Technoleg Iechyd Cymru
Health Technology Wales

# HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 041 (August 2022)

## Left atrial appendage occlusion to treat adults with non-valvular atrial fibrillation and contraindications to anticoagulation

**HTW Guidance:**

The evidence does not support the routine adoption of left atrial appendage occlusion in adults with non-valvular atrial fibrillation who have contraindications to oral anticoagulation.

There are no comparative studies of left atrial appendage device occlusion compared with standard care in adults with non-valvular atrial fibrillation in whom oral anticoagulation is contraindicated, although non-comparative observational studies suggest that left atrial appendage occlusion reduces the rate of ischaemic stroke.

The cost-utility analysis concludes that while LAAO in addition to standard care may be more effective than standard care with aspirin alone, it is cost incurring and not cost effective with an ICER of £42,302 per QALY.

### Why did Health Technology Wales (HTW) appraise this topic?

Atrial fibrillation (AF) is the most common type of heart rhythm disturbance and is characterised by an irregular and often rapid heartbeat. Since atrial fibrillation can lead to the stasis of blood and blood clot formation in the heart, blood thinners (oral anticoagulants), such as warfarin and direct-acting oral anticoagulants, are recommended for people with AF to reduce the risk of stroke. However, a proportion of people with AF cannot take these drugs due to a variety of contraindications, including a history of previous bleeding.

Left atrial appendage occlusion (LAAO) is a percutaneous treatment that involves the introduction, through the circulation, of a device that mechanically blocks the left atrium appendage, a sac at the back of the heart from which most blood clots are thought to arise.
HTW considered this topic after it was proposed by the Welsh Health Specialised Services Committee.

**The status of HTW guidance is that NHS Wales should adopt this guidance or justify why it has not been followed. HTW will evaluate the impact of its guidance.**

## Evidence Summary

Refer to Evidence Appraisal Report 041 (EAR041) for a full report of the evidence supporting this Guidance.

HTW identified and summarised evidence that addressed the following question: What is the clinical and cost effectiveness of LAAO to treat adults with non-valvular AF and contraindications to anticoagulants?

We identified a systematic review with meta-analysis of 29 non-comparative studies on the clinical follow-up of LAAO for adults with non-valvular AF and contraindications to anticoagulants. The review concluded that, based on the reported incidence rate of ischaemic stroke, LAAO is potentially effective for stroke prevention in adults with AF. Eight additional non-comparative studies were identified, which reported on the rates of ischaemic stroke events after LAAO in adults with AF and contraindications to anticoagulants. However, their findings varied and should be interpreted with caution given the limitations of this type of study design, which is more prone to bias compared to experimental studies, such as randomised control trials (RCTs).

Data from the Commissioning through Evaluation (CtE) registry in England provided evidence that LAAO is procedurally successful in about nine out of ten adults with AF with contraindications to oral anticoagulants. It was reported that LAAO is associated with a decreased risk of ischaemic events compared with historical epidemiological data in patients with a similar baseline risk.

To date, the available evidence on LAAO in adults with non-valvular AF and contraindications to oral anticoagulation appears to be at the IDEAL framework stage 2b 'exploration' for surgical interventions.

Five health economic analyses were included in a review of the economic literature. This included two directly applicable analyses that considered the perspective of the UK NHS and three partially applicable analyses that considered healthcare systems in other countries. All of the studies were assessed as having potentially serious limitations. A UK cost consequence analysis presented as part of the CtE study reported that LAAO in addition to medical therapy was more expensive than medical therapy alone, while another UK cost analysis reported that LAAO was cheaper than aspirin and no treatment at 10 years. German and Canadian cost-utility analyses concluded that LAAO was dominant (more effective and less costly) compared with aspirin or long-term apixaban, and dominant compared with aspirin alone, respectively. A Swedish cost-utility analysis found that LAAO was cost effective compared with no pharmacological antithrombotic treatment (no aspirin).

HTW developed a cost-utility analysis that compared LAAO in addition to standard care with standard care with aspirin alone, from the perspective of the UK NHS. LAAO in addition to standard care was found to be more expensive and more effective than standard care alone, but the ICER of £42,302 per QALY gained showed that it was not cost effective. However, it should be noted that, due to the lack of comparative evidence, the HTW cost-utility analysis shares some of the limitations of the already published cost-utility analyses, most notably the use, in the comparator arm, of predicted ischaemic stroke rates from the CHA2DS2-VASc tool.

In deterministic sensitivity analyses, LAAO was not cost effective in most modelled scenarios. The exceptions were scenarios in which it was assumed that there is no increase in mortality due to having AF or when the baseline age of people entering the model was reduced from 74.5 to 64.4 years. LAAO is cost effective in these scenarios because the people in the model receive the benefit for longer. In probabilistic sensitivity analysis, there was a 20% probability that LAAO is cost effective compared with standard care at a threshold of £20,000 per QALY. In threshold

analyses, it was concluded that LAAO would become cost effective compared with standard care if the cost of LAAO decreased from £15,839 in the base case to £9,039, if the base case annual risk of first ischaemic stroke was 7.32%, or if the patient age at baseline was 67 years.

The appropriate mechanism for patient engagement was determined and the patient perspective was considered where possible.

## Appraisal Panel considerations

- The Appraisal Panel noted the written evidence that had been submitted by patient organisations which highlighted the potentially devastating consequences of stroke on people's quality of life. It noted that there is an unmet treatment need in people with AF in whom anticoagulants cannot be safely administered and concluded that the availability of an alternative treatment would be welcome provided that there is robust evidence to support clinical and cost effectiveness.
- The Appraisal Panel discussed how this group of patients are currently managed in Wales. They were informed by the clinical expert and by the Welsh Health Specialised Services Committee (WHSSC) representative that LAAO is a procedure that is currently not undertaken nor commissioned in Wales; that there have been a relatively small number of Individual Patient Funding Requests (IPFRs) submitted to WHSSC for this treatment. The Panel and the clinical expert considered, however, that the number of IPFRs submitted is unlikely to reflect of the number of patients in Wales who may be suitable for this treatment and that patient numbers are likely to increase if LAAO were to be become available.
- The Panel noted that the clinical evidence in this cohort of patients is currently limited to non-comparative observational studies in which there are a relatively low number of events and small patient numbers. On the basis of a comparison of the observed rates of stroke in these studies as compared with a rate derived from a clinical estimate (using the $CHA_2DS_2$-VASc tool), the panel concluded that LAAO in addition to standard care is likely to be clinically effective overall. It noted, however, that in the absence of any directly comparative studies in this cohort of patients, this conclusion is associated with significant uncertainty.
- The Panel acknowledged that although the LAAO procedural and short to medium term clinical outcomes are satisfactory, there is uncertainty regarding the long-term outcomes of LAAO in people with non-valvular AF and contraindications to oral anticoagulation. The maximum follow-up of existing studies is two years. The Appraisal Panel noted that there are currently ongoing RCTs that are comparing LAAO with standard medical treatment in patients with AF who have contraindications to anticoagulation and in patients at high risk of stroke. It concluded that the results of these studies are likely to shed important light and a greater degree of certainty on the possible clinical effectiveness of LAAO. The Panel also noted that the forthcoming changes in UK medical device regulations and post-treatment surveillance may facilitate the tracing of long-term outcomes in patients undergoing this procedure in the future in NHS clinical practice.
- The Panel were informed by the clinical expert that careful patient selection, on the basis of clinical, anatomical and procedural risk considerations, is essential in order to ensure good clinical outcomes. It was also noted that absolute and relative contraindications to anticoagulation need to be considered carefully and that the involvement of a broad multi-disciplinary team (MDT) is mandatory in order to facilitate decision-making.
- The Panel were informed by the clinical expert that there are different LAAO devices available and that there may be differences in the procedural and long-term effectiveness of these. Attention was also drawn to the different regimes of post-procedural anti-platelet treatment that may also potentially impact on the long term clinical and cost effectiveness.

- The Appraisal Panel noted that LAAO is a complex trans-luminal procedure associated with a low incidence of potentially serious complications. The clinical expert explained that if a service were to be commenced in NHS Wales, there would need to be a sufficiently large volume of procedures to be done to overcome the 'learning curve' acquisition and maintenance of skills. He did note, however, although that there is a considerable overlap in the skills required for LAAO and other invasive procedures, such as device atrial septal defect and patent foramen ovale closure and MitraClip.
- The Appraisal Panel considered the published health economic studies and the *de novo* HTW cost-utility analysis. The Panel noted that while LAAO is currently commissioned and recommended in NHS England and in Scotland in patients with non-valvular AF in whom anticoagulation is contraindicated, decision-making has been in the absence of UK cost-utility analyses. The Panel therefore considered that the HTW *de novo* cost-utility analysis was particularly important in their decision-making since its conclusions are based on assumptions that are specifically relevant to UK NHS practice.
- The Panel were informed that the clinical effectiveness data underpinning the HTW cost-utility analysis were derived from disparate sources and so discussed the validity of applying the ischaemic stroke risk based on $CHA_2DS_2$-VASc in the standard care arm of the model. The Panel were advised by the clinical expert that $CHA_2DS_2$-VASc is well validated and is considered the gold standard for clinically assessing stroke risk in these patients.
- The Panel scrutinised several of the assumptions that were applied in the base case of the HTW cost-utility analysis and considered possible variations and alternative assumptions. The following aspects received particular attention:
  - The cost of the LAAO procedure. The panel heard that using a lower LAAO cost, which more closely aligned with a previous cost-utility analysis, but did not change the model results unless varied simultaneously with other assumptions.
  - The potential for differences in stroke severity between LAAO and standard care. The clinical expert advised that LAAO does not preclude severe strokes, and the Panel agreed with the base case assumption of no difference in stroke severity between LAAO and standard care.
  - The average age of the indicated population. The Panel heard from the clinical expert that 70% of patients with AF are over 65, and those most likely to benefit from LAAO are aged over 70. However, the Panel noted that the threshold analysis found that the baseline age of people entering the model would need to be 67 or less for LAAO to become cost effective.
- The Panel noted that other significant costs associated with stroke such as long-term home care, long-term residential care, and costs in the community to stroke sufferers and their families were not considered in the economic analysis. This reflects the NHS perspective considered by the HTW cost-utility analysis, in which only costs that are relevant to the NHS are incorporated. However, the Panel noted that due to limitations in the clinical evidence, there is considerable uncertainty in the number of strokes avoided after treatment with LAAO and this results in uncertainty around the potential cost savings of the procedure.
- The Appraisal Panel concluded from the HTW cost-utility analysis that LAAO is not cost effective in patients with non-valvular AF and contraindications to anticoagulation and noted from the threshold analysis that the procedure would need to be offered at a substantially reduced cost (£6,800 less than the base case procedural cost) in order to be cost effective.
- Overall, the Appraisal Panel concluded that the current evidence does not support the clinical or cost-effectiveness of LAAO in patients with non-valvular AF and contraindications to anticoagulation with sufficient certainty to be able to support its routine adoption in NHS Wales.
- Having noted the ongoing RCTs, the Appraisal Panel acknowledged the importance of revisiting this topic when the results of these become available.

## Responsibilities for consideration of this Guidance

Health Technology Wales (HTW) was established by Ministerial recommendation[1,2] to support a strategic, national approach to the identification, appraisal and adoption of non-medicine health technologies into health and care settings. The HTW Appraisal Panel comprises senior representation from all Welsh boards with delegated authority to produce guidance 'from NHS Wales, for NHS Wales'. The status of HTW guidance is 'adopt or justify'. There is an expectation from Welsh Government that HTW guidance is implemented with adoption regularly audited by HTW.[3]

The guidance in this document is intended to assist Welsh care system decision makers to make evidence-informed decisions when determining the place of health technologies and thereby improve the quality of care services.

The content of this HTW guidance was based upon the evidence and factors available at the time of publication. An international evidence base was reviewed and external topic experts and HTW committee members consulted to contextualise available evidence to Wales. Readers are asked to consider the generalisability of the evidence reviewed to NHS Wales and that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. It is acknowledged that evidence constitutes only one of the sources needed for decision making and planning.

This guidance does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

No part of this guidance may be used without the whole of the guidance being quoted in full. This guidance represents the view of HTW at the date noted. HTW guidance is not routinely updated. It may, however, be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the guidance given.

Standard operating procedures outlining HTW's evidence review methods and framework for producing its guidance are available from the HTW website.

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Declarations of interest were sought from all reviewers. All contributions from reviewers were considered by HTW's Assessment Group. However, reviewers had no role in authorship or editorial control and the views expressed are those of Health Technology Wales.

Chair, Health Technology Wales Appraisal Panel

1. National Assembly for Wales, Health and Social Care Committee. Access to medical technologies in Wales. December 2014.
2. Response to Recommendations from the Health & Social Care Committee: Inquiry into Access to Medical Technologies in Wales. February 2015.
3. Gething, V. Letter to all Health Board Chairs re Funding for Sacral Nerve Stimulation in Wales. VG_01655_17. September 2017.