REVEAL AF
STUDY
RESULTS
# Atrial Fibrillation (AF) and Risk for Stroke

## Stroke Prevalence

In 2013, the prevalence of stroke was 25.7 million and 6.5 million died of stroke\(^1\)

## Clinical Challenge

AF independently increases the risk of stroke 5-fold\(^1\)
- AF accounts for 1 in 4 strokes (80-89 years of age)\(^1\)
  - Ischemic strokes associated with AF are nearly twice as likely to be fatal as non-AF strokes\(^2\)
  - Stroke is the first symptom for ~20% of patients who have an AF-related stroke.\(^3\)

## AF Prevalence

Over 30 million people worldwide have documented AF\(^3,4\)
- The prevalence of patients with risk factors for AF is much higher\(^5-6\)

---

5. World Bank estimates
6. World Health Organization
# STROKE AND AF SIMILARITIES AMONG RISK FACTORS

<table>
<thead>
<tr>
<th>CHADS&lt;sub&gt;2&lt;/sub&gt; Score</th>
<th>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;-VASc Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluates ischemic stroke risk in patients with AF</td>
<td>Evaluates ischemic stroke risk in patients with AF</td>
</tr>
<tr>
<td>▪ Congestive heart failure</td>
<td>▪ Congestive heart failure</td>
</tr>
<tr>
<td>▪ Hypertension</td>
<td>▪ Hypertension</td>
</tr>
<tr>
<td>▪ Age</td>
<td>▪ Age</td>
</tr>
<tr>
<td>▪ Diabetes</td>
<td>▪ Diabetes</td>
</tr>
<tr>
<td>▪ Stroke/TIA/ thromboembolism</td>
<td>▪ Stroke/TIA/ thromboembolism</td>
</tr>
<tr>
<td></td>
<td>▪ Vascular disease</td>
</tr>
<tr>
<td></td>
<td>▪ Sex</td>
</tr>
</tbody>
</table>

Note: These same risk factors also predict AF.

CHALLENGES IN DIAGNOSING AF

- Symptoms are not a reliable indicator of AF
  - AF episodes are frequently asymptomatic\(^1-2\)
  - Approximately 1 out of 5 symptoms thought to be AF are actually due to AF\(^1,3\)

- AF is often paroxysmal
  - Difficult to detect with short-term and intermittent cardiac monitoring\(^4-6\)

Longer-term, continuous monitoring may be beneficial in high-risk patients.

REVEAL AF STUDY
OBJECTIVES

GOAL: To demonstrate the value of early screening and detection of AF via ICM monitoring in high-risk patients.

END POINTS

Primary
- Determine the incidence rate of AF lasting greater than or equal to six minutes in patients who are at high risk of having AF.

Secondary
- Identify predictors of AF onset
- Characterize the timing and nature of clinical actions relative to detection of AF

REVEAL AF STUDY
DESIGN AND PATIENT INCLUSION CRITERIA

Prospective, single-arm, open-label, multi-center, post-market study

A CHADS\(_2\) score of ≥ 3 or CHADS\(_2\) = 2 and at least 1 of the following:
- Coronary artery disease
- Renal impairment (GFR 30-60 ml/min)
- Sleep apnea
- Chronic obstructive pulmonary disease

No AF found after 24-hours of cardiac monitoring.

385 patients met the primary endpoint cohort definition

Mean follow-up: 22.5 ± 7.7 months

REVEAL AF STUDY
ENROLLMENT

446 Assessed
394 Inserted
Analysis

6 Month Follow-up
- 349 completed visits
- 16 missed visits

12 Month Follow-up
- 319 completed visits
- 28 missed visits

18 Month Follow-up
- 292 completed visits
- 34 missed visits

24 Month Follow-up
- 187 completed visits
- 13 missed visits

30 Month Follow-up
- 105 completed visits
- 4 missed visits

52 Excluded
- 25 Requested withdrawal
- 14 Inclusion/exclusion criteria not met
- 13 Other

9 Subjects inserted excluded from primary analysis cohort
- 6 CHADS₂ ≤ 2 w/o additional risk factors
- 1 Anti-arrhythmic drug
- 2 No post-insertion device data

385 patients met the primary endpoint cohort definition

Mean follow-up: 22.5 ± 7.7 months

### SUBJECT DEMOGRAPHICS AND MEDICAL HISTORY

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects with device insertion (N = 394)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Device inserted/attempted</strong></td>
<td></td>
</tr>
<tr>
<td>Reveal LINQ™ ICM</td>
<td>272 (69.0%)</td>
</tr>
<tr>
<td>Reveal™ XT ICM</td>
<td>122 (31.0%)</td>
</tr>
<tr>
<td>Gender: male</td>
<td>206 (52.3%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± standard deviation (years)</td>
<td>71.6 ± 9.8</td>
</tr>
<tr>
<td>Under 65</td>
<td>88 (22.3%)</td>
</tr>
<tr>
<td>65 to 75</td>
<td>131 (33.3%)</td>
</tr>
<tr>
<td>75 and older</td>
<td>175 (44.4%)</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>64 (16.2%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>81 (20.6%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>233 (59.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>369 (93.7%)</td>
</tr>
<tr>
<td>COPD</td>
<td>76 (19.3%)</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>104 (26.4%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>248 (62.9%)</td>
</tr>
<tr>
<td><strong>Vascular disease</strong></td>
<td></td>
</tr>
<tr>
<td>Remote cerebrovascular accident (stroke)</td>
<td>80 (20.3%)</td>
</tr>
<tr>
<td>Remote transient ischemic attack</td>
<td>76 (19.3%)</td>
</tr>
</tbody>
</table>

# CHADS<sub>2</sub> AND CHA<sub>2</sub>DS<sub>2</sub>-VASc SCORES

## Characteristic

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects with device insertion (N = 394)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHADS&lt;sub&gt;2&lt;/sub&gt; score</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± standard deviation</td>
<td>2.9 ± 0.8</td>
</tr>
<tr>
<td>1</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>2</td>
<td>158 (40.0%)</td>
</tr>
<tr>
<td>3</td>
<td>130 (33.2%)</td>
</tr>
<tr>
<td>4 or more</td>
<td>105 (26.6%)</td>
</tr>
<tr>
<td><strong>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;-VASc score</strong></td>
<td></td>
</tr>
<tr>
<td>Mean ± standard deviation</td>
<td>4.4±1.3</td>
</tr>
<tr>
<td>2</td>
<td>25 (6.3%)</td>
</tr>
<tr>
<td>3</td>
<td>79 (20.1%)</td>
</tr>
<tr>
<td>4</td>
<td>112 (28.4%)</td>
</tr>
<tr>
<td>5</td>
<td>100 (25.4%)</td>
</tr>
<tr>
<td>6</td>
<td>53 (13.5%)</td>
</tr>
<tr>
<td>7 or more</td>
<td>25 (6.3%)</td>
</tr>
</tbody>
</table>

**CHADS<sub>2</sub> subgroups of 2, 3 and 4 or more were well represented**
INCIDENCE OF ADJUDICATED AF LASTING ≥ 6 MINUTES IN DURATION


AF Detection Rate (%) vs. Number of Months Post-Insertion

- 6.2% AF detection rate at 30 days
- 20.4% AF detection rate at 6 months
- 27.1% AF detection rate at 12 months
- 29.3% AF detection rate at 18 months
- 33.6% AF detection rate at 24 months
- 40.0% AF detection rate at 30 months
# Incidence of Adjudicated AF Lasting ≥ 6 Minutes in Duration

<table>
<thead>
<tr>
<th>40%</th>
<th>123 Days</th>
<th>84.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF detection rate at 30 months.</td>
<td>was the median time to AF detection in high-risk patients.</td>
<td>of patients with AF would have been missed if only monitored for 30 days.</td>
</tr>
</tbody>
</table>

There was no significant difference in detection rates between patients with CHADS$_2$ 2, 3, and 4 or more.

Among patients who met the primary outcome of ≥6 minutes of AF:

- **10.2%** had at least one episode lasting ≥24 hours.
- **56.3%** were prescribed OAC during follow-up.
- **14.8%** were prescribed rhythm-control medication during follow-up.

AF detected through ICM monitoring was found to be actionable by physicians.

TIME TO ONSET OF DAILY AF BURDEN


NOTE: This analysis includes episodes < 6 minutes in duration, which were not adjudicated. Episode duration attributed to episodes that were adjudicated to be non-AF were excluded from the analysis.
**SUBJECT CHARACTERISTICS PREDICTIVE OF AF ONSET**

Age and BMI were the only clinical characteristics independently predictive of AF, with AF incidence higher in older and more obese patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Hazard Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.079</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.042</td>
<td>0.0198</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.122</td>
<td>0.5398</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.117</td>
<td>0.5688</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.090</td>
<td>0.7053</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.252</td>
<td>0.5541</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>0.918</td>
<td>0.6400</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>0.743</td>
<td>0.2410</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.049</td>
<td>0.8679</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.788</td>
<td>0.2319</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>0.736</td>
<td>0.2083</td>
</tr>
<tr>
<td>Family history of atrial fibrillation</td>
<td>1.923</td>
<td>0.1797</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>0.883</td>
<td>0.6066</td>
</tr>
</tbody>
</table>

### REVEAL AF STUDY SUMMARY

| AF is common in patients at high risk for AF and stroke. | **84.5% of patients with AF would have been missed** with just 30 days of monitoring. | AF detected through Reveal ICM was found to be actionable by physicians. | AF detection did not differ between CHADS\textsubscript{2} subgroups. |

“Data from the Reveal AF Study may have important public health implications regarding prophylactic AF screening and treatment in high-risk patients.”

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

**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.

---

**Medtronic**
710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA
Toll-free in USA: 800.633.8766
Worldwide: +763.514.4000
medtronic.com

UC201712606 EN ©2017 Medtronic, Minneapolis, MN. All Rights Reserved.
05/2017

Medtronic and the Medtronic logo are trademarks of Medtronic.
™ Third party brands are trademarks of their respective owners.
All other brands are trademarks of a Medtronic company.