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HOW DOES STAKEHOLDER CONSULTATION INFORM THE DEVELOPMENT OF NICE CLINICAL GUIDELINES? THE EXAMPLE OF ATRIAL FIBRILLATION: DIAGNOSIS AND MANAGEMENT

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BACKGROUND

- NICE published an updated guideline for 'Atrial Fibrillation: Diagnosis and Management' (NG196)[1] on 27 April 2021, which replaced former guideline CG180
- As part of the guideline update, NICE reviewed the recommendations for anticoagulation for the prevention of stroke, including the use of four direct acting oral anticoagulants (DOACs) which are a well-established treatment option for the prevention of stroke and other thromboembolic events in non-valvular atrial fibrillation (NVAF) patients
- Stakeholder consultation is an integral part of the NICE clinical guideline development process – comments received from stakeholders are a vital part of the robust quality-assurance and peer-review process[2]
- The NG196 guideline for Atrial Fibrillation underwent consultation during September–November 2020 and provided stakeholders (such as industry, clinical, policy and patient experts) the opportunity to review the draft recommendations and provide comment
- Stakeholders had the opportunity to comment on all aspects of the draft guideline, including draft recommendations for the use of DOACs for the prevention of stroke
  - Contrary to the original CG180 recommendation, the draft (pre-consultation) guideline favoured the use of twice-daily options (apixaban and dabigatran) over once-daily options (edoxaban and rivaroxaban): *"1.6.5 If apixaban and dabigatran are not tolerated in people with atrial fibrillation, offer anticoagulation with either edoxaban or rivaroxaban"*[3]
  - The suggested move towards a preference for the twice-daily DOACs was underpinned by research by Sterne *et al.* (2017)[4] that assessed the relative clinical- and cost-effectiveness of the four available DOACs
- Additional documents, including the Sterne *et al.* evidence review materials, were made available for stakeholder review/critique during the consultation period

OBJECTIVE

- The objective of this analysis was to perform a structured review of the consultation stakeholder comments[4] received by NICE relating to the use of DOACs in the prevention of stroke, and assess if the views expressed by stakeholders were reflected in the final NG196 guidance

METHODS

- Stakeholder responses were extracted (from publicly available material on the NICE website)[4] if they commented on the draft recommendation on the use of DOACs for stroke prevention
- The following stakeholder aspects were analysed
  - Number and type of stakeholders who responded
  - Specific views/concerns raised
  - Stakeholder responses were also categorised, with frequency of mention captured, based on whether they were supportive/neutral/advocated changes to the draft recommendation for preferential use of DOACs
- NICE's response to stakeholders (related to DOAC recommendation) was assessed and final NICE guideline NG196 was reviewed to determine whether stakeholder comments received during consultation were reflected

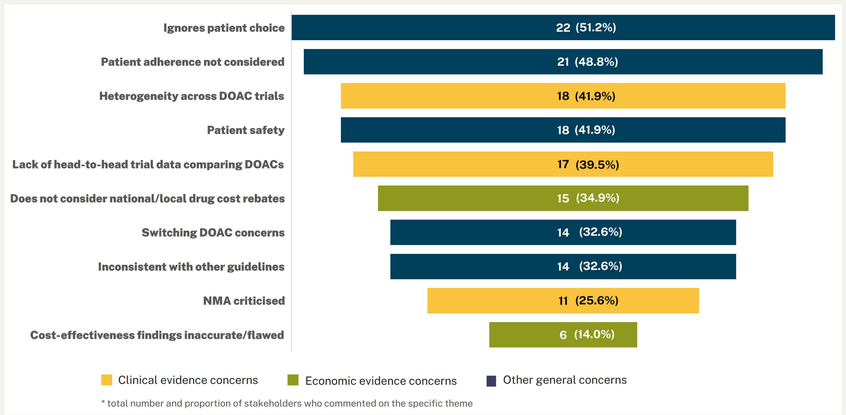
RESULTS

- A total of 43 stakeholders commented on the DOAC recommendations (**Table 1**)
  - 1 stakeholder (pharmaceutical company) was supportive of the draft recommendation favouring the twice-daily DOACs
  - 2 stakeholders were neutral (one from a pharmaceutical company and one from a professional association)
  - The majority of stakeholders (N=40; 93%) expressed concern over the draft DOAC recommendation favouring the twice-daily DOACs
  - The highest frequency of response was received from clinical commissioning groups (23.3%) followed by NHS trusts (20.9%). Interestingly, all expressed concern over the draft DOAC recommendation
- Stakeholders expressed their specific views on the draft DOAC recommendation which included key concerns related to the clinical and economic evidence presented by Sterne *et al.* as well as wider concerns related to favouring twice-daily DOACs (**Figure 1**)

Table 1 List of stakeholders (by type) who commented on the draft recommendation on DOAC use favouring twice-daily DOACs

Stakeholder type	Total number by type (%)	View on draft DOAC use recommendation		
		Supportive	Neutral	Concerned
Clinical commissioning group	10 (23.3%)			10 (23.3%)
NHS trust	9 (20.9%)			9 (20.9%)
Patient organisation / charity	5 (11.6%)			5 (11.6%)
Professional organisation	5 (11.6%)		1 (2.3%)	4 (9.3%)
Pharmaceutical company	4 (9.3%)	1 (2.3%)	1 (2.3%)	2 (4.7%)
Government department / agency	2 (4.7%)			2 (4.7%)
Health board	2 (4.7%)			2 (4.7%)
Regional evidence-based guidance group	2 (4.7%)			2 (4.7%)
Academic Health Science Network	1 (2.3%)			1 (2.3%)
District general hospital	1 (2.3%)			1 (2.3%)
Formulary committee	1 (2.3%)			1 (2.3%)
Local network	1 (2.3%)			1 (2.3%)
	43 (100%)	1 (2.3%)	2 (4.7%)	40 (93.0%)

Figure 1 Key themes raised by stakeholders* regarding draft recommendation on DOAC use



* total number and proportion of stakeholders who commented on the specific theme

- Other views of interest
  - 14 stakeholders expressed concerns related to switching from once-daily to twice-daily DOACs due to current limitations in resource, budget and capacity in the NHS
  - 14 stakeholders also highlighted that the draft DOAC recommendations are inconsistent with other DOAC guidelines including NICE technology appraisals for DOACs, Medicines Optimisation guidelines, All Wales Advice on oral anticoagulation for NVAF, as well as other well recognised international guidelines such as those published by the ESC and EMA
  - One stakeholder commented on errors identified in the health economic model code
- Stakeholder impact on NICE guideline NG196
  - In the final guideline NG196 (published in April 2021), NICE reverted to recommending use of DOACs equally: "*Recommendations 1.6.3 and 1.6.4 [of NG196 guideline] have been amended and now recommend any licensed DOAC.*"[5]
  - This recommendation was made using the NHS List prices of the four NICE recommended DOAC treatment options and does not consider any national/regional/local commercial offers
  - Within the NICE stakeholder comments document and the final guideline, NICE included expressions of agreement from the NICE committee regarding the comparative clinical effectiveness and cost-effectiveness concerns raised by stakeholders

"On further discussion, the committee accepted that there were possible limitations of the analysis by Lopez-Lopez/Sterne that made it difficult to be confident of the validity or precision of the NMA estimates. The health economic model has been revised to account for an error in the coding for the annual cost of stroke and an error in the probabilistic sensitivity analysis sampling. As a consequence of these revisions the credible intervals are now wider and the results more uncertain regarding which DOAC(s) are the most clinically and cost effective. The committee therefore are no longer confident to recommend a specific DOAC or DOACs." NICE response to stakeholders comments[5]

CONCLUSIONS

- Stakeholder comments received during the guideline development process highlighted limitations and errors within the body of evaluated evidence which led to the committee no longer being confident to recommend apixaban or dabigatran as preferred options
- Key themes emerged from the stakeholder comments with expressions of agreement from the NICE committee seen within final guideline documents – showing that stakeholders views were impactful and resulted in a change to the draft DOAC recommendation
- The final recommendation (based on NHS List prices) for any licensed DOAC for the prevention of stroke is in line with other European sources including the ESC 2020 guidelines[6] and an EMA-funded real-world study[7] which were both highlighted by stakeholders
- Our analyses emphasise the importance of a rigorous consultation exercise as part of the NICE clinical guideline process, demonstrating that NICE gives significant consideration to the views of stakeholders when developing evidence-based guidelines
- The development of NG196 provides an example of the very significant changes to draft recommendations that can result from stakeholder consultation during guideline development

QUOTES FROM FINAL PUBLISHED NICE GUIDELINE (NG196)

"Each anticoagulant has different risks and benefits that should be considered and fully discussed with the person as part of informed shared decision making."

"The committee had concerns over the lack of head-to-head comparisons, differences in the study populations and uncertainties in the economic model."

The committee *"stressed the importance of adherence and factors that might affect this, such as dosing frequency, when making the decision [on DOAC selection]"*

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