

## Editorial

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# Exploring the iceberg of inappropriateness in hemostasis testing

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Many definitions have been offered for the term ‘appropriateness’ across different English dictionaries, including “something suitable, right or fitting for a particular purpose”, “the quality of being suitable or proper in the circumstances”, and “the quality of being just right for the requirements”. The first common element that prepotently emerges from these definitions is that appropriateness is always defined according to subjective beliefs or convictions, so being vulnerable to change over time and even from culture to culture. The second important aspect refers to the fact that something that is considered appropriate in one specific circumstance may be considered inappropriate in another.

Given the objective challenge to achieve universal consensus about what should be considered appropriate or not in all human activities, the translation of this concept to laboratory medicine in general, and hemostasis testing in particular generates many additional areas of uncertainty. The term ‘appropriateness’ in laboratory medicine conventionally implies a process aimed to improving diagnostic efficiency and clinical effectiveness [1]. To put it simply, increasing the appropriateness of diagnostic testing would allow the optimization of human and economic resources, contextually offering the most useful information for improving patient outcome and maintaining the highest possible degree of safety [2].

A common misconception is that ‘inappropriateness’ may only refer to misuse or overuse of laboratory resources, thus discounting the fact that underutilization may also greatly contribute to an ‘inappropriate’

scenario. A paradigmatic example is the case of an asymptomatic patient presenting with prolonged value of activated partial thromboplastin time for whom only bleeding tests are order, thus overlooking the possibility that the prolonged clotting time may be due to the presence of lupus anticoagulant [3]. In such case, underdiagnosing an antiphospholipid syndrome may expose the patients to a greater risk of thrombosis later in life, especially in combination with other prothrombotic risk factors [4].

There is ongoing debate about the burden of inappropriateness in laboratory diagnostics, as well as on its consequences on health care economics and patient health [5]. Several lines of evidence attest that inappropriate ordering of diagnostics testing may be as high as 70% in clinical practice, the largest part due to inadequate education, lack of reliable guidance in the form of guidelines or recommendations, and medical liability issues, with modest consciousness of the unfavorable consequences deriving from this unfortunate practice [6, 7]. Inappropriate ordering of hemostasis tests not only may erode vast laboratory resources but can also generate tangible health risks, by increasing the likelihood of false-positive or false-negative results, triggering additional and often invasive investigations, or else deranging the managed care [8].

In an interesting study, published in this issue of *Diagnosis* [9], Sarkar et al. carried out a comprehensive review of 200 cases of patients evaluated for hemostatic problems, reassessing all cases to establish the appropriateness of instigated diagnostic tests. Notably, issues related to inappropriateness were uncovered in as many as 155 cases (78%), the vast majority of which (44%) were due to underutilization, 16% due to overutilization, and 18% due to both underutilization and overutilization, of laboratory testing. Overall, inappropriateness was calculated to have caused more than \$220,000 of unnecessary expenditures for the 450-bed local hospital. Translating these figures in a real-world scenario, the consequences are particularly unsettling, especially considering that clinical requests for hemostasis tests may not be evidence-based in the vast majority of patients.

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It could even be proposed that the study reported by Sarkar and colleagues [9] represents just a tip of an iceberg of inappropriate test requests. In this study, the authors randomly selected cases as part of an educational process for local discussion and training. The errors identified captured a vast array of clinical scenarios. A refocus on specific scenarios, for example, factor V Leiden requests, will similarly identify that the vast majority of such requests are inappropriate [10]. A similar specific evaluation into bleeding disorder investigation will doubtless result in similar conclusions [11]. Thus, sometimes, clinicians will order the wrong tests based on confusion or dyslexia related to roman numerals and test usage. Examples include factor (F) XI being ordered instead of FIX, FVII being ordered instead of FVIII, FV being ordered instead of FV Leiden, and FX being ordered instead of the heparin assay antiactivated FX.

Yet, many hurdles need to be overcome for expanding the practice of appropriateness in hemostasis testing. Some potential solutions entail strengthening educational interventions aimed to spread the culture and clinical significance of hemostasis testing among clinicians and laboratory professionals, especially in those laboratories in which coagulation tests are only a minor part of the daily volume of activity. The use of interpretative comments accompanying laboratory reports may also help some clinicians to more accurately interpret the data and guide them to requesting the most appropriate follow-up investigations [12]. Then the use of information technology tools, such as computerized alert system based on retesting intervals [13], may offer a reliable guidance to clinicians for limiting repeated, unnecessary, and virtually inappropriate testing. Finally, there is a wealth of expertise that can be captured in each workplace – specialist scientists and clinicians with specific expertise in hemostasis. Thus, irrespective of all potentially valuable opportunities, enhanced communication between the physicians and the laboratory remains the mainstay for performing the appropriate test, at the right time and with the right cost.

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## References

1. Pansini N, Di Serio F, Tampoia M. Total testing process: appropriateness in laboratory medicine. *Clin Chim Acta* 2003;333:141–5.
2. Lippi G, Mattiuzzi C. The biomarker paradigm: between diagnostic efficiency and clinical efficacy. *Pol Arch Med Wewn* 2015;125:282–8.
3. Poli G, Castiglioni P, Montagnana M, Favaloro EJ, Lippi G. Troubleshooting an isolate prolongation of activated partial thromboplastin time in a patient with acute myocardial infarction—a paradigmatic case report. *Ann Transl Med* 2016;4:426.
4. Favaloro EJ, Wong RC. The antiphospholipid syndrome: diagnosis, pathogenesis, laboratory testing, and management. *Semin Thromb Hemost* 2012;38:299–304.
5. Lippi G, Cervellini G, Plebani M. Less is more, but do not throw out the baby with the bathwater either! *Diagnosis* 2014;1:199–201.
6. Lippi G, Favaloro EJ, Franchini M. Dangers in the practice of defensive medicine in hemostasis testing for investigation of bleeding or thrombosis: part I—routine coagulation testing. *Semin Thromb Hemost* 2014;40:812–24.
7. Plebani M. Defensive medicine and diagnostic testing. *Diagnosis* 2014;1:151–4.
8. Favaloro EJ. The futility of thrombophilia testing. *Clin Chem Lab Med* 2014;52:499–503.
9. Sarkar MK, Botz CM, Laposata M. An assessment of overutilization and underutilization of laboratory tests by expert physicians in the evaluation of patients for bleeding and thrombotic disorders in clinical context and in real time. *Diagnosis* 2017;4:21–6.
10. Favaloro EJ, McDonald D. Futility of testing for factor V Leiden. *Blood Transfus* 2012;10:260–3.
11. Favaloro EJ, Lippi G. Problems in laboratory testing – haemophilia and beyond. *J Thromb Haemost* 2010;8:1119–20.
12. Favaloro EJ, Lippi G. Laboratory reporting of hemostasis assays: the final post-analytical opportunity to reduce errors of clinical diagnosis in hemostasis? *Clin Chem Lab Med* 2010;48:309–21.
13. Lippi G, Brambilla M, Bonelli P, Aloe R, Balestrino A, Nardelli A, et al. Effectiveness of a computerized alert system based on retesting intervals for limiting the inappropriateness of laboratory test requests. *Clin Biochem* 2015;48:1174–6.