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FARMACOGENÔMICA ACESSÍVEL NO SISTEMA ÚNICO DE SAÚDE: ALAVANCAS DE CUSTO, PAPEL DO FARMACÊUTICO CLÍNICO E O MODELO DE IMPLEMENTAÇÃO FARMA-GEN SUS

AFFORDABLE PHARMACOGENOMICS IN BRAZIL'S UNIFIED HEALTH SYSTEM: COST LEVERS, THE ROLE OF THE CLINICAL PHARMACIST AND THE FARMA-GEN SUS IMPLEMENTATION MODEL

FARMACOGENÓMICA ACCESIBLE EN EL SISTEMA ÚNICO DE SALUD DE BRASIL: PALANCAS DE COSTO, PAPEL DEL FARMACÉUTICO CLÍNICO Y EL MODELO DE IMPLEMENTACIÓN FARMA-GEN SUS

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Resumo

Introdução: Existem diretrizes clínicas para farmacogenômica, mas sua implementação no Sistema Único de Saúde (SUS) enfrenta custos dos testes, fragmentação assistencial e baixa reutilização de resultados.

Objetivo: Examinar os determinantes de custo e valor da farmacogenômica no SUS e propor o FARMA-GEN SUS, modelo de implementação proposto pelos autores e não adotado pelo Ministério da Saúde, que combina painel multigênico acionado por um primeiro gatilho clínico de alto rendimento, registro interoperável e colaboração entre farmacêuticos e prescritores.

Métodos: Ensaio crítico-propositivo fundamentado em ensaios clínicos, avaliações econômicas, estudos populacionais brasileiros e documentos normativos vigentes em 13 de outubro de 2026, complementado por buscas direcionadas em PubMed e BVS/LILACS. Evidências publicadas, cálculos ilustrativos e propostas de implementação foram analisados separadamente; não foram coletados dados clínicos primários.

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Síntese: No PREPARE, reações adversas clinicamente relevantes entre pacientes com interações gene–medicamento acionáveis ocorreram em 21,0% no grupo guiado e 27,7% no controle (OR 0,70; IC95% 0,54–0,91). A análise econômica associada identificou o preço do teste como importante determinante de custo, sem demonstrar economia para o Brasil. O modelo propõe seleção por gatilhos clínicos de alto rendimento, cobertura analítica adequada, registro estruturado, interpretação clínica e reutilização longitudinal. Um exercício ilustrativo de ponto de equilíbrio para CYP2C19–clopidogrel empregou pressupostos clínicos hipotéticos e efeito não significativo do TAILOR-PCI; com preços medianos de compras públicas (2025–2026), o custo anual incremental do ticagrelor superou amplamente os limites de equilíbrio frente ao clopidogrel, ao passo que um cenário contrafactual frente ao ticagrelor universal sugeriu possível economia. Os resultados dependem do efeito, dos preços dos medicamentos, dos custos do teste e do comparador; o exercício não constitui avaliação de custo-efetividade.

Conclusão: Não há economia demonstrada para o SUS. O FARMA-GEN SUS requer avaliação em piloto prospectivo comparativo, com mensuração de desfechos em saúde (eventos evitados, QALY), segurança, microcusteio, acesso, implementação e impacto orçamentário antes de eventual expansão.

Palavras-chave: Farmacogenética; Testes Farmacogenômicos; Assistência Farmacêutica; Sistema Único de Saúde; Avaliação de Custo-Efetividade.

Abstract

Introduction: Clinical pharmacogenomic guidelines are available, but implementation in Brazil's Unified Health System (SUS) faces testing costs, fragmented care pathways and limited reuse of results.

Objective: To examine the determinants of pharmacogenomic costs and value in the SUS and to propose FARMA-GEN SUS, an author-proposed implementation model not adopted by the Ministry of Health, combining a multigene panel triggered by a first high-yield clinical indication, interoperable records and pharmacist–prescriber collaboration.

Methods: Critical, proposal-oriented essay integrating clinical trials, economic evaluations, Brazilian population studies and regulatory documents in force on 13 October 2026, supplemented by targeted PubMed and BVS/LILACS searches. Published evidence, illustrative calculations and implementation proposals were considered separately; no primary clinical data were collected.

Synthesis: In PREPARE, clinically relevant adverse drug reactions among patients with actionable gene–drug interactions occurred in 21.0% of the guided group versus 27.7% of controls (OR 0.70; 95% CI 0.54–0.91). The associated economic analysis identified the test price as a major cost driver, without establishing savings for Brazil. The proposed model prioritises high-yield clinical triggers, fit-for-purpose analytical coverage, structured recording, clinical interpretation and later reuse. An illustrative CYP2C19–clopidogrel break-even exercise used hypothetical clinical assumptions and a non-significant effect from TAILOR-PCI; with median public-purchase prices (2025–2026), the annual incremental cost of ticagrelor far exceeded the break-even ceilings against clopidogrel, whereas a counterfactual against universal ticagrelor suggested possible savings. Results depend on effect size, medicine and test costs and the comparator; the exercise is not a cost-effectiveness study.

Conclusion: Savings for the SUS have not been demonstrated. FARMA-GEN SUS should be evaluated in a prospective comparative pilot measuring health outcomes (events avoided, QALYs), safety, micro-costed expenditure, access, implementation and budget impact before any scale-up.

Keywords: Pharmacogenetics; Pharmacogenomic Testing; Pharmaceutical Services; Unified Health System; Cost-Effectiveness Analysis.

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Resumen

Introducción: Existen guías clínicas de farmacogenómica, pero su implementación en el Sistema Único de Salud (SUS) de Brasil enfrenta costos de las pruebas, fragmentación asistencial y escasa reutilización de resultados.

Objetivo: Examinar los determinantes de costo y valor de la farmacogenómica en el SUS y proponer FARMA-GEN SUS, modelo de implementación propuesto por los autores y no adoptado por el Ministerio de Salud, que combina un panel multigénico activado por una primera indicación clínica de alto rendimiento, registro interoperable y colaboración entre farmacéuticos y prescriptores.

Métodos: Ensayo crítico-propositivo basado en ensayos clínicos, evaluaciones económicas, estudios poblacionales brasileños y documentos normativos vigentes el 13 de octubre de 2026, complementado con búsquedas dirigidas en PubMed y BVS/LILACS. Se distinguieron evidencias publicadas, cálculos ilustrativos y propuestas de implementación; no se recopilaron datos clínicos primarios.

Síntesis: En PREPARE, las reacciones adversas clínicamente relevantes entre pacientes con interacciones gen–fármaco accionables ocurrieron en el 21,0% del grupo guiado y el 27,7% del control (OR 0,70; IC95% 0,54–0,91). El análisis económico asociado identificó el precio de la prueba como determinante importante del costo, sin demostrar ahorros para Brasil. El modelo propone selección mediante indicaciones clínicas de alto rendimiento, cobertura analítica adecuada, registro estructurado, interpretación clínica y reutilización longitudinal. Un ejercicio ilustrativo de equilibrio para CYP2C19–clopidogrel utilizó supuestos clínicos hipotéticos y un efecto no significativo de TAILOR-PCI; con precios medianos de compras públicas (2025–2026), el costo anual incremental del ticagrelor superó ampliamente los límites de equilibrio frente al clopidogrel, mientras que un escenario contrafactual frente al ticagrelor universal sugirió un posible ahorro. Los resultados dependen del tamaño del efecto, los precios de los medicamentos, el costo de las pruebas y el comparador; el ejercicio no es una evaluación de costo-efectividad.

Conclusión: No se han demostrado ahorros para el SUS. FARMA-GEN SUS requiere evaluación mediante un piloto prospectivo comparativo que mida resultados en salud (eventos evitados, AVAC), seguridad, microcostos, acceso, implementación e impacto presupuestario antes de una posible expansión.

Palabras clave: Farmacogenética; Pruebas de Farmacogenómica; Servicios Farmacéuticos; Sistema Único de Salud; Análisis de Costo-Efectividad.

1. INTRODUCTION

Pharmacogenomics is no longer a predominantly descriptive field. Inherited variants in about twenty genes are now known to modify the response to roughly eighty medicines in clinical use, and international consortia publish recommendations that tell prescribers what to do once the genotype is known (Relling; Evans, 2015). The European PREPARE trial showed, under pragmatic conditions that included community pharmacies, that guiding prescribing with a 12-gene panel reduces clinically relevant adverse drug reactions (Swen et al., 2023).

In Brazil, however, pharmacogenetic testing generally remains outside routine provision in the Unified Health System (SUS), concentrated in the private sector and

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Pages: 1-35

ordered on an ad hoc basis for a single decision. A review of Brazilian pharmacogenomic research found no prospective outcome studies and no cost-effectiveness analyses of genotype-guided therapy in the country up to 2019 (Rodrigues-Soares; Suarez-Kurtz, 2019). This pattern is economically unfavourable: genetic information that may remain clinically useful for many years is paid for and used once. Without a structured record, the report tends to remain on paper or in a PDF, does not follow the patient across services, and rarely reaches the next prescriber.

The question of how to make pharmacogenomics affordable is usually framed solely in terms of the test price. This essay argues that the test price, although important, is only part of the problem. Whether pharmacogenomics can fit the SUS budget depends on how the cost of testing, interpretation and recording is spread over clinically indicated decisions that are actually implemented and that improve health outcomes. The cost per clinically indicated and implemented intervention is used here only as a secondary implementation indicator, which answers how much it costs to convert an actionable result into clinical action; it does not replace measures of value such as cost per quality-adjusted life year (QALY), cost per event avoided, net monetary benefit, budget impact and safety, because a modified prescription may be appropriate, unnecessary, neutral or harmful.

The essay proposes FARMA-GEN SUS, an author-proposed implementation model not currently adopted by the Ministry of Health. The name combines "FARMA" (pharmacy and pharmaceutical care), "GEN" (pharmacogenomics) and "SUS" (the public system in which the model is meant to be tested). The intervention is defined as a multigene pharmacogenomic panel performed when a patient first meets a high-yield clinical trigger, with the result recorded in a structured, interoperable form, interpreted by a clinical pharmacist in collaboration with the prescriber and reinterpreted for later prescriptions. This differs from a single-gene test ordered for one decision, both in cost and in potential value.

Previous publications by the authors examined the legal and institutional conditions and policy barriers to integrating pharmacogenomics into the SUS (Floriano; Menezes, 2026), the effects of the SUS digital transformation on equity of

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access (Floriano et al., 2026) and the implementation of pharmacogenetic testing in community pharmacies through middle-range theory and implementation science (Floriano, 2026a, 2026b). Table 1 summarises what each of these works did not address and what the present essay adds, so that overlap can be assessed.

Table 1 – Previous publications by the authors and contribution of this essay

Previous work	Object	What it did not address	New contribution of this essay
Floriano and Menezes (2026)	Legal, institutional and policy conditions for integrating pharmacogenomics into the SUS	Cost decomposition; economic heuristic; care pathway; data model	Cost and value levers; illustrative break-even with sensitivity analysis; defined intervention
Floriano et al. (2026)	Digital transformation of the SUS and equity of access	Pharmacogenomics; genetic data governance	Pharmacogenetic record proposal for the RNDS and data-governance requirements
Floriano (2026a)	Middle-range theory for implementing pharmacogenetics in community pharmacies	Public provision in the SUS; economic analysis; regulatory update	SUS-specific model; comparator analysis; regulatory framework in force on the cut-off date
Floriano (2026b)	Evidence synthesis in implementation science and the PPCPM framework for community pharmacies	Cost per person tested; comparator; judicial and sanitary status; pilot design	Phased pilot with stopping criteria and outcome-based indicators

Source: prepared by the authors.

As Table 1 shows, the specific contribution of this essay is an economic framing of the cost and value levers, an illustrative break-even exercise with an explicit sensitivity analysis, the definition of the FARMA-GEN SUS intervention and an updated regulatory and data-governance analysis. None of these elements was the object of the previous works.

2. METHODS

This is a critical, proposal-oriented essay. Sources were purposively selected to answer four questions: (i) what is the clinical evidence of benefit from panel-guided treatment; (ii) what do economic evaluations show about the determinants of cost; (iii) how does Brazilian genetic diversity affect the composition of a useful panel; and (iv) which Brazilian regulations govern provision, recording and professional practice. Priority was given to clinical trials, systematic reviews of economic evaluations, allele-

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frequency studies in Brazilian cohorts, guidelines of the Clinical Pharmacogenetics Implementation Consortium (CPIC) and federal regulations and court decisions in force on the cut-off date of 13 October 2026.

To keep evidence, calculation and proposal apart, the text separates three levels. Level 1, demonstrated evidence, comprises results of published trials, economic evaluations, frequency studies and legal acts (sections 3 to 7). Level 2, illustrative calculation, comprises the expected-value heuristic and the break-even exercises, which combine explicitly hypothetical clinical assumptions with observed public-purchase prices and do not constitute an economic evaluation (section 8). Level 3, implementation hypothesis, comprises the FARMA-GEN SUS model, which must be tested prospectively (section 9). Statements drawn from sections 3 to 7 that are the authors' own proposals, such as the prioritisation of gene–drug pairs, are identified as such.

This is not a systematic or scoping review, and no effect estimate was statistically pooled. The figures cited reproduce the denominators and estimators of the original publications.

To reduce selection bias in the economic evidence, a complementary PubMed search was run on 13 October 2026, with no date limit, using the strategy ("pharmacogenetic*"[Title/Abstract] OR "pharmacogenomic*"[Title/Abstract] OR "Pharmacogenomic Testing"[MeSH Terms]) AND ("cost effectiveness"[Title/Abstract] OR "cost utility"[Title/Abstract] OR "economic evaluation"[Title/Abstract] OR "Cost-Benefit Analysis"[MeSH Terms]) AND (Brazil*[Title/Abstract] OR Mexico[Title/Abstract] OR Colombia[Title/Abstract] OR "Latin America"[Title/Abstract] OR Argentina[Title/Abstract] OR Chile[Title/Abstract] OR Peru[Title/Abstract]). The search returned 11 records; two were primary economic evaluations from a Latin American perspective and one described an implementation programme in a Brazilian public institution, all discussed in section 3.3. An additional multilingual search was run in the Virtual Health Library (BVS) portal on 13 October 2026 using the terms (pharmacogenetic* OR pharmacogenomic* OR farmacogenetic* OR farmacogenomic*) AND ("cost effectiveness" OR "economic evaluation" OR "cost benefit" OR "custo-efetividade" OR "avaliação econômica") AND (Brazil OR Brasil

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OR Mexico OR México OR Colombia OR Chile OR Argentina OR Peru OR "Latin America" OR "América Latina"). The final export contained 14 records: eleven tagged MEDLINE, two PubMed-not-MEDLINE and one LILACS. The three records discussed in section 3.3 were retrieved again; the sole LILACS-indexed record, on the pharmacogenomics of first-line gastric-cancer therapy, was also represented by a MEDLINE record and was not a primary economic evaluation. No additional primary economic evaluation indexed specifically in LILACS was identified. Records from both searches, which overlapped substantially, were screened by title and abstract independently by two authors against the objectives of this essay, and the second author reviewed the screening decisions and approved the final selection. Both searches were intended to reduce selection bias, not to map all Latin American economic evaluations; country coverage and retrieval remain limited, and Embase, EconLit and health technology assessment reports were not searched.

3. WHAT THE INTERNATIONAL EVIDENCE SUPPORTS (LEVEL 1)

3.1 Clinical benefit

PREPARE was a pragmatic, open-label, multicentre, cluster-randomised crossover trial conducted in 18 hospitals, nine community health centres and 28 community pharmacies in seven European countries. Of 41,696 patients assessed, 6,944 were enrolled (3,342 in the guided group and 3,602 in the control group) and genotyped for 50 variants in 12 genes. In the subgroup with an actionable result for the index drug (n = 1,558), clinically relevant adverse drug reactions occurred in 152 of 725 patients (21.0%) in the guided group and in 231 of 833 (27.7%) in the control group (OR 0.70; 95% CI 0.54–0.91), an absolute difference of 6.8 percentage points. In the whole population exposed to the index drug, the incidences were 21.5% and 28.6% (OR 0.70; 95% CI 0.61–0.79) (Swen et al., 2023).

Three limitations constrain the transferability of this result to the SUS. The open-label design allows bias in the assessment of adverse reactions: in critical correspondence, authors observed that even participants without an actionable result, who could not benefit from guided adjustment, showed a similar odds ratio (OR 0.68; 95% CI 0.60–0.78), suggesting that knowledge of allocation influenced event reporting (Rogers et al., 2023). Loss to follow-up was higher in the guided group

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(11.0%) than in the control group (7.9%) (Swen et al., 2023). And 97.7% of participants self-identified as of European, Mediterranean or Middle Eastern ancestry, a composition very different from that of Brazil (Swen et al., 2023). PREPARE also tested a complex strategy (test, guideline-based recommendation, prescriber, pharmacist, information system and awareness) and does not allow the effect of any single component, including the pharmacist, to be isolated. It therefore establishes clinical and operational plausibility, including in pharmacies, but does not provide Brazilian parameters.

3.2 Test price as a major economic driver

The cost-utility analysis of 6,930 PREPARE participants, from the perspective of national health systems, estimated an incremental ratio of €12,020 per QALY (95% CI €10,957–€13,356), which the authors described as marginally cost-effective (Fragoulakis et al., 2026). The most relevant finding for this essay lies in the cost breakdown: with the test price included, the guided strategy cost on average €21.4 more per patient; in a scenario analysis that excluded the test price from the cost calculation, which the authors associate with a pre-emptive approach in which the result is already available, the difference became favourable, at approximately €103.6 per patient (Fragoulakis et al., 2026). This is a counterfactual exercise. In a real pre-emptive programme the test cost is not zero; rather, it is amortised over several decisions over time. The scenario shows that, in that analysis, the test price was a major driver of the sign of the result, not that it is the decisive variable in every health system, nor that the savings are transferable to the SUS.

The analysis has weaknesses that should be acknowledged. Utility was derived from a visual analogue scale, the QALY gain was very small (0.00178) and the horizon mainly reflects trial follow-up (Fragoulakis et al., 2026). Even so, the direction of the finding is consistent with the wider literature. A systematic review of 108 economic evaluations of drugs with CPIC guidelines found 71% of results to be cost-effective or cost-saving, notably for clopidogrel (22 of 23 favourable studies), but few data on multigene and pre-emptive testing (Morris et al., 2022). An umbrella review published in 2026 included 211 unique evaluations, 71.1% of which concluded in favour of cost-effectiveness, concentrated in a few high-income countries (Ochi et

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al., 2026). In cardiovascular care, favourable findings are likewise restricted to a few gene–drug pairs (Zhu et al., 2020).

The operational implication is that, for the SUS, the challenge is not only to demonstrate efficacy but to design a form of provision in which the test cost is amortised across many clinically useful decisions over time. This is what North American pre-emptive programmes sought by integrating the genotype into the electronic health record and clinical decision support (Dunnenberger et al., 2015).

3.3 Economic and implementation evidence in middle-income countries

The complementary search identified two primary economic evaluations in the region. In Brazil, a decision-tree model estimated that isoniazid dosing guided by NAT2 genotype in drug-susceptible tuberculosis would cost US$ 476 per QALY gained, with incremental ratios below gross domestic product per capita in 99% of probabilistic simulations (Rens et al., 2020). In Chile, acenocoumarol dosing guided by CYP2C9 and VKORC1 in atrial fibrillation yielded an incremental ratio of US$ 436.86 per QALY and remained cost-effective even at test prices well above the US$ 190 charged in the country (Mena et al., 2026). Both model a single gene–drug pair rather than a multigene panel. They are illustrative examples rather than a comprehensive mapping of the region, and suggest that testing targeted at a high-yield indication can have a favourable economic result in middle-income systems when local parameters are favourable.

In the Brazilian public sector, the National Cancer Institute set up, with Ministry of Health funding, a pharmacogenomics programme for fluoropyrimidines, irinotecan and thiopurines, applied to 100 outpatients with gastrointestinal cancer and 162 children with acute lymphoblastic leukaemia and later extended to other centres; the authors themselves list continuous funding, staff training, prescriber uptake and evidence of cost-effectiveness as challenges (Suarez-Kurtz et al., 2020).

Thailand provides the most frequently cited example among middle-income countries. The national economic evaluation of HLA-B*15:02 screening before carbamazepine compared three strategies (testing, not testing and directly replacing carbamazepine with more expensive alternatives) and estimated incremental ratios of 222,000 baht per QALY in epilepsy and 130,000 baht per QALY in neuropathic

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pain, with 343 patients tested to prevent one case of Stevens-Johnson syndrome or toxic epidermal necrolysis; the prevalence of the severe reaction and the positive predictive value of the test were the most influential parameters (Rattanavipapong et al., 2013). At a university hospital in Bangkok, HLA-B tests rose from 94 in 2011 to 2,880 in 2020, half of them requested by public hospitals, and reimbursement by government and insurance schemes was cited among the factors behind this growth (Koomdee et al., 2022). The lesson for the SUS is twofold: public funding targeted at a high-risk pair is feasible in a middle-income setting, and value depends on local parameters, which makes the Thai result non-transferable to Brazil, where HLA-B*15:02 is rare (Rodrigues-Soares; Suarez-Kurtz, 2019).

4. WHERE THE COST LIES

The retail price of a panel is only one component of the total cost of a pharmacogenomics service. Table 2 breaks this cost down and indicates, for each component, the lever capable of reducing it and who controls that lever. The table is an analytical construct of the authors based on the cited literature.

Table 2 – Cost components of a pharmacogenomics service and levers for reduction

Component	What it includes	Lever for reduction	Who controls it
Laboratory test	Supplies, collection, processing, quality control, retests	Panel with adequate analytical coverage; proportionate technology; procurement at scale	Health manager and laboratory
Report and interpretation	Phenotype inference, clinical recommendation, reinterpretation after guideline updates	Open, versioned guidelines; interpretation separated from genotyping	Health manager and pharmacist
Patient selection	Identifying who benefits at the first trigger	High-yield clinical triggers	Pharmacist and prescriber
Conversion into decisions	Medication review, communication with prescriber, recording	Documented, intelligible recommendation; collaborative protocols	Pharmacist and prescriber
Recording and reuse	Fixed: information model, RNDS integration, training. Recurrent: maintenance, audit, security, support	Minimal information model; access at the point of care	Digital health management
Consequences	Adverse events, admissions, late switches	Expected reduction with clinically indicated, implemented intervention (to be measured)	Health system

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Source: prepared by the authors based on Swen et al. (2023), Fragoulakis et al. (2026) and Dunnenberger et al. (2015).

Table 2 shows that only the first component depends directly on the laboratory. Patient selection, conversion into decisions and reuse depend on service organisation and professional practice, which suggests that lowering the test price alone does not guarantee access. Integration and governance costs have a fixed part (development of the information model, integration with the RNDS, training, infrastructure) and a recurrent part (maintenance, guideline updates, reinterpretation, audit, security and user support); reuse dilutes only the fixed part and may generate additional recurrent costs.

5. SEVEN LEVERS TO MAKE PHARMACOGENOMICS AFFORDABLE IN THE SUS

5.1 A panel with analytical coverage suited to the Brazilian population

Panels designed and validated mainly in other populations should not be transferred to the Brazilian population without evaluation. In two Brazilian cohorts of more than one thousand individuals, three DPYD variants classified as tier 1 by the Association for Molecular Pathology were not identified; another 13 variants had frequencies of 1% or less, and the remaining 21 ranged from 1.2% (NUDT15*3) to 76.4% (CYP3A5*3) (Suarez-Kurtz, 2025). This finding informs the assessment of yield and coverage, but it does not demonstrate that these variants are absent in all Brazilians, nor does it justify their automatic exclusion. The final panel composition should weigh frequency, analytical validity, severity of the preventable event, coverage of rare or structural variants and the risk of falsely reassuring results.

The same study recommends that variant selection should not be based on race/colour categories, because frequency follows individual ancestry proportions rather than self-identification (Suarez-Kurtz, 2025; Suarez-Kurtz et al., 2012). Diversity also calls for caution in the opposite direction. Among Yanomami and Munduruku Indigenous people, the four DPYD variants prioritised by international guidelines were not detected (Suarez-Kurtz; Basta; Perini, 2026); for these groups, a negative result on a conventional panel does not mean absence of risk of fluoropyrimidine toxicity. Among the Paiter-Suruí, 41% would have an indication for dose reduction, or consideration of dose reduction, of thiopurines based on the

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combined TPMT/NUDT15 genotype, a proportion three to four times higher than in any other population described (Perini; Basta; Suarez-Kurtz, 2024). The implication is not a reduced panel defined by ethnic identity, nor the use of Indigenous identity as a genetic proxy. It is the need for expanded or adapted analytical coverage, based on validated evidence, individual assessment and community governance, with the participation of Indigenous peoples in decisions about testing, data use and return of results.

5.2 Technology proportionate to the clinical question

For a defined set of variants, targeted genotyping with probes or arrays tends to cost less than sequencing and yields results that are simpler to interpret. Broad genome sequencing has a role in research and in the National Programme of Genomics and Precision Public Health – Genomas Brasil (Brasil, 2025b), but it is not a prerequisite for routine pharmacotherapeutic decisions. The main exception is CYP2D6: structural and copy-number variants are common in Brazilians (Bertholim-Nasciben et al., 2023) and, if not assessed, the inferred phenotype may be wrong. Technological proportionality is therefore defined gene by gene.

5.3 Timing and target population of initial testing

In a São Paulo cohort of 1,171 older adults with whole-genome sequencing, 98.0% carried at least one high-risk phenotype in genes with level 1A evidence; 42.0% used at least one drug at that level; and, among these, 18.9% had a high-risk gene–drug interaction (Bertholim-Nasciben et al., 2023). Multiplying these proportions indicates that about 8% of the cohort had an actionable interaction in use at that time. This figure refers to contemporaneous use and does not measure future exposure, reuse or lifetime benefit, so it should not be read as an estimate of lifetime yield. A low contemporaneous rate of actionable gene–drug interactions suggests that the timing and target population of initial testing may materially affect short-term implementation yield.

For this reason, the model proposes that initial provision be linked to high-yield clinical triggers: initiation of a drug with a strong guideline and serious consequences of error (Table 3). The panel is performed at the first trigger and remains available, subject to reinterpretation, for later prescriptions involving other pairs. Table 3

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Pages: 1-35

distinguishes the published evidence for each pair from the priority proposed by the authors.

Table 3 – Examples of clinical triggers: published evidence and priority proposed by the authors

Gene(s) – drug(s)	Clinical trigger	Evidence: guideline	Evidence: Brazilian or population data	Priority proposed by the authors*
CYP2C19 – clopidogrel	Start of antiplatelet therapy after acute coronary syndrome or angioplasty	CPIC 2022 (Lee et al., 2022)	Loss-of-function alleles frequent in Brazilians (Santos et al., 2011); clopidogrel is the SUS comparator (Brasil, 2011)	First wave
DPYD – fluorouracil, capecitabine	Before the first chemotherapy cycle	CPIC 2017 (Amstutz et al., 2018)	4% of patients with activity score < 2 in a São Paulo cohort (Cereser et al., 2026); canonical variants not detected in Amazonian Indigenous people (Suarez-Kurtz; Basta; Perini, 2026)	First wave
TPMT, NUDT15 – azathioprine, mercaptopurine	Start of thiopurine	CPIC 2025 (Maillard et al., 2026)	High frequency of risk genotypes among the Paiter-Suruí (Perini; Basta; Suarez-Kurtz, 2024)	First wave
CYP2D6 – codeine, tramadol	Prolonged opioid analgesia	CPIC 2021 (Crews et al., 2021)	Structural variation common; requires adequate assay coverage (Bertholim-Nasciben et al., 2023)	Second wave, conditional on assay coverage
SLCO1B1, ABCG2, CYP2C9 – statins	Start of therapy or muscle intolerance	CPIC 2022 (Cooper-DeHoff et al., 2022)	No Brazilian outcome data identified	Second wave, to be assessed by the committee
CYP2C9 – non-steroidal anti-inflammatory drugs	Chronic use in older adults or with bleeding risk	CPIC 2020 (Theken et al., 2020)	Phenotype distribution varies with ancestry (Suarez-Kurtz, 2023)	Second wave, to be assessed by the committee

Source: prepared by the authors based on the references cited. *The priority column is the authors' judgement, not a finding of the cited studies; final selection would be the task of a clinical-scientific committee using the criteria listed in section 5.3.

The priority column in Table 3 reflects the authors' judgement and is not a recommendation derived from the cited studies. A formal prioritisation by a clinical-scientific committee should consider, in addition to allele frequency and severity of the preventable event: quality of the evidence; availability of an alternative therapeutic action; time to result relative to the clinical decision; cost of the test and of the

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

alternative; laboratory capacity and analytical validity; equity; budget impact; consequences of false-negative results; and availability of the comparator in the SUS.

5.4 Reuse, reinterpretation and retesting

The germline genotype is stable, but the clinically usable result can become incomplete as new alleles are recognised, functional classifications change, guidelines are updated, or a new method detects variants (including structural ones) that the original panel did not assess. Genetic data can therefore be reused longitudinally provided that analytical coverage remains adequate. Three situations should be distinguished: reuse, when the recorded result is applied to a new prescription; reinterpretation, frequently needed, when the same genotype is translated again under an updated guideline or classification; and retesting or extended genotyping, occasionally needed, when coverage is insufficient for the decision at hand. Reuse amortises the test cost across decisions, which is consistent with the change of sign in the PREPARE economic analysis when the test price was removed (Fragoulakis et al., 2026), but reinterpretation and occasional retesting have costs of their own. Moreover, reuse only occurs if the result is structured, accessible at the point of care and protected (section 7).

5.5 Scale and public procurement

The unit price of supplies and processing tends to fall with volume, standardisation and competition. Centralised procurement based on a public technical specification of the panel, together with public and university reference laboratories, could reduce the laboratory component. The Genomas Brasil programme, organised by Ministry of Health Ordinance GM/MS No. 6,581/2025 (Brasil, 2025b), may in future provide infrastructure or expertise, but its existence does not show that there is idle laboratory capacity, that such capacity could be allocated to FARMA-GEN SUS, that its laboratories are validated for the proposed pharmacogenes or that there is budget for routine care; these conditions would have to be documented before any pilot. The specification should require reports in an open format and interpretation based on public guidelines, to avoid supplier lock-in.

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

5.6 Interpretation based on open guidelines

The recommendations of CPIC and the Dutch Pharmacogenetics Working Group (DPWG) are public, updated and used by trials and implementation programmes (Swen et al., 2023; Dunnenberger et al., 2015). Proprietary reports that embed closed interpretation make the service more expensive and hinder updating when a guideline changes. A public service can separate genotyping, which can be contracted on the market, from clinical interpretation, carried out by the system's own professionals on the basis of open and versioned references.

5.7 Converting results into clinically indicated decisions

An actionable result that does not reach the prescriber, or reaches the prescriber without clinical context, generates no benefit. Conversion requires a professional who identifies the eligible patient, gathers current medicines, renal and hepatic function and interactions, translates the genotype into an intelligible recommendation and documents the prescriber's response. The goal is not to maximise the number of modified prescriptions, which could create a perverse incentive, but to ensure that clinically indicated changes are implemented. In the proposed model this is the role of the clinical pharmacist, examined next.

6. CLINICAL PHARMACY FUNCTIONS IN FARMA-GEN SUS

Law No. 13,021/2014 defines the pharmacy as a service unit intended to provide pharmaceutical care and health care (Brasil, 2014). Resolution No. 585/2013 of the Federal Council of Pharmacy (CFF) sets out the clinical duties of pharmacists, including medication review, pharmacotherapeutic follow-up and documentation of interventions (Conselho Federal de Farmácia, 2013a). In public civil action No. 0060624-78.2013.4.01.3400, brought by the Federal Council of Medicine, the 17th Federal Civil Court of the Federal District Judicial Section declared CFF Resolution No. 586/2013, which regulated pharmacist prescribing (Conselho Federal de Farmácia, 2013b), unconstitutional and unlawful, prohibited its nationwide application and ordered its immediate suspension in a judgment of 18 November 2024 (PJe document ID 2158791341), on the grounds that only a federal law could confer such prescribing powers and that the resolution conflicted with Law No. 12,842/2013 (Brasil, 2013a); the judgment stated that it was subject to mandatory appellate review;

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

motions for clarification were rejected on 3 April 2025, and a procedural order electronically signed on 2 December 2025 (PJe document ID 2226558151) called for a response to an appeal, which documents appellate proceedings without establishing their outcome (Brasil, 2024). In public civil action No. 1024895-51.2025.4.01.3400, concerning CFF Resolution No. 5/2025, the same court suspended the resolution through an interim order of 31 March 2025 (PJe document ID 2179584479) (Brasil, 2025c) and, in a judgment signed on 9 October 2026 (PJe document ID 2294660694), upheld the claim, declared the resolution unconstitutional, unlawful and null, prohibited its nationwide application and made the interim relief definitive at first instance; the judgment expressly stated that it was subject to mandatory appellate review (Brasil, 2026d). The documents examined do not establish that either judgment has become final or whether later appellate decisions have modified its effects. Accordingly, neither resolution is treated as a general authorisation for independent pharmacist prescribing or for unilateral modification of treatment prescribed by another professional. FARMA-GEN SUS separates pharmacotherapeutic assessment, interpretation and evidence-based recommendations from prescribing acts, and requires renewed verification of the judicial and regulatory framework before implementation.

In FARMA-GEN SUS, the proposed role of the clinical pharmacist comprises five functions: (i) identification of eligibility according to indication criteria defined in a protocol, such as the triggers in Table 3; (ii) pre-test counselling, including on the limitations of the test; (iii) integrated interpretation of genotype, current medicines, phenoconversion by enzyme inhibitors and inducers, organ function and clinical context; (iv) evidence-based recommendation to the responsible prescriber when the adjustment depends on the prescriber's decision; and (v) follow-up, recording the decision, adverse events and reuse of the result. The model does not assume unilateral changes to another professional's prescription.

These functions are proposed as mechanisms acting on selection, interpretation, communication and follow-up; their incremental contribution has not been demonstrated and must be measured. The evaluation design should separate the effect of the genetic information, the effect of medication review and their

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Vol: 13.21
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Pages: 1-35

interaction, since attributing the entire benefit of an intensive pharmaceutical service to genotyping would overestimate the value of the test, and vice versa. Pharmacist time is a real programme cost: in the pilot, micro-costing should include minutes per consultation, salary and workload, training, documentation, communication with the prescriber and future reviews and reinterpretations.

Pharmacist functions may be performed in primary care units or in community pharmacies; the essay does not assume that one setting is superior, and the feasibility, reach and cost of each setting are hypotheses to be measured, particularly in view of the conflict of interest declared by the first author. Sample collection is a regulatory matter distinct from counselling. Under the framework in force at the cut-off date, Anvisa Resolution RDC No. 978/2025, as amended by RDC No. 986/2025 and RDC No. 1,043/2026, allows a pharmacy to be classified as a Type I service, which performs the test on site and does not store or transport biological material, except for quality-control purposes (Agência Nacional de Vigilância Sanitária, 2025, 2026). A Type I pharmacy therefore cannot simply collect a sample and send it to a central laboratory. RDC No. 1,043/2026 revised the rules on itinerant services, which must be linked to a Type II or Type III service and refer the material only to that service, and on the organisation of the pre-analytical phase (Agência Nacional de Vigilância Sanitária, 2026). These provisions may open logistical routes for a SUS pilot built on public Type II or Type III infrastructure, but they do not turn private community pharmacies into collection points. Any arrangement must be checked against the regulatory text in force before the pilot.

Package inserts approved by the Brazilian Health Regulatory Agency (Anvisa) present a further practical obstacle: for 19 gene–drug pairs with strong or moderate CPIC recommendations, pharmacogenetic information appears scattered across seven different sections, with poor agreement with other regulatory agencies (Suarez-Kurtz, 2026). The pharmacist interpreting the result must therefore rely on guidelines, and the proposal of a standardised pharmacogenetic section in package inserts would facilitate this work (Suarez-Kurtz, 2026).

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

7. A REUSABLE RECORD: RNDS AND DATA GOVERNANCE

The RNDS is the national health interoperability infrastructure (Brasil, [2026b]), and Decree No. 12,560/2025 regulates the RNDS and the SUS Digital Platforms, including proportionate data processing and data protection impact assessments (Brasil, 2025a). Integrating a structured pharmacogenetic record into the RNDS is, in this essay, a technical proposal rather than an implemented functionality. The suggested minimum data set contains only the variants actually analysed, method and limitations, diplotype where applicable, inferred phenotype, guideline used and interpretation version (Table 4). Storing the whole genome in the network is not proposed.

Table 4 is a conceptual starting point, not an information model. A pilot would require, at least: a coding standard and semantic interoperability with the RNDS; a representation of alleles, diplotypes and phenotypes that follows international nomenclature; recording of the analytical method, of the variants covered and of uncertainty; versioning of the translation rules and of the guideline used; a standard drug terminology; and governance for updating interpretations, defining who issues a new interpretation, how prescribers are notified and how previous versions are preserved.

Genetic data relating to a natural person are sensitive personal data under the General Personal Data Protection Law (Brasil, 2018) and carry a particular risk of reidentification, including of relatives. In addition to access by care purpose and professional profile, audit trail, encryption, minimisation and clear information for the data subject, data governance should define: retention periods; safeguards against reidentification; rules for secondary use; an incident-response plan; and procedures for exceptional research access, subject to ethical approval. The legal basis for processing is defined institutionally for each processing operation, not selected by the professional at each access. A negative result should be recorded as "not detected among the variants assessed", and a guideline update should generate a new interpretation without deleting the previous one. Commercialisation or sharing with insurers or employers is outside the scope of the model, but this exclusion does not

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

replace governance: the pilot protocol must list permitted and prohibited uses, sharing rules, conditions for secondary research and audit procedures.

Table 4 – Proposed minimum content of the interoperable pharmacogenetic record

Block	Elements
Identification	Patient identifier according to national standards; test identifier; dates of collection and analysis
Test	Laboratory and technical lead; method; list of variants actually covered; limitations (including structural variation) and analytical uncertainty
Result	Genotype or diplotype in standard nomenclature; inferred phenotype; translation rule and its version; negative result described as "not detected among the variants assessed"
Recommendation	Drug (standard terminology) and indication; guideline and version; clinical interpretation and reinterpretation history; responsible professional; date
Decision and follow-up	Prescriber's decision and justification; monitoring; subsequent clinical event
Security	Purpose of access; professional profile; audit log. The legal basis is defined institutionally for the processing operation, not chosen at each access

Source: prepared by the authors based on Brasil (2025a), Brasil (2018) and Dunnenberger et al. (2015).

Table 4 restricts the record to what is needed for clinical decision-making and traceability. Separating result, recommendation and decision allows the interpretation to be updated when a guideline changes, without losing the history of what was recommended and decided.

8. AN EXPECTED-VALUE HEURISTIC AND ILLUSTRATIVE BREAK-EVEN EXERCISES (LEVEL 2)

To make explicit what must hold for pharmacogenomics to fit the budget, the following heuristic formulation of the expected net cost per person tested, over a defined horizon, is proposed:

$$NC = C_t + C_s + C_i - \Sigma_k [\, p_k \cdot a_k \cdot d_k \cdot r_k \cdot \Delta C_k \,] \quad (1)$$

C_t is the full cost of the test (collection, analysis and report); C_s, the cost of pharmaceutical care, including reinterpretations; and $C_i = F_i/N + R_i$, the cost of integration and governance per person, where F_i is the fixed cost (information model, RNDS integration, training, infrastructure) shared among N people tested over the horizon and R_i the recurrent cost per person (maintenance, updates, audit, security,

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DOI: 10.66104/y3x8xb05
Pages: 1-35

support). For each gene–drug pair k, p_k is the probability of clinically relevant exposure to the drug within the horizon; a_k, the probability of an actionable result correctly identified by the panel used; d_k, the conditional probability that the information generates a recommendation to change; r_k, the probability that this recommendation is accepted and implemented; and ΔC_k, the avoided cost attributable to the intervention relative to the comparator. Events and costs for the different k must be defined without overlap, to avoid double counting in people taking several medicines. NC is negative when the strategy saves resources; when it is positive, it must be weighed against the health benefit according to the Brazilian methodological guidelines (Brasil, [2026a]).

The expression is a didactic heuristic, not an economic model sufficient for an incorporation decision. It does not explicitly incorporate time, discounting, mortality, utilities, recurrent events, correlation between exposures, competing risks, future costs, guideline changes, parameter uncertainty or the value of information, all of which a cost-utility analysis, a state-transition model and a budget impact analysis would have to address. Its value is to show that economic value depends jointly on exposure, actionability, recommendation, implementation and clinical consequence, and that a multigene panel triggered by one indication differs from a single-gene test: C_t is higher, but the sum may include other pairs over time. Because auditable Brazilian parameters were not available for all terms of the expression, NC was not calculated with real values and no savings for the SUS were inferred. Sections 8.1 and 8.2 only illustrate how the expression behaves.

8.1 Illustrative break-even exercise: CYP2C19–clopidogrel

The SUS comparator for this pair is the national protocol for acute coronary syndromes approved by Ordinance GM/MS No. 2,994/2011, which incorporated clopidogrel 75 mg into the SUS procedures table and provided for its supply after hospital discharge (Brasil, 2011); ticagrelor was not incorporated for the prevention of thrombotic events in acute coronary syndrome (Ordinance SCTIE/MS No. 8/2013, based on Conitec Recommendation Report No. 41) (Brasil, 2013b), and prasugrel was not incorporated for diabetic patients with acute coronary syndrome undergoing primary angioplasty (Ordinance SCTIE/MS No. 60/2020) (Brasil, 2020). In the

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Vol: 13.21
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Pages: 1-35

sources consulted (Conitec decisions and court technical notes), we found no subsequent decision incorporating either drug for these indications up to the cut-off date, a point that should be rechecked before any pilot. The relevant comparison for the SUS is therefore current protocol treatment with clopidogrel versus the same protocol with genotype-guided modification for eligible patients, in which carriers of loss-of-function alleles would receive an alternative P2Y12 inhibitor. The incremental cost must represent what would actually change after incorporation, including the acquisition of an alternative not currently provided.

Consider patients undergoing percutaneous coronary intervention over a 12-month horizon. In TAILOR-PCI, among carriers of CYP2C19 loss-of-function alleles, the composite ischaemic outcome (cardiovascular death, myocardial infarction, stroke, stent thrombosis and severe recurrent ischaemia) occurred in 4.0% of the genotype-guided group and 5.9% of the conventional clopidogrel group (HR 0.66; 95% CI 0.43–1.02; p = 0.06), a difference of 1.9 percentage points that did not reach statistical significance in the prespecified analysis (Pereira et al., 2020). The exercise therefore does not treat this difference as an established causal effect; it uses it as one value in a sensitivity range. In a sample of the Brazilian general population, the frequency of the CYP2C19*2 allele ranged from 10.4% in Amerindians to 20.2% in people of African descent, and the *3 allele was not detected (Santos et al., 2011); under Hardy-Weinberg equilibrium, this corresponds to about 20% to 36% carriers of at least one loss-of-function allele, with a central value close to 31%.

Restricting expression (1) to this pair, the net cost is zero when $f \cdot d \cdot r \cdot (\Delta \cdot q \cdot H - D) = C_t + C_s + C_i$, where f is the proportion of carriers, Δ the absolute reduction in the outcome, q the proportion of avoided events that would have led to hospital admission, H the mean cost of admission, d and r the probabilities of recommendation and acceptance, and D the annual incremental medicine cost per carrier. For ticagrelor 90 mg twice daily instead of clopidogrel 75 mg once daily, $D = 730 \cdot p_t - 365 \cdot p_c = 365 \cdot (2 \cdot p_t - p_c)$, where p_t and p_c are unit prices; the limit is therefore expressed as an annual incremental cost and not as a difference per tablet. For H, the mean value of the hospital admission authorisation (AIH) for acute myocardial infarction in the SUS in 2025, R$ 5,764.59, obtained from the SIH/SUS, is used (Paiva

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

et al., 2026). With f = 0.31, d = 1 and r = 0.85, Table 5 shows the maximum annual incremental cost D compatible with break-even for different effect sizes and three totals of test, service and integration costs: two hypothetical values (R$ 20 and R$ 150) and the price of a commercial multigene pharmacogenetic test, R$ 987 per patient, used in a Brazilian cost-utility analysis from the supplementary health system perspective (Andrade-Silva et al., 2023), taken here as an order of magnitude for C_t alone.

Table 5 – Illustrative break-even: maximum annual incremental medicine cost per carrier (D, R$) compatible with zero net cost, by effect size (Δ), proportion of hospitalised events (q) and total cost per person tested

$C_t + C_s + C_i$	q	Δ = 0	Δ = 0.010	Δ = 0.019	Δ = 0.030
R$ 20	0.50	none	none	none	10.57
R$ 20	0.75	none	none	6.24	53.80
R$ 20	1.00	none	none	33.63	97.04
R$ 150	0.50 to 1.00	none	none	none	none
R$ 987, commercial multigene test (Andrade-Silva et al., 2023)	0.50 to 1.00	none	none	none	none

Source: prepared by the authors. Hypothetical values: f = 0.31, d = 1, r = 0.85, H = R$ 5,764.59, the mean AIH for acute myocardial infarction in 2025 reported by Paiva et al. (2026); Δ = 0.019 corresponds to the non-significant difference in TAILOR-PCI (p = 0.06) (Pereira et al., 2020). $D = \Delta \cdot q \cdot H - (C_t + C_s + C_i)/(f \cdot d \cdot r)$. "None": the ceiling is negative, i.e. no alternative more expensive than clopidogrel reaches break-even. Not an economic evaluation.

Under the hypothetical values adopted, the scenario reaches break-even against clopidogrel for everyone only with a combination that is unlikely: an effect at least as large as that observed in TAILOR-PCI, a high proportion of hospitalised events, an almost free test and an alternative whose annual additional cost would remain below a few tens of reais. With Δ = 0 or 0.01, or with costs of R$ 150 or R$ 987 per person, no alternative that is more expensive than clopidogrel reaches break-even. To compare these ceilings with observed prices, purchase records for clopidogrel 75 mg and ticagrelor 90 mg tablets were extracted from the open files of the Health Price Database (Banco de Preços em Saúde, BPS) for 2025 and 2026, downloaded on 13 October 2026 (Brasil, 2026c). Records for other presentations or

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Vol: 13.21
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Pages: 1-35

fixed-dose combinations were excluded, and prices were expressed in R$ per tablet. Table 6 summarises the prices and the resulting values of D. With the median prices of all purchases, D was about R$ 2,724 per carrier per year; even with the lowest ticagrelor price recorded, it was about R$ 1,788, roughly 18 times the highest break-even ceiling in Table 5. Reaching break-even at that price, with q = 1 and costs of R$ 20, would require an absolute reduction of about 32 percentage points in the composite outcome, more than five times the event rate observed in the clopidogrel arm of TAILOR-PCI. The result does not show that genotyping "does not save resources" in the SUS; it shows that, under these assumptions, any case for the strategy against the current comparator would rest on health gain, to be measured as an incremental cost-effectiveness ratio, rather than on savings.

Table 6 – Unit prices of clopidogrel 75 mg and ticagrelor 90 mg in public purchases (BPS, January 2025 to September 2026) and derived annual incremental cost (D) and counterfactual ceiling

Scenario	Ticagrelor 90 mg, R$/tablet (n)	Clopidogrel 75 mg, R$/tablet (n)	D = 365·(2·p_t − p_c), R$/year	Ceiling for C_t + C_s + C_i vs universal ticagrelor, R$
Median, all purchases	3.91 (12)	0.356 (110)	2,724	1,598
Median, administrative purchases only	3.30 (7)	0.35 (102)	2,281	1,338
Lowest ticagrelor price; clopidogrel median	2.63 (1)	0.356 (110)	1,788	1,048

Source: prepared by the authors from the open files of the Banco de Preços em Saúde for 2025 and 2026 (Brasil, 2026c), downloaded on 13 October 2026 (purchase dates 22 January 2025 to 23 September 2026). Ceiling = (1 − f)·r·D with f = 0.31 and r = 0.85. Purchases include administrative and court-ordered acquisitions by municipal and state institutions; a fixed-dose acetylsalicylic acid + clopidogrel record was excluded. Values are illustrative and are not an economic evaluation.

The BPS data in Table 6 have limitations: records depend on reporting by purchasing institutions and are not a national price; ticagrelor had only 12 purchases in five states, five of them made to comply with court orders, which suggests ongoing judicial demand for a medicine not incorporated in the SUS; and a few clopidogrel records had implausibly high unit prices, probably unit errors, to which the median is robust. Prices paid in a future centralised purchase could differ.

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

The exercise has further limitations. The AIH value for myocardial infarction is a reimbursement, not the economic cost of admission, and does not represent the cost of the whole composite outcome: stroke, stent thrombosis, reintervention, death and severe ischaemia have different costs and consequences, and the parameter q addresses only the frequency of admission. A real evaluation should disaggregate events, use micro-costing or actual SUS costs, include direct medical and subsequent costs, adopt an adequate time horizon with discounting and use prices from a predefined period and purchasing perspective, updated at the time of analysis. It should also model the panel actually proposed rather than a single-gene test, and represent the uncertainty of Δ probabilistically.

8.2 Counterfactual sensitivity scenario: universal ticagrelor

Because universal ticagrelor is not the SUS comparator, the following scenario is a counterfactual sensitivity analysis and does not carry the same analytical weight as section 8.1. In POPular Genetics, the standard arm received ticagrelor or prasugrel, whereas in the genotype-guided arm non-carriers received clopidogrel and carriers received ticagrelor or prasugrel; the guided strategy was non-inferior for net adverse clinical events (5.1% versus 5.9%; $p < 0.001$ for non-inferiority) and resulted in fewer major or minor bleeding events (9.8% versus 12.5%; HR 0.78; 95% CI 0.61–0.98) (Claassens et al., 2019). The scenario below simplifies this protocol into a comparison with universal ticagrelor, which is acceptable only as hypothetical modelling.

If non-carriers, about two thirds of patients, switched from ticagrelor to clopidogrel without loss of efficacy, the maximum test price compatible with break-even would be approximately $(1 - f) \cdot r \cdot (730 \cdot p_t - 365 \cdot p_c) - C_s - C_i$; with f = 0.31 and r = 0.85, each R$ 1.00 in the unit price of ticagrelor raises this ceiling by about R$ 428, without counting the reduction in bleeding. With the BPS median prices (Table 6), the ceiling for the sum $C_t + C_s + C_i$ would be about R$ 1,598 per person tested, or about R$ 1,048 with the lowest ticagrelor price recorded. A commercial multigene test priced at R$ 987 (Andrade-Silva et al., 2023) would fall below the ceiling in all three price scenarios, leaving about R$ 611, R$ 351 or R$ 61, respectively, for pharmaceutical care and integration; with the lowest ticagrelor price,

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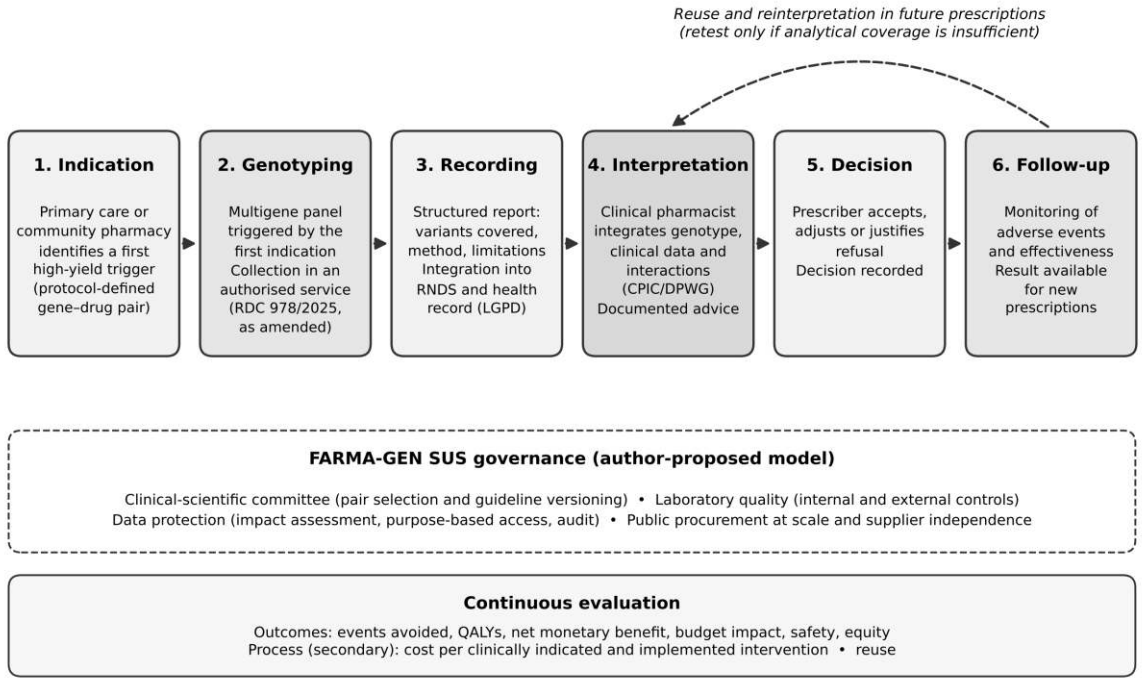
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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

the margin would therefore be very narrow. Under these price differences, therefore, the genotype-guided strategy could be cost-saving relative to a strategy in which everyone receives ticagrelor. Whether this holds depends on negotiated procurement prices, the full costs of the test and of the service, the time needed to obtain the result without delaying treatment and the clinical guidelines in force.

9. THE FARMA-GEN SUS MODEL (LEVEL 3: IMPLEMENTATION HYPOTHESIS)

Figure 1 summarises the author-proposed model. The pathway starts with the first high-yield clinical trigger identified in primary care or in a pharmacy, moves through multigene genotyping in an authorised service and structured recording, and reaches pharmacist interpretation and the prescriber's decision. Follow-up returns the result to the system for future prescriptions, with reinterpretation when guidelines change and retesting only when analytical coverage is insufficient. The pathway is supported by a governance layer, with a clinical-scientific committee for pair selection and guideline versioning, laboratory quality, data protection and public procurement, and by a continuous evaluation layer.

Figure 1 – The FARMA-GEN SUS model (author-proposed): care pathway, governance and evaluation



Source: prepared by the authors.

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Pages: 1-35

Figure 1 shows that the expected value of the model lies in the cycle rather than in any single step: the result recorded at step 3 returns to step 4 with each new prescription, without a new test unless coverage is insufficient. The governance and continuous evaluation layers support all steps and define the criteria for continuing or stopping the pilot.

The proposed implementation follows four phases with progression criteria: (i) preparation, with regulatory analysis according to the rules then in force, data protection impact assessment and a protocol approved by an ethics committee; (ii) feasibility, with interoperability tests using synthetic data, pharmacist training and documentation of the laboratory capacity to be used; (iii) a prospective comparative pilot in territories with different care capacities, comparing current protocol treatment with the same protocol plus FARMA-GEN SUS, with micro-costing; and (iv) economic and budget impact evaluation according to the guidelines of the National Commission for the Incorporation of Technologies in the SUS (Conitec) (Brasil, [2026a]), with a decision on expansion. Serious adverse events attributable to the pathway, critical unavailability of results or a relevant privacy incident are stopping criteria. Table 7 lists the minimum indicators.

Table 7 – Minimum indicators for pilot evaluation

Dimension	Indicator
Health outcomes (primary)	Predefined clinically relevant adverse drug reactions; ischaemic and bleeding events, disaggregated; hospital admissions; safety events attributable to the pathway
Economic value	Micro-costed cost per person tested (including pharmacist time, fixed and recurrent integration costs); incremental cost per QALY and per event avoided; net monetary benefit; budget impact
Implementation (secondary)	Cost per clinically indicated and implemented intervention; recommendations issued, accepted, declined with justification and unanswered; time to decision; proportion of changes judged clinically appropriate on audit
Process	Eligible patients informed; tests completed; median request-to-result time; results available at the point of care
Reuse	Subsequent prescriptions that consulted the result; reinterpretations; retests needed and avoided
Equity	Indicators above stratified by region, age and digital barriers

Source: prepared by the authors based on Brasil ([2026a]) and Swen et al. (2023).

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

The indicators in Table 7 distinguish health and economic outcomes, which define value, from process indicators, which describe implementation. Stratification by region, age and digital barriers makes it possible to check whether any cost reduction is accompanied by an equitable distribution of benefits.

10. EQUITY

A strategy that lowers the cost per test may at the same time widen inequalities if it mainly benefits urban, digitally connected people living close to laboratories. The evaluation of FARMA-GEN SUS should stratify provision, test completion, time to result, receipt of interpretation and therapeutic change by region, age and digital barriers, and maintain a care pathway for people who do not use apps. For Indigenous populations, documented differences in allele frequencies (Suarez-Kurtz; Basta; Perini, 2026; Perini; Basta; Suarez-Kurtz, 2024) call for adapted analytical coverage and individual assessment, not identity-based panels, together with free, prior and informed consultation and community governance over testing, data and return of results.

11. LIMITATIONS

This essay is not a systematic review; the purposive selection of sources may have missed relevant experiences, particularly in Latin America. The complementary searches in PubMed and in the BVS portal (including LILACS-indexed records) did not name every country in the region or all relevant terminology, were not designed as systematic searches, and no formal inter-rater agreement statistic was calculated; Embase, EconLit, health technology assessment reports and institutional literature were not systematically searched, which remains a limitation for regional economic evidence. The exercises in section 8 are illustrative: they use a clinical effect that was not statistically significant, the AIH value for myocardial infarction as a proxy for the cost of a composite outcome, a reimbursement rather than an economic cost, drug prices from a public-purchase registry that depends on institutional reporting and a single commercial test price from the supplementary sector, and are not an economic evaluation. The clinical and economic evidence comes mainly from European populations and high-income systems. The regulatory and judicial analysis reflects acts and decisions in force on 13 October 2026 and will need updating before any

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

implementation. The first author works in a community pharmacy, which is material to the interpretation of the role proposed for pharmacies.

12. CONCLUSION

No savings from pharmacogenomics have been demonstrated for the SUS, and this essay does not claim them. Its contribution is a framework for formulating and testing the hypothesis that pharmacogenomics may become economically viable in the SUS if patient selection, laboratory cost, clinical implementation and reuse are jointly optimised: a multigene panel triggered by a first high-yield indication, with analytical coverage suited to the Brazilian population, interpretation based on open guidelines, collaborative work between clinical pharmacists and prescribers within the current regulatory limits, and a minimal, protected and reinterpretable record. The illustrative exercises show that the economic result depends heavily on effect size, comparator and prices. FARMA-GEN SUS must therefore be evaluated in a prospective Brazilian pilot, with micro-costing and health outcomes such as events avoided, QALYs and net monetary benefit, before any proposal for expansion.

DECLARATIONS

Author contributions (CRediT): João Fernandes Floriano: conceptualisation, investigation, formal analysis, visualisation and writing – original draft. Maria Elizabeth Menezes: validation, investigation (independent screening of search records) and writing – review and editing. Both authors approved the final version and are accountable for all aspects of the work.

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Conflict of interest: João Fernandes Floriano works professionally and in a management role in a private community pharmacy, a sector discussed in this essay. This interest is material to the interpretation of the role proposed for community pharmacies; for this reason, the essay makes no claim about the superiority of pharmacies over other care settings and treats their feasibility, reach and costs as

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Vol: 13.21
DOI: 10.66104/y3x8xb05
Pages: 1-35

hypotheses to be measured. Maria Elizabeth Menezes declares no conflicts of interest.

Ethical aspects: The study used only published, publicly available information and therefore did not require review by a Research Ethics Committee, in accordance with Brazilian National Health Council Resolution No. 510/2016.

Data availability: No primary data were generated, and every source used is cited in the reference list. The break-even calculations can be reproduced from the formulas and values given in section 8 and Tables 5 and 6; the BPS extraction used the public files cited in the references.

Use of generative artificial intelligence: Consensus (Consensus NLP) and Claude (Anthropic) were used as aids for literature discovery and organisation, and Claude also for revising the text, translating it into English and formatting it according to the journal's guidelines. These tools did not replace the reproducible PubMed search described in the Methods or the verification of sources: every reference was checked by the authors against primary sources (authors, title, year, volume, pages and DOI or official text). The tools were not used to generate data. All content was reviewed, validated and edited by the authors, who take full responsibility for its accuracy, integrity and originality.

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