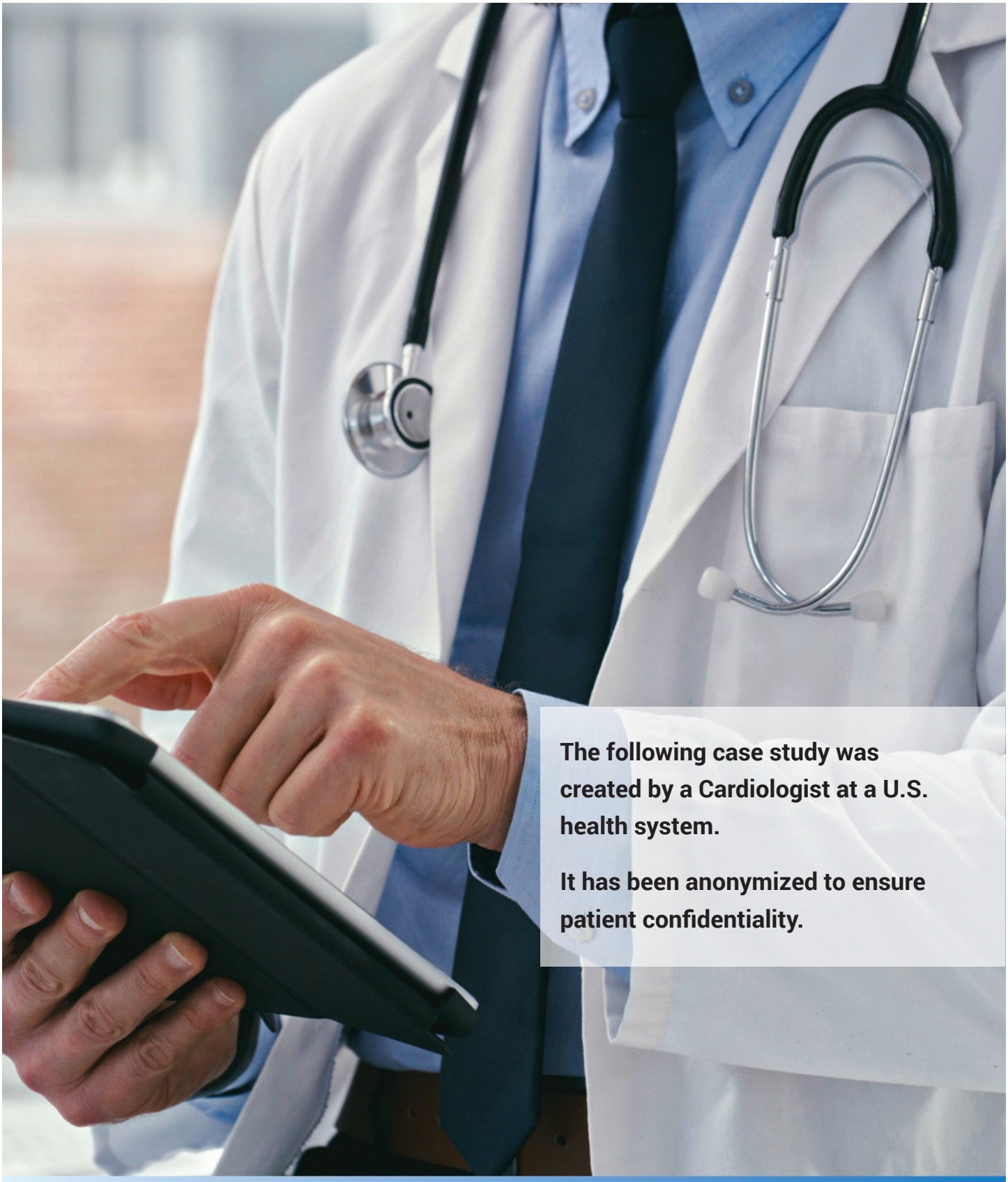
A Compelling Case for Integrated Genomic Decision Support



The following case study was created by a Cardiologist at a U.S. health system.

It has been anonymized to ensure patient confidentiality.

"This afternoon I saw a 59-year-old ICU physician in follow up with hypertension, rheumatoid arthritis, and established coronary artery disease who had recently undergone PCI with stenting of a left anterior descending artery lesion. He was highly motivated to pursue aggressive secondary prevention. At follow-up, his medications included ticagrelor, atorvastatin, bempedoic acid, hydroxychloroquine, nebivolol, and olmesartan. His LDL cholesterol was already well controlled at <50 mg/dL Based on emerging evidence for cardiovascular risk reduction, we discussed adding low-dose colchicine, and the patient wished to proceed."

Shortly after the prescription was written, the pharmacist filling it contacted me. She noted that the combination of ticagrelor and atorvastatin can substantially increase colchicine exposure, raising the risk of serious toxicity—including rhabdomyolysis, pancytopenia, and multiorgan failure. I asked why this interaction had not been flagged more prominently by our existing drug–drug interaction software. She shared her frustration that this limitation is something she encounters repeatedly in routine practice. Because discontinuing ticagrelor was not an option, she recommended switching from atorvastatin to rosuvastatin and dosing colchicine every other day.

At the time these decisions were made, the patient had not yet undergone pharmacogenomic testing. As a result, colchicine dosing would have been adjusted without knowledge of his CYP3A4 or P-glycoprotein (ABCB1) activity—both central to colchicine clearance. Pharmacogenomic testing was then ordered and I asked the patient to hold the colchicine until PGx data is available.This represented a genuine near-miss. Had the patient later developed atrial fibrillation and been treated empirically with diltiazem(common practice)—a potent CYP3A4 and P-glycoprotein inhibitor—colchicine levels could have risen into a profoundly toxic and potentially fatal range, even at what would otherwise be considered a low dose.

This episode involved one patient, one prescriber, one pharmacist, and one afternoon. Harm was avoided only because a highly experienced pharmacist recognized a non-obvious, stacked interaction and intervened in real time. That level of vigilance does not scale.

As we begin to accumulate hundreds (we already have) and soon thousands of pharmacogenic profiles, clinicians will be managing patients with multiple genetic variants interacting with increasingly complex medication regimens. The number of possible drug–gene–drug interactions will become unmanageable for individual clinicians or small expert teams.

"Without computer-assisted, pharmacogenomics-aware clinical decision support that continuously integrates medications, genetics, renal function, age, and evolving clinical context, our health system will be exposed to extraordinary and unnecessary risk. Near-misses like this will not remain near-misses; they will become preventable adverse drug events, some of them catastrophic."

There is an additional scenario that deserves explicit attention because it introduces a new – and largely unrecognized – form of liability: the situation in which pharmacogenomic testing has been performed and results exist, but no clinical software is in place to manage, interpret, and apply those results at the point of care.

In this setting, the health system possesses information indicating altered drug metabolism or transport – such as reduced CYP3A4 or P-glycoprotein activity – but that information is effectively inert. It may exist as a PDF, a scanned report, or a discrete lab result, yet it is not computationally integrated into prescribing workflows. Clinicians are implicitly expected to remember, reinterpret, and manually apply complex genomic data across time, across medications, and across care settings. This expectation is not realistic and does not reflect how modern clinical care must function.

From a risk perspective, this is more dangerous than not testing at all. Once pharmacogenomic data exist, (and it already does), the system can no longer plausibly claim ignorance. If a patient with documented reduced colchicine clearance later experiences toxicity after a predictable drug stack – such as the addition of a CYP3A4 or P-glycoprotein inhibitor – the question will not be whether the interaction was theoretically knowable. The question will be why known genetic risk was not operationalized, surfaced, and acted upon.

"If we continue this process the failure will no longer be one of individual clinical judgment. It will be an institutional failure."

This creates a fundamental shift in liability. Responsibility moves away from individual clinicians and toward the health system itself. Generating pharmacogenomic data without providing the infrastructure to use it implies an institutional decision to create high-complexity, high-risk information without the tools required to manage it safely. That responsibility cannot reasonably be transferred to individual prescribers relying on memory, vigilance, or static alerts.

As pharmacogenomic testing scales, this gap will widen. We will see this in new medications, new specialists become involved, and acute events introduce drugs that were not anticipated at the time of the original prescription. Without automated, continuously updating decision support, previously "safe" regimens can become dangerous overnight – despite the relevant genetic risk having been known all along.

In short, pharmacogenomic testing without integrated clinical decision support (that includes phenoconversion) does not reduce risk. It redistributes it – and amplifies it. It creates a false sense of precision while quietly

increasing exposure to preventable adverse drug events. From both a patient-safety and enterprise-liability standpoint, generating pharmacogenomic data obligates the health system to manage that information intelligently, dynamically, and at scale. Mentioning the enormous cost savings that would accrue seems somewhat superfluous in view of the case described above.

Note: In this real-world example, a provider recognizes the need for continuously updated genomic decision support and notes that genetic testing without workflow integration does not reduce risk on its own. Genetics is rapidly becoming an integral part of medical care, and with proper electronic health record integration can protect both patients and the enterprises that serve them.

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