Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EFFECTIVENESS OF INRatio2 PT/INR MONITOR

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
1.	Consultee 10: Alere	Section1	We do not agree that the INRatio2 PT/ INR monitor is only recommended for use in research for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. The reasons are as follows: - The INRatio2 PT/ INR monitor has been validated against laboratory standard methods in several validation studies. It is an accurate method for patients to self-monitor their INR. - The INRatio2 PT/ INR monitor is easy to use and gets high patient satisfaction scores in clinical studies. - The INRatio2 PT/ INR monitor has been shown in real life clinical use to achieve high TTR, which has been shown to lead to improved clinical outcomes. - The assessment seeks to determine the effectiveness of a device that is only one element in the pathway for managing patients undergoing coagulation treatment. Patient management by	Thank you for your comment which the Committee considered. The Committee considered the performance of the InRatio2 PT/INR compared with the gold standard of laboratory based INR testing and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EFFECTIVENESS OF INRatio2 PT/INR MONITOR

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
			their physician, VKA dosing, patient diet and behaviour will ultimately impact their clinical outcome. Therefore we believe the correct assessment is against the gold standard lab test and patient acceptability/ usability. - Other monitors, such as glucometers, are similarly assessed versus the lab standard and patient ease of use. They are not evaluated separately based on clinical outcome in any NICE guidance. - INRatio 2 PT/ INR monitor is used widely across the world, in clinic and self-testing/self-management applications, with good user experience and acceptable correlation to laboratory gold standard methods. We accept that the majority of published evidence obtained by the assessment panel utilised the CoaguChek devices but this does not mean that INRatio 2 PT/ INR monitor (or any other device that correlates well with acceptable gold standard methods) would not also achieve the same outcomes. The assessment findings for INRatio 2 PT/ INR monitor could be seen as undermining the effectiveness of the device and have implications and	

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EFFECTIVENESS OF INRatio2 PT/INR MONITOR

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
			may cause unnecessary concern for existing patients using the INRatio 2 PT/ INR monitor.	
2.	Consultee 10: Alere	Section 4	The main purpose of self-testing of INR is to free the patient from the inconvenience and cost of testing at a clinic and to encourage behaviour that allows patients to improve their TTR. Therefore the appropriate comparator is lab testing of INR. The device itself is only providing information about part of the clinical pathway. Patient management by their physician, VKA dosing, patient diet and behaviour will ultimately impact their clinical outcome. The most important assessment is the ability of the device to accurately, rapidly and conveniently deliver an INR result and be easy for the patient to use. According to this NICE assessment, INRatio2 PT/ INR monitor performs these functions well and to an acceptable standard. Other monitors, such as glucometers, are similarly assessed versus the lab standard and patient ease of use. They are not evaluated separately based on clinical outcome in any NICE guidance.	Thank you for your comment which the Committee considered. The Committee considered the performance of the InRatio2 PT/INR compared with the gold standard of laboratory based INR testing and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EFFECTIVENESS OF INRatio2 PT/INR MONITOR

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
3.	Consultee 10: Alere	Section 7	We do not agree that the INRatio 2 PT/ INR monitor is only recommended for use in research for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. The reasons are as follows: - The INRatio 2 PT/ INR monitor has been validated against laboratory standard methods in several validation studies. It is an accurate method for patients to self-monitor their INR. - The INRatio 2 PT/ INR monitor is easy to use and gets high patient satisfaction scores in clinical studies. - The INRatio 2 PT/ INR monitor has been shown in real life clinical use to achieve high TTR, which has been shown to lead to improved clinical outcomes. - INRatio 2 PT/ INR monitor is used widely across the world, in clinic and self-testing/self-management applications, with good user experience and acceptable correlation to laboratory gold standard methods.	Thank you for your comment which the Committee considered. The Committee considered the performance of the InRatio2 PT/INR compared with the gold standard of laboratory based INR testing and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EFFECTIVENESS OF INRatio2 PT/INR MONITOR

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
			- Other monitors, such as glucometers, are similarly assessed versus the lab standard and patient ease of use. They are not evaluated separately based on clinical outcome in any NICE guidance.	

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EQUIVALENCE OF TECHNOLOGIES

4.	Consultee 10: Alere	Section1	The INRatio2 PT/ INR monitor has been shown to have equivalent performance in clinical studies and in audit data from patient use to the CoaguChek XS system (evidence provided in support).	Thank you for your comment which the Committee considered. The Committee considered the performance of the InRatio2 PT/INR and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.
5.	Consultee 10: Alere	Section 5	We agree that the lower cost structure of INRatio 2 PT/ INR monitor means that it has improved cost effectiveness compared to CoaguChek. However we do not accept that an exclusive INRatio 2 PT/ INR monitor study on clinical effectiveness is required to support this model. The technical performance of the INRatio 2 PT/ INR monitor correlates with the lab testing method and with the CoaguChek XS product. When both monitors were included in a clinical effectiveness study, there was no significant difference noted between the monitors, using the same clinical population and studied by the same clinical team (Azarnousch et al., 2011). This is further supported by data from The National Thrombosis Service in the Netherlands. An analysis of data from 5846 patients using either the CoaguChek XS or	Thank you for your comment which the Committee considered. The Committee considered the performance of the InRatio2 PT/INR compared with the gold standard of laboratory based INR testing and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.

			INRatio 2 PT/ INR monitor for INR monitoring, showed there were no significant differences. We would like to submit this additional data as evidence in support that the INRatio2 PT/ INR monitor has equivalent performance to CoaguChek XS in routine patient use, and that as both devices accurately measure INR in patient's hands, the impact on clinical outcomes is equivalent.	
6.	Consultee 10: Alere	Section 6	6.3 There is no substantive evidence that the usability of the INRatio 2 PT/ INR monitor has a large impact on patient behaviour. In this NICE assessment it was noted that patients favoured the INRatio 2 PT/ INR monitor (41% preferred) compared to the CoaguChek system (36%). In addition, the technical performance of the INRatio 2 PT/ INR monitor correlates with the lab testing method and with the CoaguChek XS product. When both monitors were included in a clinical effectiveness study, there was no significant difference noted between the monitors, using the same clinical population and studied by the same clinical team (Azarnousch et al., 2011). This is further supported by data from The National Thrombosis Service in the Netherlands that we are submitting in support. An analysis of data from 5846 patients using	Thank you for your comment which the Committee considered. The Committee considered the usability of the InRatio2 PT/INR and decided to change sections 5.24 and 6.5 of the guidance.

			either Coaguchek XS or INRatio 2 PT/ INR monitor showed there were no significant differences between the devices.	
7.	Consultee 10: Alere	Section 6	6.7 It is noted that CoaguChek XS is only used in 4 out of the 26 trials included. The differences between the CoaguChek XS and CoaguChek S are quite significant, as highlighted in this document. In addition, it is important to note that the technology principles on which the devices deliver the INR result are completely different (iron particle movement vs. electrochemical enzyme activity). It is not made clear why the committee assumed that the 2 CoaguChek devices are equivalent but goes on to suggest that this data cannot be used to support the INRatio 2 PT/ INR monitor. If the data from the Coaguchek S device can be used to support the CoaguchekXS system, because they are both correlated to the lab standard INR result, then it follows that the data can also be used to support the INRatio 2PT/INR monitor, as it has been shown that the INRatio 2 PT/ INR monitor correlates with the lab standard, has equivalent performance to CoaguChek XS when included in the same clinical study (Azarnousch et al., 2011) and in routine patient use (data from 2877	Thank you for your comment. The Committee considered your comment and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EQUIVALENCE OF TECHNOLOGIES

			INRatio 2PT/INR users from The National Thrombosis Service in the Netherlands submitted in support).	
8.	Consultee 10: Alere	Section 6	We do not agree with the statement that that there was insufficient evidence to determine if self-monitoring with the INRatio2 PT/INR monitor would represent a cost-effective use of NHS resources. Patients using the INRatio 2 PT/ INR monitor have been proven to have an accurate INR result, maintain a high TTR (DeSantis et al., in press, provided as evidence in support) and perform equivalently to CoaguChek XS in side by side comparison studies (Azarnousch et al., 2011) and routine patient use (National Thrombosis Service, Netherlands, provided as evidence in support). The INRatio 2 PT/ INR monitor has been compared with CoaguChek XS for patient acceptability and was preferred (Hemkens et al., 2008). Therefore we suggested that it is relevant to include the INRatio 2 PT/ INR monitor in the model developed for cost effectiveness. The CoaguChek XS system itself was only included in 4 of the trials, and has significant differences with CoaguChek S as highlighted above and with an ISI 1.0 vs 1.6. It is not explained clearly why this difference was accepted for CoaguChek XS but not for the INRatio 2 PT/ INR	Thank you for your comment. The Committee considered your comment and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.3, 6.4 and 6.5 of the guidance.

			monitor.	
9.	Consultee 10: Alere	Section 7	The INRatio 2 PT/ INR monitor has been shown to have equivalent performance in clinical studies and in audit data from patient use to the CoaguChek XS system (evidence provided in support).	Thank you for your comment which the Committee considered. The Committee considered the performance of the InRatio2 PT/INR and decided to change sections 1.2, 5.6, 5.7, 5.8, 6.4 and 6.5 of the guidance.
10.	Consultee 2: Atrial Fibrillation Guideline Development Group (Guideline Development Group)	Section 1	1. The document specifically refers to the Coaguchek XS system yet most, if not all, the studies considered within the document were undertaken using the Coaguchek S system. The technologies are not the same despite their being marketed by the same manufacturer. I would question the validity therefore of recommending the XS system based on data from the S system.	Thank you for your comment which the Committee considered. The Committee considered the performance of the CoaguChek S and XS systems compared to the gold standard of laboratory-based INR testing and noted that the precision and accuracy of the 2 CoaguChek versions correlated with that of laboratory-based measurements. The Committee decided to change section 6.3 of the guidance.
11.	Consultee 5: Roche	Section 4	As acknowledged by the committee in section 6.4, some of the clinical trials considered used older	Thank you for your comment which the Committee considered.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EQUIVALENCE OF TECHNOLOGIES

	Diagnostics		versions of the technology and the improved reliability and accuracy of the current XS system means that the latest CoaguChek XS system obtains results that are comparable with results obtained with older versions.	The Committee considered the performance of the CoaguChek S and XS systems compared to the gold standard of laboratory-based INR testing and noted that the precision and accuracy of the 2 CoaguChek versions correlated with that of laboratory-based measurements. The Committee decided to change section 6.3 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EXTERNAL VALIDITY OF STUDIES

12.	Consultee 2: Atrial Fibrillation Guideline Development Group (Guideline Development Group)	Section 1	2. The data on reduction of thrombo-embolic events are based on studies which were mainly undertaken outside the UK. Thus the anticoagulation control within the routine care arms tends to be less than that obtained in the UK. There have been no UK studies which have demonstrated reduction in clinical events associated with self-management.	Thank you for your comment which the Committee considered. The Committee discussed the heterogeneity in the trials and the applicability of the pooled results from the meta-analysis of the trial data to the UK population. It noted that the meta-analysis results showed low statistical heterogeneity and concluded that self-monitoring offered clinical benefit because it was likely to result in a significant reduction in thromboembolic events. The Committee concluded that the pooled effect estimates from the meta-analysis were likely to be applicable to the UK because there are no confounding biological differences between people receiving vitamin K antagonist therapy in the UK and those in other countries. Please see section 6.2 of the guidance.
13.	Consultee 7: NHS Professional	Section 6	Studies which have compared patient self-monitoring with standard monitoring have significant heterogeneity in the 'standard' The standard service for INR monitoring is very variable with wide quality of control. There is no 'one standard' model as a comparator of this technology. This results in	Thank you for your comment which the Committee considered. The Committee discussed the heterogeneity in the trials and the applicability of the pooled results

			erroneous interpretation of data available. Studies from different countries cannot be extrapolated to UK as the service models for INR monitoring vary from one country to another and many times within a country there are several models.	from the meta-analysis of the trial data to the UK population. It noted that the meta-analysis results showed low statistical heterogeneity and concluded that self-monitoring offered clinical benefit because it was likely to result in a significant reduction in thromboembolic events. The Committee concluded that the pooled effect estimates from the meta-analysis were likely to be applicable to the UK because there are no confounding biological differences between people receiving vitamin K antagonist therapy in the UK and those in other countries. Please see section 6.2 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EVIDENCE ON SELF-MONITORIING

14.	Consultee 2: Atrial Fibrillation Guideline Development Group (Guideline Development Group)	Section 1	3. The document recommends self-management for both mechanical valves and atrial fibrillation however no data are presented which separates these conditions out. As far as I am aware there has been no specific AF analysis.	Thank you for your comment which the Committee considered. The Committee heard from clinical specialists that the clinical outcomes for people with atrial fibrillation are similar to those for people with artificial heart valves. The Committee noted that it was not possible to isolate the data for people with atrial fibrillation but concluded that it was likely that self-monitoring would result in similar clinical benefits in people with atrial fibrillation to those achieved in people with artificial heart valves. Please see section 6.7 of the guidance.
15.	Consultee 2: Atrial Fibrillation Guideline Development Group (Guideline Development Group)	Section 2	4. The health economics section needs clarifying. It is stated that 2 previous health economic analyses have been undertaken which concluded that self-management is not cost-effective within the NHS. The analysis therefore uses non-UK data to populate what is a fairly complex model. This is both disingenuous and potentially misleading. In terms of costs, it is clear that self-management is more costly than routine care within the NHS. Thus to demonstrate cost-effectiveness there needs to be an effect over and above that seen in routine care. As stated in 1 above,	Thank you for your comment which the Committee considered. The Committee discussed the heterogeneity in the trials and the applicability of the pooled results from the meta-analysis of the trial data to the UK population. It noted that the meta-analysis results showed low statistical heterogeneity and concluded that self-monitoring offered clinical benefit because it was likely to result in a significant reduction in thromboembolic events.

			this has not been seen in UK studies. Neither has there been a demonstrable improvement in INR control in terms of TTR. Thus the conclusion of the original analyses remains valid. It would be more appropriate to undertake sensitivity analysis in order to determine at what level of either improvement in outcome or reduction in cost self-management would become cost-effective. 5. There needs to be much more clarity regarding the distinction between self-testing and self-management.	The Committee concluded that the pooled effect estimates from the meta-analysis were likely to be applicable to the UK because there are no confounding biological differences between people receiving vitamin K antagonist therapy in the UK and those in other countries. Please see section 6.2 of the guidance. The Committee considered the cost-effectiveness analysis and concluded that self-monitoring is cost effective in light of the reduction in thromboembolic events seen in the pooled results of the trial data. Please see section 6.8 of the guidance. The Committee considered the differences in clinical outcomes and cost-effectiveness between self-testing and self-management. Please see sections 6.6 and 6.9 of the guidance.
16.	Consultee 7: NHS Professional	Section 5	The comparator used is INR testing by lab based or point of care device. This can only be a comparator for patient self testing and not self management. Self management must compare the decision making for warfarin dosage which is widely variable between	Thank you for your comment which the Committee considered. Clinical experts and attendees at the scoping workshop agreed that INR testing in primary or

			various services. This is highlighted in several publications. Due to such wide variability in the 'standard monitoring' the studies are not comparable and therefore patient self management efficacy remains unproven.	secondary care using laboratory analysers or point-of-care tests constitutes current NHS practice and is therefore, the comparator in this assessment. This enables an assessment of the potential benefit that may be gained by using the technology in the NHS compared with current practice. The Committee discussed the heterogeneity in the trials and the applicability of the pooled results from the meta-analysis of the trial data to the UK population. It noted that the meta-analysis results showed low statistical heterogeneity and concluded that self-monitoring offered clinical benefit because it was likely to result in a significant reduction in thromboembolic events. The Committee concluded that the pooled effect estimates from the meta-analysis were likely to be applicable to the UK because there are no confounding biological differences between people receiving vitamin K antagonist therapy in the UK and those in other countries. Please see section 6.2 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: EVIDENCE ON SELF-MONITORIING

17.	Consultee 8: BMS-Pfizer	Section 6	The BMS-Pfizer Alliance notes that although there is a significant improvement in thromboembolic (TE) events in self-management and self-monitoring, there is no significant improvement in TTR. Conversely, for self-testing, there is a significant improvement in TTR, but no significant improvement in TE events. The Committee therefore conclude that the clinical and cost-effectiveness associated with self-testing is likely to have been under-estimated. We suggest that this discrepancy warrants further discussion at the next Committee meeting.	Thank you for your comment which the Committee considered. The Committee noted that the largest trial in the assessment of self-testing did not show a reduction in clinical adverse events but did show an increase in the time in therapeutic range (Matchar et al. 2010). The Committee also noted that this trial had a high standard of coagulation control in the control arm, which could explain why no statistically significant difference in clinical adverse events was detected between the self-testing group and the standard care group was detected. The Committee concluded that the high standard of coagulation control in the control arm of the trial may not reflect general UK clinical practice and so it was plausible that the increase in time in therapeutic range would lead to a statistically significant reduction in clinical adverse events if compared with UK standard coagulation control practice. Please see section 6.6 of the guidance.
18.	Consultee 8: BMS-Pfizer	Section 6	We note that the studies included in the evidence review are quite old and that the management of	Thank you for your comment.

			warfarin may have improved since these studies were conducted. The results of the meta-analysis are being driven by four large studies that were published in 2008, 2005, 2005 and 2001 respectively. The potential impact of this on the results does not appear to have been considered by the Committee and we suggest this should be discussed at the next Committee meeting.	The Committee discussed the applicability of the pooled results from the meta-analysis of the trial data to the UK population. It noted that the meta-analysis results showed low statistical heterogeneity and concluded that self-monitoring offered clinical benefit because it was likely to result in a significant reduction in thromboembolic events. The Committee concluded that the pooled effect estimates from the meta-analysis were likely to be applicable to the UK because there are no confounding biological differences between people receiving vitamin K antagonist therapy in the UK and those in other countries. Please see section 6.2 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: TECHNOLOGIES

19.	Consultee 3: BIVDA	Section 2	Three CE marked technologies had been identified as being relevant to the assessment, as outlined in the consultation document, although only two were taken forward ? both manufactured by BIVDA members.	Thank you for your comment which the Committee considered. The assessment consisted of a systematic review of the evidence on test performance and clinical-effectiveness data for the CoaguChek XS system, the INRatio2 PT/INR monitor, the ProTime microcoagulation system and comparator tests. The ProTime microcoagulation system was in the assessment but has been removed from this guidance because it is no longer available to the NHS and its successor model is not intended for patient self-monitoring. Please see section 5.1 of the guidance.
20.	Consultee 3: BIVDA	Section 4	The committee has identified two relevant tests, from Roche and Alere both members of BIVDA, and we understand that they will be responding to the consultation separately. However, it has been raised with us that there should be enhanced clarity over the descriptions of the tests.	Thank you for your comment which the Committee considered. All comments received at consultation have been considered by the Committee.
21.	Consultee 5: Roche Diagnostics	Section 4	Section 4.6 could be a clearer description of the currently marketed versions of the CoaguChekÂ® XS system: The CoaguChek XS Plus system is intended for use by healthcare professionals only and therefore	Thank you for your comment. The Committee considered your comment and decided to change section 4.6 of the guidance.

			not suitable for INR self-monitoring. Â As this guidance relates to INR self-monitoring, we recommend removing the final sentence in 4.6. for clarity.	
22.	Consultee 7: NHS Professional	Section 4	The point of care coagulometers should not be used for testing INR in individuals not on Vitamin K antagonists	Thank you for your comment which the Committee considered. This guidance is on 'Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease'.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: DOSING SOFTWARE

23.	Consultee 5: Roche Diagnostics	Section 6	The conclusions of the committee, in particular in sections 6.3 and 6.7, highlight the cost-effectiveness of self-monitoring using the CoaguChek XS system based on the clinical effectiveness in reducing thromboembolic events compared to standard care and thus we fully endorse the committee's conclusions and recommendations. We do not think that the inclusion of dosing-software cost (discussed in 6.10) will significantly affect the cost-effectiveness of self-monitoring. Services that use dosing software will incur the same cost per patient for the software whether the patient is attending clinic or participating in a self-monitoring scheme and there may be small additional cost for automated solutions (e.g. telephone systems or texts) that further support self-management.	Thank you for your comment which the Committee considered. The Committee considered an additional analysis by the External Assessment Group that investigated the impact of an additional cost for dose adjustment software on the base-case ICERs for self-managing. The Committee noted that the additional cost of software would need to be greater than £190 per patient per year to substantially affect the cost-effectiveness of self-managing with the coagulometers. The Committee concluded that the additional cost of software was unlikely to exceed this value and therefore, even with this potential additional cost, self-managing with the point-of-care coagulometers would still represent a cost-effective use of resources in the NHS. Please see section 6.11 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: POPULATION - VTE

24.	Consultee 1: Children's Heart Federation Charity	Section 1	The Children's Heart Federation welcomes the widening access of INR self-testing machines to people on long-term vitamin K antagonist therapy. We do however feel concerned that limiting access to those who have atrial fibrillation or heart valve disease does not include all those with VTE who require life/long term anticoagulation, denying these people the same ability to manage their chronic health conditions. We believe all children with heart conditions on long-term Warfarin should have access to self-testing, including those who have had heart operations, for instance the Fontan procedure.	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases.
25.	Consultee 9: AntiCoagulation Europe	Section 1	1.1 Limiting the indication for heart disease and Atrial Fibrillation excludes people with types of thrombophilia that require life/long term anticoagulation with the consequences being that they will be denied access to the devices which can help them manage their chronic health conditions, if this is their preferred choice.	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: POPULATION - VTE

26.	Consultee 9: AntiCoagulation Europe	Section 1	Needs further clarification and consideration as to the exclusion of the wider VKA population to avoid discrimination and inequalities to access self monitoring devices for the purpose of decreasing a VTE event	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases.
27.	Consultee 9: AntiCoagulation Europe	Section 3	Any person who requires long term VKA should not be excluded because the current VTE Guidelines do not routinely recommend offering people the choice of self – management and self –monitoring for patients being treated for VKA (CG144 section 1.4.1) In section 1.2.5 – reference is made to offering VKA beyond 3 months to patients where their risk of VTE is high. It is these patients who, when making a decision as to whether to continue with Warfarin, could benefit from access to self monitoring devices for managing their healthcare effectively and with minimal clinical	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases. Details on updating the clinical guideline can be found in clinical guideline

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: POPULATION - VTE

			intervention such as having to regularly attend clinics in primary and secondary care. If these (Coaguchek +) Guidelines reflected the whole of the population affected, the VTE Guidelines could be amended / reviewed accordingly.	144.
28.	Consultee 9: AntiCoagulation Europe	Section 5	5.15 Evidence shows that self –management halved the risk of thromboembolic events compared to that of standard care. Heart valve patients and AF sufferers will benefit from access to the devices and the subsequent benefits of reducing the risk of a VTE. This disadvantages the rest of the VKA long term user population and their healthcare outcomes. How can this be justified when an individual who has been diagnosed with a clotting disorder requiring warfarin is advised that they won't be able to access a device to help them manage their treatment effectively? 5.17 Evidence indicates that there is significant reduction in death for self –managers – see above for comments for disadvantaging those outside of scope	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: POPULATION - CHILDREN

29.	Consultee 9: AntiCoagulation Europe	Section 1	The term 'people' needs to be defined – does this include children too? 1.2 Alludes to children and their carers. Does the recommendations go far enough in stating that parents will be able to access the devices **as choice** for their children and at what age does a child become responsible for own healthcare decisions i.e. a 'minor' needing VKA therapy for heart disease or for inherited thrombophilia condition needing treatment or prophylaxis in their teens?	Thank you for your comment. The Committee considered your comment and decided to change section 1 of the guidance.
30.	Consultee 1: Children's Heart Federation Charity	Section 2	We welcome the recommendation that patients and carers should receive training for effective use of the Coaguchek XS system. Â The Children?s Heart Federation currently fund INR machines for children with heart conditions who are on long term Warfarin therapy and one requirement to receive the machine is that training is undertaken. It would be useful if the guidance provided information regarding Â at what age a child can be expected to self-monitor and manage their INR.	Thank you for your comment which the Committee considered. The Committee concluded that the decision for a patient to self-monitor should be made after a thorough discussion and subsequent agreement between the patient and the healthcare professional. Please see section 6.13 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: CLINICAL GUIDELINE

31.	Consultee 5: Roche Diagnostics	Section 1	The recommendations of the committee are clear and concise and we hope that they will lead to a wider awareness of the benefits of self-monitoring for people on long-term vitamin K antagonist therapy in the NHS. Â We would therefore find it very beneficial and important for clinicians and patients if the final recommendations of this guidance are included in verbatim in the updated NICE clinical guideline for atrial fibrillation that is scheduled for publication a month before (June 2014) this guidance and thus facilitate uptake and implementation of this guidance.	Thank you for your comment which the Committee considered. NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice. The NICE clinical guideline on atrial fibrillation refers to the diagnostics guidance on self‑monitoring of vitamin K antagonist therapy
32.	Consultee 3: BIVDA	Section 9	The recommendations have put forward 7 items of related guidance in this section. BIVDA consider these as appropriate, however it is important to note that some of these including the Atrial Fibrillation guidance have been recently updated; reference to these updates could be made.	Thank you for your comment which the Committee considered. NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice. The NICE clinical guideline on atrial fibrillation refers to the diagnostics guidance on self‑monitoring of vitamin K antagonist therapy
33.	Consultee 5: Roche Diagnostics	Section 9	This section could benefit from a reference to the updated AF guideline and it would be very beneficial for clinicians and patients to incorporate the final recommendations of this assessment in verbatim in	Thank you for your comment which the Committee considered. NICE intends to develop tools, in association with

			the updated NICE clinical guideline for atrial fibrillation to raise awareness for INR self-monitoring.	relevant stakeholders, to help organisations put this guidance into practice. The NICE clinical guideline on atrial fibrillation refers to the diagnostics guidance on self‑monitoring of vitamin K antagonist therapy.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: NOACs

34.	Consultee 6: Bayer	Section 3	Under ?diagnostic and care pathways?, when discussing the new oral anticoagulants (NOACs) (3.11), the draft guidance currently states: ?However, they may be unsuitable for some people such as people with mechanical heart valves, people with renal or liver dysfunction and those taking concurrent drugs that cannot be taken with the new oral anticoagulants.? The above implies that all the NOACs are unsuitable for all people with renal or liver dysfunction. However, this does not accurately reflect the licence recommendations, which not only differ from product to product, but also depend on the degree of impairment, ranging from no dose reduction required through to contraindications, and including use with caution, or dose reductions for certain groups. The individual SmPCs should be consulted for each product. We suggest that the text should be amended to ?However, they may be unsuitable for some people such as people with mechanical heart valves, certain	Thank you for your comment. The Committee considered your comment and decided to change sections 3.11 and 6.14 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: NOACs

			people with renal or liver dysfunction and those taking concurrent drugs that cannot be taken with the new oral anticoagulants. The individual Summary of Product Characteristics should be consulted for specific details.?	
35.	Consultee 8: BMS-Pfizer	Section 6	We welcome the acknowledgement of the NICE guidance relating to the novel oral anticoagulants (NOACs) in section 3.11. However, we agree with the decision to exclude the NOACs from this diagnostic appraisal, and we suggest that is not relevant to consider the risks and benefits associated with treatment in a diagnostic appraisal outlined in section 6.13. Specifically, these considerations are: That people receiving warfarin who have stable international normalised ratios are unlikely to switch to new oral anticoagulants because of the risk of bleeding when switching between different anticoagulant therapies? and ?that clinical concerns remain about the use of the new oral anticoagulants because there is currently no reliable way to reverse bleeding should it occur, and there is no test that can reliably monitor the level of the drugs or assess patient adherence to treatment.? We suggest that these considerations could be	Thank you for your comment. The Committee considered your comment and decided to change sections 3.11 and 6.14 of the guidance.

			removed from the DCD and future documentation relation to this appraisal. Alternatively, NICE may consider clarifying this section by stating that the influence of these clinical considerations, and the degree to which they are addressed, may impact upon the number of patients still using warfarin.	
36.	Consultee 8: BMS-Pfizer	Section 12	On page 10 of the DAR it notes that: "According to the NICE clinical guideline on AF... the most effective treatment considered for the treatment of atrial fibrillation is dose-adjusted warfarin..." **We suggest that this statement contradicts the recent NOAC technology appraisals and should be removed or updated accordingly in order to reflect the existence of the NOACs.**	Thank you for your comment which the Committee considered. This statement is not included in the diagnostics guidance. The Diagnostics Assessment Report was released for consultation in November 2013. All comments received on the DAR were considered at that time.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: IMPACT ON PATIENTS

37.	Consultee 3: BIVDA	Section 3	The use of POC coagulometers enable the patient to independently monitor the clotting tendency of their blood, thus providing a more positive patient experience, as well as improving understanding. This improved awareness and understanding will mean that patients take less regular visits to the GP, thereby freeing up resources.	Thank you for your comment which the Committee considered. The Committee's considerations of the benefits of self-monitoring for patients are described in sections 6.12 and 6.13 of the guidance.
38.	Consultee 4: Heart Rhythm Charity	Section 3	The use of the Coagucheck would enable those patients unable to travel to manage their INR at home and those younger patients would not need to attend regular appointments, possibly affecting work commitments, both parties will then enjoy a better, less stressful quality of life.	Thank you for your comment which the Committee considered. The Committee's considerations of the benefits of self-monitoring for patients are described in sections 6.12 and 6.13 of the guidance.
39.	Consultee 3: BIVDA	Section 5	The committee has put forward an extensive evidence base towards the clinical effectiveness of self monitoring using both tests outlined. BIVDA agree that Point of Care Testing brings forward a range of benefits to the patient and health service.	Thank you for your comment which the Committee considered.
40.	Consultee 3: BIVDA	Section 6	Section 6 outlines the cost-effectiveness of self monitoring in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. It also compares self monitoring of anticoagulation status and self testing for diabetes. BIVDA agree with the conclusions of the report to the extent that there self monitoring brings benefits to	Thank you for your comment which the Committee considered. The Committee's considerations of the benefits of self-monitoring for patients are described in sections 6.10, 6.12 and 6.13 of the guidance.

			patients and families, and allows them more independence and control. The Committee also concluded that there are different considerations for self-monitoring of coagulation status to those made for self-testing for diabetes, and that the decision for a patient to self-monitor should be made after a thorough discussion and subsequent agreement between the patient and the healthcare professional. BIVDA concur with this statement, as all self monitoring and testing should be appropriate.	
41.	Consultee 9: AntiCoagulation Europe	Section 6	6.5 Self – testers could potentially convert to self – managers when supported by their healthcare professionals. If a patient is only restricted to using a monitor for self –testing; they may not fully benefit from the opportunity to engage in the long term management of their condition. ACE acknowledges that the convenience of self – testing with monitored dose adjustments being provided by healthcare professionals may still be necessary for some people(or carers) whilst others with education, training and encouragement will embrace the process with confidence and competence	Thank you for your comment which the Committee considered.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: IMPACT ON PATIENTS

42.	Consultee 9: AntiCoagulation Europe	Section 6	6.9 and 6.11 The Committee has reflected on the impact of INR monitoring and the significant burden on the individual, their carers and family. This should not be understated in addressing the overall benefits of engaging patients in the management of their chronic conditions in terms of quality of life, financial outlay and time required for INR monitoring. Overall, if patients are better controlled, there will be a reduced risk of a clotting or bleeding event which in turn will reduce hospital admissions and management of associated conditions such as Post Thrombotic Syndrome.	Thank you for your comment which the Committee considered. The Committee's considerations of the benefits of self-monitoring for patients are described in sections 6.10, 6.12 and 6.13 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: IMPLEMENTATION

43.	Consultee 4: Heart Rhythm Charity	Section 6	The patient must be fully informed as to the use of this form of INR monitoring when first assessed as requiring Warfarin.	Thank you for your comment. The Committee considered your comment and decided to change section 1.3 of the guidance.
44.	Consultee 3: BIVDA	Section 8	As previously stated, BIVDA is an advocate of appropriate self-monitoring, and believes that this is an important aspect of the patient pathway. Therefore we welcome the efforts put forward by NICE to make tools available for appropriate self-monitoring so that any barriers to doing so are overcome. This includes training and on-going support for patients and carers.	Thank you for your comment which the Committee considered.
45.	Consultee 3: BIVDA	Section 8	As outlined in section 6.11, the committee has stated that there is variation in access to self-testing strips. It is important that materials aimed at both primary and secondary care (including CCGs)are available to support implementation of this guidance.	Thank you for your comment which the Committee considered. NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice.
46.	Consultee 5: Roche Diagnostics	Section 8	Although the committee discussed differences in INR self-monitoring and self-testing for diabetes (section 6.12), we like to highlight that the majority of insulin-dependent patients self-manage whereas only a minority of patients self-monitor their INR. In our opinion, this difference can be explained by the lack	Thank you for your comment which the Committee considered. Please see section 6.13 for the Committee's considerations of the similarities between self-monitoring coagulation status and self-managing

			of support/awareness for INR self-monitoring in the current service model. We therefore welcome the effort by NICE to make tools available that help overcome barriers to adopt patient INR self-monitoring and recommend that tools include examples of service specifications that address training and ongoing support for patients INR self-monitoring. It is essential that materials aimed at CCGs and GPs that help to reduce the variation in access to self-testing strips on formularies, acknowledged by the committee in section 6.11, will be available to support implementation of this guidance.	diabetes. NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice.
47.	Consultee 9: Anti Coagulation Europe	Section 8	This is necessary to raise awareness, education and information for CCGs, clinicians, patients and their carers. Will stakeholders be approached directly to assist in the development of the tools and what is the timeframe here?	Thank you for your comment which the Committee considered. NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice.

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 1

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 11 March 2014

THEME: OTHER COMMENTS

48.	Consultee 4: Heart Rhythm Charity	Section 1	Arrhythmia Alliance welcomes the recommendation for Self monitoring.	Thank you for your comment
49.	Consultee 5: Roche Diagnostics	Section 5	We have no further comments and have commented on the substantial evidence supporting the clinical effectiveness of self-monitoring with CoaguChek XS compared to standard care, supported by a robust evidence base of 22 RCTs using the CoaguChek system, and the economic analysis indicating that self-monitoring is highly cost-effective or cost-saving compared to standard care in our comments to the diagnostic assessment report.	Thank you for your comment

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: LEVEL OF EVIDENCE

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
1	Consultee 1: Roche Diagnostics	Section 1|Comment on Section 1: Provisional recommendations	The revised recommendations of the committee for CoaguChek XS (1.1) remain concise. However, we are surprised by the change in recommendations for InRatio2/INR. There is still a considerable difference in evidence on clinical effectiveness that should be stated in the section: 22 RCTs using the CoaguChek system versus none for InRatio2/INR. Considering the importance of accurate and reliable test results and the consequent risk of stroke or bleeding, the level of evidence available for CoaguChek XS gives confidence in the safety and effectiveness of self-management using the system. The fact that both monitors were found to be comparable to laboratory-based INR testing in terms of precision and accuracy may not imply equal safety or clinical benefits in practice as acknowledged in section 6.5.	Thank you for your comment The Committee considered the evidence that showed the 2 coagulometers had a broadly similar performance in precision and accuracy with regard to time in therapeutic range measurement when compared with the gold standard of laboratory-based INR testing and therefore concluded that it was appropriate to extrapolate the clinical-effectiveness data from the CoaguChek system to the INRatio2 PT/INR monitor. Please see sections 6.3 and 6.4 of the guidance. The Committee considered your comment and decided to change section 6.5 of the

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: LEVEL OF EVIDENCE

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
				guidance
2	Consultee 1: Roche Diagnostics	Section 5|Comment on Section 5: Outcomes	The section highlights the substantial evidence supporting the clinical effectiveness of self-monitoring with CoaguChek XS compared to standard care, supported by a robust evidence base of 22 RCTs using the CoaguChek system. In contrast, no RCT data on InRatio2/INR was identified. The assumptions of equal clinical effectiveness between the systems (5.42) is very severe given this difference in evidence and Â considering the importance of accurate and reliable test results and the consequent risk of stroke or bleeding.	Thank you for your comment The Committee considered the evidence that showed the 2 coagulometers had a broadly similar performance in precision and accuracy with regard to time in therapeutic range measurement when compared with the gold standard of laboratory-based INR testing and therefore concluded that it was appropriate to extrapolate the clinical-effectiveness data from the CoaguChek system to the INRatio2 PT/INR monitor. Please see sections 6.3 and 6.4 of the guidance. The Committee considered your comment and decided to change section 6.5 of the

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: LEVEL OF EVIDENCE

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
				guidance
3	Consultee 1: Roche Diagnostics	Section 6|Comment on Section 6: Considerations	The economic analysis and the recommendations rely on the assumption of equal clinical effectiveness of the systems (CoaguChek XS and InRatio2/INR) and equal resource use. Clinical effectiveness data from randomized controlled trials is however only available for the CoaguChek system. The fact that both monitors were found comparable to laboratory-based INR testing in terms of precision and accuracy does not imply equal clinical benefits in practice. As acknowledged in 6.5, the usability of the monitor influences outcomes. Resource use may also be different: an NHS report (CEP 2006) found test failure rates of 20-30% for InRatio, which increases strip costs and may affect patient confidence and continuation of self-monitoring. Continuation and success may also be affected by the requirements for almost double the blood volume with the InRatio system compared to CoaguChek XS.	Thank you for your comment The Committee considered the evidence that showed the 2 coagulometers had a broadly similar performance in precision and accuracy with regard to time in therapeutic range measurement when compared with the gold standard of laboratory-based INR testing and therefore concluded that it was appropriate to extrapolate the clinical-effectiveness data from the CoaguChek system to the INRatio2 PT/INR monitor. Please see sections 6.3 and 6.4 of the guidance. The Committee considered your comment and decided to change section 6.5 of the

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: LEVEL OF EVIDENCE

Comment number	Name and organisation	Section number	Comment	NICE/EAG considerations
				guidance

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: EQUIVALENCE OF COAGUCHEK VERSIONS

4	Consultee 3: Atrial Fibrillation Guideline Development Group	Section 3|Comment on Section 3: The clinical need and practice	Pgs 31-32: Committee concluded that it was appropriate to pool the results of trials using different versions of the CoaguChek system and that these pooled results could demonstrate the clinical effectiveness of self-monitoring using the CoaguChek XS version of the system. Could the committee please justify this decision given that only 2 trials used the XS system which has a completely different INR end-point detection to the S system?	Thank you for your comment which the Committee considered. The Committee noted that there are substantial technical differences between the CoaguChek S system and the CoaguChek XS system and heard from clinical specialists and the manufacturer that changes had been made to the different versions to improve reliability and accuracy. The Committee considered the performance of the CoaguChek S and XS systems compared with the gold standard of laboratory-based INR testing and noted that the precision and accuracy of the 2 CoaguChek versions correlated with that of laboratory-based measurements. The Committee concluded that results from the

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: EQUIVALENCE OF COAGUCHEK VERSIONS

				CoaguChek XS system were likely to be at least as good as those obtained from trials in which previous versions of the system were used. Please see section 6.3 of the guidance.

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: ASSESSMENT OF EVIDENCE

5	Consultee 3: Atrial Fibrillation Guideline Development Group	Section 3|Comment on Section 3: The clinical need and practice	Pg 29: However, the ICERs for the CoaguChek XS system and the INRatio2 PT/INR monitor only rose above Â£20,000 per QALY gained when the baseline time in therapeutic range was set at greater than 72.6%. Could they please clarify that this means that self-management is only cost-effective if routine care provides a TTR of less than 72.6% and whether this is clinic based or patient based?	Thank you for your comment which the Committee considered. A further analysis was carried out for the atrial fibrillation cohort using the baseline risks seen for participants with better INR control in standard care, assuming a constant relative risk reduction for thromboembolic events associated with self-monitoring. As the INR time in therapeutic range increased in the control group, and the baseline risk of thromboembolic events consequently dropped, the cost effectiveness of self-monitoring also decreased. However, the ICERs for the CoaguChek XS system and the INRatio2 PT/INR monitor only rose above £20,000 per QALY gained when the baseline time

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: ASSESSMENT OF EVIDENCE

				in therapeutic range was set at greater than 72.6%
6	Consultee 3: Atrial Fibrillation Guideline Development Group	Section 4|Comment on Section4: The diagnostics tests	Pg 33: The Committee concluded that the high standard of coagulation control in the control arm of the trial may not reflect general UK clinical practice and so it was plausible that the increase in time in therapeutic range would lead to a statistically significant reduction in clinical adverse events if compared with UK standard coagulation control practice. Could the committee please justify this conclusion given that they use different assumptions within the economic analysis?	Thank you for your comment which the Committee considered. The Committee discussed the impact of 1 large trial by Matchar et al. (2010) (see section 6.6) on the cost effectiveness of self-testing and noted that although this trial did not show a reduction in clinical adverse events, it did show an increase in the time in therapeutic range. The Committee discussed the impact on the ICERs for self-testing if the economic model was driven by time in therapeutic range rather than adverse events. The Committee concluded that self-testing may be more cost effective if the model had been

				based on time in therapeutic range. The Committee also considered the costs of self-managing and self-testing and noted that self-testing was more expensive because of higher administration costs. The Committee heard from the External Assessment Group that if the pooled-effect estimates from self-monitoring were applied to self-testing, self-testing would become cost effective even with the higher administration costs this incurred. The Committee concluded that it was likely that the increase in time in therapeutic range shown for self-testing in the trial would lead to a reduction in adverse events compared with standard clinical practice in the UK. The Committee therefore concluded that it was likely that the clinical

				benefits of self-testing had been underestimated in the economic analyses and that both self-testing and self-managing were cost effective. Please see sections 6.6 and 6.9 of the guidance

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: QUALITY ASSURANCE

7	Consultee 1: Roche Diagnostics	Section 1|Comment on Section 1: Provisional recommendations	Section 1.4 should mention the need for internal and external quality control assurance (comment to section 6.15).	Thank you for your comment. The Committee considered your comment and decided to change section 1.4 of the guidance.
8	Consultee 1: Roche Diagnostics	Section 6|Comment on Section 6: Considerations	For the CoaguChek XS systems an established NEQAS EQA scheme exists (Kitchen 2012). Parallel testing on the same reagents is well established for CoaguChek. It is not clear whether there is a specific scheme for InRatio2/INR and if parallel tests on different reagents lead to equally robust quality assurance.	Thank you for your comment. The Committee considered your comment and decided to change section 1.4 of the guidance.

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: POPULATION

9	Consultee 2: AntiCoagulation Europe	Section 1|Comment on Section 1: Provisional recommendations	As stated throughout this consultation, Â ACE raises concerns over limiting recommendation to AF and heart disease as it discriminates against those individuals who need long term warfarin treatment for other thrombophilia conditions(some which may be inherited) ACE acknowledges that the current Management of VTE guidelines state that people should not be routinely offered the choice of self monitoring for VTD prevention (CG 144 section 1.4.1) In section 1.2.5 of the VTD guidelines, it refers to extending anticoagulant treatment beyond 3 months. People who may be advised to undertake longterm anticoagulation therapy will be disadvantaged if they cannot access or have choice over managing their treatment as and when it is convenient for them to check their INR levels. Â There is clinical evidence that people who self -manage can obtain higher TTR levels reducing their risk of further clots. The VTE guidelines are due for review in 2015 and we trust that in the event of these proposed guidelines being restricted to the two conditions; the VTD review will offer all patients choice and access to self monitoring if the patient selects to remain on warfarin as treatment for any condition	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases. Details on updating the clinical guideline can be found in clinical guideline 144.
10	Consultee 2: AntiCoagulation Europe	Section 3|Comment on Section 3: The	3.4 As mentioned in section 1, acknowledging that there are a number of conditons but focusing on AF and Heart failure to the exclusion of other conditions 'infers' that other long term warfarin users are	Thank you for your comment which the Committee considered.

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: POPULATION

		clinical need and practice	potentially at less risk and their chronic health conditions are not as important a consideration as AF or Heart disease. Those requiring long term treatment for the prevention of blood clots Â would have been advised of their risk and the importance of embarking on anticoagulation therapy to avoid further Â clotting episodes. If people cannot access the devices and/or will be denied the ability to obtain the strips on prescription then they should be offered the choice of staying on warfarin and commiting to the regular monitoring protocols offered in secondary and primary care or the alternative, if eligible, of being offered the opportunity to start treatment with a NICE Approved new oral anticoagulant which does not require Â the demands of regular INR monitoring	The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases. Details on updating the clinical guideline can be found in clinical guideline 144.
11	Consultee 2: AntiCoagulation Europe	Section 6|Comment on Section 6: Considerations	6.14 'The Committee concluded that, because the new oral anticoagulants would not be suitable for all people who need anticoagulant therapy, and there are many people who will receive warfarin therapy rather than new oral anticoagulant therapy, self-monitoring coagulometers are still of clinical importance to the NHS and patients' The Committee's conclusions are not based on looking at the 'whole' warfarin dependent population who could benefit from managing their	Thank you for your comment which the Committee considered. The scope of the diagnostics guidance is for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: POPULATION

			health effectively with a coagulometer. This comment does not fairly reflect the impact on people who fall outside of the proposed indications and therefore how can Â 'clinical importance to the NHS and patients' be qualifed when some patients will not be eligible to self monitor simply because their conditions are not included Â under the proposed guidelines. If the Committee reviewed it's decision here, we suspect that the floodgates would hardly open but it would be deemed fair and equitable for all those who Â currently need to take Â long term warfarin (and may not have any other choice of treatment) to obtain the freedom and control to manage their risk of clotting with a device available for this purpose.	fibrillation or heart valve disease. NICE clinical guideline 144 provides guidance on monitoring coagulation status in people with venous thromboembolic diseases. Details on updating the clinical guideline can be found in clinical guideline 144.

Self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease: point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor)

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: NOACs

12	Consultee 5: Bayer	Section 6|Comment on Section 6: Considerations	In relation to the ?considerations? regarding the new oral anticoagulants (NOACs), we would like to make the following comments about rivaroxaban as specified in the Summary of Product Characteristics (SmPC): ? When converting patients from VKAs to rivaroxaban, INR values will be falsely elevated after the intake of rivaroxaban. The INR is not valid to measure the anticoagulant activity of rivaroxaban, and therefore should not be used. Whilst a specific reversal agent antagonising the pharmacodynamic effect of rivaroxaban is not available, administration of a specific procoagulant reversal agent such as prothrombin complex concentrate (PCC), activated prothrombin complex concentrate (APCC) or recombinant factor VIIa (r-FVIIa) can be considered for the management of bleeding. There is no need for monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine. However, if clinically indicated rivaroxaban levels can be measured by calibrated quantitative anti-factor Xa tests. Bayer plc. SmPC, Xarelto 20mg film-coated tablets. Last updated: 06/01/2014. Available at: http://www.medicines.org.uk/emc/medicine/25586/SPC/Xarelto+20mg+film-coated+tablets/	Thank you for your comment. The Committee considered your comment and decided to change section 6.14 of the guidance.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: OTHER COMMENTS

13	Consultee 4: Alere Ltd	Section 4|Comment on Section4: The diagnostics tests	Please add to Section 4.9: Test strips are supplied in quantities of 12 or 48 strips, are individually foil wrapped and can be stored at room temperature.	Thank you for your comment. The Committee considered your comment and decided to change sections 4.4 and 4.9 of the guidance.
14	Consultee 1: Roche Diagnostics	Section 8|Comment on Section 8: Related NICE guidance	This section could benefit from a reference to the updated NICE clinical guideline for atrial fibrillation, currently in development. It would be very beneficial for clinicians and patients to incorporate the final recommendations of this assessment in verbatim in the updated to raise awareness for INR self-monitoring.	Thank you for your comment which the Committee considered. NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice. The NICE clinical guideline on atrial fibrillation refers to the diagnostics guidance on self‑monitoring of vitamin K antagonist therapy
15	Consultee 6: AF Association		We welcome the update and the recommendation by NICE to offer this option if: • the patient prefers this form of testing and • the patient or their carer is both physically and cognitively able to do the self-monitoring effectively.	Thank you for your comment.

Point-of-care coagulometers (the CoaguChek XS system and the INRatio2 PT/INR monitor) for self-monitoring coagulation status in people on long-term vitamin K antagonist therapy who have atrial fibrillation or heart valve disease

CONSULTATION 2

Diagnostics Consultation Document – Comments
Diagnostics Advisory Committee date: 13 May 2014

THEME: OTHER COMMENTS