DECIDE
Developing and Evaluating Communication strategies to support Informed Decisions and practice based on Evidence
GRADE

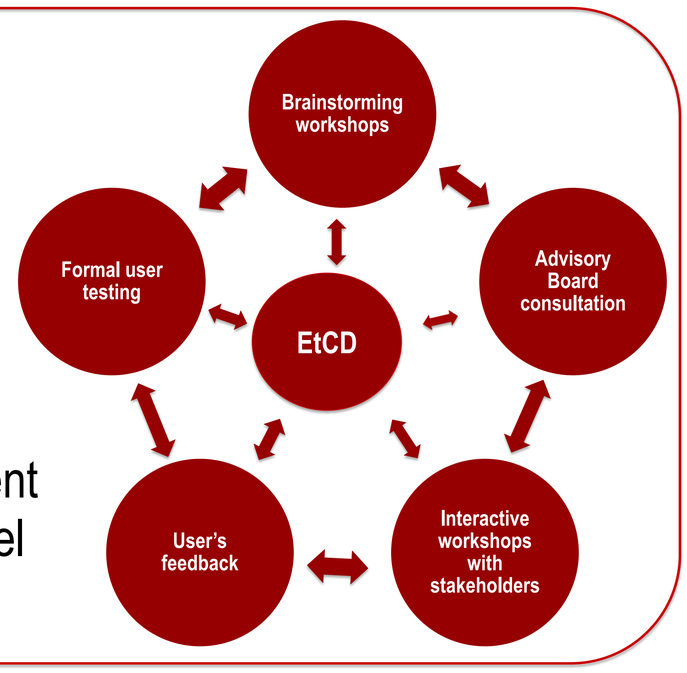
Work Package 2

Policymaker and manager focussed strategies for communicating evidence-based recommendations

Going from evidence to coverage decision

Objective: Development of *tools* and *strategies* targeted to WP2's audience: policy makers, managers and their support staff with responsibility for making coverage decisions. These coverage decisions are defined as decisions by third party payers (public or private health insurers) about whether and how much to pay for drugs, tests, devices or services and under what conditions and can take place at national and/or regional level depending on the type of interventions.

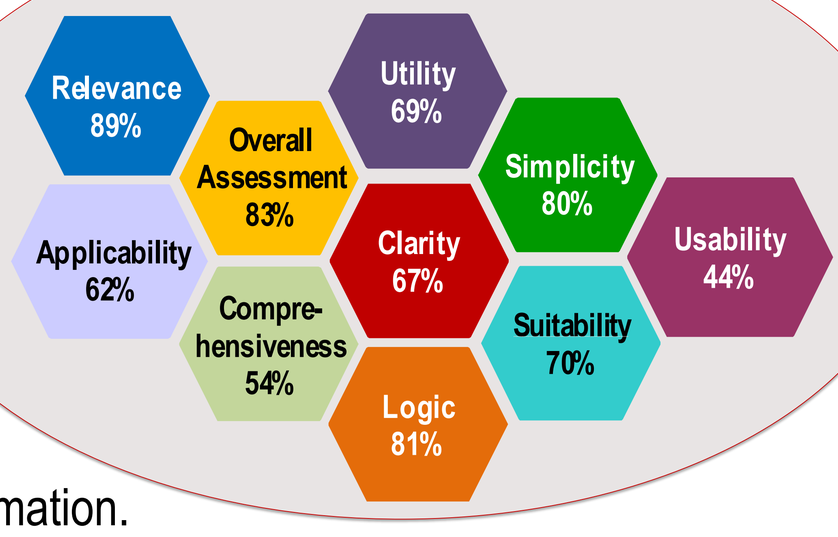
Methods: The initial development of an optimal presentation format was based on the work of the GRADE working group.
The **development process** includes different strategies used in parallel and iteratively.



Results

- 7 Frameworks developed:
  - 3 on drugs (bevacizumab+Paclitaxel , Palivizumab, NOACs)
  - 3 on high cost technologies (MRI, DUS, Da Vinci Robot)
  - 1 on device (Inferior vena cava filter)
- 6 National and International workshops organised

Users' feedbacks:



Evidence to Coverage Decision Framework (EtCD)

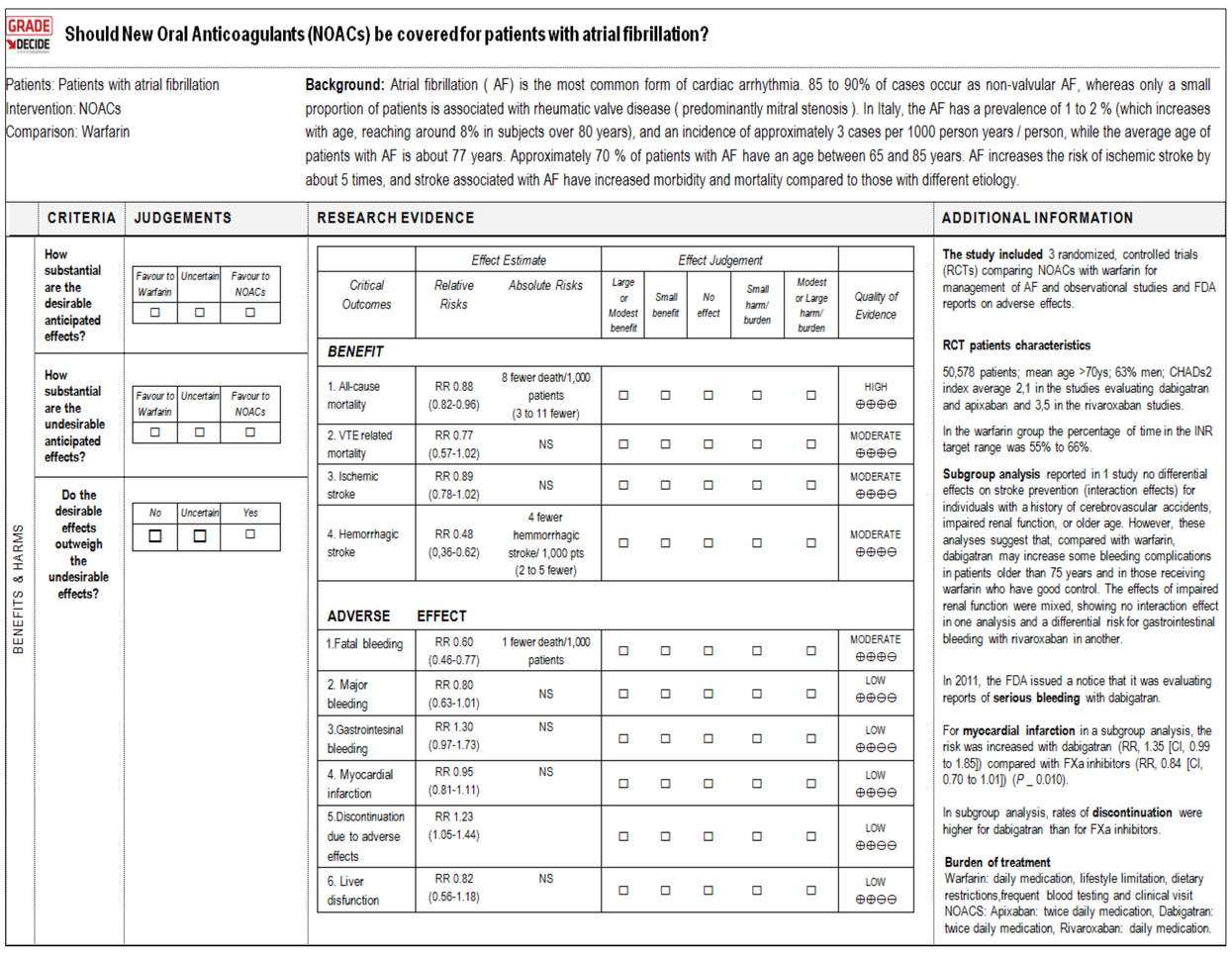
The EtCD is structured in 3 sections:

Section 1: clinical question, PICO, background information.

Section 2: domains, criteria, judgement, research evidence, additional information.

Section 3: balance between desirable and undesirable consequences, decision, restrictions, justification and implementation considerations.

Domain	Criteria
Problem	Is the problem a priority?
Value	Is there important uncertainty about how much people value the main outcomes?
Certainty of the evidence	What is the overall certainty of the evidence of effects?
Benefits & Harms	How substantial are the desirable anticipated effects? How substantial are the undesirable anticipated effects? Do the desirable effects outweigh the undesirable effects?
Resource use	How large are the resource requirements? How large is the incremental cost relative to the net benefit?
Equity	What would be the impact on health inequities?
Acceptability	Is the option acceptable to key stakeholders?
Feasibility	Is the option feasible to implement?



GRADE DECIDE **Should New Oral Anticoagulants (NOACs) be covered for patients with atrial fibrillation?**

Patients: Patients with atrial fibrillation
Intervention: NOACs
Comparison: Warfarin

Background: Atrial fibrillation (AF) is the most common form of cardiac arrhythmia. 85 to 90% of cases occur as non-valvular AF, whereas only a small proportion of patients is associated with rheumatic valve disease (predominantly mitral stenosis). In Italy, the AF has a prevalence of 1 to 2 % (which increases with age, reaching around 8% in subjects over 80 years), and an incidence of approximately 3 cases per 1000 person years / person, while the average age of patients with AF is about 77 years. Approximately 70 % of patients with AF have an age between 65 and 85 years. AF increases the risk of ischemic stroke by about 5 times, and stroke associated with AF have increased morbidity and mortality compared to those with different etiology.

BENEFITS & HARMS

CRITERIA	JUDGEMENTS
How substantial are the desirable anticipated effects?	Favour to Warfarin ☐ | Uncertain ☐ | Favour to NOACs ☐
How substantial are the undesirable anticipated effects?	Favour to Warfarin ☐ | Uncertain ☐ | Favour to NOACs ☐
Do the desirable effects outweigh the undesirable effects?	No ☐ | Uncertain ☐ | Yes ☐

RESEARCH EVIDENCE

Critical Outcomes	Effect Estimate: Relative Risks	Effect Estimate: Absolute Risks	Effect Judgement: Large or Modest benefit	Small benefit	No effect	Small harm/ burden	Modest or Large harm/ burden	Quality of Evidence
BENEFIT								
1. All-cause mortality	RR 0.88 (0.82-0.96)	8 fewer death/1,000 patients (3 to 11 fewer)	☐	☐	☐	☐	☐	HIGH ⊕⊕⊕⊕
2. VTE related mortality	RR 0.77 (0.57-1.02)	NS	☐	☐	☐	☐	☐	MODERATE ⊕⊕⊕⊖
3. Ischemic stroke	RR 0.89 (0.78-1.02)	NS	☐	☐	☐	☐	☐	MODERATE ⊕⊕⊕⊖
4. Hemorrhagic stroke	RR 0.48 (0,36-0.62)	4 fewer hemmorrhagic stroke/ 1,000 pts (2 to 5 fewer)	☐	☐	☐	☐	☐	MODERATE ⊕⊕⊕⊖
ADVERSE EFFECT								
1.Fatal bleeding	RR 0.60 (0.46-0.77)	1 fewer death/1,000 patients	☐	☐	☐	☐	☐	MODERATE ⊕⊕⊕⊖
2. Major bleeding	RR 0.80 (0.63-1.01)	NS	☐	☐	☐	☐	☐	LOW ⊕⊕⊖⊖
3.Gastrointesinal bleeding	RR 1.30 (0.97-1.73)	NS	☐	☐	☐	☐	☐	LOW ⊕⊕⊖⊖
4. Myocardial infarction	RR 0.95 (0.81-1.11)	NS	☐	☐	☐	☐	☐	LOW ⊕⊕⊖⊖
5.Discontinuation due to adverse effects	RR 1.23 (1.05-1.44)		☐	☐	☐	☐	☐	LOW ⊕⊕⊖⊖
6. Liver disfunction	RR 0.82 (0.56-1.18)	NS	☐	☐	☐	☐	☐	LOW ⊕⊕⊖⊖

ADDITIONAL INFORMATION

The study included 3 randomized, controlled trials (RCTs) comparing NOACs with warfarin for management of AF and observational studies and FDA reports on adverse effects.

RCT patients characteristics

50,578 patients; mean age >70ys; 63% men; CHADs2 index average 2,1 in the studies evaluating dabigatran and apixaban and 3,5 in the rivaroxaban studies.

In the warfarin group the percentage of time in the INR target range was 55% to 66%.

Subgroup analysis reported in 1 study no differential effects on stroke prevention (interaction effects) for individuals with a history of cerebrovascular accidents, impaired renal function, or older age. However, these analyses suggest that, compared with warfarin, dabigatran may increase some bleeding complications in patients older than 75 years and in those receiving warfarin who have good control. The effects of impaired renal function were mixed, showing no interaction effect in one analysis and a differential risk for gastrointestinal bleeding with rivaroxaban in another.

In 2011, the FDA issued a notice that it was evaluating reports of **serious bleeding** with dabigatran.

For **myocardial infarction** in a subgroup analysis, the risk was increased with dabigatran (RR, 1.35 [CI, 0.99 to 1.85]) compared with FXa inhibitors (RR, 0.84 [CI, 0.70 to 1.01]) (*P* _ 0.010).

In subgroup analysis, rates of **discontinuation** were higher for dabigatran than for FXa inhibitors.

Burden of treatment
Warfarin: daily medication, lifestyle limitation, dietary restrictions,frequent blood testing and clinical visit
NOACS: Apixaban: twice daily medication, Dabigatran: twice daily medication, Rivaroxaban: daily medication.

References:

- Treweek S, Oxman AD, Alderson P, Bossuyt PM, Brandt L, Brożek J, Davoli M, Flottorp S, Harbour R, Hill S, Liberati A, Liira H, Schünemann HJ, Rosenbaum S, Thornton J, Vandvik PO, Alonso-Coello P; DECIDE Consortium Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice Based on Evidence (DECIDE): protocol and preliminary results. Implement Sci. 2013 Jan 9;8:6.
- Parmelli E, Amato L, Saitto C, Davoli M; Gruppo di Lavoro "DECIDE Italia. DECIDE: developing and evaluating communication strategies to support informed decisions and practice based on evidence. Recenti Prog Med. 2013 Oct;104(10):522-31.

WP2 Group: Laura Amato, Luciana Ballini, Massimo Brunetti, Roberto D'Amico, Marina Davoli, Luca De Fiore, Rossana De Palma, Eliana Ferroni, Marien Gonzalez Lorenzo, Nicola Magrini, Lorenzo Moja, Francesco Nonino, Salvatore Panico, Donato Papini, Elena Parmelli, Vanna Pistotti, Silvia Pregno, Carlo Saitto, Gianni Virgili, Gustavo Zanoli.

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no 258583.