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Precision Prescribing Under Unequal Genomic Representation: A Normative and Methodological Framework for Artificial Intelligence–Enabled Pharmacogenomics Across Ancestry, Polypharmacy, and Changing Clinical Contexts

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ABSTRACT

Artificial intelligence–enabled pharmacogenomics promises to extend precision prescribing by integrating genomic variation with increasingly rich clinical information. Its validity, however, depends on more than predictive performance. Pharmacogenomic evidence has been generated from populations, variant catalogs, assays, and implementation environments that differ substantially in genomic representation, while the clinical meaning of genotype may change as co-medications, disease state, organ function, and treatment history alter drug exposure and phenotype. This article develops a normative and methodological account of precision prescribing under these conditions. It separates population representation from individual ancestry inference, ancestry from race, germline genotype from current metabolic phenotype, and prediction from clinical action. Unequal genomic representation is treated as an evidentiary problem that affects which variants are discovered, characterized, measured, and validated, whereas polypharmacy and changing clinical context are treated as interpretation problems that can modify the translation from genotype to expected drug response. The resulting argument is that representation-aware pharmacogenomic systems require explicit evidence provenance, patient-level genomic characterization, context-sensitive phenotype updating, uncertainty handling, and safeguards against extrapolation beyond adequately characterized populations. Equity therefore cannot be evaluated only after deployment or reduced to average predictive parity. It must be considered across evidence generation, variant interpretation, clinical decision support, monitoring, and the distribution of uncertainty itself. . A representation-aware approach can strengthen AI-enabled pharmacogenomic prescribing only when ancestry, genomic variation, medication context, and clinical change remain analytically distinct and are recombined at the point of individual treatment decision.

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Introduction

Pharmacogenomics has moved from the proposition that inherited variation may contribute to variable drug response toward increasingly operational forms of genotype-guided prescribing. Yet the evidence base supporting this transition has not developed uniformly across populations. Ancestry and sex remain unevenly represented in pharmacogenomic research, affecting the breadth of variants, haplotypes, allele frequencies, and clinical relationships that have been characterized [1]. This matters for AI-enabled prescribing because computational systems cannot recover population-specific biological or clinical information that was never adequately observed, measured, or represented in the evidence used to construct or evaluate them.

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Population pharmacogenomic variation also differs across biogeographic groups, including variation in the frequencies of alleles assigned functional or therapeutic significance [2]. Such differences do not imply that membership in a population group determines an individual's genotype or drug response. They instead show why evidence generated predominantly in one set of populations may have incomplete external validity in another. The same problem is visible at the measurement level. Comparisons between broader sequencing approaches and targeted pharmacogenetic testing indicate that predefined panels can fail to capture variants present in people whose genomic backgrounds were less influential when those panels were designed [3]. Representation therefore concerns more than the demographic composition of a training cohort; it also concerns which variants are discoverable, which are included in assays, which receive functional characterization, and which populations contribute to validation.

These issues become particularly important when population-level genomic information is incorporated into AI-supported treatment prediction. Population pharmacogenomic analyses demonstrate geographically structured patterns in clinically relevant variation, while broader genomic work continues to document substantial diversity gaps in datasets and reference resources [4, 5]. The methodological implication is not that ancestry should be inserted into a predictive model as a corrective variable. Doing so could reproduce the very simplification the representation problem exposes. Instead, a prescribing system must distinguish evidence about population-level variation from evidence about the individual patient's genotype, phenotype, medication exposure, and current clinical state.

A second difficulty is that even accurately measured germline variation does not operate in an invariant clinical environment. Pharmacogenomic interpretation frequently begins with a genotype-to-phenotype translation and then proceeds toward treatment selection or dose adjustment. In practice, concomitant drugs, inhibition or induction of metabolic pathways, organ dysfunction, disease progression, adherence, treatment history, and other changes can modify the relationship between genotype and current drug disposition. An AI system that treats genomic information as a static personal attribute may therefore be technically sophisticated while remaining clinically incomplete.

The central question is consequently twofold: for whom is the pharmacogenomic evidence sufficiently representative, and under what current clinical conditions does a genomic prediction remain a defensible basis for prescribing? This article addresses that question through a normative and methodological framework rather than through a new empirical dataset. It first examines how unequal representation enters AI-enabled pharmacogenomic evidence, then distinguishes ancestry from individual genomic information and analyzes how polypharmacy and changing clinical context modify genotype-based inference. The later sections translate those distinctions into requirements for representation-aware pharmacogenomic decision systems and their equitable clinical implementation.

Unequal Genomic Representation in AI-Enabled Prescribing

Unequal genomic representation becomes clinically consequential through several different mechanisms that should not be collapsed into a single measure of dataset diversity. One mechanism concerns who contributes genomic observations. Another concerns which variants can be detected by the chosen assay. A third concerns whether detected variants have been functionally characterized well enough to support phenotype assignment. A fourth concerns whether gene–drug relationships have been validated in populations sufficiently similar to those in whom a system will be deployed. Population-level analyses demonstrating ancestry-associated pharmacogenomic structure illustrate the first problem [4], whereas broader evaluations of genomic diversity show why simply enlarging an already homogeneous evidence base does not necessarily resolve it [5].

This distinction changes how representation should be evaluated in AI-enabled prescribing. A model may contain individuals from several nominal population categories while still depending on variant annotations, haplotype definitions, reference panels, or clinical evidence derived mainly from a narrower genomic background. Conversely, a relatively small dataset may contain informative variation if it was designed to sample genomic diversity relevant to the prediction problem. Representation is therefore not adequately summarized by the proportion of participants assigned to demographic categories. The relevant question is whether the evidence system contains the variation needed to support the claims made for the populations in which the model will operate.

The problem is especially visible when pharmacogenomics is developed with communities whose genomic diversity, historical experiences of research, or patterns of clinical care differ from those underlying dominant reference resources. Work on community-engaged pharmacogenomics in Indigenous populations emphasizes that implementation cannot be separated from community partnership, governance, data stewardship, and locally relevant evidence [6]. These considerations have methodological consequences. A model that performs acceptably according to an aggregate validation statistic may still be poorly justified for a community if the relevant alleles were insufficiently characterized, if phenotype translation was not established in that population, or if genomic data were collected under governance arrangements that undermine legitimate use.

Representation failures may also propagate from discovery into clinical translation. Oncology provides a clear example because germline and somatic genomic evidence increasingly inform treatment, yet the evidence supporting pharmacogenomic testing has not been generated equally across ancestral groups. Analyses of equitable pharmacogenomic implementation in oncology have highlighted barriers spanning variant discovery, test content, clinical evidence, guideline development, and access to testing [7]. The important methodological point is that downstream fairness cannot be guaranteed solely by recalibrating an algorithm. If an actionable variant was not discovered, was omitted from a test, or lacks reliable functional interpretation, the resulting limitation precedes model fitting.

An equity perspective therefore requires attention to the entire evidentiary chain. Research on pharmacogenetic translation in underrepresented populations argues that representational imbalance may influence who benefits from pharmacogenomic discovery and implementation [8]. Yet the normative concern should be stated carefully. Unequal representation does not mean that every currently used pharmacogenomic association is invalid outside the population in which it was initially studied, nor does it mean that every population requires an entirely separate evidence base. The problem is one of claim-specific transportability: whether the variant, functional assignment, gene–drug relationship, treatment context, and decision rule have enough evidentiary support for the person to whom a recommendation is being applied.

For AI-enabled prescribing, this yields three different questions that conventional performance reporting can obscure. First, coverage validity asks whether the relevant genomic variation is observable and adequately represented. Second, interpretive validity asks whether the detected variant can be translated into a sufficiently reliable functional phenotype. Third, decision validity asks whether that phenotype supports the clinical recommendation under the patient's current circumstances. An algorithm may perform well at the third task in a subgroup for whom the first two tasks have already been solved while remaining poorly justified in patients whose variants or functional annotations are incompletely represented.

This separation also clarifies why demographic balancing alone is insufficient. Representation is not merely a statistical property of a training sample; it is a property of the evidence pathway linking population sampling to variant discovery, measurement, functional interpretation, model evaluation, and clinical action. The methodological and equity consequences differ depending on where that pathway is weak.

The distinct consequences of these representation failures are summarized in **Table 1**. The analytical purpose is to distinguish evidence deficits that may look similar in an aggregate dataset but require different remedies before AI-supported pharmacogenomic recommendations can be trusted.

Table 1. Distinct representation failures in AI-enabled pharmacogenomics and the validity questions they create

Representation failure	What is inadequately represented	How the deficit enters AI-enabled prescribing	Methodological consequence	Equity consequence	Evaluation required before clinical reliance
Population sampling deficit	Genomic variation carried by populations rarely enrolled in discovery or validation research	Training and validation evidence contain limited exposure to relevant alleles, haplotypes, or genomic backgrounds	External validity is uncertain even when aggregate discrimination appears acceptable	Underrepresented patients may receive recommendations supported by thinner evidence	Population-specific coverage analysis and subgroup validation with explicit uncertainty
Variant-discovery deficit	Rare, population-enriched, or structurally complex pharmacogene variation	Clinically relevant variation may be absent from model inputs or variant knowledge bases	Prediction can appear confident despite incomplete genomic observability	Patients carrying poorly characterized variants may be systematically assigned to default categories	Variant-spectrum audit against the intended clinical population
Assay-content deficit	Variants not included on targeted tests or calling pipelines	The model receives an incomplete genotype rather than an explicitly uncertain genotype	Missing biological information may be mistaken for absence of actionable variation	Test design may perform unevenly across genomic backgrounds	Analytical coverage assessment by gene, variant class, and population
Functional-annotation deficit	Detected variants whose functional effect is poorly characterized	Genotype is available but phenotype assignment is unstable or unknown	Uncertainty shifts from measurement to interpretation	Patients with understudied variants may receive less actionable or less reliable guidance	Functional-evidence grading and explicit indeterminate states
Gene–drug evidence deficit	Clinical response evidence for a variant–drug relationship in relevant populations or contexts	Model extrapolation extends beyond populations or settings represented in clinical evidence	Transportability of the recommendation is uncertain	Unequal evidence may translate into unequal confidence in treatment recommendations	Claim-specific external-validity assessment
Validation deficit	Independent testing across populations, sites,	Apparent model performance may reflect the	Generalization cannot be inferred from internal performance alone	Weak external validation can conceal population-specific error	External and stratified validation using clinically relevant endpoints

	or clinical environments	development setting			
Implementation-access deficit	Access to testing, specialist interpretation, or decision support	Evidence exists but is unequally available in practice	Clinical utility becomes conditional on workflow and infrastructure	Benefits accrue preferentially to patients in better-resourced settings	Monitoring of testing access, actionable-result delivery, and recommendation uptake

Ancestry, Polypharmacy and Changing Clinical Context

Genetic ancestry is relevant to pharmacogenomics because the distribution of pharmacogene variants and haplotypes differs across populations, and some loci show substantial ancestry-associated structure [9]. Its relevance, however, is easily overstated. Ancestry is neither a substitute for an individual's genotype nor equivalent to socially assigned race. The distinction matters because race reflects social classification and lived exposure to structural conditions as well as, imperfectly, population history; treating it as a genetic variable can biologize social categories and obscure both sources of variation [10]. A representation-aware system must therefore avoid two opposite errors: ignoring population structure when it affects genomic evidence, and converting population structure into deterministic patient-level inference.

Individual prescribing should begin with measured patient-level genomic information when the relevant genotype is available. Pharmacogenomics provides a framework for translating inherited variation into information about drug disposition, efficacy, or toxicity, but genomic variation is only one contributor to observed treatment response [11]. Standardized allele nomenclature is essential because different laboratories and knowledge resources must refer consistently to the same pharmacogene haplotypes [12]. Likewise, genotype-to-phenotype translation requires explicit conventions. Consensus efforts for CYP2D6 demonstrate that even before current medications are considered, phenotype assignment can vary unless activity scoring and translation procedures are standardized [13].

This establishes an important sequence: ancestry may inform the expected distribution of variation and the adequacy of evidence coverage, whereas the individual's measured genotype informs pharmacogenomic interpretation. Even that interpretation remains conditional. A genetically predicted phenotype represents an expectation under specified assumptions about enzyme activity and exposure; it is not necessarily a permanent description of the patient's effective metabolic state.

The clinical value of pharmacogenomics nevertheless extends beyond theoretical prediction. Multigene implementation studies have shown that genotype-guided prescribing can reduce clinically relevant adverse drug reactions under defined conditions [14]. Such evidence supports clinical use, but it also increases the importance of getting the interpretive context right. Panel testing expands the number of gene–drug relationships simultaneously available to clinicians and creates the possibility that several recommendations will become relevant during a patient's treatment trajectory [15]. For patients using many medicines, the question is no longer simply whether a pharmacogenomic result is actionable. It is whether the action remains appropriate in the presence of current co-medications and clinical conditions.

This is particularly important in older and medically complex populations. Actionable pharmacogenetic genotypes can coexist with polypharmacy and exposure to inhibitors or inducers of the same metabolic pathways that genotype-based recommendations seek to characterize [16]. Observational evidence from veterans similarly demonstrates that pharmacogenomic phenotypes and complex medication use frequently intersect [17]. These findings do not establish that polypharmacy always invalidates genotype-guided recommendations. They establish that the medication list is part of the phenotype-interpretation environment.

Drug–drug–gene interactions provide the clearest mechanistic example. Models of cytochrome-mediated interaction show how an inhibitor or inducer can alter the phenotypic expression expected from genotype, while broader analyses of drug-gene and drug–drug–gene interactions emphasize that genetic and non-genetic influences can combine rather than act independently [18, 19]. In practical terms, a patient genetically predicted to have normal or increased metabolic capacity may behave differently when a strong inhibitor suppresses the relevant enzyme. Conversely, induction can increase effective metabolic activity in ways not represented by a static genotype label. The inference needed for prescribing is therefore not simply genotype → phenotype → dose, but genotype + current exposures + relevant physiology → context-specific phenotype → clinical decision.

Clinical data support the importance of this distinction. Large psychiatric pharmacogenomic datasets have documented CYP2D6 phenoconversion, illustrating that a genotype-derived phenotype may diverge from the phenotype expected under the patient's actual medication exposure [20]. Phenoconversion should not be generalized into the claim that every interacting medicine negates pharmacogenomic information. Its methodological importance lies elsewhere: a prescribing system must be able to recognize conditions under which genotype-derived phenotype requires revision.

The same principle extends beyond inhibition and induction. Renal and hepatic function can alter drug clearance independently of pharmacogene variation; disease state may change pharmacodynamics or competing risks; adherence determines realized exposure; previous intolerance may modify acceptable therapeutic choices; and treatment history may alter the value of trying another agent even when genomic evidence favors it. These factors do not all have equivalent mechanistic relationships to pharmacogenomics, and they should not be compressed into one generic “clinical context” score. They belong to different stages of the treatment inference.

Temporal change further distinguishes pharmacogenomic information from a complete prescribing recommendation. Germline genotype is largely stable, but the clinical meaning attached to it can change. A result obtained years earlier may remain analytically valid while a recommendation derived from it becomes inappropriate after a new interacting drug is introduced, renal function declines, treatment goals change, or an alternative therapy becomes available. A clinically useful AI system should consequently preserve stable genomic information while permitting repeated reinterpretation against updated clinical data.

This dynamic view also constrains how ancestry should enter AI models. Population or ancestry information may identify evidence gaps, suggest that a panel has incomplete coverage, or indicate that functional interpretation is less certain for a particular variant spectrum. It should not be allowed to override an observed patient genotype or to become a shortcut for an unmeasured genotype. Where uncertainty remains because a variant is poorly characterized, the correct output may be reduced confidence, additional testing, expert review, or temporary abstention rather than imputation from ancestry.

The practical distinctions among stable genomic information, ancestry-related evidence context, modifiable drug exposure, physiological change, and treatment history are summarized in **Table 2.** Each modifier changes a different part of the pharmacogenomic inference and therefore calls for a different updating rule.

Table 2. Clinical-context modifiers that change the interpretation or actionability of pharmacogenomic information

Contextual element	What remains stable	What may change	Point in the pharmacogenomic inference affected	Appropriate system response	Unsafe shortcut to avoid
Genetic ancestry / population background	The patient's measured genotype	Confidence in how completely relevant variation and evidence are represented	Evidence coverage and external validity	Display population-specific evidence limitations and assay-coverage uncertainty	Using ancestry as a substitute for genotype
Germline pharmacogene genotype	Underlying inherited sequence	Functional interpretation when novel or incompletely characterized variants are encountered	Genotype-to-phenotype translation	Retain the genotype while updating annotation as evidence changes	Treating an uncertain genotype as a known phenotype
Enzyme inhibition by co-medication	Genotype	Effective metabolic activity	Phenotype expression	Recalculate or qualify phenotype when inhibition is clinically material	Applying the genetic phenotype without considering inhibitors
Enzyme induction by co-medication	Genotype	Effective metabolic activity and exposure	Phenotype expression and dose expectation	Reassess the predicted drug-exposure relationship	Assuming genotype fixes metabolic capacity
Polypharmacy involving multiple pathways	Genotypes	Net exposure and interaction configuration	Translation from multiple gene–drug results to one medication plan	Evaluate interacting recommendations jointly rather than independently	Acting on each gene–drug pair in isolation
Renal or hepatic dysfunction	Genotype	Clearance, exposure, toxicity risk, and appropriateness of standard dosing	Pharmacokinetic translation and clinical action	Integrate organ-function constraints with PGx guidance	Interpreting PGx as sufficient for dose selection
Disease-state change	Genotype	Pharmacodynamic response, competing risks, and therapeutic priorities	Clinical actionability	Re-evaluate whether the same genomic recommendation remains clinically relevant	Treating the original indication and risk profile as permanent
Treatment history and previous response	Genotype	Expected value of repeating, avoiding, or switching therapy	Decision layer	Incorporate prior benefit, intolerance, and treatment failure	Recommending a genetically favored drug without regard to prior outcome
Addition or withdrawal of medication	Genotype	Interaction structure and potentially the expressed phenotype	Temporal update of phenotype and recommendation	Trigger reassessment when clinically relevant perpetrators appear or disappear	Treating a past PGx recommendation as permanently current
Change in available evidence or guidance	Genotype	Interpretation of variant function or recommended action	Knowledge layer	Version and update the clinical interpretation while preserving the original laboratory result	Freezing interpretation at the date of testing

The implication is that representation-aware pharmacogenomics requires two forms of updating that should remain conceptually separate. Evidence updating asks whether the genomic knowledge supporting a recommendation remains adequate for the patient's variant and population context. Clinical updating asks whether the patient's current medications, physiology, disease state, and treatment history still support the action originally associated with that genomic result. The

methodological framework developed in the next section uses this separation to determine when AI-supported pharmacogenomic inference can proceed, when it requires qualification, and when uncertainty should block automatic treatment recommendation.

Proposed Representation-Aware Pharmacogenomic Framework

A representation-aware system should preserve the distinction between evidence sufficiency and patient-specific interpretation. Population exposure to medicines carrying evidence-based pharmacogenomic information is itself uneven, meaning that deployment begins in a clinical landscape where opportunities to benefit from pharmacogenomics are not equally distributed [21]. Implementation barriers likewise extend beyond predictive modeling to evidence standards, reimbursement, laboratory processes, electronic records, education, and clinical workflow [22]. The framework therefore treats representation, interpretation, action, and reassessment as separate functions rather than compressing them into a single model output.

Once genomic information has been generated, it should remain available as structured, reusable information while the clinical interpretation attached to it is allowed to change. Clinical decision-support implementations illustrate how genomic results can be stored and repeatedly surfaced as treatment circumstances evolve [23, 24]. Equity should also be an explicit implementation objective rather than a retrospective subgroup analysis [25]. Standardized resources such as CPIC can anchor gene–drug interpretation [26], while examples such as DPYD-guided fluoropyrimidine prescribing demonstrate the need to connect validated genomic evidence to a defined therapeutic context [27]. Updated TPMT/NUDT15 guidance further illustrates why ancestry-associated frequency differences can inform evidence appraisal without becoming a substitute for measured genotype [28].

Operationally, representation-aware prescribing requires safeguards matched to distinct failure points rather than one global confidence threshold **(Table 3)**.

Table 3. Safeguards linking genomic representation, dynamic phenotype interpretation, and clinical action

Safeguard function	Trigger for reassessment	Information that must remain distinct	Permissible system response	Condition requiring qualification or blocked automation
Evidence-coverage check	Patient or variant poorly represented in discovery, annotation, or validation evidence	Population representation; individual genotype	Report evidentiary coverage and uncertainty	Relevant variation or transportability is insufficiently characterized
Genomic-identity check	New or discordant laboratory result	Ancestry; race; measured genotype	Use measured genomic result as the patient-level substrate	Ancestry label is being used to impute an unmeasured genotype
Functional-interpretation check	Novel allele, uncertain function, or revised annotation	Variant detection; functional phenotype	Preserve genotype and update phenotype assignment as evidence changes	Functional status is unresolved
Clinical-context check	Medication addition/withdrawal, organ-function change, disease progression, or treatment failure	Germline genotype; current effective phenotype; present clinical state	Recalculate or qualify interpretation	A static historical recommendation conflicts with current exposure or physiology
Decision-action check	PGx information becomes therapeutically relevant	Prediction; guideline-supported action; patient-specific constraints	Recommend, defer, escalate for review, or abstain	Evidence does not justify an automatic prescribing action
Equity-monitoring check	Deployment across populations or sites	Overall performance; coverage gaps; uncertainty; access; overrides	Audit who receives testing, confident interpretation, and implemented recommendations	Aggregate accuracy conceals systematically thinner evidence or higher uncertainty in particular populations

These safeguards imply that uncertainty should be located rather than merely quantified. A system should be able to state whether uncertainty arises because genomic coverage is weak, functional interpretation is unresolved, interacting treatment has altered the expected phenotype, or the clinical evidence is insufficiently transportable. Only then can uncertainty change the appropriate action rather than becoming another undifferentiated score.

The resulting decision field therefore separates evidence adequacy, patient-level interpretation, dynamic clinical context, and equity safeguards while allowing reassessment whenever one of these layers becomes unstable **(Figure 1)**.

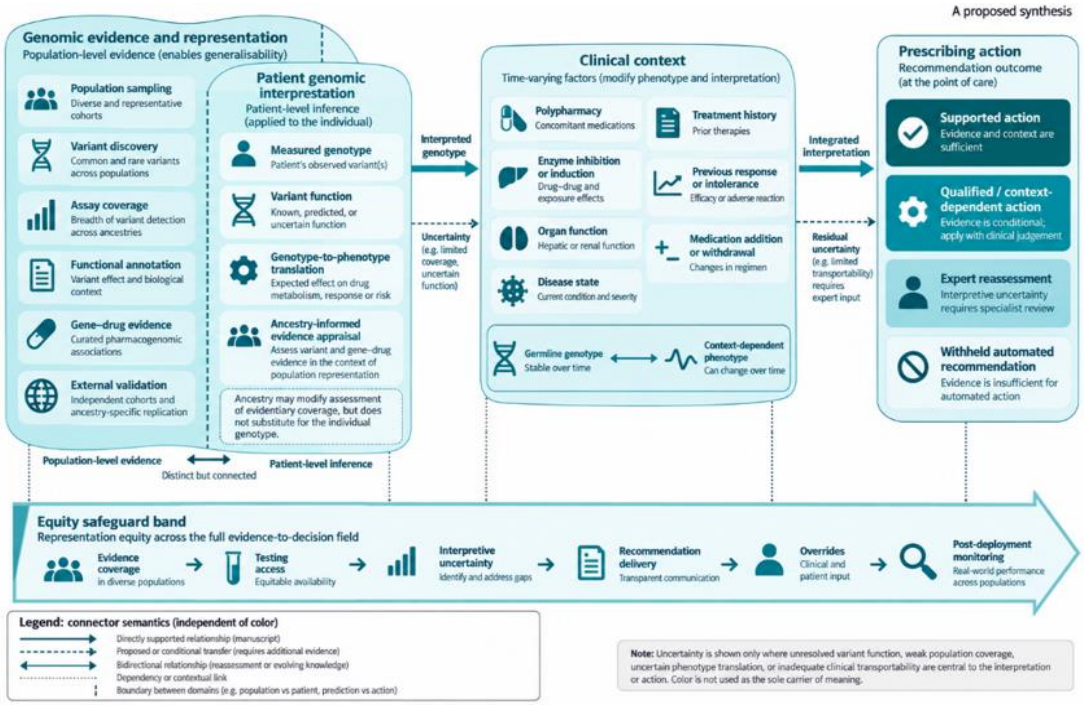


Figure 1. When pharmacogenomic evidence is sufficient, conditional, or insufficient for a prescribing action.

Equity and Clinical Implementation Implications

Representation-aware precision prescribing changes the meaning of equity. It is insufficient to compare average prediction errors after deployment if the underlying genomic evidence is substantially thinner for some populations. Pharmacogenomic research in African populations illustrates both the depth of human genomic diversity and the continuing gaps in population-relevant evidence and implementation resources [29]. Equity assessment should therefore ask whose variation has been characterized, whose variants remain uncertain, and whose treatment decisions consequently carry greater inferential uncertainty.

Greater sample size alone cannot answer that question. Genomic analyses show that increasing ancestral diversity can add information that is not recovered simply by expanding a much larger but comparatively homogeneous dataset [30]. For AI-enabled pharmacogenomics, this supports evaluating representation as informational coverage rather than demographic arithmetic. A smaller but deliberately diverse evidence resource may answer questions that a larger homogeneous dataset cannot, although diversity itself does not remove the need for rigorous validation.

Post-deployment evidence should then test whether pharmacogenomic expectations survive contact with clinical practice. Real-world dose data can recover established pharmacogenomic associations while also showing that some expected relationships are difficult to observe in routine records [31]. Such non-recovery should prompt examination of adherence, co-medication, phenotype modification, prescribing behavior, data quality, and treatment selection before being interpreted as biological absence. Longitudinal biobank-linked electronic health records further show how medication-response trajectories can support pharmacogenetic discovery and replication across clinical contexts [32].

Equitable implementation therefore requires monitoring more than access to testing. Health systems should examine the distribution of interpretable results, uncertain variants, phenoconversion risk, clinically actionable recommendations, overrides, specialist escalation, and opportunities for reassessment. A population that receives testing but disproportionately receives uncertain or weakly transferable interpretations has not necessarily achieved equivalent pharmacogenomic benefit. Conversely, uncertainty should not justify withholding innovation indefinitely from underrepresented populations. It should trigger proportionate safeguards: better evidence generation, explicit uncertainty communication, contextual reassessment, shared clinical judgment, and continued outcome monitoring.

The framework consequently treats equity as an evidentiary and clinical property of the entire prescribing process. The relevant objective is not to erase biologically meaningful population variation or to make ancestry invisible. It is to prevent population labels from standing in for patient-level genomic evidence while ensuring that differences in the depth of supporting evidence are visible at the point where treatment decisions are made.

Conclusion

AI-enabled pharmacogenomic prescribing is most defensible when it distinguishes three questions that are often merged: whether the genomic evidence adequately represents the relevant variation, whether the individual patient's genotype can be translated into a reliable functional interpretation, and whether that interpretation remains clinically valid under current medications and changing physiological or therapeutic conditions. Ancestry can inform appraisal of evidence coverage but

cannot substitute for measured genotype; genotype can inform expected phenotype but cannot replace assessment of polypharmacy and current clinical state. Representation-aware precision prescribing therefore requires continuous linkage between stable genomic information, revisable interpretation, dynamic clinical context, and explicit equity safeguards. Its clinical value depends not on eliminating uncertainty, but on identifying where uncertainty enters and allowing that uncertainty to qualify, redirect, or temporarily block automated prescribing action.

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