Data for a Common Clinical Dilemma

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A patient receiving warfarin for atrial fibrillation experiences worsening of her chronic obstructive pulmonary disease with purulent sputum. You want to start an antibiotic. Her international normalized ratio (INR) has been rock stable at 2.5. Should you adjust the dose of warfarin? Would the answer be different if she was just ill and you were not going to use an antibiotic? Does it depend on the antibiotic? This is a common medicine (warfarin) and a common situation (upper respiratory tract infection), and yet there are no easy real-world answers.

Harnessing the power of linked medical, pharmacy, and laboratory records and an anticoagulation database, Clark and coauthors show that upper respiratory tract infection increases the risk of excessive anticoagulation even without antibiotics, probably because of a combination of eating less, using acetaminophen-containing medications, and developing fever. With antibiotics, the risk increases a bit more, but the difference is not statistically significant. Antibiotics interfering with warfarin metabolism (metronidazole and trimethoprim-sulfamethoxazole) were more likely to result in clinically concerning increases in INR (≥5.0). Of importance to us as clinicians is that most patients had minimal changes in the INR with antibiotics, indicating that we should not lower warfarin dosages preemptively. On the other hand, we can take from this study that patients with respiratory tract illness, especially those receiving an antibiotic that interferes with warfarin metabolism, as well as women, patients with cancer, and those with an elevated baseline INR, are at higher risk for excessive anticoagulation and should have additional INR monitoring.