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# North American and British guidelines for anti-thrombotic therapy: are we reaching consensus?

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APLAs: antiphospholipid antibodies
IUGR: intrauterine growth restriction
IPC: intermittent pneumatic compression
IVC: inferior vena caval
LMWH: low-molecular-weight heparin
PE: pulmonary embolism
UFH: unfractionated heparin
VTE: venous thromboembolism

## Introduction

The management of thrombotic conditions, hypercoagulable states, and anticoagulant therapy in pregnant women remains a clinical challenge. Pulmonary embolism (PE) continues to be the leading cause of maternal mortality in the Western world [1–4] and venous thromboembolism (VTE) in pregnancy is an important cause of maternal morbidity [5]. Pregnant women with mechanical heart valves also appear to be at particularly high risk for thromboembolic events, with reported incidences as high as 60% [6]. Many such events present as valve thrombosis, which is associated with mortality rates ranging from 30% to 67% [7]. The use of anticoagulant therapy during pregnancy is also problematic because of the potential for fetal, as well as maternal, complications. Finally, the amount of high quality data upon which to base management decisions in this patient population is limited, with the majority of published reports consisting of uncontrolled studies or case series. Indeed, even when controlled studies are available, they often have important methodological limitations.

Clinical practice guidelines are written to improve patient care by reducing practice variability through the dissemination of recommendations for effective practice based on the best current evidence [8]. Although guidelines may be based on a consensus "expert opinion" or non-systematic review of the literature, evidence-based practice guidelines are developed through a clear definition of questions to be addressed, systematic identification of studies to be included, careful review and evaluation of the quality of available research evidence, and the provision of specific recommendations [8,9]. Consequently, these types of guidelines are much less susceptible to bias.

A number of evidence-based clinical practice guidelines addressing the management of anticoagulant therapy and thrombotic diseases in pregnancy have been commissioned by organizations in North America and the United Kingdom including: the American College of Chest Physicians (ACCP) [10]; the Society of Obstetricians and Gynaecologists of Canada (SOGC) [21]; the Royal College of Obstetricians and Gynaecologists (RCOG) [16–18]; the British Committee for Standards in Haematology (BCSH) – a subcommittee of the British Society of Haematology [12–15]; and

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Table 1
Comparison of guideline grading systems

| Grade/ level | Description |
|---|---|
| **American College of Chest Physicians (ACCP) [10,11]** | |
| | Unlike other systems, the strength of any recommendation is based on the trade-off between benefits, risks, burdens, and costs, as well as the level of confidence in estimates of those benefits and risks; in addition to the quality of the evidence upon which the recommendations are based |
| Grade 1A | Strong recommendation (desirable effects clearly outweigh undesirable effects or vice versa), high quality evidence (consistent evidence from randomized trials without important limitations or exceptionally strong evidence from observational studies) |
| Grade 1B | Strong recommendation (desirable effects clearly outweigh undesirable effects or vice versa), moderate quality evidence (evidence from randomized controlled trials with important limitations – inconsistent results, methodological flaws, indirect or imprecise – or very strong evidence from observational studies) |
| Grade 1C | Strong recommendation (desirable effects clearly outweigh undesirable effects or vice versa), low or very low quality evidence (evidence for at least one critical outcome from observational studies, case series, or from randomized, controlled trials with serious flaws or indirect evidence) |
| Grade 2A | Weak recommendation (desirable effects closely balance with undesirable effects or vice versa), high quality evidence (consistent evidence from randomized trials without important limitations or exceptionally strong evidence from observational studies) |
| Grade 2B | Weak recommendation (desirable effects closely balance with undesirable effects or vice versa), moderate quality evidence (evidence from randomized controlled trials with important limitations – inconsistent results, methodological flaws, indirect or imprecise – or very strong evidence from observational studies) |
| Grade 2C | Weak recommendation (desirable effects closely balance with undesirable effects or vice versa), low or very low quality evidence (evidence for at least one critical outcome from observational studies, case series, or from randomized, controlled trials with serious flaws or indirect evidence) |
| **British Committee for Standards in Haematology (BCSH) [12–15]** | |
| | *See under Royal College of Obstetricians and Gynaecologists* |
| **Royal College of Obstetricians and Gynaecologists (RCOG) [16–18]** | |
| Grade A | Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation |
| Grade B | Requires the availability of well conducted clinical studies but no randomized clinical trials on the topic of recommendation |
| Grade C | Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality |
| **Scottish Intercollegiate Guidelines Network (SIGN) [19,20]** | |
| Grade A | At least one high quality meta-analysis, systematic review of randomized controlled trials or randomized trial with very low risk of bias and directly applicable to the target population OR a body of evidence consisting principally of well-conducted meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with a low risk of bias and demonstrating overall consistency of results |
| Grade B | A body of evidence including high quality systematic review of case control or cohort studies, high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal, directly applicable to the target population and demonstrating overall consistency of results OR extrapolated evidence from at least one high quality meta-analysis, systematic review of randomized controlled trials or randomized trial with very low risk of bias or well-conducted meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with a low risk of bias and demonstrating overall consistency of results |
| Grade C | A body of evidence including well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal, directly applicable to the target population and demonstrating overall consistency of results OR extrapolated evidence from high quality systematic review of case control or cohort studies, high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal |
| Grade D | Non-analytic studies (e.g. case reports or case series) or expert opinion OR extrapolated evidence from well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal |

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