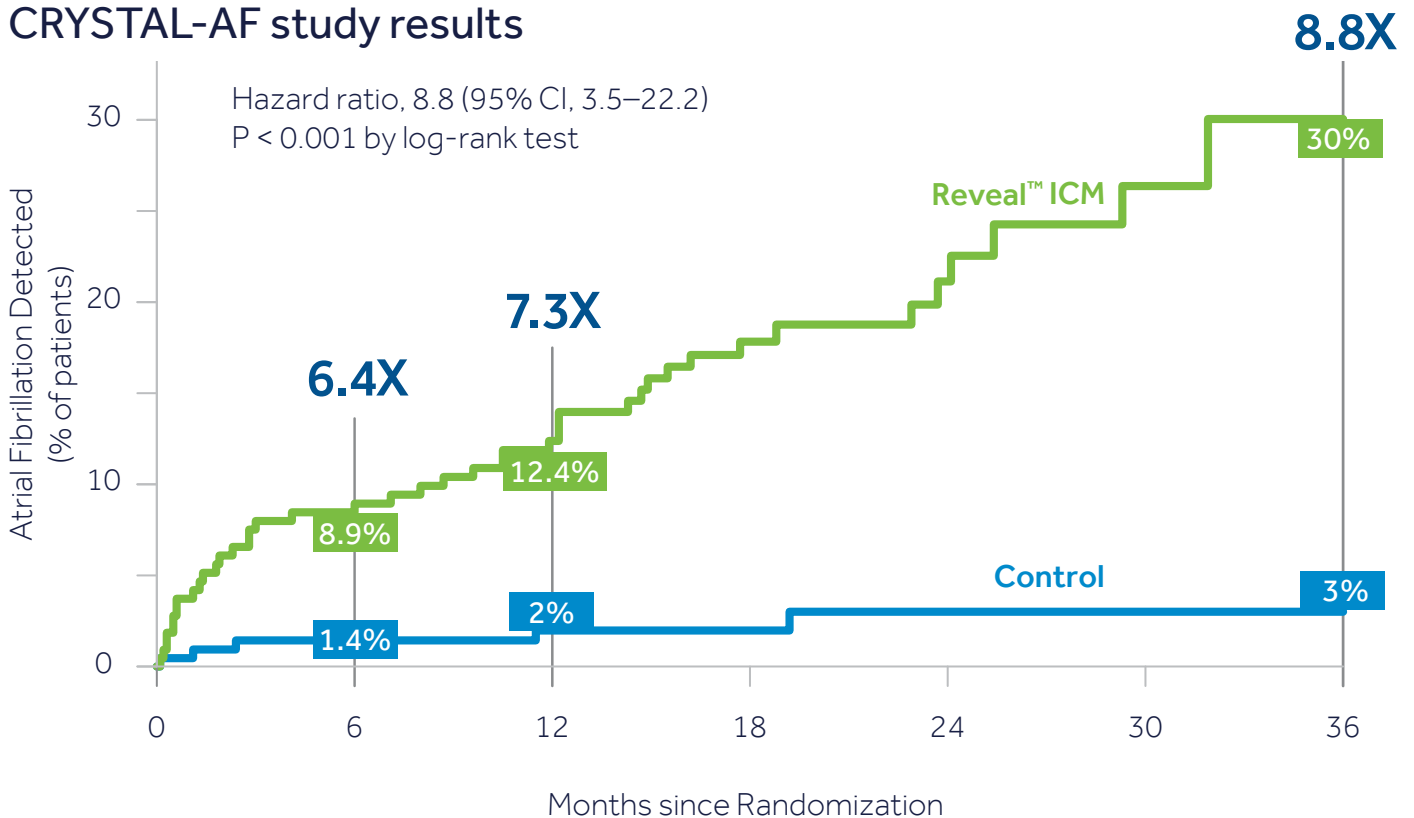
79%

of first AF episodes are asymptomatic at 12 months.³

THE CRYSTAL-AF STUDY DEMONSTRATES THE SUPERIORITY OF ICM FOR AF DETECTION

As published in the *New England Journal of Medicine*³

CRYSTAL-AF study results



▪ **30%** AF detected at 3 years vs. 3% for SOC.

▪ Multiple studies show that **short-term monitoring is NOT sufficient for AF detection in cryptogenic stroke.**^{12,13}

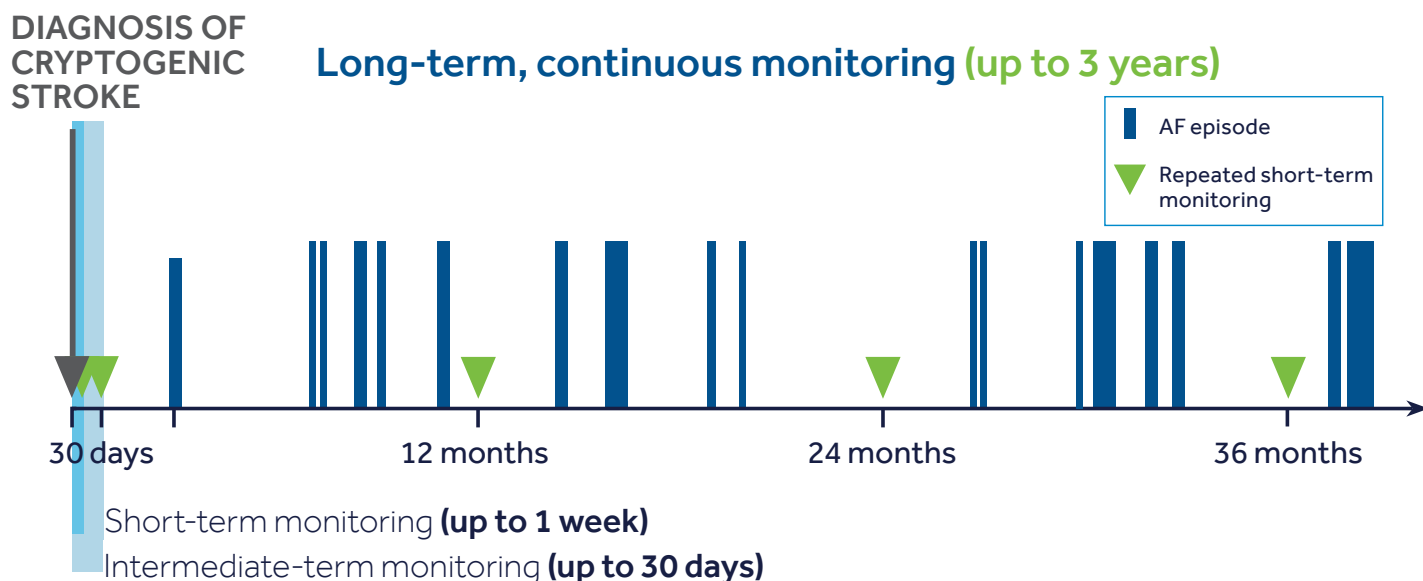


“Atrial fibrillation after cryptogenic stroke was most often asymptomatic and paroxysmal and thus unlikely to be detected by strategies based on symptom-driven monitoring or intermittent short-term recordings.”

– Sanna, et al. *N Engl J Med.*³

30-DAY CARDIAC MONITORING IS NOT ENOUGH

Short-term and intermediate-term cardiac monitoring may miss many patients with paroxysmal AF³



Note: Illustration purposes only.

Considerations for monitoring of cryptogenic stroke patients:

Yield

88%

of patients who had AF would have been missed if only monitored for 30 days.*^{3,14}

Patient Outcomes

55%

lower stroke recurrence for cryptogenic stroke/TIA patients when AF is detected by an ICM and treated.¹⁵

Patient Experience

< 5%

of ischemic stroke patients who initially receive short-term external cardiac monitoring (up to 30 days) go on to receive an ICM.¹⁶

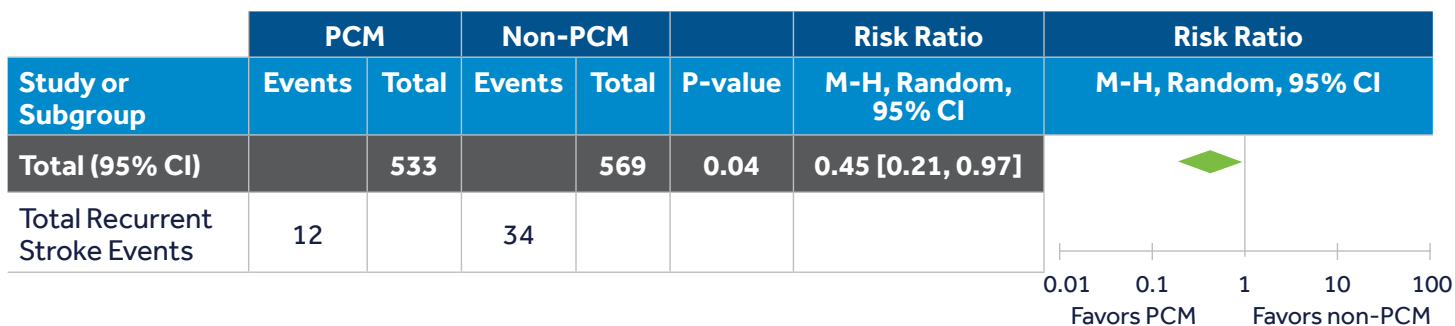
*Based on Kaplan-Meier estimates.



SECONDARY STROKE REDUCTION

As published in *Stroke*¹⁵

Study objective: Evaluate the impact of prolonged cardiac rhythm monitoring (PCM) on secondary stroke prevention using data from available to date randomized clinical trials (RCTs) and observational studies.



The above forest plot represents the differences between prolonged (favors PCM) and conventional (favors non-PCM) cardiac rhythm monitoring in the risk of recurrent stroke.

The meta-analysis included 4 studies for a total of 1,102 patients:

Study Name	Study Type	Conventional Cardiac Monitor Method	Total Number of Patients
Brown ESUS-AF	OS	30-day noninvasive ambulatory ECG monitoring	117
CRYSTAL-AF	RCT	ECG monitoring at scheduled and unscheduled visits at the discretion of the site investigator	441
FIND-AF	RCT	At least 2 hours ECG monitoring	398
Rodriguez-Campello, et al.	OS	24–36 hours ECG monitoring	146

WITH PROLONGED CARDIAC MONITORING

Patients who underwent PCM compared to conventional cardiac monitoring show:

2.5x

Increased incidence of AF detection.¹⁵

**FIND
AF.**

2.1x

Increased incidence of anticoagulant initiation.¹⁵

**TREAT
AF.**

55%

Decreased risk of recurrent stroke.¹⁵

**REDUCE
STROKE.**



The use of prolonged cardiac monitoring has a potential impact on secondary stroke prevention, as patients with cryptogenic IS/TIA undergoing PCM had higher rates of AF detection and anticoagulant initiation and lower stroke recurrence.¹⁵

INFORM YOUR CLINICAL DECISIONS WITH THE REVEAL LINQ™ ICM SYSTEM

Up to 3 YEARS of continuous
cardiac monitoring

The Reveal LINQ insertable cardiac monitoring system transforms your ability to diagnose atrial fibrillation with its proven AF detection algorithm.



The world's smallest,
most accurate
insertable cardiac
monitor^{17,18}



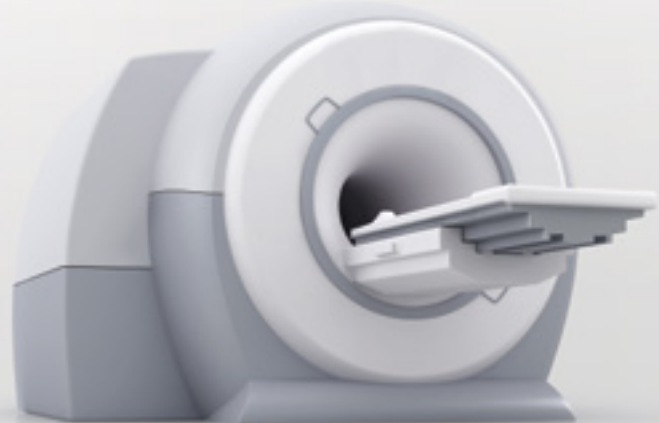
99.7%

AF episode
detection accuracy

Industry's highest
AF episode detection
accuracy rate.^{19,20}

1.5T & 3T MRI CONDITIONAL

No post-insertion wait time or
patient positioning restrictions*

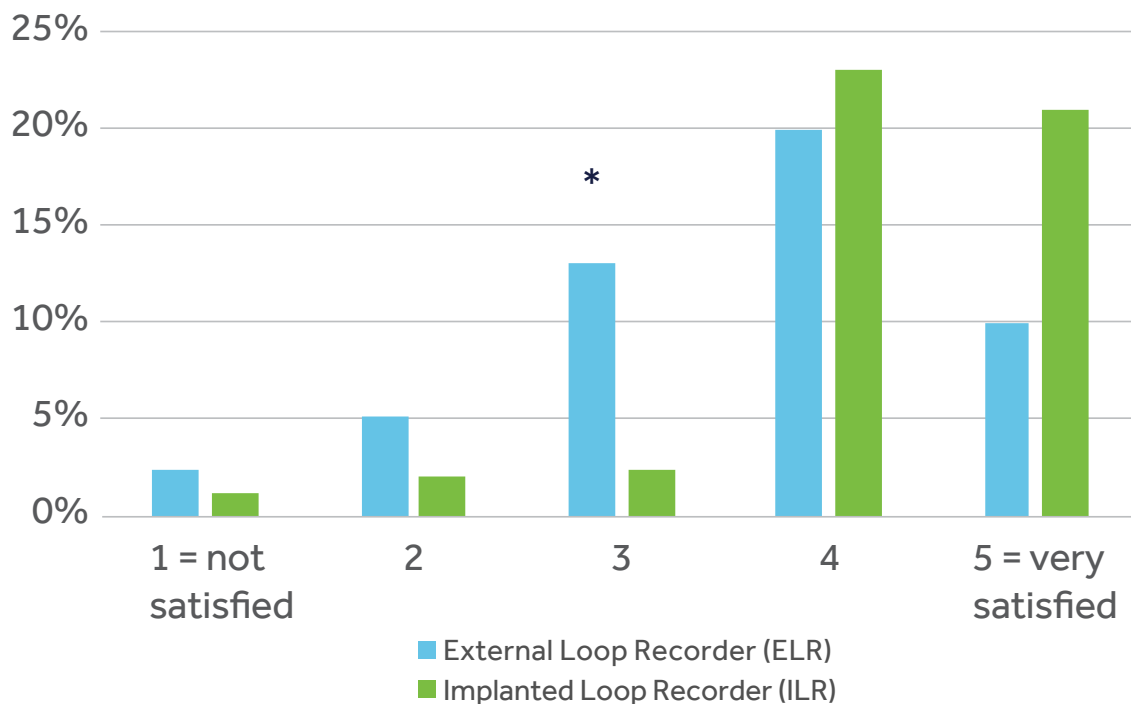


*Reveal LINQ has been demonstrated to pose no known hazards in a specified MRI environment with specified conditions of use. Please see the Reveal ICM clinician manual or MRI technical manual for more details.

PATIENTS ARE MORE SATISFIED WITH ICMs THAN EXTERNAL WEARABLE MONITORS²¹

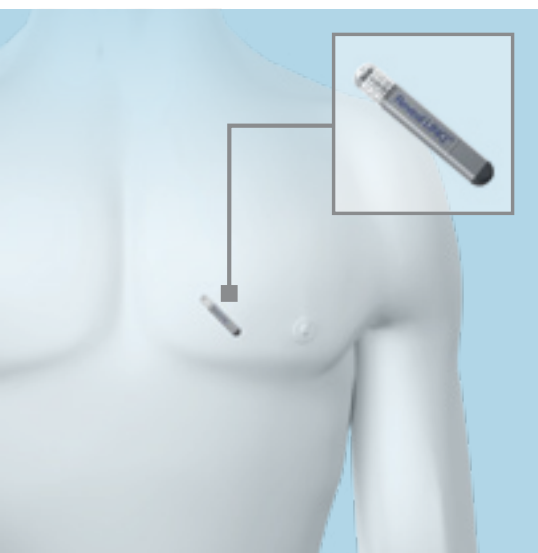
Percentage of patients “very satisfied” with monitoring strategy was higher in ILR vs. ELR arm (21% vs. 10%)²¹

Patient Satisfaction with Monitoring Strategy



Overall Chi-square = 34.4; $p < 0.001$.

* = Bonferroni-adjusted pairwise comparison of column proportions $p < 0.05$.



- The Reveal LINQ ICM is inserted just under the skin of the patient's chest in a short and simple procedure.
- The heart monitor is one-third the size of a AAA battery (1.2 cc) and is not visible in most patients.
- Use of the Reveal LINQ system doesn't require a change in daily activities.

GUIDELINES RECOMMEND ICM FOR PATIENTS WITH CRYPTOGENIC STROKE^{5,6}

2019 AHA/ACC/HRS Atrial Fibrillation Guidelines

Recommends use of implantable loop recorder (ILR) in patients with cryptogenic stroke (Class IIa, LOE B-R*)⁵

RECOMMENDATIONS	COR	LOE
In patients with cryptogenic stroke (i.e., stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF.	IIa*	B-R

2016 ESC AF Guidelines

ICM recommendation for cryptogenic stroke (Class IIa, LOE B†)⁶

RECOMMENDATIONS	COR	LOE
In stroke patients, additional ECG monitoring by long-term, noninvasive ECG monitors or implanted loop recorders should be considered to document silent AF.	IIa*	B

*Class IIa is Benefit >> Risk and LOE B-R is moderate quality of evidence from 1 or more RCTs or meta-analysis of moderate-quality RCTs.

†Endorsed by the European Stroke Organization (ESO). Class IIa is weight of evidence/opinion is in favor of usefulness/efficacy. LOE B is data derived from a single randomized clinical trial or large nonrandomized studies.

WHEN TO CONSIDER LOOKING FOR AF IN CRYPTOGENIC STROKE PATIENTS



Reveal LINQ ICM Indications*

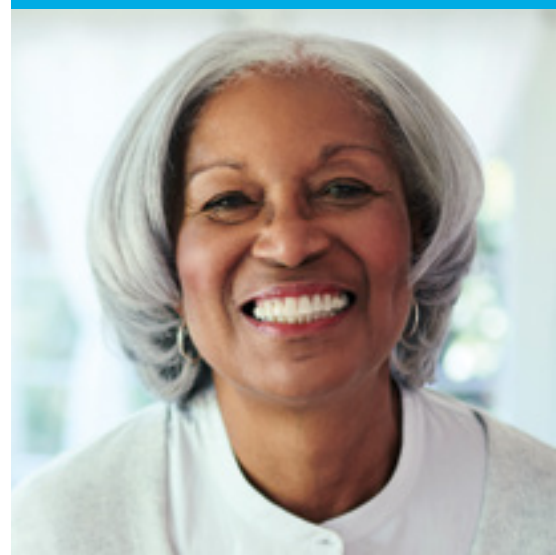
- Patients with clinical syndromes or situations at increased risk of cardiac arrhythmias
- Patients who experience transient symptoms such as dizziness, palpitation, syncope, and chest pain, that may suggest a cardiac arrhythmia

Appropriate

- Stroke detected by CT or MRI that is not lacunar²²
- Absence of extracranial or intracranial atherosclerosis causing $\geq 50\%$ luminal stenosis in arteries supplying the area of ischaemia²²
- No major-risk cardioembolic source of embolism²²
- No other specific cause of stroke identified (e.g., arteritis, dissection, migraine/vasospasm, drug misuse)²²
- First event — stroke or high-risk TIA[†]
- CHADS₂ score ≥ 2 (minimal risk factors)

Not Appropriate

- Indication for chronic anticoagulation or already on anticoagulation
- Patients with a relative contraindication for long-term anticoagulation and not appropriate for LAA closure device



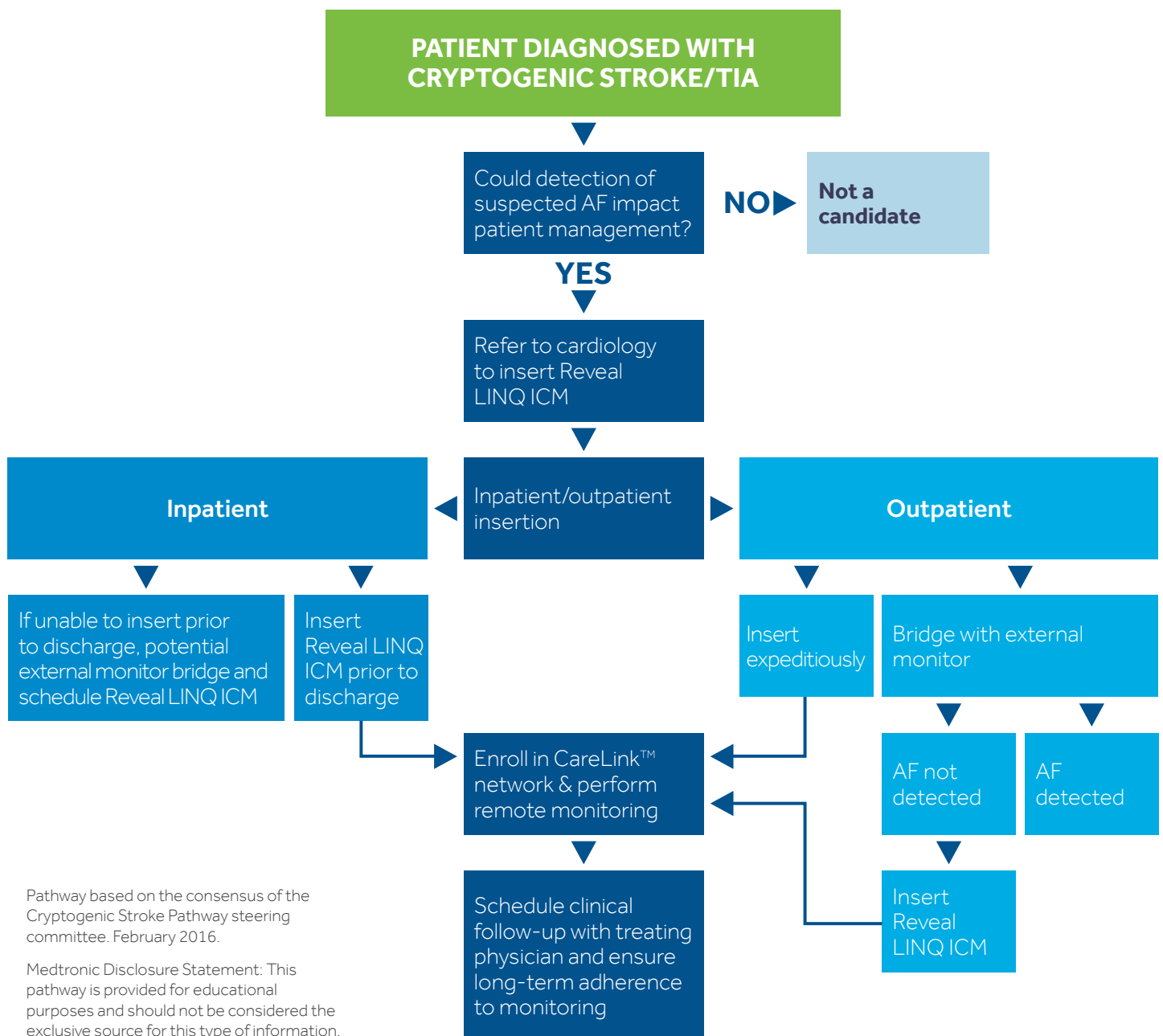
*See full brief statement for complete indications for use.

[†]ABCD2 Score > 5 .

Pathway based on the consensus of the Cryptogenic Stroke Pathway steering committee, February 2016.

PLANNING THE CRYPTOGENIC STROKE PATHWAY

Many cryptogenic stroke patients are lost to follow-up. Pathways for transition of care and follow-up help to ensure these patients receive better care.



Pathway based on the consensus of the Cryptogenic Stroke Pathway steering committee. February 2016.

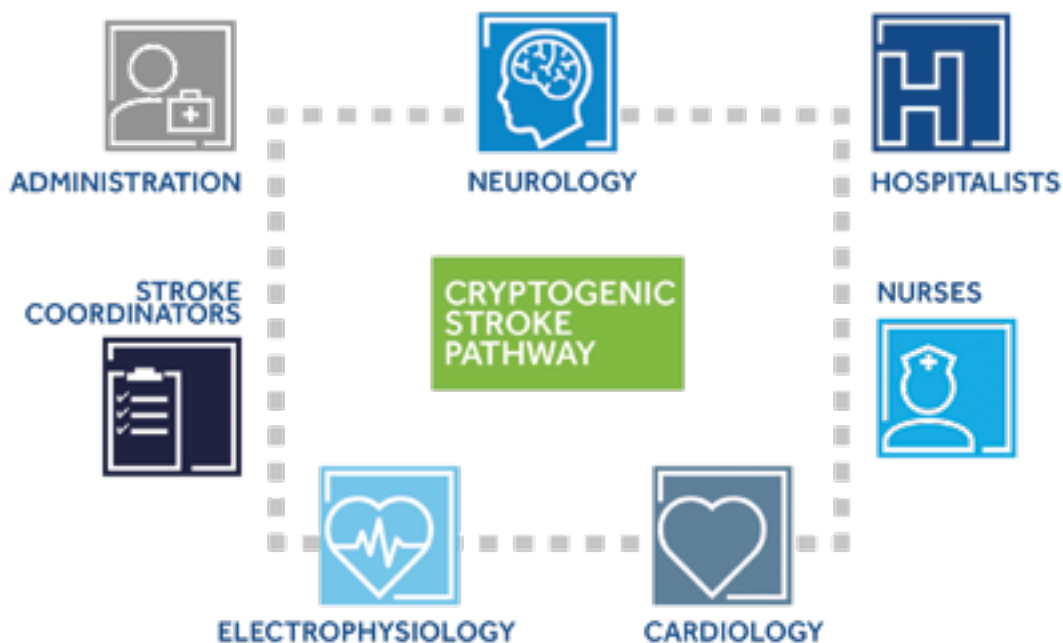
Medtronic Disclosure Statement: This pathway is provided for educational purposes and should not be considered the exclusive source for this type of information. It is the responsibility of the practitioner to exercise independent clinical judgment.

Refer to the brief statement for indications, warnings/precautions, and complications for the Reveal LINQ ICM.

A MULTIDISCIPLINARY APPROACH TO IMPROVE CARE

Why establish a cryptogenic stroke pathway?

Establishing a monitoring pathway to detect and treat AF can significantly reduce a patient's risk for another stroke. When developing a cryptogenic stroke pathway, it is important to include all stakeholders involved in the care of the patient.



PATHWAY TIPS

- Less than 5% of ischemic stroke patients who initially receive short-term external cardiac monitoring (up to 30 days) go on to receive an ICM.¹⁶
- Ischemic stroke patients seen by an electrophysiologist are 4x more likely to receive an ICM than a patient seen by a practitioner from a different specialty.¹⁶
- The diagnostic yield of 30 days of monitoring is likely to be limited. Data suggest a rationale for proceeding directly to ILR prior to hospital discharge in cryptogenic stroke patients.²³

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Brief Statement

Indications

Reveal LINQ™ LNQ11 Insetable Cardiac Monitor and Patient Assistant

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 specifically been 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 Insetable 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.

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.

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 complications/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 these devices to sale by or on the order of a physician.

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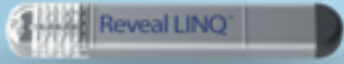
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SUPERIOR ACCURACY

Industry's highest AF episode detection accuracy rate.^{19,20}



Reveal LINQ
Insetable Cardiac Monitoring System

30% AF DETECTED AT 3 YEARS WITH ICM vs. 3% for SOC³

CRYSTAL-AF study found that continuous monitoring with Reveal LINQ ICM is superior to standard monitoring for the detection of AF in cryptogenic stroke patients.³



SHORT-TERM MONITORING IS NOT ENOUGH

88%
of patients who had AF would have been missed if only monitored for 30 days*³

PROLONGED CARDIAC MONITORING AND SECONDARY STROKE PREVENTION



55%
Lower stroke recurrence in patients with cryptogenic stroke/TIA undergoing prolonged vs. conventional cardiac monitoring.¹⁶

*Based on Kaplan-Meier estimates.