National Institute for Health and Care Excellence

Medical technologies evaluation programme

DHT 005 Zio XT for detecting cardiac arrhythmias

Consultation comments table

Final guidance MTAC date: 24 July 2020

There were 53 consultation comments from 18 consultees:

- 10 NHS professional
- 1 manufacturer (sponsor)
- 5 organisations
- 2 others

Of the 53 comments, 5 were duplicates and have been removed. The comments are reproduced in full, arranged in the following themes:

- Recommendations (comments 1 to 13)
- Technology (comments 14 to 21)
- Clinical evidence (comments 22 to 32)
- Cost modelling (comments 33 to 40)
- NHS consideration (comments 41 to 47)
- General (comment 48)

This document also contains:

- Appendix A: External assessment centre (EAC) review of the real-world evidence submitted during consultation (page 40)
- Appendix B: External assessment centre (EAC) additional economic analysis (page 41)

#	Consultee ID	Role	Section	Comments	NICE response
Recommendation (n=9)					
1	2	Healthcare professional	Recommendation 1.2	There is currently no gold standard for accuracy of diagnostic cardiac monitors. In fact, compared to current practice of Novacor R-test, the diagnostic yield of ZIO XT is superior in my opinion from the data we have received from both cardiac monitors enabling more informed clinical decision making	Thank you for your comment. The committee understood there is no gold standard for accuracy of ambulatory ECG monitors. The committee considered additional information from the company and the consultation comments received and decided to change the recommendations from research to supporting the case for adoption subject to further data collection. Section 1 of the guidance and the rationale for why the committee made the recommendations has been updated accordingly.
2	4	Healthcare professional	Recommendation	As far as I am aware, there is no gold standard for accuracy of ECG. The accuracy of currently available technology such as 12 lead ECG or Holter monitoring is not known. Holter monitoring is an outdated technique. A simple Zio patch service model has appeal as it allows a seamless integration with any virtual digital outpatient service. I have used over 100 Zio patches in the last 8 years and am confident the clinical information provided by the Zio patch is superior to other technologies for providing ambulatory ECG monitoring. In my personal experience, the diagnostic yield from Zio patch use is far greater than with conventional rhythm monitoring modalities, presumably reflecting the ease of obtaining prolonged assessment for up to 14 days. In my department the cost of the Zio patch has often been cited as inhibitory for general use in the	Thank you for your comment. The committee values comments from clinicians about their experience using the technology. The committee considered additional information from the company and the consultation comments received and decided to change the recommendations from research to supporting the case for adoption subject to further data collection. Section 1 of the guidance and the rationale for why the committee made the recommendations has been updated accordingly.

				NHS. However, I feel that this is compensated by the increase in diagnostic yield, which prevent the requirements for repeat testing or indeed more expensive/invasive assessment with implantable loop recorders. In addition, an increase in diagnostic yield for atrial fibrillation, will have significant cost-saving benefits, as a large numbers of stroke cases may be prevented, with earlier use of anticoagulant medication. In addition, use of a Zio service, may result in cost-savings for valuable cardiac technician time, who skills can be redeployed in more complex environments such as the pacing department or cardiac cath lab.	
3	11	Manufacturer	Recommendation	iRhythm has presented to NICE further evidence in a highly confidential commercial technical dossier (commercial in confidence) to directly answer the Committee's questions around accuracy and address the uncertainties raised by the Committee. This dossier provides in-depth technical information regarding processes and specifications of the technology and personnel workflow utilised during the commissioning and execution of the service. We would like to direct the Committee to particular sections of the dossier, which directly address questions around accuracy: Executive Technical Summary; Addendum 8: 8.1 Zio XT ECG Report (Sample) 8.5 Detailed impedance and pause explanation 8.6 Methodology explanation around modified Lead II position 8.7 Clinical Reference Manual (includes skin prep and device placement) previously submitted as part of the clinical submission	Thank you for your comment. The committee considered the comment, the technical information supplied and the external assessment centre's review of this data carefully (see sections 3.8, 3.9 and 4.4 of the guidance) The committee decided to change the draft research recommendations to a recommendation which supported Zio XT as an option for ambulatory ECG monitoring subject to further data collection. The committee accepted that the Zio XT software demonstrates good per-episode performance for detecting cardiac arrhythmia and this is likely to translate to good per-patient performance. Section 1 of the guidance and the rationale for why the committee made the recommendations has been updated accordingly.
4	6	Manufacturer	Recommendation	The committee acknowledged the evidence demonstrating the increased diagnostic yield with the Zio Service vs the comparator (Section 3.4).	Thank you for your comment.

				Increased diagnostic yield enables a clinician to diagnose or rule out clinically significant arrhythmia in a greater number of patients. It is this ability to confidently rule out arrhythmia in more patients that clinicians say is an important part of the value of the Zio Service. They tell us that when they can rule out arrhythmia, patients do not need to return for a follow-up appointment and can be discharged with a letter to the GP. Enabling patients to be discharged without a follow-up appointment will reduce the pathway burden of outpatient appointments. Also in the current context of COVID-19, the Zio Service enables patients to be monitored entirely remotely, without the need to attend a hospital appointment, thus further reducing the burden on outpatients. Several NHS Trusts are in the process of reconfiguring services to do more activity virtually, and are looking to adopt the Zio Service to support this pathway transformation. The Zio Service also reduces other resource use within the pathway such as that associated with DNAs (does not attend) and repeat tests. Feedback from clinicians suggests that DNAs for Holter fitting appointments is as high as 24% and even higher since COVID. Repeat tests with current monitoring approaches also add to the resource use. The percentage of Holter tests that are currently repeated (27%) was accepted by the EAC. It also accepted that the Zio test would be unlikely to be repeated due to the high diagnostic yield. Good real-world evidence exists within the current NHS user base that supports this claim that increased diagnostic yield will reduce resource use,	The committee decided to change the draft research recommendations to a recommendation which supported Zio XT as an option for ambulatory ECG monitoring subject to further data collection (please also see NICE's response to consultation comment 3). The committee accepted that Zio XT Service improves diagnostic yield and patient wear time. It also accepted that the Zio XT software demonstrates good per-episode performance for detecting cardiac arrhythmia and this is likely to translate to good per-patient performance (see section 4.4 of the guidance). Section 1 of the guidance and the rationale for why the committee made the recommendation has been updated accordingly. The committee acknowledged the plausible benefits that a service such as Zio XT may offer in the current COVID-19 situation however it noted that the use of Zio XT in this situation is not within the scope of this evaluation. The committee considered there is uncertainty about resource use for ambulatory ECG monitoring in the NHS, particularly about repeat test costs and the impact of Zio XT on follow-up appointments. This is described in sections 4.11 and 4.12 of the guidance document. Real-world evidence on the use of Zio XT in the NHS was submitted by 2 healthcare professionals during consultation. The EAC reviewed the evidence submitted but did not consider it added anything to the existing evidence base. It concluded that clear conclusions about efficacy could not be drawn

				in particular outpatient appointments and repeat testing	from the results because there was not enough information on the patient populations. This is described in section 3.10 of the guidance document.
5	8	Healthcare professional	Recommendation 1.1	There is relatively little published evidence, but abundant clinical experience that evidences strong superiority of the Zio XT over standard Holter recordings. As a physician working exclusively in the field of arrhythmia management for over 25 years, I have read more than 5,000 Holter monitors and ordered tens of thousands. My personal experience of using this advice has led me to switch entirely to the Zio XT when the option is available (ie for my private patients). The current COVID-19 pandemic highlights an additional advantage: It reduces the need for patients to attend healthcare institutions. This is vital for the coming months, but will remain relevant to a lesser extent for the long term. Attending hospital exposes our patients to a risk of many infections. This device can be delivered by post, applied by the patient and returned without contact with health care professionals. This will always save the patient from unnecessary risk and inconvenience.	Thank you for your comment. The committee considered additional information from the company and the consultation comments received and decided to change the recommendations from research to supporting the case for adoption subject to further data collection (please also see NICE's response to consultation comment 2). Section 1 of the guidance and the rationale for why the committee made the recommendations has been updated accordingly. The committee acknowledged the plausible benefits that a service such as Zio XT may offer in the current COVID-19 situation however it noted that the use of Zio XT in this situation is not within the scope of this evaluation (please also see NICE's response to consultation comment 4)
6	13	Other	Recommendation	What is the gold standards for accuracy? Holter monitoring and Patient Activated Recording have been widely accepted as standard care. Zio have compared favourably in some studies compared these technologies (Barrett 2014, Esyenck 2019)	Thank you for your comment. The committee understood there is no gold standard for accuracy of ambulatory ECG monitors. Please also see NICE's response to consultation comment 1.
7	6	Healthcare professional	Recommendation 1.1	Assessing the accuracy of a service like this is potentially challenging as a 12-lead ECG is the Gold standard for arrhythmia detection, but for ambulatory ECG there is no absolute 'gold standard' and every form of ambulatory ECG has two aspects to its accuracy - the device itself and then the person making final interpretation. The	Thank you for your comment. The committee values comments from clinicians about their experience using the technology. The committee understood there is no gold standard for accuracy of ambulatory ECG

				latter will of course vary between different hospitals to a greater or lesser extent. I have been using the Zio Service for several years now and whilst initially apprehensive about it, I have found it to be very reliable and accurate - at least comparable to our standard holter service.	monitors. Please also see NICE's response to consultation comment 1.
8	6	Healthcare professional	Section 4.3	This is an important question and reasonable, but what is the gold standard to reference it against? Holter monitoring accuracy will also vary depending on the experience of the physiologist providing in interpretation, which may vary person to person or between hospitals to an extent	Thank you for your comment. Please see NICE's response to consultation comment 1.
9	12	Professional organisation		I am frankly confused as to why the technology is not being recommended by NICE especially in the circumstances we find ourselves in now. From a patients position and talking from a position of someone who has used the frankly, clunky and cumbersome holter for paroxysmal AF this technology would be a significant upgrade to what is standard of care both from a tech and data analysis point of view but also from a QOL position for a patients. Wait times for holters are too long and put the patient at risk if they have a suspected arrhythmia. I am assuming deployment of this technology does not require people to go into hospital, is convenient and simple to wear, excluding the need maybe to shave body hair, but this is the case for a holter with leads anyway. It is innovative, discreet and a comfortable way for a patient to be diagnosed with an uncomfortable and or dangerous arrhythmia. With the increased risk of COVID-19, where people with hospital appointments are in the main, nervous about attending hospitals, a service like this technology significantly reduces the burden on outpatient services, is safer for patients and their carers and reduces anxiety and should be seen as important as, the streamlining of regular appointments to telephone / video calling, reducing all but the most	Thank you for your comment. The committee considered additional information from the company and the consultation comments received and decided to change the recommendations from research to supporting the case for adoption subject to further data collection (please also see NICE's response to consultation comment 1). Section 1 of the guidance and the rationale for why the committee made the recommendations has been updated accordingly. The committee acknowledged the plausible benefits that a service such as Zio XT may offer in the current COVID-19 situation however it noted that the use of Zio XT in this situation is not within the scope of this evaluation. Please also see NICE's response to consultation comment 1. See response to comment 4 regarding COVID-19.

				"red flag" of situations to face to face. Consider this. In our recent submission to a Select Committee request, we asked over 800 patients in our community a pertinent question - "If you became unwell during the pandemic, would you be anxious about contacting your medical teams - 63% said they would. This continues to be the case where people are very anxious about engaging with their medical teams still. This alone demonstrates why this recommendation needs to be considered and in my humble opinion is incorrect.	
10	18	Professional organisation	Recommendations	The BCS agrees with the draft guidance from NICE. Our members felt that wearable devices like this – and importantly we note that Zio is only one of a number of similar devices – do offer patients a more convenient means of recording their heart rhythm over long periods of time. We believe that such devices will be well-tolerated by patients for long periods of time, and we note, for example, that they can be worn in the shower. The device appears easy to use and so may be something that can be used in primary care, rather than the patients having to come to a hospital cardiology department. Remote monitoring of the device would mean the patients would not need to come back into the hospital after use, saving both patient and physiologist time. The package offered by the manufacturers of this device includes the reporting of the recordings made by externally employed physiologists. This is included in the cost of the device, which is not reusable. BCS feels that there are both risks and benefits of this approach. The benefits would include potentially shorter waiting times for ambulatory cardiac recording. In the NHS it is not unusual for patients to have to wait to get Holter monitoring and then again to be given a result. If an external company can augment the capacity of the NHS to offer outpatient cardiac recording by providing such	Thank you for your comment. Based on technical information submitted during consultation and the external assessment centre's review of this data, the committee decided to change the recommendation from research to supported as an option for ECG monitoring subject to further data collection (see NICE's response to consultation comment 3). The committee agreed that Zio XT Service improves diagnostic yield and patient wear time compared with standard care. It also agreed that the Zio XT software demonstrates good per-episode performance for detecting cardiac arrhythmia and this is likely to translate to good per-patient performance. The committee does however encourage the collection of further information on how using Zio XT affects resource use in the NHS and it's long-term consequences (see sections 4.11 and 4.12 of the guidance). Section 1 of the guidance and the rationale for why the committee made the recommendation has been updated accordingly.

				a service, this may well improve patient waiting times and experience. BCS has, like the NICE committee, some reservations about how the reporting service will be staffed. If reporting is done by physiologists who have left the NHS to work for the private company, then this would not be of net benefit to the NHS, but rather an additional staffing constraint in an allied health profession that is particularly limited already. If reporting is done by physiologists not trained to the same high standard as we are used to in the NHS, there is an uncertainty as to whether the quality of the reporting would be as high as is generally the case for NHS trained and regulated cardiac physiologists. In summary, BCS welcomes the draft NICE guidelines. We note that Zio is only one of many technologies in this developing area. We would be keen to support increased research into the clinical effectiveness of the use of such technologies in a UK population.	
11	18	Professional organisation		Regarding the accuracy and utility of the devices, BCS agrees with NICE's view that more research work is needed to demonstrate that the use of these devices increases useful diagnostic information above and beyond existing technologies. One particular concern voiced by members relates to this whole emerging field, rather than to just this one device. Clinicians are not sure yet which asymptomatic arrhythmias detected by such devices are clinically significant. BCS are well aware that there is a coherent hypothesis that may well prove to be of great benefit to patients, i.e. asymptomatic episodes of atrial fibrillation may increase the risk of thromboembolic risk and such risk could be reduced by use of anticoagulant therapy in such cases. We hope that, in time, the use of such devices will be shown to improve outcomes through increased detection of arrhythmias. However, as yet, most cardiologists in the UK feel that there is not a compelling evidence	Thank you for your comment. Please see NICE's response to consultation comment 10.

				base to confirm (or refute) this hypothesis. There are many unanswered questions, such as what constitutes a significant amount of asymptomatic atrial fibrillation, in terms of increased thromboembolic risk. BCS feels that for Zio or similar devices to be used on any scale in the NHS, it would need to be demonstrated that their use in high risk populations led not only to an increased detection of arrhythmia or an increased prescription of anticoagulants, but also a reduction in thromboembolic events, without excessive increased adverse events. Cost effectiveness would also be of importance, not only against existing recording options but also against competitor technologies that may outperform Zio.	
12	14	Patient organisation		1. Zio is easy for patients to use and therefore more likely to adhere to using it. 2. They can wash and shower with it on. It is easy to post back without another visit to the hospital 3. One lead monitoring have been proven to be sufficient for AF 4. It appears to be more cost-effective. 5. The ZIO service to detect AF will increase diagnosis and therefore more patients will be anticoagulated and reduce the number of AF-related strokes meeting the NHS Long Term Plan goals and objectives.	Thank you for your comment. NICE values the input of patient organisations, which offer an important patient perspective. The adverse outcomes associated with this disease area means that the detection of cardiac arrhythmia will continue to be a health care priority. Engagement with patient organisations is an important way to ensure that NICE achieves the best possible outcomes for patients. Evidence shows that the monitoring with Zio XT is well accepted by patients. The committee acknowledged that people find Zio XT convenient and easy to use and are more likely to wear Zio XT for longer. This is described in section 4.1 of the guidance document. The committee decided to change the case for adoption from research recommendations to supported (see NICE's response to consultation comment 3). Section 1 of the guidance and the rationale for why the committee made the recommendation has been updated accordingly.

13	15	Patient organisation		1. Zio is easier for patients to use and hence compliance is better - they can shower with it on and they can send it back. 2. One lead monitoring is more than sufficient for diagnostic purposes 3. Although cost effectiveness evidence was heterogenous in outcomes I suspect it is more cost-effective. 4. Granted more research is needed to compare its accuracy against traditional holter monitoring to detect AF but i think it is good for AF diagnosis.	Thank you for your comment. Please see NICE's response to consultation comment 12.
The technology (n=8)					
14	2	Healthcare professional	Section 2.1	From our experience so far of using ZIO XT, the amount of artefact content that we have seen on our reports is much lower than current practice devices in the NHS (Novacor R-Test, cardiomemo). The benefit of utilizing a single biosensor is the reduction in risk of losing valuable ECG data. In current practice, should an ECG wire be pulled / caught on an object and disconnected or accidentally detached whilst asleep at night, all data for that disconnected time period is lost. A single leadless biosensor negates the risk - to a large extent - of losing ECG data by minimizing the amount of components which could be susceptible to failure (i.e. in R-tests / Cardiomemo the gel electrodes, wires, detachable monitors may all be prone to disconnection).	Thank you for your comment and for sharing your experience. The committee considered this comment carefully but decided not to update the guidance. Section 2.1 is intended to give a brief description of the technology only. The lack of external leads or wires and the possible reduction in noise artefacts is covered by section 2.4 of the guidance.
15	2	Healthcare professional	Section 2.2 to 2.4	See comment also from subsection 2.1. Whilst using the ZIO XT, the turnover of patients that we can monitor has dramatically increased. This has meant reduced waiting times for test appointment and results from 6-10 weeks, down to just under 3 weeks. This enhances the NHS opportunity to treat patients much quicker and prevent the potential for hospital stays for patients. The time we spend on analysis within the NHS is	Thank you for your comment and for sharing your experience. The committee considered this comment carefully but decided not to update the guidance. Section 2.2 to 2.4 are intended to describe the main innovative aspects of the technology. The possible reduction in time

				also reduced so that we can focus on training staff in other areas such as Echocardiography, Pacing / ICD implant and follow up and Cath Lab.	needed for NHS staff to analyse ECG data is covered by section 2.4 of the guidance.
16	2	Healthcare professional	Section 2.5 to 2.7	Full disclosure recording from devices such as ZIO XT enable capture of all potential arrhythmias across 14 days. Current practice devices provided for longer than 48hrs only provide a snapshot and selected arrhythmias. Some symptoms may be fairly infrequent and only occur at days 12-14 of recording for which ZIO XT would be ideal to capture these events. The diagnostic yield again prevents the need for re-testing which incurs its own costs and multiple patient attendances.	Thank you for your comment. The committee considered this comment carefully but decided not to update the guidance based on this comment.
17	11	Manufacturer	Section 2.2 to 2.4	Unlike the comparator, the Zio biosensor is single-use, avoiding the need for decontamination between use The Zio biosensor is also designed with sustainability targets in mind. The existing ambulatory cardiac monitoring industry uses tens of thousands of disposable AA or AAA batteries each year to power their devices. Lead wires, electrode patches and antiquated or broken devices also end up in landfills. Conversely, iRhythm designed the Zio XT biosensor with the environment in mind. iRhythm recycles 100% of each device returned following patient wear; no part of the device ends up in a landfill.	Thank you for your comment. The committee considered this comment carefully but decided not to update the guidance. The single-patient use of the technology is described in section 2.1 of the guidance.
18	11	Manufacturer	Section 4.6	The company would like to inform the Committee of the following: NHS Digital Toolkit: iRhythm has completed and published the NHS Digital Toolkit for 19/20, under ODS code 8K977 (iRhythm Technologies). The Zio Service meets all the standards and requirements within the toolkit. NHSX guidelines: To the greatest extent possible, iRhythm supports compliance with the NHSX guidelines and follows the five principles. The Zio	Thank you for your comment. The committee considered your comment carefully. Section 4.8 of the guidance has been revised to reflect the updated information available and the committee discussions and conclusion.

				Service does not yet support patient record interoperability standards (such as FHIR) as it does not generate or store patient healthcare records per se; it simply create reports. NHS Digital Application Questionnaire (DAQ): iRhythm does not produce a mobile app nor a patient-facing web-based service, so significant proportions of the DAQ are not applicable. However, as a CE-marked device delivered through an ISO 13485:2016-conformant QMS, the Zio Service meets the relevant usability, efficacy and clinical safety standards contained within the DAQ. Privacy/GDPR expectations are also met, as further evidenced in the NHS Digital Toolkit submission, and the information security processes for the Zio Service are in excess of the requirements of the DAQ. Information Security Governance: iRhythm has a current SOC 2 attestation, both Type 1 and Type 2. This covers the organisation and processes that deliver the service and the information technology supporting, and confirms that the security controls in place are both appropriate and operating effectively.	
19	8	Healthcare professional	Section 2.2 to 2.4	As a physician working and conducting research in arrhythmias I have worn Holter monitors for periods of up to 72 hours on many occasions as part of various research studies. I can attest that it is an unpleasant experience because of the electrodes and loose wires involved - it leaves the wearer highly restricted and unable to wash. As there is no pain, this adverse effect is not captured in the published literature, but is very real to patients.	Thank you for your comment and sharing your experience. The committee considered your comment carefully but decided not to update the guidance. Section 4.1 of the guidance refers to the potential increased patient acceptability and convenience of Zio XT compared with Holter monitors.
20	13	Other	Section 2.2 to 2.4	The qualitative benefits of Zio is worth highlighting e.g. enables normal activity (showering and bathing) and is discreet Holter monitors are not waterproof and in practice can be restricting or an issue for long term	Thank you for your comment. The committee considered your comment carefully but decided not to update the guidance. The possible benefits highlighted in

				monitoring. Some patients have been known to removed monitors and reapply poorly affecting recording. In some cases the monitors has been damaged by water and other fluids. Having discreet monitor is also important to highlight. There are incidents where patients have been called out by officials or the public for having a wired device attached them.	this comment are covered by section 2.3 of the guidance. Section 4.1 of the guidance refers to the potential increased patient acceptability and convenience of Zio XT compared with Holter monitors.
21	6	Healthcare professional	Section 2.5 to 2.7	I don't think the Zio Service should be considered as a replacement for holter services but as an extension and enhancement of them. there will always remain within cardiology a role for a multi-channel recording as provided by a holter, or a recording limited to 24 hours. However, prolonged ambulatory monitoring beyond 48 hours is where this service excels, particularly in the detection of AF where extended monitoring is far more likely to result in a diagnostic ECG being recorded. The longer the recording the greater the diagnostic yield, with pacemakers or ILRs being the extreme (and very expensive) end. From a non-invasive ECG perspective the Zio biosensors seems very acceptable to patients and most are very happy wearing it for close to 14 days. this acceptance from patients is important as many cannot or will not wear a conventional holter for that duration, thereby reducing the utility of these.	Thank you for your comment. The committee considered your comment and decided to amend section 2.6 of the guidance to more accurately reflect Zio XT's position in the care pathway. Section 4.2 of the guidance describes the committee's discussion on the diagnostic yield of Zio XT compared with 24-hour Holter monitoring. Section 4.1 of the guidance refers to the potential increased patient acceptability and convenience with Zio XT compared with Holter monitors.
Clinical evidence and experience (n=11)					
22	3	Healthcare professional		I have been using the Zio device for several years for identification of arrhythmias and particularly AF. I have found it extremely useful and the diagnostic yield appears to be higher than for alternative tools. I have detected PAF in a number of patients in whom previous ECG monitoring had been unremarkable. The patients find it convenient and unobtrusive, and it is particularly useful in patients with exercise induced symptoms.	Thank you for your comment and sharing your experience.

23	11	Manufacturer	Section 3.2	The refusal by 20% of patients to use the Holter is an important observation in this study and an important factor in the diagnostic yield – the likelihood that the test will produce the information needed to make a diagnosis. If patients are refusing to participate in the Holter test, this will impact on the yield of that test as, in those patients, the test is not providing any information - zero diagnostic yield. This study also demonstrates the considerable limitations with the current monitoring approach, which impact on the ability of the approach to yield information to inform a treatment plan	Thank you for your comment. The committee considered this comment carefully but decided not to update the guidance.
24	11	Manufacturer	Section 3.6	Increased diagnostic yield identifies a greater number of patients with clinically relevant arrhythmia (such as AF) who would benefit from medical intervention to reduce their risk of stroke. If undetected and left untreated, AF is a significant risk factor for stroke and other morbidities [NICE Clinical Guidelines CG180]. Detecting AF and initiating appropriate treatment is aimed at preventing complications, particularly stroke, and alleviating symptoms [NICE Clinical Guidelines CG180]. Closing this detection gap (in terms of the number of people who have AF but in whom it is undetected) is one of the objectives in the Long Term Plan. “Where 100 people with AF are identified and receive anticoagulation medication, an average of four strokes are averted, preventing serious disability or even death.” [NHS Long Term Plan].	Thank you for your comment. The committee considered this comment carefully but decided not to update the guidance.
25	13	Other	Section 3.2.	While it is true the result might have been biased by drop out rate, I would highlight the Holters drop rate was similar in both arms. This also highlights different in patient comfort between holter versus Zio which is an important qualitative measure to consider.	Thank you for your comment. The committee considered this comment carefully. It amended the wording to section 3.2 to make it clearer that the withdrawal rate was high in both arms of the study because 20% of people declined Holter monitoring. .

26	16	Professional organisation		The accuracy of the Zio patch appears to be very good in assisting with clinical decision making. The diagnostic yield with the Zio patch appears to be very high, and this is beneficial in reducing workload and, hence, costs. The Zio patch is likely to be highly beneficial to the NHS owing to the long duration of ambulatory monitoring of 14 days, coupled with ease of use and analysis. The Zio patch is patient friendly, with single-use technology in a remote setting. This is more convenient and safe for the patients and staff.	Thank you for your comment. The committee considered additional information from the company and the consultation comments received and decided to change the recommendations from research to supporting the case for adoption subject to further data collection (please also see NICE's response to consultation comment 1). Section 1 of the guidance and the rationale for why the committee made the recommendations has been updated accordingly.
27	1	Healthcare professional		I have been using Zio XT for over 1 year. As an end user, following are my views about this device: 1) there is positive feedback from patients. Zio is very convenient and tends to stay in place for the entire 2 weeks. It has a low profile and can be worn while showering. Event marker button is easy to operate. Patients do not need to travel and can return the device by post. It is a convenient device that allows patients to continue normal activities. 2) It has a much better diagnostic yield and symptom-ecg correlation over a standard Holter from prolonged monitoring. 3) There is lack of randomised trial data on diagnostic accuracy for automated detection and classification of arrhythmias. This usually is unlikely to make a difference as report data is first reviewed by a iRhythm physiologist and later by the specialist. 4) In appropriately selected patients, diagnostic yield from Zio could potentially reduce the requirement for loop recorder implants. 5) I feel it will be a cost effective device in the longer term due to higher diagnostic yield, and potential to reduce the need for repeated Holter ECGs. 6) I do not feel that having the Zio service, risks losing resources and physiologists. To the contrary,	Thank you for your comment and sharing your experience. The committee values comments from clinicians about their experience using the technology. Please see NICE's response to consultation comment 1. Please see NICE's response to consultation comment 4 regarding COVID-19.

				freeing up physiologists' time allows them to provide expertise in other areas within the department. 7) The ability to log in to iRhythm from anywhere to view a report is valuable. 8) NICE has comprehensively looked into the available evidence from studies comparing Zio with Holters and the diagnostic yield. 9) During Covid, company is able to provide the device directly to the patients with instructions to fit it on the chest and operate. 10) Recording quality is usually very good, including during periods of exercise with minimal or no artefacts.	
28	5	Healthcare professional		I wanted to share my personal experience with the Zio patch, which I have been using as a Cardiology Consultant for my private practice for over 3 years. This has been an extremely useful diagnostic tool, which has transformed my practice. It is convenient for both me and my patients. Regarding its sensitivity, I have not had any experience of non-diagnostic tests due to interference or artefacts. It allows me to investigate patients with infrequent arrhythmias, which was not possible with the existing systems. I have at least 2 examples of patients for whom the use of the Zio patch established the diagnosis and the patient could avoid the invasive procedure of an implantable loop recorder insertion. I also believe it is important to consider the patient convenience and the fact that this service can be delivered without the need of the patient to attend the clinic. This is extremely important in the current COVID19 circumstances and may be relevant in the future as well. It also fits with the direction of travel towards ambulatory diagnostics and delivery of care. I believe that, although the data are not available at this stage, the use of Zio patches in the NHS will help reduce the number of patients not attending for	Thank you for your comment and sharing your experience. The committee values comments from clinicians about their experience using the technology. Please see NICE's response to consultation comment 1. Please see NICE's response to consultation comment 4 regarding COVID-19.

				their appointments for ECG monitors and allow Departments to reallocate their staff to other services (no need to have ECG technicians analysing tapes the whole day). In my opinion the cost of technicians' pay should be incorporated in the cost effectiveness analysis of the Zio patch service. Finally, introducing the Zio patch in the current era of COVID19 pandemic will allow us to clear the backlog of ECG monitors without the need for patients to attend the hospital.	
29	7	Healthcare professional		I am a consultant stroke neurologist. We have been using the Zio service since March 2020 for detection of paroxysmal atrial fibrillation (AF) following stroke and transient ischaemic attack (TIA) in secondary care (stroke unit and TIA clinic), funding having been rapidly agreed due to COVID-19. Prior to this we had wished to implement an improved solution to our ambulatory ECG monitoring service that was delivered through cardiac testing. We have found this service to be invaluable and a huge improvement on our previous service (outpatient 5 day ambulatory ECG event recorder), due to: - Reduced "Did Not Attend" (DNA) rate. We had a high DNA rate of 20-30%. We have not had any patients refuse to wear the Zio patch. This is of high importance given that AF-related strokes tend to be more severe, and more elderly people with more co-morbidities are at increased risk of AF. While we have not investigated who did not attend their appointments, it seems probable that people who are more disabled or frail are more likely to not attend, which is the group more likely to have AF. A convenient test such as the Zio that does not require another hospital attendance is therefore very desirable.	Thank you for your comment and sharing your experience. The committee values comments from clinicians about their experience using the technology. Please see NICE's response to consultation comment 1. The committee considered the use of Zio XT to cost saving or cost neutral but that there are likely to be additional benefits which have not been captured in the current cost modelling (see sections 4.10 and 4.11 of the guidance). Please see NICE's response to consultation comment 4 regarding COVID-19.

				- Ability to provide the service without an additional hospital attendance. This has been particularly important due to COVID-19. Patients who had their appointments cancelled as cardiac testing could not carry out monitor fitting have had monitors sent out to them, with a very high adherence rate. Zio patches have been easily fitted on the ward and in TIA clinic. - Increased diagnostic yield: on the basis of the first 116 Zio patients, 6% have detected AF compared with approximately 2% previously. This is despite use amongst a broad range of patients, not only those in whom other causes of stroke have been largely ruled out (e.g. inclusion criteria for EMBRACE and CRYSTAL-AF studies). Average wear time has been 12.2 days, median 13.8 days. Fewer than 7% of patients wore the monitors for 5 days or less, and perhaps half of these were traced to monitors falling off due to fitting technique of a particular staff member. Diagnostic yield is important, since a diagnosis of AF can be readily verified by the requesting physician by accessing the report on the online portal, and I would anticipate that this would always be done prior to anticoagulation. - Convenience and patient satisfaction. 48 of 116 patients returned patient satisfaction questionnaires. Of these, the average scores for wear comfort, ability to go about normal activity, ease of use and “would wear again in the future” were all at or above 4.25 (4 being “agree”, 5 being “strongly agree”). - Hidden costs in the previous service, including lost monitors, regular replacement of analysis workstation and staff costs. I think that the ability to verify the diagnosis of AF readily using the online portal makes the determination of specificity less important. Also, it is difficult to assess negative predictive	

				value/specificity in the post-stroke/TIA population as it is difficult to be certain that a patient does not have paroxysmal AF. I think the resource savings in terms of requirements of providing an outpatient service are potentially underestimated due to hidden costs in alternative services. I also think that the need to reduce hospital attendances during the COVID-19 pandemic makes the Zio service much more important. Draft NICE recommendations approve use of implantable loop recorders, which are more expensive, invasive, require additional hospital attendances and technology, and lacks evidence on clinical benefit beyond AF detection. Failure to recommend the Zio service appears inconsistent with this.	
30	17	Other		Section Guidance statement Comment NICE question Are the recommendations sound and a suitable basis for guidance to the NHS? This guidance in its current form would make it almost impossible for innovation to be adopted within the NHS in this key area. In the current climate I feel that the benefits of the Zio service would have key benefits in reducing pressures on the NHS and protecting vulnerable patients with unnecessary exposure to hospital settings. The guidance do not appear to factor in the COVID-19 pandemic and its consequences to delivering safe, efficient and effective healthcare: • Growing backlog of patients • Patient reluctance to attend face-to-face clinic appointments. • Increased infection risk to staff and patients during fitting of traditional Holter monitors	Thank you for your comment. The committee considered all comments and new data received during consultation. The recommendations changed from research to supported as an option for ambulatory ECG monitoring subject to further data collection. Please see NICE's response to consultation comment 1. After consultation, the EAC conducted further sensitivity analysis using the 2 scenarios that best reflected current clinical practice, and threshold analysis concerning the number of repeat tests after a negative test result with standard care. The committee considered Zio XT to be cost saving or broadly cost neutral, but the magnitude of cost saving is uncertain. Sections 3.15, 3.17 and 4.11 have been added to the guidance and section 4.9 has been amended to reflect this. Please see

				• Infection control / disinfecting existing resuable equipment Zio service: • Enables vulnerable and at-risk patients access to ambulatory ECG monitoring without the need to attend a clinic appointment or even leave their home • Reduces the requirement for outpatient attendance and repeat testing within the whole diagnostic pathway • Single-use equipment which minimises infection risk NICE question Are there any equality issues that need special consideration and are not covered in the medical technology consultation document? Elderly, frail, comorbid and disabled patients are currently at the highest risk of morbidity and mortality from COVID 19 and disproportionately affected in terms of their ability to attend hospital outpatient appts. 1.2 Little evidence to show its likely effect on resource use in the NHS Research is recommended to address uncertainties about the resource use associated with Zio XT monitoring compared with standard care, in particular the number of outpatient visits and repeat tests needed. Efficiency of resource use will be a priority in the post COVID era 1. The Zio service has evidence of greater diagnostic yield vs standard of care and also expected to be associated with: • Reduction in outpatient appointments within the pathway, especially:	response to consultation comment 4 regarding COVID-19.

				o reduction in follow-up OPD appts (increased diagnostic yield means that patients can be discharged back to the GP with a management plan (if positive diagnosis for AF) or reassurance if arrhythmia ruled out) • Higher diagnostic yield (+95%) – either rule in or rule out - means reduced requirement for repeat tests (again reduction in outpatient appts and resource use) • Reduced requirement for costly implantable loop recorder testing due to higher diagnostic yield • Increased detection of incidental of AF. Identifying and managing more AF leads to reduced incidence of stroke, particularly in those with cryptogenic stroke / TIA (NNT of around 12 to prevent one stroke per year in secondary prevention) 2. Zio uses single equipment vs standard Holter or event recorder monitoring, which uses reusable equipment; This has implications for patient safety, decontamination, availability of equipment and is expected to have significant reduction in resource use 3.3 The UK-based randomised controlled trial has a high withdrawal rate because there was a high refusal rate for the Holter monitor 20% of the randomised participants refused to use the 24-hour Holter monitor. This may have biased results. According to the study authors, the study was adequately powered for the primary outcome. An independent power analysis carried out by the EAC found that the randomised controlled trial was likely to be underpowered because of the high withdrawal rate. The 20% refusal of patients to use the Holter monitor is an important factor in consideration of the diagnostic yield and the	

				considerable limitations with the current monitoring approach. This impacts adversely to inform a treatment plan or confidently rule out clinically significant arrhythmia 3.4 Evidence suggests that monitoring with Zio XT increases diagnostic yield The clinical and economic relevance of this statement appears to have been overlooked in the recommendations, which focuses only on accuracy. It is the significantly increased diagnostic yield vs standard practice that enables substantially more patients with arrhythmia (such as AF) to be identified, and therefore managed appropriately. Closing this detection gap is the one of key goals in stroke prevention strategies. It is one of the 3 Cardiovascular Ambitions within the NHS long term plan. 3.6 There is no evidence to show that an increased diagnostic yield with Zio XT improves clinical outcomes. The mention of diagnostic yield in a section discussing accuracy seems out of place here. Ipso facto an increased diagnostic yield identifies a greater number of patients with AF who would benefit from anticoagulation to reduce their risk of stroke. Anticoagulation has been proven to reduce the risk of further stroke in patients with stroke/TIA and AF. This improved clinical outcome can therefore be assumed, particularly given that increasing the diagnosis of patients with AF so that they can be appropriately managed is one of the objectives of the Long Term Plan. 3.10 The EAC revised the base-case (cardiology and stroke) models to address some potential limitations:	

				• the cost of an outpatient visit before discharge was included for all tests. Section 3.11: The EAC did a scenario analysis to explore the impact of repeat monitoring after a negative test. Zio XT was cost incurring when all monitoring was repeated after a negative test. When monitoring with a 24-hour Holter or a 7-day cardiac event recorder was repeated after a negative first test, but Zio XT was not repeated, the technology was cost saving. A negative test result often does not require an OPD follow-up appt (as opposed to an inconclusive or positive result). The increased diagnostic yield with Zio means clinically significant arrhythmia can be confidently ruled out (negative test result) in substantially more patients than with standard Holter monitoring. Clinicians can discharge these patients back to the GP, without the need to see them again for a follow-up review in OPD. It is critical that this reduction in OPD follow-up appts is included in the modelling in order for it to provide meaningful outcomes. 4.2 The evidence shows that Zio XT can improve diagnostic yield and patient acceptability There is strong evidence that embracing the Zio service enhances diagnostic yield and can result in a leaner, more streamlined and efficient pathway with significant reduction in downstream resource utilisation and improved clinical outcomes. It appears the evidence that supports this was not properly factored into the final recommendations.	
31	10	Healthcare professional		We conducted a service evaluation of the Zio service, the results of which we have shared with NICE by email as part of these comments. We found the Zio Service was associated with significantly higher diagnostic yield (significant arrhythmia detected in 30% of Zio patients vs only	Thank you for your comment. The committee considered your comment and the submitted evidence carefully. The EAC reviewed the evidence submitted (see Appendix A of this document) but did not consider it added anything to the existing

				8.6% in Holter patients) than the Holter, enabling us to confidently rule in or rule out clinically relevant arrhythmias in a far greater number of patients. On the back of this service evaluation, a business case is currently being considered by the Trust Board to introduce the Zio Service as an alternative to the ambulatory current monitoring approach (Holter) in patients with intermittent symptoms or those who are asymptomatic but present with other reasons to suspect arrhythmia such as stroke/TIA or syncope. The business case presents a service redesign whereby a large proportion of patients are sent the Zio monitor to fit at home. The service redesign also anticipates that, in a significant proportion of patients monitored with Zio, the higher diagnostic yield will enable a virtual follow-up or a letter to the GP for the patient to be managed in primary care or discharged. With the challenges presented by the current COVID-19 pandemic, we expect adoption of the Zio service to substantially reduce the requirement for patients to attend hospital appointments. As well as significant savings in resources such as outpatient appointments, repeat tests and staff time, we also expect waiting times for diagnosis or rule out of arrhythmia to be reduced. If you have any questions or require further information, then please do not hesitate to contact me.	evidence base. It concluded that clear conclusions about efficacy could not be drawn from the results because there was not enough information on the patient populations. This is described in section 3.10 of the guidance document. After consultation, the committee changed the recommendations to supported subject to further data collection. Please see response to consultation comment 4 regarding COVID-19.
32	9	Healthcare professional		On behalf of our Staffordshire STP's pilot of holters for detecting paroxysmal AF I'd like to submit the following evidence for the NICE guidance review – derived from 2 practices in northern Staffordshire (third practice trial is underway. We used the Zio holter for 20 x 2 ie 40 patients selected by the GPs in two practices according to our service design pathway (see attached) between	Thank you for your comment and sharing the results of your local evaluation of the Zio XT service. Please see NICE's response to comment 31.

				September 2019 & January 2020 and found from the zio analyses & a consultant cardiologist's independent interpretation of the analyses: • 92.5% of patients were found to have an arrhythmia (40% with multiple arrhythmia) • High levels of patient compliance even for extended wear times of 14 days (average 12.1 days) showing patient acceptance • Average analysable time of 97.3%, demonstrating high level of accuracy and rhythm capture • Average number of days to 1st symptomatic arrhythmia was 3.5 days. (We concluded that routine 24/48hr Holter monitoring would have been insufficient to diagnose the arrhythmia in the majority of patients) • 57.5% of patients were subsequently managed by their GP without needing a cardiology referral Our experience in Staffordshire STP for these two CCGs where practices based indicates that adoption of the Zio Service in primary care has the potential to significantly transform the pathway for diagnosing and managing patients with suspected cardiac arrhythmia by identifying and treating more patients arrhythmia in primary care and reducing cardiology referrals. So we've one more practice in Northern Staffs now underway – their start was delayed by COVID. Then we'd hope to write this up.	

				We based our service design pathway on the Ealing pilot of zio holters but amended the selection criteria according to our clinical thinking –. Hope this helps	
Cost (n=8)					
33	2	Healthcare professional	Section 2.8	Offset from this is the savings in patient ambulance transport / taxi transport and driving down the cost of potential hospital stays by earlier arrhythmia recognition. Delivery of devices to patient homes also lowers the risk of patient failure to attend rates within NHS trusts.	Thank you for your comment. NICE Medical Technology Evaluation Programme considers costs from an NHS and personal social services perspective only, as stated in the scope for this evaluation. Costs to the individual patient (such as those for transport) were therefore out of scope and not considered in any economic analyses. The rationale and context for cost-consequence analysis is described in section 7.3.1 of the Medical Technology Evaluation methods guide. The committee considered the comment carefully and decided not to change the guidance based on this comment. Section 2.8 of the guidance was amended however to state the revised costs of Zio XT.
34	2	Healthcare professional	Section 3.2	At Liverpool Heart and Chest Hospital, we were seeing failure to attend rates as high as 24% for 24 hr Holter devices using spot-check daily audits. We have currently sent out 50 ZIO XT patches and only received positive feedback about the fact that the device comes to the patient and saves the patient time and money in terms of transport, parking fees, having relatives bring them for a test, petrol, taxi / bus / train fares.	Thank you for your comment and sharing your experience. The committee considered the comment carefully and decided not to change the guidance. Please refer to NICE's response to consultation comment 33 regarding costs to the patient.
35	11	Manufacturer	Section 3.8	The EAC noted (in the Supporting Documentation) that, 'although relevant to the decision problem, none of the estimates from the evidence base were used to populate the company's economic model.'	Thank you for your comment. As this comment refers to the overview of the external assessment centre's report, no change to the guidance was made.

				There were limitations to using these studies in determining the cost impact of the Zio Service to the NHS. Mostly these relate to the fact that they did not consider the resource impact on the patient pathway, instead just focusing on comparing just the cost of monitoring. Also, one of the studies was based in the US, where healthcare utility is distinctly different from the UK, so the conclusions cannot be translated to the NHS setting. The economic model submitted by the company specifically examined the impact of the Zio Service on the entire NHS patient pathway and the resources used.	
36	11	Manufacturer	Section 3.10	The EAC replaced the cost estimate for a 24-hour Holter assessment from PLICS data of £158 with an estimate from NHS reference costs of £141. This change reduced the cost of the comparator in the stroke and cardiology models. The costing model submitted by the company used a Patient-Level Information and Costing System (PLICS) cost reference instead of an NHS Reference Cost to reflect the current move from costing based on averages to costing based on the actual care individual patients receive. PLICS is intended to provide detailed information about how resources are used at patient-level, for example, staff, drugs, and diagnostic tests. All acute trusts are now required to calculate their costs at patient level and, from 2019, the national cost collection for acute trusts is PLICS rather than NHS reference costs. The modelling used published PLICS cost data from 2016/17. More recent PLICS cost datasets are not publicly available to reference. Although in 2016/17, the collection of PLICS was not yet mandatory, 62 providers contributed to the 2016/17 dataset and the PLICS cost used for EY51	Thank you for your comment. The committee considered the comment carefully. The committee agreed that NHS reference costs are representative of costs incurred by hospitals in delivering monitoring services, and that the costs for cardiology are the most relevant costs to use. The reference cost data have the advantage of being more to up to date than the PLICS data and are derived from a national sample. The committee decided not to change the guidance.

				(OPROC – Outpatient procedures) was based on data from 329,000 tests. The EAC replaced the PLICS cost of £158 with the NHS reference cost just for Cardiology. However, in the current NHS Reference Costs (2017/18), the following specialty-specific costs for cardiac monitoring are listed for relevant outpatient services: • Cardiology: £141 • Stroke medicine: £328 • Transient Ischaemic Attack: £172 Although we recognise that Cardiology accounts for around two-thirds of the tests represented in the NHS Reference costs, the range of cost is large, across 62 specialty outpatients: a median value of £214 per test, IQR = £153-£307. We therefore believe that not only does the cost of £158 used in the company's modelling represents a more current methodology for calculating activity cost (PLICS), it is also a conservative estimate when considering the full range of NHS reference costs for that activity, and does not justify further down-rating. NB. On page 107 of 156 of the External Assessment Centre report: Zio XT Service for detecting cardiac arrhythmias it states that The EAC replaced the cost estimate for a 24-hour Holter assessment from PLICS data of £165. This is a typo. The cost estimate that they replaced was £158 as stated above, not £165	As this comment refers to the external assessment centre's report, no change to the guidance was made.
37	11	Manufacturer	Section 3.10	The inclusion of an outpatient assessment prior to discharge following a negative test result in the cardiology model increased the costs of the technology more than the comparator, since the Zio Service produces more negative results; ie the Zio Service is able to rule-out arrhythmia in more patients, rather than yield an inconclusive result.	Thank you for your comment. The committee considered the comment carefully and decided not to change the guidance. The external assessment centre did not consider the inclusion of an 'inconclusive' result to be useful because of the lack of data to inform this parameter. This was further

				Clinical opinion confirms that it is the higher diagnostic yield of the Zio Service and the ability to confidently rule out arrhythmia (as well as rule in), and therefore discharge the patient back into the community without further follow-up in outpatients, that contributes to the reduced burden on resource use. To not allow the distinction between the follow-up of a negative test vs an inconclusive test, and to assume all patients are followed-up in outpatients regardless of test result, ignores a significant element of the potential cost and system benefit of the Zio System. The inclusion of outpatient appointments for all test results is counter conducive to NHS England strategic intentions to reduce unnecessary secondary care follow up appointments. This is especially the case now with the COVID-19 pandemic, where there is a significant move to manage patients remotely wherever possible.	validated with advice from clinical experts and was accepted by the committee. The committee agreed that there is considerable heterogeneity in the follow-up of patients with negative results. The committee understood that, in practice, many patients were not followed up with an outpatient visit after a negative result. The committee had considered the results of the external assessment centre's sensitivity analysis in which alternative scenarios where considered with respect to outpatient follow-up appointments after tests. After consultation, NICE sought additional clinical expert advice regarding outpatient appointments and the EAC did further sensitivity analysis using the 2 scenarios that best reflected clinical practice. Section 3.15 has been added to the guidance and section 4.9 amended to reflect this. Please refer to NICE's response to consultation comment 4 regarding the use of Zio XT in relation to the COVID-19 pandemic.
38	11	Manufacturer	Section 3.10	The EAC has introduced an error to the Downstream stroke model that fundamentally changes the cost outcome for Zio relative to the comparator. This was raised by the company at the Fact Check stage prior to the last Committee meeting, but it was not adequately addressed at that time. Again, the company would like to refer to the Economic submission, page 40 (Section 2.3 Assumptions used to extrapolate clinical outcomes), where it points out that the Downstream Stroke model is an 'extrapolatory scenario' and that no costs of monitoring are included in this model, as this element has already been captured in the process model. The Stroke Downstream model should be considered as supplementary to the main	Thank you for your comment. The committee considered the comment carefully. The committee understood that the company submitted a model which considered only the downstream treatment costs over one year for patients at risk of stroke, and the external assessment centre modified this model to include the costs of assessment and diagnosis. The committee agreed the change was needed to provide a fuller picture of the costs per person in this population, over one year. The committee decided not to change the guidance

				Stroke model, yielding an aggregate cost, and it should not be considered in isolation as it does not incorporate the diagnostic process captured in the Stroke model. The approach currently adopted by the EAC results in a loss of process detail from the overall Stroke care flow and runs the risk of misrepresenting the true costs. The Economic Submission states: The primary models evaluate only process costs and therefore there are no clinical extrapolations used. An exploratory scenario analysis has been carried out on the Stroke Model to evaluate the potential impact of increased sensitivity and decreased time to diagnosis associated with the use of Zio versus either Holter or Cardiac Event Recorder (CER). This analysis uses literature-based results to estimate: • 1 year risk of stroke with or without AF • 1 year risk of stroke with AF when anticoagulated • Delay from decision to monitor to point when results are available for each technology • 1 year direct medical costs associated with stroke The analysis assumes that all patients diagnosed with AF will be started on anticoagulation. The annual risk of stroke is estimated based on the proportion of time off or on anticoagulation, based on the mean delay to monitoring results being available. Patients monitored with Holter or CER undergo one repeat test in the absence of a positive result. Patients monitored with Zio undergo a single test only.	

				No costs of monitoring are included in this model, as this element has already been captured in the process model.	
39	8	Healthcare professional		It would be worth comparing the cost of this service to traditional Holter recordings in £ per day rather than as a procedure cost.	Thank you for your comment. The committee considered your comment carefully but decided not to change the guidance.
40	6	Healthcare professional		this is always difficult to full model and I applaud the committee and what they have done. Factors to consider, but can be hard to model include: - DNAs for Holter fitting appointments; fewer follow-up outpatient appointments needed if diagnosis made earlier; reduce resource use associated with the downstream costs associated with avoided clinical sequalae such as stroke/TIA events but also better care for patients in hopefully detecting AF earlier and avoiding strokes	Thank you for your comment. The Committee considered you comment carefully and decided not to update the guidance. The committee had considered the results of the external assessment centre's sensitivity analysis in which alternative scenarios were considered with respect to outpatient follow-up appointments. In addition, the downstream stroke model captured the economic consequences of an increased risk of recurrent stroke from delayed or missed diagnosis of atrial fibrillation within the first year. After consultation, the committee also concluded that there are likely to be benefits to using Zio XT which have not been captured in the cost modelling (see section 4.10). It recommended further data collection to obtain information about resource use and the long-term consequences of using Zio XT (see section 4.12)
NHS consideration (n=7)					
41	11	Manufacturer	Section 2.2 to 2.4	To expand on this point, adoption of the Zio Service helps to resolve some of the workforce issues faced by the cardiac physiology profession. Traditionally Holter analysis is undertaken by Band 5 or Band 6 qualified cardiac physiologists, or by associate practitioners overseen by qualified cardiac physiologists. NHS departments are under resourced and skills of a cardiac physiologist are required in all areas of invasive and non-invasive	Thank you for your comment. The committee considered your comment carefully and decided not to update its conclusion about the impact of adoption of Zio XT on the NHS workforce in section 4.7, which notes that it not clear what the impact will be across the NHS.

				cardiology for face-to-face appointments; for example exercise testing, echocardiograms or for interventional cardiology procedures. Ambulatory ECG monitoring performed remotely will free up valuable NHS resource for these other areas. Additionally, due to the efficiency of the iRhythm ZEUS ECG analysis system, which performs a first pass analysis of the ECG data, the cardiac technician time involved in the analysis is substantially reduced compared with the comparator. This enables a reduced headcount requirement to analyse the same number of clinical records. The Zio Service should be viewed as a support and enhancement to current cardiac physiologist workforce, in particular in relation to the current challenges presented by COVID-19. The Zio Service retains the ability of the cardiac physiologist to interpret the clinical data quickly, efficiently and remotely.	Please refer to NICE's response to consultation comment 4 regarding the use of Zio XT in relation to the COVID-19 pandemic.
42	8	Healthcare professional	Section 2.2 to 2.4	In my clinical work I have personally read more than 5,000 Holter recordings. The process is time consuming, occupying between 10 and 60 minutes of the time of a professional per 24-hour period of recording analyzed depending on the quality of the recording and the complexity of the rhythm observed. This is grueling work; in the UK it is more often undertaken by physiologists rather than physicians, but this is still a drain on the staff of the NHS.	Thank you for your comment and sharing your experience. The committee considered this comment carefully but decided not to update these sections of the guidance. Please see the response to comment 41 about the impact on the NHS workforce.
43	13	Other	Section 2.2 to 2.4	Zio long-term monitoring of 14 days have been showed in at least one study to produce increased diagnostic yield for AF and reduce need for additional testing. As a diagnostic manager and cardiac scientist, I think it is important to highlight, as repeated tests have significant financial, operational, staffing challenges for us.	Thank you for your comment and sharing your experience. Please refer to NICE's response to consultation comment 1 regarding the diagnostic yield for Zio XT.

					The committee had considered the external assessment centre's economic analyses which captured the impact of repeat testing after an inconclusive test result with Holter monitoring or cardiac event recorders. After consultation, the external assessment centre did a threshold analysis to assess the number of repeat tests in the current care arm needed to equalise the cost of Zio XT Service and current care. Section 3.17 of the guidance has been added to reflect this.
44	13	Other	Section 2.2 to 2.4	During COVID19 and indeed before the "analysis" burden of holters was significant for diagnostics managers and cardiac scientists. Zio patch technology which provides a comprehensive analysis and reporting as well as a reduction in repeat tests (according to some studies) may reduce this burden. It would in turn free-up cardiac scientific staff to focus other important areas of diagnostic delivery.	Thank you for your comment. Please refer to NICE's response to consultation comment 4 regarding the use of Zio XT in relation to the COVID-19 pandemic.
45	11	Manufacturer	Section 4.7	Adoption of the Zio Service helps to resolve some of the workforce issues faced by the cardiac physiology profession. Traditionally Holter analysis is undertaken by Band 5 or Band 6 qualified cardiac physiologists, or by associate practitioners overseen by qualified cardiac physiologists. NHS departments are under resourced and skills of a cardiac physiologist are required in all areas of invasive and non-invasive cardiology for face-to-face appointments; for example exercise testing, echocardiograms or for interventional cardiology procedures. Ambulatory ECG monitoring performed remotely will free up valuable NHS resource for these other areas. Additionally, due to the efficiency of the iRhythm ZEUS ECG analysis system, which performs a first pass analysis of the ECG data, the cardiac technician time involved in the analysis is substantially reduced compared with the	Thank you for your comment. Thank you for highlighting the recommendations in the review into cardiac physiology services in England by the SCST (Society for Cardiological Science and Technology) The committee considered this comment carefully but decided not to change this section of the guidance. Please see the response to comment 41 about the impact on the NHS workforce. Please refer to NICE's response to consultation comment 4 regarding the use of Zio XT in relation to the COVID-19 pandemic.

				comparator. This enables a reduced headcount requirement to analyse the same number of clinical records. In addition to this, iRhythm has the ability to rapidly scale-up, utilising the model adopted in the US, which employs individuals with relevant cardiac related credentials such as associate practitioners, registered nurses and paramedics, with a significant (minimum 2 years) amount of arrhythmia interpretation experience. This would require ensuring they pass the international CCT (Certified Cardiographic Technician) qualification within 90 days and supporting them to achieve SCST accreditation within the first 6 months of employment. These measures would significantly support the cardiac physiology workforce for the long-term future, whilst ensuring no depletion in quality due to the strict measurable processes that the company has in place. The Zio Service should be viewed as a support and enhancement to current cardiac physiologist workforce, in particular in relation to the current challenges presented by COVID-19. The Zio Service retains the ability of the cardiac physiologist to interpret the clinical data quickly, efficiently and remotely. The joint review into cardiac physiology services in England by the SCST (Society for Cardiological Science and Technology) and the BCS (British Cardiovascular Society) was set up to make recommendations to NHS England, Health Education England and across the health and care system about the innovations in service delivery, models of care and workforce configuration. This was published in May 2015, set out 12 recommendations to transform services and patients' experience of cardiovascular disease care. The following recommendations are pertinent to the Zio Service:	

				RECOMMENDATION 2 The Review recommends that models of delivery for cardiac physiology services are redesigned to improve clinical quality, affordability, patient experience and sustainability. These new models recognise the need to give patients the best health outcomes by giving them the skills for appropriate self-management of their cardiac conditions; providing services in the community closer to where patients live; and providing urgent and emergency treatment as soon as it is needed to return patients to health. RECOMMENDATION 3 With the rapid development of information technology (IT) innovations, the Review recommends that NHS England strengthens the IT and telecommunications infrastructure available across healthcare providers to support web based, secure archiving which will allow for the transfer of electronic images and data with patients as they meet care providers along their clinical pathway. This will improve the quality of the information available to clinicians, reduce the duplication of investigations, and facilitate timely and accurate diagnosis and the provision of effective treatment and care. RECOMMENDATION 4 Those technological innovations which are already available, and which have been shown to improve clinical outcomes and patients' experience of care, should be adopted at pace and scale. With the rapid development of technology and the need to promote adoption, the Review recommends that a 'horizon scanning' function is established for the rapid review of innovations, evaluation of their clinical benefit, and to make recommendations for their timely adoption across cardiac physiology services.	

				RECOMMENDATION 5 The Review recommends that all cardiac physiology investigations are delivered to defined and consistent quality standards (including the maintenance and calibration of equipment) and that these form a core component of the commissioning of services. These standards should be consistently and uniformly applied without variation by time, day or place of service provision. The Review recommends that NHS England establishes a partnership working group jointly chaired by the British Cardiovascular Society (BCS) and the Society for Cardiological Science and Technology (SCST) to agree a quality framework (including quality standards and key performance indicators) aligned to that of other medical disciplines. RECOMMENDATION 7 The Review recommends that urgent action is taken to address the considerable shortfall in the current cardiac physiology workforce at all levels across the career framework. The current workforce is inadequate to meet current demand, with marked variations in access to cardiac physiology investigations and significant waiting lists in some areas; and, in addition, it will be inadequate to meet future demands if the proposed service changes and resulting efficiency gains outlined above are not implemented alongside an expansion in the workforce.	
46	11	Manufacturer	Section 4.6	The company was told informed that this work would be carried out in parallel with the guidance development and would inform the recommendations. To date, this work to assess Zio XT's compliance with digital standards and to explore the use of artificial intelligence in the technology has not taken place.	Thank you for your comment. Please see NICE's response to consultation comment 18 regarding Zio XT's compliance with digital standards.
47	11	Manufacturer		The draft NICE guidance for the Zio Service does not take account of the new and highly relevant challenges facing patients and healthcare providers	Thank you for your comment. The committee considered your comment carefully and decided not to change the guidance.

				arising from the COVID-19 pandemic. Patients who are either unable or unwilling to attend hospital appointments face increased mortality risk from delayed diagnosis and treatment, and for those patients who do venture into hospital for a cardiac monitor fitting, there is an increased risk of virus infection. Similarly, healthcare providers are facing acute challenges directly caused by the pandemic, especially dealing with a growing backlog of patients who need cardiac monitoring, as well as the longer term service redesign that will be required to adapt to new ways of working. In the second phase of the response to COVID-19, NHS organisations are being asked to 'lock in beneficial changes' that have been brought about in response to the virus, including 'rapid scaling of new technology-enabled service delivery options'. As more and more patient consultations are being carried out remotely, providers are looking for ways to ensure that patients only attend hospital appointments where absolutely necessary. The COVID-19 pandemic has also created new health inequalities in terms of patient access to care. Many high risk and vulnerable patients are now unable or unwilling to attend hospital appointments for cardiac monitoring due to the risk of the virus, and as such place themselves at a much higher and unnecessary risk from delays to diagnosis and treatment. These issues are especially significant when considering reports that a wide range of arrhythmias complicate the course of COVID-19 and patients with cardiovascular risk factors represent an especially vulnerable population.	Please refer to NICE's response to consultation comment 4 regarding the use of Zio XT in relation to the COVID-19 pandemic.

				In direct support of the current and future challenges, the Zio Service integrates with new virtual ways of working such as digital outpatients, while addressing the need for scalable and proven remote cardiac monitoring. In direct support of the clinical and patient needs created by COVID-19, iRhythm launched a 'Direct To Patient' shipping mechanism for the Zio Service, enabling patients to receive and fit the at home, without the need to visit a hospital or clinic. The Zio Service directly addresses the issues created by COVID-19: o 100% remote diagnostic pathway – helps to reduce risk to patients and NHS staff o Improves patient access to cardiac monitoring (helps to reduce back-log and reduces delays to care) by removing the need to attend a hospital or clinic appointment and directly helps to overcome scenarios where patients are unable or unwilling to attend a hospital appointment. o Single-use biosensor – reduced risk of infection (versus the reusable monitoring equipment of the comparator, which requires decontamination between each patient) o A Direct to Patient delivery model, which has been proven in a clinical study – Steinhubl SR et al. Effect of a home-based wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation. The mSToPS Randomized Clinical Trial. JAMA 2018;320(2):146–155. o Helps to reduce newly emerging health inequalities arising from issues around access to care	
General (n=1)					
48	18	Professional organisation		In summary, BCS welcomes the draft NICE guidelines. We note that Zio is only one of many technologies in this developing area. We would be keen to support increased research into the clinical	Thank you for your comment.

				effectiveness of the use of such technologies in a UK population.	

Appendix A: external assessment centre (EAC) review of the real-world evidence submitted during consultation

One NHS Trust and one STP provided feedback on the use of Zio XT Service that included results from their experience.

The Trust reported that Zio XT Service resulted in higher diagnostic yield versus Holter monitoring, with arrhythmia detected in 30% of people in the Zio XT Service group compared with 8.6% in Holter monitoring group. The population size and patch wear time for these groups were not provided. Two GP practices within an STP reported that Zio XT Service detected an arrhythmia in 92.5% of 40 patients (40% with multiple arrhythmia). There was no comparative result for Holter monitoring. The diagnostic accuracy and population characteristics within either of these patient cohorts were not available. Consequently, it is unclear why there is a wide discrepancy in the percentage of people found to have arrhythmia between the Trust and GP practice results. Additionally, the STP reported that 57.5% of patients were subsequently managed by their GP, therefore less than half of patients were referred to cardiology. Without more detail, this highlights the uncertainty over the extent to which an increase in diagnostic yield affects outcomes.

The two GP practices reported high levels of patient compliance for extended wear times of 14 days (average 12.1 days) and an average analysable time of 97.3%. The practices reported that the average number of days to first symptomatic arrhythmia was 3.5, concluding that routine 24 or 48hr Holter monitoring would have been insufficient to diagnose the arrhythmia in most patients.

Both the Trust and the STP suggested that adoption of Zio XT Service has the potential to significantly transform the pathway for diagnosing and managing patients with suspected cardiac arrhythmia by identifying and treating more patients with arrhythmia in primary care and reducing cardiology referrals.

Clear conclusions about efficacy cannot be currently be drawn from these results due to a lack of detail provided about the patient population. This level of evidence may satisfy tier 1 evidence requirements as per the digital evidence standards framework: credibility, relevance and acceptability.

Appendix B: external assessment centre (EAC) additional economic analysis

Sensitivity analysis examining the impact of a reduced price for Zio sensor and changes in the likelihood of ILR use

The EAC undertook sensitivity analysis to examine the impact of a lower price for Zio Service of £265 and a lower cost for ILR of £2062.17. The EAC also examined the impact of increased use of ILR. The EAC tested increased probabilities of 5% and 10% of testing with ILR following a negative/inconclusive first test result. The EAC modified the stroke and cardiology models to ensure consistency in the pathway to the use of ILR after either conventional testing or Zio. In the original EAC stroke model, the conventional pathway included a fork to ensure that the number of patients without a second test matched data from HES; there was a 2% probability of ILR use if a further test was implemented. The EAC amended the model to ensure a 2% probability of an ILR after a negative conventional test while preserving the probability of no further testing after a conventional test at 73% as reported in HES. This change increases the likelihood of ILR use in the conventional testing pathway. In the original EAC cardiology model there was a 2% probability of ILR use after a negative/inconclusive test with Holter or CER, but a 2% probability of ILR use only after an inconclusive test with Zio. The EAC added a 2% probability of ILR use after a negative test with Zio, consistent with its use in the EAC model after Holter or CER. In contrast, to the changes in the stroke model, these changes to the cardiology model increased the likelihood of ILR use after Zio Service. No changes were made to the downstream stroke model as this does not consider the use of ILR.

The EAC examined these changes under three scenarios regarding the likelihood of a follow-up outpatient visit. Firstly, the changes were examined under the base case which assumes an outpatient visit after all test results. Second, the changes were examined under an assumption that outpatient visits occur after tests except where the test is negative and is not repeated. Finally, the changes were examined under an assumption in which outpatient visits occur only after a positive test or where a patient proceeds to an ILR. For the second and third scenarios the EAC further amended each the model to include the cost of a further outpatient visit following the result of a repeat test if the final test was positive.

Stroke model

Base case – outpatient visit after every test

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£423.13	£493.94	-£70.81
Original EAC model – reduced Zio cost	£423.13	£454.44	-£31.31
Revised model	£463.49	£498.26	-£34.77
Revised model - reduced ILR cost	£441.61	£478.85	-£37.24
Revised model - reduced Zio & ILR cost	£441.61	£439.34	£2.27
Revised model – reduced costs, 5% chance of ILR	£493.41	£493.58	-£0.17
Revised model – reduced costs, 10% chance of ILR	£579.75	£583.97	-£4.22

Revisions to the stroke model under the base case assumption increase the cost of current care by increasing the probability that an ILR will be placed. However, current care is still cheaper than Zio Service. Zio Service remains cost incurring after a fall in the cost of ILR, but becomes cost saving when the cost of Zio Service is reduced. Increasing the likelihood of ILR use has a marginally negative impact on cost savings with Zio Service. This is because increased likelihood reduces the possibility of a further conventional test (albeit not by much).

Scenario – no outpatient test after any negative test not repeated

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£326.71	£381.14	-£54.43
Original EAC model – reduced Zio cost	£326.71	£341.64	-£14.93
Revised model	£353.59	£384.10	-£30.51
Revised model - reduced ILR cost	£331.70	£364.69	-£32.99
Revised model - reduced Zio & ILR cost	£331.70	£325.18	£6.52
Revised model – reduced costs, 5% chance of ILR	£385.77	£382.79	£2.98
Revised model – reduced costs, 10% chance of ILR	£475.88	£478.80	-£2.92

In this scenario negative tests not repeated do not require an outpatient visit. The change in the model structure has a very small effect on the cost of Zio Service as this arm incorporates some patients receiving current care. It has a much larger effect on current care, increasing the cost by nearly £30 and reducing the additional cost of Zio Service to around £25. Change in the cost of

ILR has little impact on incremental costs. When the cost of Zio Service is reduced to £265, Zio Service becomes cost saving. Cost savings for Zio Service reduce as the likelihood of an ILR after a negative test increases. This is a product of the revised model structure. Under current care a negative test has a 70% chance of not being repeated and a 2% chance of leading to an ILR with the remaining patients being retested. In contrast, after a Zio negative test the only further possibility of testing is the use of an ILR. As a consequence, as the likelihood of an ILR increases the number of retests falls in the current care arm which offsets the increased cost of ILR in the current care arm.

Scenario – outpatient test after positive tests or before ILR

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£252.10	£371.07	-£118.97
Original EAC model – reduced Zio cost	£252.10	£331.57	-£79.47
Revised model	£301.76	£378.54	-£76.78
Revised model - reduced ILR cost	£279.87	£359.13	-£79.26
Revised model - reduced Zio & ILR cost	£279.87	£319.63	-£39.76
Revised model – reduced costs, 5% chance of ILR	£339.58	£377.84	-£38.26
Revised model – reduced costs, 10% chance of ILR	£439.08	£474.85	-£35.77

In this scenario only positive tests and tests leading to use of an ILR require an outpatient visit. In the original analysis this scenario was highly cost incurring for Zio Service due to the reduction in the costs of additional testing in the current care arm (after the removal of an outpatient visit cost.) Again, the impact of the revised model structure is large; the additional cost for Zio Service falls to around £80. The change in the cost of Zio Service, inevitably impacts; at a lower cost of £265, the additional cost of Zio Service is around £40. Changes in the cost of ILR or likelihood of ILR fitting has little impact on relative costs.

Cardiology model

Base case – outpatient visit after every test

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£465.96	£466.78	-£0.82
Original EAC model – reduced Zio cost	£465.96	£428.56	£37.4
Revised model	£465.96	£483.48	-£17.52
Revised model - reduced ILR cost	£448.35	£473.47	-£25.12
Revised model - reduced Zio & ILR cost	£448.35	£435.24	£13.11
Revised model – reduced costs, 5% chance of ILR	£489.74	£461.63	£28.11
Revised model – reduced costs, 10% chance of ILR	£558.73	£505.6	£53.13

Revisions to the cardiology model under the base case assumption increase the cost of Zio Service by allowing for use of an ILR following a negative result. Zio Service remains cost incurring after a fall in the cost of ILR, but becomes cost saving when the cost of Zio Service is reduced. Cost savings increase as the likelihood of ILR use increases as this is higher under current care (due to a larger proportion of inconclusive/negative scans).

Scenario – no outpatient test after any negative test not repeated

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£420.11	£398.53	£21.58
Original EAC model – reduced Zio cost	£420.11	£360.31	£59.80
Revised model	£387.23	£429.73	-£42.50
Revised model - reduced ILR cost	£369.62	£419.72	-£50.10
Revised model - reduced Zio & ILR cost	£369.62	£381.50	-£11.18
Revised model – reduced costs, 5% chance of ILR	£411.97	£409.19	£2.78
Revised model – reduced costs, 10% chance of ILR	£482.55	£455.33	£27.22

Revisions to the model to estimate the proportion of repeat tests which are negative and not requiring an outpatient follow-up reduced the cost of the conventional arm in comparison to the previous scenario analysis run by the EAC, and Zio Service becomes cost incurring. Changes in the cost of ILR have a modest impact, increasing the incremental cost of Zio Service. The cost increase is offset by a reduction in the cost of Zio Service, but not eliminated. Zio Service becomes cost saving when the likelihood of ILR use increases to 5%.

Scenario – outpatient test after positive tests or before ILR

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£319.77	£354.52	-£34.75
Original EAC model – reduced Zio cost	£319.77	£316.30	£3.47
Revised model	£331.12	£417.45	-£86.33
Revised model - reduced ILR cost	£313.51	£407.45	-£93.94
Revised model - reduced Zio & ILR cost	£313.51	£369.22	-£55.71
Revised model – reduced costs, 5% chance of ILR	£360.60	£397.95	-£37.35
Revised model – reduced costs, 10% chance of ILR	£439.08	£445.82	-£6.74

Table 2 – Cardiology model, no outpatient test after all negative tests (except where ILR is fitted)

Costs under both current care and Zio Service rise in this scenario after the EAC amended the model to estimate the proportion of repeat tests which are positive and incur an outpatient visit, but this effect is most pronounced with Zio Service due to its higher sensitivity. Zio Service remains cost incurring in this scenario after a reduction in the price of Zio Service; it approaches cost neutrality when the chance of ILR use is 10%.

Downstream stroke model

Base case – outpatient visit after every test

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£1216.62	£1237.45	-£20.63
Original EAC model – reduced Zio cost	£1216.62	£1192.45	£24.17
Revised model	*Unchanged*	*Unchanged*	*Unchanged*
Revised model - reduced Zio cost	£1216.62	£1192.45	£24.17

Table 3 – Downstream stroke model, no outpatient test after negative tests not repeated

Amendments to the downstream stroke model were not required in the base case as the model does not incorporate the use of ILR. Reduction in the cost of Zio Service leads to a cost saving with Zio Service.

Scenario – no outpatient test after any negative test not repeated

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£1145.86	£1118.31	£27.45
Original EAC model – reduced Zio cost	£1145.86	£1073.31	£72.55
Revised model	£1087.40	£1118.31	-£30.91
Revised model - reduced Zio cost	£1087.40	£1073.31	£14.04

Table 3 – Downstream stroke model, no outpatient test after negative tests not repeated

The EAC revised this model to account for the likelihood of a positive test and then a further outpatient visit following a repeat test. After the revision Zio Service was cost incurring. Zio Service was cost saving at a price of £265.

Scenario – outpatient test after positive tests or before ILR

Sensitivity analysis	Cost of current care	Cost of Zio Service	Cost saving with Zio
Original EAC model	£1039.52	£1118.31	-£78.79
Original EAC model – reduced Zio cost	£1039.52	£1073.31	-£33.79
Revised model	*Unchanged*	*Unchanged*	*Unchanged*
Revised model - reduced Zio cost	£1039.52	£1073.31	-£33.79

Table 4 – Downstream stroke model, no outpatient test after all negative tests (except where ILR is fitted)

Under an assumption of an outpatient visit following a positive test only, Zio Service is cost incurring when compared against current care, and remains so when the price of Zio Service is reduced.

Sensitivity analysis on the number of repeat tests under current care

All three models were constructed to ensure that the number of repeat tests under current care matched observations in Hospital Episode Statistics (HES), at least in the base case. However, the data from HES includes exercise stress tests, and may not be an accurate estimate of the number of retests using Holter and CER in the model populations. Consequently, sensitivity analysis was undertaken to assess the number of repeat tests which equalised the cost of Zio Service and current care. In the base case there are 1.389 tests per patient in the conventional care arms.

Scenario	Number of tests
Cardiology model – base case	1.30
Cardiology model – no outpatient visit after negative tests not repeated	1.43
Cardiology model – outpatient visit after positive test	1.78
Stroke model – base case	1.37
Stroke model – no outpatient visit after negative tests not repeated	1.36
Stroke model – outpatient visit after positive test	1.71
Downstream stroke model – base case	1.31
Downstream stroke model – no outpatient visit after negative tests not repeated	1.34
Downstream stroke model – outpatient visit after positive test	1.59

Conclusions

In general, the reduction in cost of Zio Service, along with amendments to the cost and pathway to ILR fitting, are sufficient to make Zio Service cost saving in the base case, and in a scenario in which negative tests not repeated do not lead to an outpatient visit. If a further assumption is made that all negative tests except those leading to use of an ILR do not require an outpatient visit, Zio Service is cost incurring.

The impact of changes in the cost of ILR or the likelihood of testing with ILR are minimal in the stroke model and modest in the cardiology model, reflecting changes made by the EAC to align the models with regard to the pathway to the use of an ILR.