NEW ORAL ANTICOAGULANTS AND ATRIAL FIBRILLATION

Differentiating between “no proof of difference” and “proof of no difference” for new oral anticoagulants

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In the past few years, network meta-analysis has increasingly been used in research on comparative effectiveness.\textsuperscript{1} Recently, 13 meta-analyses of new oral anticoagulants for the prevention of stroke and systemic embolism in patients with atrial fibrillation have been conducted and published over a short time.\textsuperscript{2} Although simultaneous publication of numerous meta-analyses on the same subject has disadvantages in terms of scientific redundancy,\textsuperscript{3} it has the advantage that the degree of concordance of individual results can later be verified.\textsuperscript{4}

In Italy, the relative effectiveness of new oral anticoagulants in atrial fibrillation has attracted the interest of scientific societies, and two position papers have been published on the therapeutic equivalence of these agents.\textsuperscript{5} \textsuperscript{6} Italian professionals, scientific societies, and decision makers are currently interested in therapeutic equivalence because of a national regulation that was issued at the end of 2012.\textsuperscript{7} Under this new regulation, within the NHS, local tendering for drugs belonging to the same pharmacological class is no longer allowed unless our national medicines agency certifies that the agents are therapeutically equivalent.

All of the studies in the 13 meta-analyses mentioned above were aimed at demonstrating “no proof of difference” among these drugs and not at assessing equivalence (“proof of no difference”).\textsuperscript{8} One exception is a study that tested the equivalence margins of these drugs but applied this analysis to an endpoint of safety, and not to the “typical” endpoints of effectiveness (stroke and systemic embolism).\textsuperscript{9}

From a practical and scientific perspective, the ongoing Italian experience of managing new oral anticoagulants emphasises that evidence based studies should focus more on differentiating between “no proof of difference” and “proof of no difference.”\textsuperscript{10}

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