Title	Relative versus absolute drug-therapy benefits and safety: Lessons from ARISTOTLE
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Relative versus absolute drug-therapy benefits and safety: Lessons from ARISTOTLE

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Introduction: ARISTOTLE was a double-blind, double-dummy, randomised clinical trial in patients with atrial fibrillation and one other risk factor for stroke, and compared oral anticoagulation with warfarin (targeted to achieve an international normalised ratio [INR] of 2.0 to 3.0) versus apixaban (5 mg x 2 daily).[1] Whilst apixaban conferred significantly greater efficacy (stroke/embolic event prevention) and was safer (less frequent bleeding), consideration of these issues in relative terms can be uninformative. To appreciate the overall cost-effectiveness of such treatments, absolute benefits should be considered.

Methods & Results: As previously described,[2] we therefore derived unadjusted estimates of relative risk (RR) and number needed to treat (NNT)/year values for prophylaxis with apixaban compared to warfarin for principal efficacy and safety endpoints published in ARISTOTLE (Table).

No. of patients (median follow-up)	Pre-specified endpoint	%RR (95% confidence interval)	NNT/year (95% confidence interval)
Apixaban - 9120	Stroke / systemic embolism	80 (66 to 96)	303 (169 to 1501)
Warfarin - 9003	Haemorrhagic stroke	51 (35 to 75)	428 (273 to 987)
(1.8 years)	Death from any cause	90 (80 to 100)	238 (119 to ∞)

Discussion & Conclusion: Whilst the favourable RR values pertaining to apixaban for stroke / systemic embolism, haemorrhagic stroke, and death seem striking, in absolute terms (NNT/year) the benefits appear less impressive. Moreover, treatment with the newer oral anticoagulants is currently much more costly than using warfarin, though the long-term impact of embolic events and major bleeds are both financially and emotionally devastating. Thus, when allocating resources for thromboembolic prophylaxis in patients with atrial fibrillation, the meagre absolute number of additional events prevented with apixaban must be weighed against the consequential long-term accrued savings as well as those from avoidance of INR monitoring.

References

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The effects of cigarette smoke on lipopolysaccharide-mediated inflammatory responses in airway epithelial cells

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Introduction: Chronic obstructive pulmonary disease (COPD) is a highly prevalent disease. Cigarette smoke is the major cause by stimulating the production of inflammatory chemokines, such as interleukin-8 (IL-8) and monocyte chemoattractant protein-1 (MCP-1), causing chronic inflammation in the airways. However, cigarette smoking might induce an immunosuppressive effect upon lung infection by bacteria, such as *Pseudomonas aeruginosa* during acute exacerbation in COPD, leading to bacteria colonisation in the airways and further chronic inflammation in the airway of COPD.

Methods: Human bronchial epithelial cells (BEAS-2B) were cultured and treated with 2% cigarette smoke medium (CSM), 1 μg/mL lipopolysaccharide (LPS) or in combination for 24 hours. Supernatant was collected and analysed by enzyme-linked immunosorbent assay for the measurements of IL-8 and MCP-1.

Results: Exposure of BEAS-2B cells to 2% CSM induced a significant increase in both IL-8 ($n = 3$; $P < 0.05$), and MCP-1 ($n = 3$; $P < 0.001$) and 1 μg/mL LPS also induced significant increase in IL-8 and MCP-1 ($n = 3$; $P < 0.001$). However, LPS-induced release of IL-8 and MCP-1 was significantly suppressed by 2% CSM ($n = 3$; $P < 0.001$).

Conclusion: Our data demonstrated that both cigarette smoke and LPS alone can induce the release of IL-8 and MCP-1. However, cigarette smoke has immunosuppressive effect as it reduces LPS-induced IL-8 and MCP-1. This immunosuppressive effect of cigarette smoke might be due to the impairment of the immune response of the airway epithelial cells, leading to bacteria colonisation in the airways, hence becoming more prone to infection.