WATCHMAN™: A CLINICALLY PROVEN AND SAFE THERAPY FOR YOUR NVAF PATIENTS

1. WATCHMAN reduces the risk of stroke in NVAF patients as effectively as warfarin
2. WATCHMAN *also* reduces the long-term risk of bleeding associated with warfarin
3. WATCHMAN is a one-time, minimally invasive treatment option
4. WATCHMAN LAAC is the only device with proven safety, efficacy and patient benefits from RCTs and prospective registries
5. WATCHMAN has been implanted in more than 20,000 patients worldwide and is the only device of this kind approved by the FDA

Asses the risks of stroke and bleeding in your NVAF patients with the **Stroke-Bleed Risks Calculator app** available on the Apple App-Store or Android Google Play.

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FIND AN IMPLANTING CENTRE NEAR YOU AT:

www.watchman.com/uk

Refer your patient to one of the medical centres across EU that is certified to implant WATCHMAN.

Contact: contact@watchman.com

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THINK OUTSIDE THE PILLBOX

WATCHMAN™

LEFT ATRIAL APPENDAGE CLOSURE DEVICE

A proven one-time procedure that reduces the risk of stroke in your non-valvular atrial fibrillation (NVAF) patients and the risk of bleeding that comes with a lifetime of oral anticoagulant use.

www.watchman.com/uk/hcp

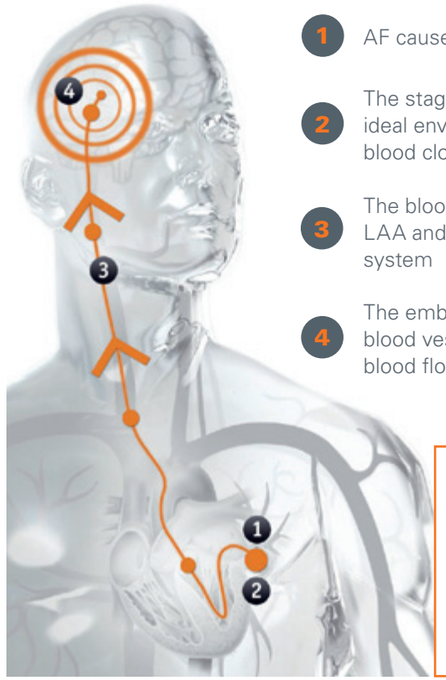
PATIENTS WITH ATRIAL FIBRILLATION ARE AT AN INCREASED RISK OF STROKE

Atrial Fibrillation (AF) increases the risk of stroke by 5 times.[1]

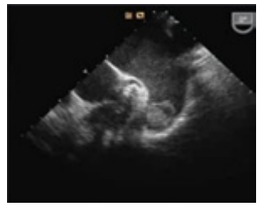
Strokes in patients with AF are:

- #1 Cause of long-term disability
- #3 Leading cause of death

In non-valvular atrial fibrillation patients (NVAF), 90% of left atrium blood clots originate in the left atrial appendage (LAA).[2]



1. AF causes blood to stagnate in the LAA
2. The stagnant blood becomes an ideal environment for a thrombus or blood clot to form
3. The blood clot dislodges from the LAA and travels through the arterial system
4. The embolism lodges itself in the blood vessels of the brain, restricting blood flow and causing a stroke



TREATMENT OPTIONS

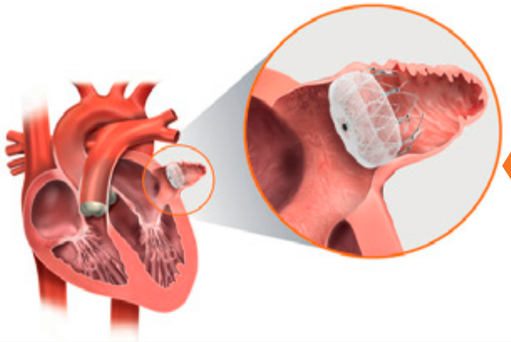
Oral anticoagulation (OAC) with vitamin K antagonists (VKA) or non-VKA oral anticoagulants (NOAC) are good treatment options for some patients.

However

- discontinuation of the OAC therapy rates remain high (at 2 years, 50% of patients on VKA and 30% on NOAC treatment[3])
- bleeding risks are not eliminated
- other AF patients have contraindications to OAC, or a history of bleeding on OAC, or may suffer a systemic thromboembolisation event despite adequate OAC

REDUCING THE RISK OF STROKE WITH WATCHMAN™ LEFT ATRIAL APPENDAGE CLOSURE (LAAC) DEVICE

The WATCHMAN LAAC procedure is a local, minimally invasive therapy that reduces the risk of stroke and the risk of bleeding that comes with the use of OACs in non-valvular atrial fibrillation patients (NVAF).



The WATCHMAN device is designed to close off the LAA, preventing the migration of blood clots.

The WATCHMAN device is a self-expanding nitinol frame covered by a permeable fabric (PET) to facilitate endothelialisation.

It is available in 5 different sizes to adapt to individual LAA anatomy (from 21 to 33 mm diameter).

WHICH OF YOUR NVAF PATIENTS ARE RIGHT FOR WATCHMAN?

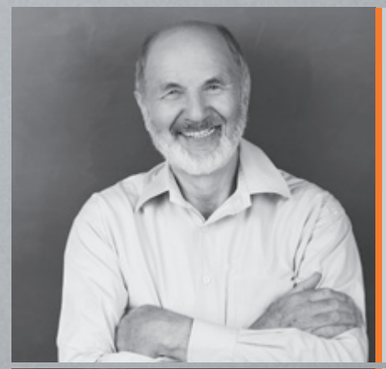
The WATCHMAN device may be an appropriate option for your NVAF patients who:

1. Are at an increased risk of stroke (CHA_2DS_2-VASc≥2)*
2. Are contraindicated or intolerant to oral anticoagulants
3. Have a history of bleeding while taking oral anticoagulants
4. Have suffered a prior stroke or transient ischemic attack (TIA)

- Patients who are NOT ELIGIBLE for OAC therapy can now BENEFIT from a therapy to protect them from stroke
- Patients who are ELIGIBLE for OAC therapy can REDUCE the risk of bleeding that comes with life-long usage of OAC

*__C__=congestive heart failure; __H__=hypertension; __A_2__=age≥75 years; __D__=diabetes mellitus; __S_2__=prior stroke or transient ischemic attack or thromboembolism; __V__=vascular disease; __A__=age 65–74 years; __Sc__=sex category

PATIENT PROFILES



NIKOLAS, 77 contraindicated to OAC

Occupation: Retired teacher

Medical conditions: NVAF; Hypertension; Previous TIA

CHA_2DS_2-VASc score: 5 - **HAS-BLED score:** 3

Nikolas has a history of bleeding, especially gastrointestinal, which makes him contraindicated to oral anticoagulants.

What approach do you take with your NVAF patients who cannot take OAC?

GWEN, 65 previous bleeding events

Occupation: Home healthcare assistant

Medical conditions: NVAF; Hypertension; Previous TIA

CHA_2DS_2-VASc score: 5 - **HAS-BLED score:** 3

Gwen is currently taking 100 mg of aspirin daily. She experienced gastrointestinal bleeding on warfarin and on apixaban. She has been taking only ASA since her last GI bleed.

What approach do you take with your NVAF patients who experienced bleeding?

ABIGAIL, 72 high risk for bleeding

Occupation: Retired flight attendant

Medical conditions: NVAF; Hypertension; Diabetes

CHA_2DS_2-VASc score: 4 - **HAS-BLED score:** 3

Abigail has severe kidney dysfunction, which precludes her from being able to use several kinds of oral anticoagulants. Her physician also believes she is at high risk for bleeding as a result of her kidney failure.

What approach do you take with your NVAF patients who are at a high risk of bleeding?

Case description for educational purposes; not real patient cases.

HOW THE WATCHMAN™ IMPLANT WORKS

WATCHMAN LAAC is a one-time, minimally invasive procedure that closes off the LAA, preventing the migration of blood clots.

The procedure is performed under general anaesthesia or conscious sedation in a catheterisation laboratory using a standard transseptal technique.

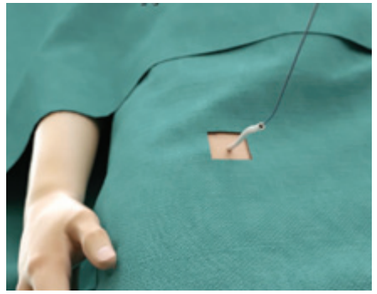
The procedure usually lasts about an hour and patients typically stay in hospital for a day.

In the EWOLUTION prospective registry, WATCHMAN was successfully implanted in ***98.5%*** *of patients*[*4]

The Implant Procedure

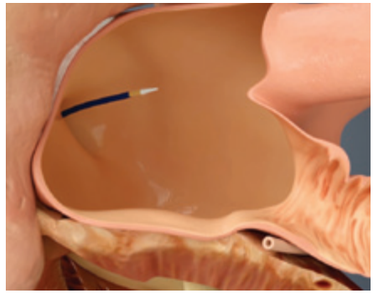
1

Using a standard percutaneous technique, a guidewire and vessel dilator are inserted into the femoral vein.

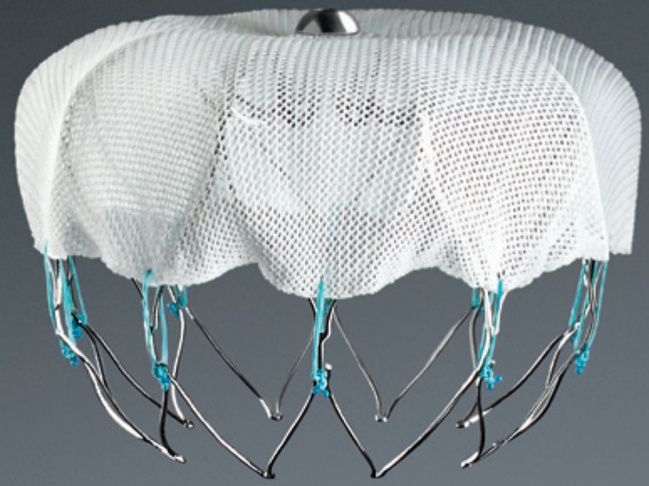


2

The implant procedure is performed with fluoroscopy and transesophageal echocardiography (TEE). The interatrial septum is crossed using a standard transseptal access system.

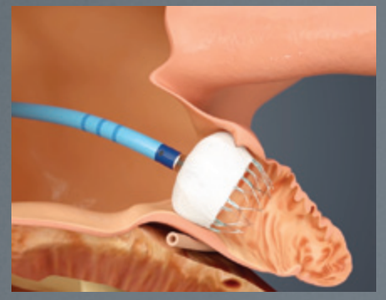


*The most common reason for the deployment failures was unfavourable anatomy or mismatch between the size of the device and the LAA.



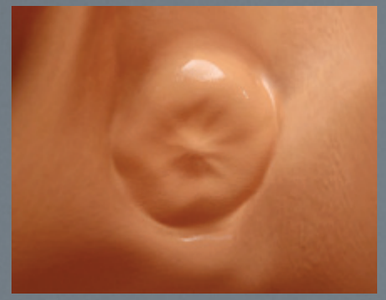
3

WATCHMAN is then deployed and released in the LAA.



4

Heart tissue grows over the WATCHMAN implant and the LAA is permanently sealed.



Post Procedure

Following the procedure, physicians may prescribe clopidogrel and aspirin daily for up to six months to patients contraindicated to OAC therapy. After stopping clopidogrel, patients remain on aspirin.

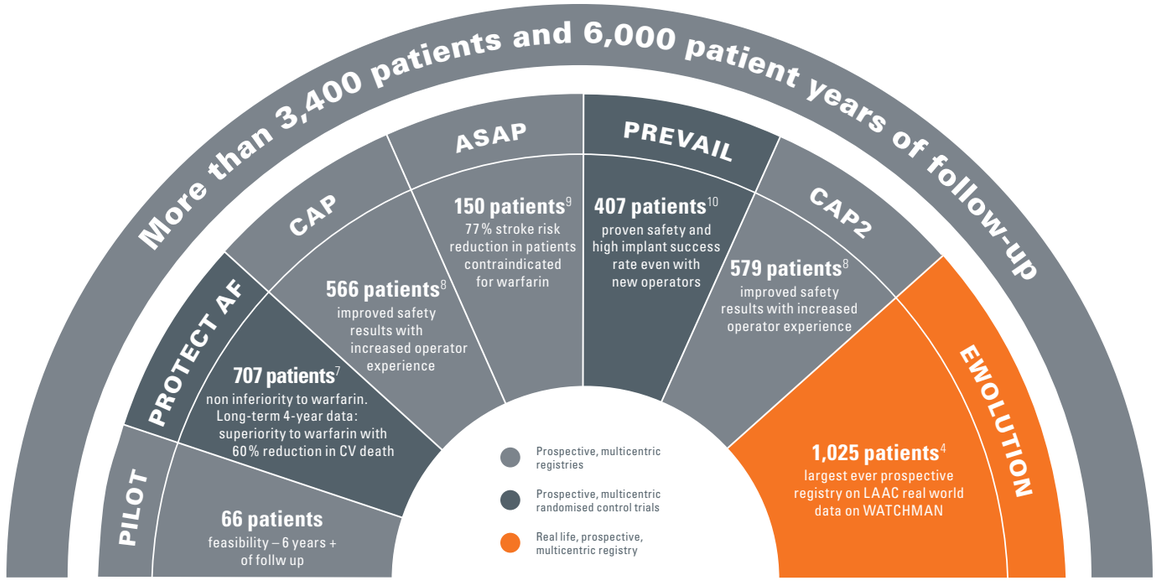
Patients who are eligible for OAC therapy take aspirin and warfarin for about 45 days or until the device endothelialises.

After stopping warfarin, patients should begin clopidogrel and continue aspirin daily for 6 months post-implant and then remain on aspirin.

WATCHMAN: A CLINICALLY PROVEN THERAPY

The WATCHMAN clinical evidence consists of over 3,400 patients studied in 2 randomised trials (with over 5 years of follow-up of PROTECT AF and 3 years of follow-up of the PREVAIL) and 4 prospective registries.

The WATCHMAN implant reduces the risk of stroke as effectively as warfarin and the long-term risk of bleeding associated with warfarin use.[5,6]



The WATCHMAN device demonstrated comparable stroke risk reduction and statistically superior reductions in haemorrhagic stroke (85% reduction), disabling stroke (63% reduction) and cardiovascular death (56% reduction) compared to warfarin over long-term follow-up in the PROTECT AF Study.[11,12]

PROTECT AF 5-YEAR PRIMARY EFFICACY RESULTS

	Event Rate		Rate Ratio	Posterior Probabilities	
	WATCHMAN	Warfarin	(95 % CI)	Non-Inferiority	Superiority
Primary Efficacy	2.2	3.7	0.61 (0.42, 1.07)	> 99.9 %	95.4 %
Stroke (all)	1.5	2.2	0.68 (0.42, 1.37)	99.9 %	83 %
Systemic Embolism	0.2	0.0	N/A	N/A	N/A
Death (CV/ unexplained)	1.0	2.3	0.44 (0.26, 0.90)	> 99.9 %	> 98.9 %

WATCHMAN Group N=463
WARFARIN Group N=244

In a patient-level meta-analysis of 2 randomised controlled trials (PROTECT AF and PREVAIL; N=1,114), the WATCHMAN implant was compared with warfarin and showed comparable primary efficacy results to warfarin.[6] WATCHMAN significantly reduced haemorrhagic stroke (HR: 0.22; P=0.004), cardiovascular/ unexplained death (HR: 0.48; P=0.006) and major bleeding events >7 days post-procedure (HR: 0.51; P=0.002).[6]

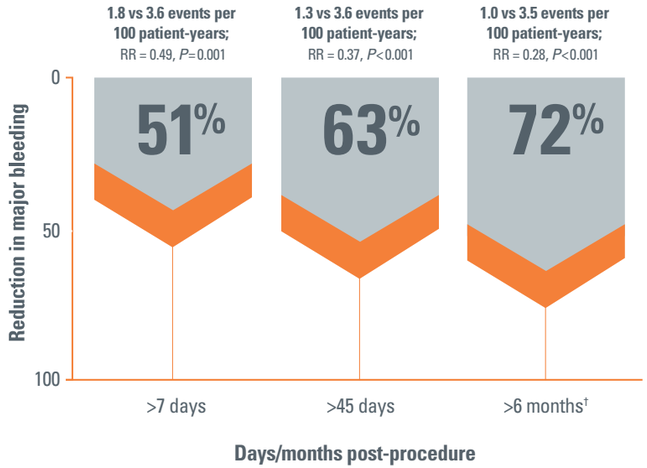
The patient-level meta-analysis of the PROTECT AF and PREVAIL trials found that the longer a patient has a WATCHMAN implant, the greater the reduction in bleeding events.[5]

At 6 months post-procedure, WATCHMAN reduced major bleeding events vs warfarin by 72% (1.0 vs 3.5; *P*<0.001).[5]

* Major bleeding defined as adverse event that was assigned one of several bleeding codes and was adjudicated by an independent Clinical Events Committee as significant (life-threatening or resulting in hospitalisation , prolongation of hospitalisation, substantial disability, or death).

WATCHMAN REDUCED BLEEDING EVENTS VS WARFARIN*

The longer a patient has a WATCHMAN implant, the greater the reduction in bleeding events[5]



STUDY DESIGN

The patient-level meta-analysis of the PROTECT AF and PREVAIL trials also compared the relative risk of major bleeding with WATCHMAN and long-term warfarin therapy. In both trials, patients who were randomly assigned to WATCHMAN continued to take warfarin and aspirin 45 days after the procedure. Transesophageal echocardiography was then performed to confirm adequate left atrial appendage (LAA) sealing (peridevice leak <5 mm in diameter). If the LAA was adequately sealed, patients discontinued warfarin and were treated with aspirin and clopidogrel for 6 months after the procedure, followed by ongoing aspirin therapy. If LAA sealing was inadequate, patients remained on warfarin and aspirin and did not receive clopidogrel. Post-hoc analyses were performed at 3 intervals (7 days, 45 days, and 6 months post-procedure) to assess the procedural complications and relative risk to events like major bleeding.[5]

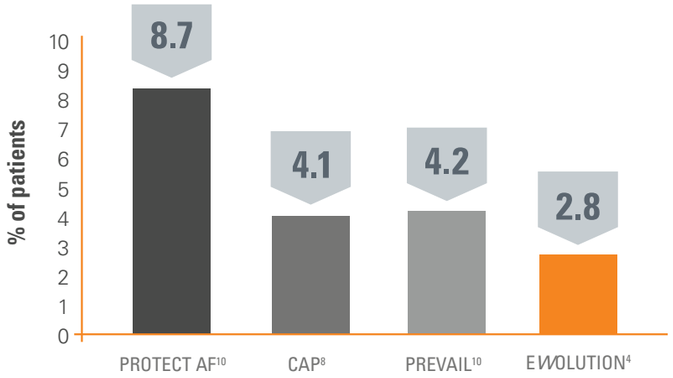
†PROTECT AF followed patients for five years.

WATCHMAN DEMONSTRATED FAVORABLE SAFETY OUTCOMES IN CLINICAL STUDIES

E*W*OLUTION (Registry on WATCHMAN Outcomes in Real-Life Utilisation) is the largest prospective real-life LAAC registry with over 1,000 patients studied.[4]

- 72% pts contraindicated to OAC[13]

Serious adverse procedure or device related events (SAE)* at 7 days



* SAE: Serious Adverse Event - Composite of vascular complications includes cardiac perforation, pericardial effusion with tamponade, ischemic stroke, device embolisation, and other vascular complications

REFERENCES

1. Holmes DR, Atrial Fibrillation and Stroke Management: Present and Future. Seminars in Neurology 2010;30:528–536.
2. Blackshear JL and Odell JA, Appendage Obliteration to Reduce Stroke in Cardiac Surgical Patients with Atrial Fibrillation. Annals of Thoracic Surg (1996).
3. Martinez C, et al., Therapy Persistence In Newly Diagnosed Non-Valvular Atrial Fibrillation Treated with Warfarin or Noac, A Cohort Study. Thromb Haemost. 2016; 115:31–39.
4. Boersma LVA et al., Implant Success and Safety of Left Atrial Appendage Closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION Registry. Eur Heart J. 2016;37(31):2465-74.
5. Price MJ, et al., Bleeding outcomes after left atrial appendage closure compared with long-term warfarin. JACC Cardiovasc Interv. 2015;8(15):1925-1932.
6. Holmes DR Jr, et al., Left atrial appendage closure as an alternative to warfarin for stroke prevention in atrial fibrillation: a patient level meta-analysis. J Am Coll Cardiol. 2015;65(24):2614-2623.
7. Holmes DR et al., Lancet 2009; 374:534-42.
8. Circulatory System Devices Panel: WATCHMAN® Left Atrial Appendage Closure Therapy Sponsor Presentation. 2014 FDA Circulatory System Devices Panel.
9. Reddy VY, et al. JACC.2013 Jun 25;61(25):2551-6.
10. Holmes DR et al., Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. JACC 2014; Jul 8;64(1):1-12.
11. Reddy VY, et al., Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. JAMA. 2014;312(19):1988-1998.
12. Reddy VY et al., presented at TCT 2014.
13. Bergmann M.W. EWOLUTION: 3-months outcome of Left Atrial Appendage Closure with the WATCHMAN device in Europe Presented at EuroPCR.2016.