Research Square

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From Access to Appropriate Use: Reimbursement Design for Pathogen Nucleic Acid Diagnostics across Six Health Systems, 2014–2026

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Abstract

Background

Pathogen nucleic acid diagnostics answer questions that culture, antigen detection and serology cannot answer within the treatment-decision window — slow-growing and fastidious organisms, paucibacillary disease, and genotypic resistance — yet are persistently reimbursed below that value; we ask whether that mismatch is transitional or structural.

Methods

We compare six health systems (China, the United States, Germany, France, England, Japan) under a most-different-systems design, tracing three index technology classes defined by target scope — single-pathogen detection with or without a resistance-conferring variant; multi-pathogen targeted detection by multiplex or isothermal amplification or panel enrichment with sequencing; and untargeted metagenomic sequencing of the primary specimen — through a three-gates framework (approval, price assignment, coverage) using primary policy documents, 2014–2026, under confidence-tiered verification.

Results

All six systems impose the same three gates, but the binding gate differs: China's price-item gate is being removed by the 2026 national price-item guideline (trial), which standardises item definitions but not price levels, so the binding constraint migrates to insurance listing rather than disappearing; the United States binds at clinical-utility evidence; Germany at coverage. A "double squeeze" of inpatient diagnosis-related-group bundling and outpatient price compression (Medicare's ratcheted PAMA repricing, repeatedly deferred; China's volume-based procurement cuts of 47–77%; Japan's FY2014 256-item fee cut) suppresses adoption of cost-effective tests. Five innovation carve-outs echoing the coverage-with-evidence-development concept underperform for diagnostics: Germany's inpatient innovation channel (NUB) integrated 105 of more than 3,400 methods into regular payment in 2005–2020 (single peer-reviewed source); Medicare's molecular-panel coverage policy excludes metagenomic sequencing from its scope, with no affirmative coverage elsewhere. Regulatory review itself ranges from months (Japan's targets; US 510(k) goals) to multiple years (China's Class III elapsed times; EU notified-body backlogs). For metagenomic sequencing, Gate 1 is a laboratory-accreditation regime rather than product review, and the longest lags sit at the approval–payment interface (median 5.7 years from FDA authorisation to nominal Medicare coverage in a 2016–2019 cohort; diagnostics' lags were shorter).

Conclusion

The reimbursement gap is structural and is best explained by the externalisation of diagnostic value across budget silos; closing it requires diagnostic-specific payment design coupled to prescriber competency in test selection.

Implications for policy makers

Publish test-level prices or tariffs for nucleic acid diagnostics: implicit rationing of laboratory budgets then becomes explicit and auditable — England's 2026/27 genomic tariffs and China's 2026 national price-item guideline are the first large-scale natural experiments in test-level price transparency, with effects not yet observable.

When paying for a new test conditionally, reimburse the test together with the stewardship programme that produces its outcome benefit — France's RIHN 2.0 supplies the contract template.

Credit avoided antibiotic days and bed-days to the budget that orders the test, and exempt diagnostics with graded evidence of cost-effectiveness from across-the-board procurement and fee-cut rounds.

Implications for the public:

Faster access to accurate infection tests means the right treatment sooner and fewer unnecessary antibiotics, slowing antibiotic resistance.

Payment rules decide whether tests reach patients: an unpriced or uncovered test may not be offered, even if effective.

1. Introduction

1.1 Background and motivation

Over the past fifteen years, pathogen nucleic acid diagnostics — syndromic multiplex polymerase chain reaction (PCR) panels, metagenomic next-generation sequencing (mNGS), and World Health Organization (WHO)-endorsed nucleic acid amplification tests (NAATs) such as Xpert MTB/RIF — have moved to the front line of infectious-disease management because they answer questions that culture, antigen detection and serology cannot answer within the treatment-decision window (slow-growing and fastidious organisms, paucibacillary disease, genotypic resistance; Supplementary Material S10), with an unusually well-documented value proposition: molecular rapid diagnostic testing reduced mortality (odds ratio 0.66), time to therapy and length of stay in bloodstream infection when coupled to antimicrobial stewardship [(1)], and Xpert MTB/RIF costs US$41–138 per disability-adjusted life-year averted in high-burden settings (2011 price levels) [(2)]. The clinical centre of gravity is respiratory: the respiratory tract is the principal portal through which the pathogens targeted by the index assays enter the host, and the usual starting point of the systemic dissemination — bloodstream infection and sepsis — that these technologies are increasingly used to resolve. Yet payment remains persistently weak: diagnostic value is informational and hierarchically mediated [(3)], most dossiers stop at accuracy rather than outcomes, outcome-grade trials number only about 37 per year (2012 estimate) [(4)], and the benefits accrue outside the laboratory budget that bears the test cost.

Since 2020, fiscal pressure has pushed dissimilar systems towards a common instrument set [(5, 6)]: inpatient testing is absorbed into prospective bundles (diagnosis-related groups [DRGs] and national variants — France's GHS, Japan's DPC, the US IPPS, China's DIP), while outpatient testing faces explicit price compression (Protecting Access to Medicare Act [PAMA] repricing, fee-schedule point cuts, volume-based procurement [VBP]). The systems themselves remain profoundly different: health expenditure ranged from 17.6% of gross domestic product (GDP) in the United States (2023, CMS National Health Expenditure basis) [(7)] to 5.6% in China on the OECD basis (China's official measure is approximately 7.2%) [(8)]. The clinical questions that make these tests non-substitutable — organisms whose culture is unavailable within the decision window, paucibacillary disease in which smear and culture sensitivity collapses, serology that post-dates the treatment decision, and sub-species characterisation returnable by no non-molecular method — are documented with their performance evidence in Supplementary Material S10.

1.2 Research gap

Cross-country scholarship on diagnostic reimbursement is sparse and dated: existing mappings document drug–diagnostic desynchronisation in European companion diagnostics [(9)] and fragmented access pathways for in vitro diagnostic (IVD) devices across five systems [(10)], both stopping at route description. This study addresses five deficits: *temporal* (no peer-reviewed comparison reaches the 2024–2026 policy frontier); *geographic* (China, the largest natural experiment in diagnostic price and volume compression, is absent); *disease-area* (prior comparisons are oncology-centric, whereas infectious-disease nucleic acid diagnostics face a harsher regime despite stronger cost-effectiveness evidence); *mechanism* (which of the sequential gates binds remains unanalysed); and *evidence-economics* (the mismatch between payer evidence demands and diagnostics' evidence-production capacity [(4)]).

1.3 Research questions

A third family of institutions mediates between these pressures and access: temporary innovation carve-outs, including Germany's NUB (Neue Untersuchungs- und Behandlungsmethoden, "new examination and treatment methods") and Zusatzentgelt (ZE, supplementary payment), France's RIHN 2.0, the US Molecular Diagnostic Services (MolDX) programme, and the Early Value Assessment (EVA) of England's National Institute for Health and Care Excellence (NICE). This study asks three questions:

- **RQ1 (descriptive-comparative)**: How do the payment architectures of six health systems (China, United States, Germany, France, England, Japan) govern the three sequential reimbursement gates (regulatory approval, price/code assignment, and coverage decision) for pathogen nucleic acid diagnostics across the three classes defined in Section 2.2 — single-pathogen detection with a resistance variant, multi-pathogen targeted detection, and untargeted metagenomic sequencing? Which gate is binding in each system?

- **RQ2 (mechanistic)**: Through what mechanisms do convergent cost-containment instruments — inpatient prospective bundling (DRG/DIP/GHS/DPC/IPPS) and outpatient price compression (PAMA medians, fee-schedule point cuts, VBP) — create a structural "double squeeze" that suppresses adoption of nucleic acid diagnostics even where clinical value and cost-effectiveness are established?
- **RQ3 (normative/design)**: To what extent do emerging innovation carve-outs (NUB/ZE, RIHN 2.0, MolDX technical assessment, NICE EVA, China's special-case deliberation / carve-out payment) embody "coverage with evidence development," why do they underperform for diagnostics (whose value is informational and externalised across budget silos), and what diagnostic-specific design features would correct this misalignment?

1.4 Contributions

The study makes four contributions: an analytical framework — a "three gates × gate-sequencing" model showing that the gates are universal but which gate binds, and when, differs systematically; a two-dimensional account in which system archetype locates the binding gate while technology attributes — registration route, outcome-evidence tractability, platform openness and target content — determine the difficulty of passage; the first six-system, primary-source-verified account of pathogen molecular diagnostic reimbursement through the 2025–2026 policy frontier; and a diagnostic-specific carve-out design proposal motivated by the documented underperformance for informational technologies of device- and drug-shaped instruments built on coverage-with-evidence-development logic [11].

2. Methods

2.1 Study design

This study is a comparative policy analysis under a most-different-systems logic: six health systems differing maximally in financing, provision and administrative tradition are examined for convergent payment mechanisms governing one technology class, IVDs for pathogen detection. The unit of analysis is the payment pathway of an index test in a defined care setting; the observation window is 2014–2026. No reporting guideline exists for comparative policy analysis; the study is instead reported against a bespoke transparency protocol covering verbatim source extraction, dual independent verification and confidence tiering (Supplementary Material S1).

2.2 Case selection

Selection was theory-driven: financing archetype predicts the instrument through which laboratory services are paid. The six systems span four financing archetypes condensed from the leading deductive classifications of OECD health systems [12, 13]: Bismarck-type social health insurance (Germany, France), a tax-funded national health service (England), a market-based public–private hybrid (United States), and universal social insurance with strong state price administration (Japan; and China, extending the comparison beyond the OECD). The four-type scheme merges the two social-insurance subtypes (social and etatist) of the five-type source classification and groups China with Japan — a simplification that affects only the granularity of the archetype axis, not the gate analysis, which is conducted per system. Three index technology classes span a clinical-maturity gradient while holding the disease area constant, defined by target scope rather than by product or platform (Supplementary Material S11): (i) single-pathogen detection, either as a stand-alone pathogen target or combined with a defined resistance-conferring sequence variant (first-layer amplification by PCR or isothermal methods; second-layer readout by fluorescent hydrolysis probes, or by melting-curve analysis resolving point mutations directly); (ii) multi-pathogen targeted detection, by multiplex PCR or isothermal amplification (first layer), read out (second layer) by fluorescent probe panels, melting-curve analysis, ligation-dependent probe amplification with fragment sizing (MLPA), or sequencing after panel enrichment by multiplex amplification or hybrid capture; and (iii) untargeted metagenomic sequencing of the primary specimen, an unbiased library prepared without target primers. Within class (i) the two tiers behave differently at the gates: long-listed single-target respiratory NAATs (influenza A/B, M. pneumoniae) are priced and covered in every system studied, whereas the resistance-variant tier — traced here through tuberculosis NAAT with rpoB detection — is newly itemised and unevenly covered; the contrast is itself evidence that the binding gates identified here act on newly created items rather than on molecular testing as such. Xpert MTB/RIF serves as the class exemplar rather than a vendor case: its selection follows WHO endorsement and evidence maturity rather than market prominence, and the gates analysed bind the technology class, including domestically registered equivalents (Section 3.5). All three index technologies are reference points rather than market

proxies — the syndromic-panel exemplar's manufacturer reports an approximately 70% share of its multiplex segment, whereas China's tuberculosis NAAT market pairs the leading imported platform with a larger domestic assay ecosystem, and mNGS is delivered as a centralised laboratory service in both China and the United States (Supplementary Material S7). A routine tier of long-listed respiratory NAATs (influenza, M. pneumoniae and similar single-target tests) passes all three gates in every system and serves as the no-binding-gate baseline (Supplementary Material S7). One delivery-mode boundary is explicit: the three-gates framework applies to institution-based testing, whereas home and point-of-care testing follow a different regulatory logic. Regulators distinguish *self-testing* — a lay person performing any part of the assay, which requires product approval with an explicit self-test indication and lay-user evidence — from *self-collection for laboratory analysis*, which is not self-testing and follows the lighter specimen-receptacle-plus-laboratory-accreditation path (Supplementary Material S8). Home-use NAAT self-tests are essentially absent outside the United States (where Lucira's LAMP-based home COVID/flu test is the exception); everywhere else in this comparison, home NAAT is delivered as self-collection with central laboratory analysis. Home testing therefore does not enter the gate analysis: its constraints are product approval and service licensing, not the price-item/coverage sequence examined here. (Covariate scope decision: Supplementary Material S4.)

2.3 Analytical framework

1. **2.3.1 Three gates.** Grounded in Fryback–Thornbury's efficacy hierarchy [3] and Bossuyt's pathway logic [14], we define three sequential gates every system imposes on any new IVD seeking payment (per-system instantiations: Table 1): **Gate 1 (regulatory/market authorisation)**, the legal right to market or perform the test; **Gate 2 (price/code assignment)**, a billable identifier and price — or, in England, the *absence* of test-level prices; and **Gate 3 (coverage/funding decision)**, whether and on what terms the payer pays. The gates are universal, but *which gate binds* differs systematically (Section 3.1).
2. **2.3.2 Double squeeze.** We define the **double squeeze** as the simultaneous exposure of diagnostics to (a) inpatient prospective bundling, which absorbs tests into fixed case payments and thereby converts laboratories from profit centres into cost centres — routine inpatient testing showed "major decreases" after Medicare's 1983 Prospective Payment System [15] — and (b) outpatient price compression of administered fees (Section 3.3).
3. **2.3.3 Externality-misalignment lens.** To evaluate innovation carve-outs we apply an **externality-misalignment lens**: a diagnostic's cost falls on one budget silo, whereas its benefits arise outside the paying silo [1, 16]. Five systems' carve-out mechanisms (Japan excepted) echo the logic of coverage with evidence development (CED) [11], and cross-country evidence documents their operation as inpatient add-on or supplementary payments [17]; CED frameworks demand outcome-level evidence diagnostics rarely supply [18].
4. **2.3.4 Operationalising the binding gate.** A gate is classified as binding when an approved technology observably stalls there, evidenced by the documented absence of a price item or listing, measurable application or rejection statistics, or explicit exclusionary policy text; a binding gate is distinguished from a rate-limiting step, the slowest clock upstream (Section 3.2). Where no product-approval route exists (metagenomic laboratory-developed tests [LDTs]), Gate 1 mutates into a laboratory-accreditation regime. With six systems the diagnosis is hypothesis-generating, not statistically identified (evidence mapping: Supplementary Material S2).
5. **2.3.5 Method classes: two-layer decomposition and trade-offs.** Because gate behaviour attaches to method classes, we fix the classification here. Every index test decomposes into two layers. The first layer amplifies, generates signal from, or enriches target nucleic acid: thermal-cycling PCR (mature and quantitative, but requiring amplicon-contamination control in separated laboratory areas and around one to three hours of thermal cycling); isothermal amplification (LAMP, RPA — faster, instrument-simple and tolerant of inhibitors, but harder to multiplex, weakly quantitative, and run closed because aerosolised amplicon carries over into subsequent reactions); CRISPR-based signal generation (Cas12/Cas13 collateral cleavage — sequence-specific signal amplification, typically following a brief isothermal pre-amplification and not yet standardised); or, for sequencing-based assays, target enrichment by multiplex-PCR amplification or hybrid capture — shotgun metagenomics amplifying nothing, trading per-target sensitivity for unrestricted target scope. The second layer reads the product: fluorescent probes (real-time hydrolysis-probe fluorescence; melting-curve analysis resolves point mutations without sequencing); ligation-dependent probe amplification read by fragment sizing (MLPA); direct colour or lateral-flow readout for simplified formats; or sequencing (Sanger, second- or third-generation), the only readout able to reveal unanticipated variants. These trade-offs are the operating knowledge on which pathogen-related clinicians must select tests — the prescriber-competency premise to which Section 4.3 returns as a payment condition. (Per-class enzyme systems, primer and probe design and platform attributes: Supplementary Material S11.)

2.4 Data sources

Evidence was assembled from primary policy documents — statutes, fee schedules and coverage decisions (NHSA and provincial bureaus; US CMS; G-BA and InEK; HAS and Journal Officiel; NHS England and NICE; MHLW) — and from literature searched in PubMed/PMC and Web of Science, June–August 2026, with an upstream Chinese-language policy survey produced within our institution used as a secondary source; every factual claim carried into the manuscript was re-verified against primary documents [19] (Supplementary Material S1). Verification followed dual-source triangulation with confidence tiering (Tier A asserted directly; Tier B source-noted; Tier C excluded; protocol: Supplementary Material S1). Because a document-based comparison is bounded by what each system publishes, we audited public data availability for six data classes per system — price catalogues, coverage decisions and their rationale, procurement awards, review statistics, test volumes and provider-level charging — recording whether each cell is published in full, partially published, not published, or available only on application (Supplementary Material S7). Throughout we distinguish retrieval gaps (public documents not located) from publication gaps (data classes a system does not generate or does not publish); the institutional absence of a data class was treated as a finding about the payment architecture, not as missing data.

2.5 Measurement-basis disclosures

Measurement bases are disclosed rather than silently harmonised: every health-expenditure figure carries its year and accounting basis [8]; US IVD market-size estimates (US$24–54 billion, inconsistent scopes; Tier C) are excluded from main claims; COVID-19 testing fees serve only as fee-trajectory illustrations.

Search and archival record. All web-based (non-journal) sources cited in this study were retrieved programmatically and archived. We logged every URL with its retrieval status, byte count and, where retrieval failed, the reason. Of 275 logged URLs, 226 (82.2%) were retrieved in full; 29 were blocked by the host (HTTP 403, Cloudflare challenge or connection refused), 8 returned HTTP 404 or resolved to a dead domain, and 12 yielded only an article-level record rather than the primary document. Failures were concentrated in two groups: United States official sources (11 of 43 blocked — 10 on cms.gov, which refuses programmatic access, and one oig.hhs.gov report whose host was unreachable but whose content was recovered from the indexed official PDF) and vendor/think-tank/press sources (17 of 145 blocked). Official sources for Germany, France, the EU, England, Japan and WHO were retrieved without failure (38/38). The full per-URL log, including failure reasons, accompanies this study in the evidence archive; group tallies appear in Supplementary Material S12.

3. Results

3.1 Payment architectures and the three gates (RQ1)

Applying the three-gate framework (Section 2.3.1), we map each system's payment architecture onto the gate sequence (Table 1), diagnose which gate binds (Table 2), and examine subnational divergence.

3.1.1 Gate map across six systems.

Table 1

Six-system comparison of payment architectures across the three reimbursement gates.

System	Financing archetype; health expenditure (basis/year)	Gate 1: regulatory route	Gate 2: price/code mechanism	Gate 3: coverage/funding decision	Dominant inpatient handling
China	Social health insurance with public provision; 5.6% of GDP (OECD, 2023) [8]	National Medical Products Administration (NMPA) registration	Provincial price-item catalogues → National Guideline for Laboratory-Test Price Items (Aug 2026, trial; 662 main items) [23]	Insurance-catalogue listing (province-decided)	DRG/DIP bundle (all 393 pooling regions by April 2025) [65, 66]
United States	Market-based public–private hybrid; 17.6% of GDP (2023, CMS NHE) [7]	Food and Drug Administration (FDA) clearance, or Clinical Laboratory Improvement Amendments (CLIA) laboratory-developed test (LDT) status	Current Procedural Terminology (CPT)/Proprietary Laboratory Analyses (PLA) codes priced on the Clinical Laboratory Fee Schedule (CLFS) under the Protecting Access to Medicare Act (PAMA)	National/Local Coverage Determinations (NCDs/LCDs); MolDX DEX (Diagnostics Exchange) Z-code plus technical assessment (TA) [25]	Medicare Severity diagnosis-related group (MS-DRG)/Inpatient Prospective Payment System bundle
Germany	Bismarck-type social health insurance (SHI); 12.3% (OECD, 2024) [8]	CE marking under the European Union In Vitro Diagnostic Regulation (IVDR)	Uniform Value Scale (EBM); laboratory and molecular items in Chaps. 32/11/19 are set as fixed euro amounts (Eurobeträge), not points × Orientierungswert	Federal Joint Committee (G-BA) decision under § 135 SGB V (outpatient "ban with reservation of permission"); § 137c SGB V (inpatient "permission with reservation of ban")	G-DRG bundle (NUB/ZE add-ons)
France	Bismarck-type SHI; 11.5% (OECD, 2024) [8]	CE marking under IVDR	Nomenclature des Actes de Biologie Médicale (NABM) B-point catalogue (92nd version, 985 acts; standard 60% reimbursement) [27]	Haute Autorité de Santé (HAS) SA/ASA assessment → Union Nationale des Caisses d'Assurance Maladie (UNCAM)/NABM listing; Liste des Produits et Prestations Remboursables (LPPR) listing for device-type IVDs after HAS SA/ASA evaluation	Groupes homogènes de séjour (GHS) DRG bundle
England	Beveridge-type tax-funded national health service; 11.1% (OECD, 2024) [8]	UK Conformity Assessed (UKCA)/CE marking	No routine test-level prices: NHS Payment Scheme block/aligned payment and incentive (API) flows; unbundled Community Diagnostic Centre items; first national genomic-test tariffs, NHS Payment Scheme 2026/27 (cancer and rare-disease scope; published 26 March 2026, in effect 1 April 2026) [97]	NHS England commissioning; National Genomic Test Directory (NGTD) for genomic tests (pathogen genomics excluded; UK Health Security Agency [UKHSA] remit) [30]	Healthcare Resource Group (HRG)-based blended payment

Note. Health-expenditure shares are OECD-basis figures from Health at a Glance 2025 (2024 or nearest available year) [8], except the United States, shown on the CMS National Health Expenditure basis (2023) [7]; China's official national health-expenditure measure is approximately 7.2% of GDP. Cell-level gate instantiations are sourced in Sections 3.1–3.3 and 4.3.

System	Financing archetype; health expenditure (basis/year)	Gate 1: regulatory route	Gate 2: price/code mechanism	Gate 3: coverage/funding decision	Dominant inpatient handling
Japan	Universal social insurance with strong state price administration; 10.6% (OECD, 2024) [8]	Pharmaceuticals and Medical Devices Agency (PMDA) approval	National medical fee schedule (Shinryo hoshu tensuhyo; 1 point = JP¥10) — fee listing *is* the coverage decision	Identical to Gate 2 (Central Social Insurance Medical Council [Chuikyo] listing)	Diagnosis Procedure Combination/per-diem payment system (DPC/PDPS) bundle

Note. Health-expenditure shares are OECD-basis figures from Health at a Glance 2025 (2024 or nearest available year) [8], except the United States, shown on the CMS National Health Expenditure basis (2023) [7]; China's official national health-expenditure measure is approximately 7.2% of GDP. Cell-level gate instantiations are sourced in Sections 3.1–3.3 and 4.3.

Four structural regularities emerge from Table 1. First, Gate 1 binds nowhere in our disease area: closed-cartridge NAATs, syndromic panels and even mNGS (as CLIA LDTs or in-house IVDR tests) are legally performable somewhere in every system, although the IVDR's Article 5(5) regime materially tightens the conditions for in-house metagenomic tests [20]. Second, Gates 2 and 3 are institutionally fused only in Japan, where fee-schedule listing simultaneously sets price and confers coverage; everywhere else the two gates are separable, and access failures occur precisely in the gap between them.

Third, the inpatient column is strikingly uniform: prospective bundles absorb test costs in all six systems (DRG/DIP, MS-DRG, G-DRG, GHS, HRG, DPC), so meaningful variation concentrates in outpatient and carve-out channels — the empirical basis for Section 3.3. Fourth, outpatient price-setting mechanisms diverge widely even where the underlying fiscal lever is shared.

3.1.2 Binding-gate diagnosis per country. The binding gate differs systematically. In **China**, Gate 2 historically bound — many new molecular tests "have no price item, and without a price item hospitals cannot charge" [21]; in practice, absent a dedicated item, hospitals billed through generic proxy items (per-gene or pathogen nucleic-acid catch-alls), with the item applied varying across institutions and provinces — the national reform's own rationale records regional catalogues ranging from about 4,000–5,000 to more than 20,000 items, with identical item names carrying different content across provinces (Supplementary Material S6). The constraint therefore bound not as an absolute bar but as improvised, inconsistent proxy billing, with coverage following the proxy item's status rather than any evaluation of the test itself. The sixth batch of national price governance (2025) capped provincial molecular-test prices [22] (Tier B) and the National Guideline for Laboratory-Test Price Items (662 main items, August 2026) establishes a unified national price-item framework (trial), with provincial execution in progress [23], shifting the constraint to province-decided insurance listing, which Anhui's 2025 notice provisionally withholds [24]. In the **United States**, Gate 3 binds as an *evidence* gate: Medicare coverage runs through MolDX Z-code registration and technical assessment of analytic validity, clinical validity and clinical utility [18, 25], and the MolDX Local Coverage Determination (LCD) L38988 — issued by Palmetto GBA and binding the four MolDX contractor jurisdictions (28 states) rather than the nation — conditions syndromic-panel coverage on peer-reviewed outcome evidence [25]. In **Germany**, diagnostic applications to the inpatient innovation channel were "almost exclusively rejected" — InEK declined all companion-diagnostic applications on record (26; an institutional review — Tier B). In **France**, reimbursement is legally conditioned on prior NABM listing [27], and tariff-setting historically lagged favourable HAS opinions by years, leaving HAS-endorsed molecular tests without payable codes [28]. In **England**, absent test-level prices for the tests examined here, commissioning binds: NICE diagnostics guidance carries no statutory funding mandate [29], and pathogen sequencing sits outside the National Genomic Test Directory (NGTD) [30]. In **Japan**, mixed self-pay billing is prohibited as a general rule (with statutory exceptions under the evaluation and selection schemes), and fee-schedule listing fuses Gates 2 and 3 into one discretionary decision, binding through facility-gating and volume conditions rather than price [31], and metagenomic sequencing remains unlisted entirely (Supplementary Material S5).

The six diagnoses exhibit a systematic pattern: *which gate binds tracks the financing archetype* — state price-administered systems bind at the price or fee-listing gate (China historically; Japan durably), Bismarck-type systems at the coverage or listing gate (Germany; France), the market-based hybrid at the evidence gate, and the tax-funded service at the commissioning gate (Table 2).

Table 2
Binding-gate diagnostic matrix, six systems.

System	Gate 1 (regulatory)	Gate 2 (price or code)	Gate 3 (coverage/funding)	Binding gate (evidence type)
China	NMPA technical review (Class III); real 24–60 months (Tier B)	Provincial catalogues → national guideline 2026	Insurance listing (province-decided)	Gate 2→3 migration (documented absence + exclusion texts)
United States	FDA 510(k)/De Novo; LDTs CLIA-only post-vacatur	CPT/PLA codes; CLFS/PAMA pricing	NCDs/LCDs; MolDX technical assessment	Gate 3 as evidence gate (LCD restriction and exclusion texts)
Germany	IVDR notified body (Class C); 13–18 months	EBM fixed euro amounts	G-BA decisions; NUB/ZE add-ons	Gate 3 (application/rejection statistics)
France	IVDR notified body; same EU lane	NABM B-point tariffs	HAS SA/ASA → UNCAM/LPPR listing	Gate 2/3 sequencing lag (documented listing delays)
England	UK MDR 2002; CE recognised to 2030	No routine test-level prices	NHS England/NGTD commissioning	Gate 3 commissioning (absence of funding mandate)
Japan	PMDA review; 7–12-month targets	Fee-schedule listing	Fused with Gate 2 (Chuikyo listing)	Gate 2 = 3 listing (facility and volume conditions)

Table 2 operationalises the classification rule of Section 2.3.4, recording for each system the instrument occupying each gate and the evidence type on which the classification rests; given the six-system design, the pattern is hypothesis-generating rather than statistically identified.

3.1.3 Subnational divergence. National gate maps conceal within-system variance: identical molecular tuberculosis tests are insurance-listed in some Chinese provinces (Xinjiang, 2019) yet uninsured or provisionally excluded in others (Tianjin, documented 2020; Anhui, 2025) [24, 32, 33] (Section 3.5), and in Germany even NUB Status-1 methods require hospital-by-hospital negotiation, achieved by only 32.9% of acute hospitals in 2013 [34] — whereas in the United States, MolDX makes Medicare outpatient panel coverage uniform across the four MolDX MAC jurisdictions spanning 28 states [35]. Which gate binds for a given patient can therefore depend on province or hospital negotiating capacity, a second-order access inequality that cost-containment and carve-out instruments reinforce rather than soften. Such divergence is observable only where subnational units publish: Chinese provinces publish listing notices, whereas German hospital-level negotiation outcomes and Japanese facility-level notifications are not centrally published, so the visible concentration of divergence in China partly reflects this observability asymmetry (Supplementary Material S7). Subnational variation is therefore a property of all six systems rather than of China alone: United States coverage is determined by regional contractors, with the MolDX policies cited here binding contractor jurisdictions spanning 28 states; German innovation payments are negotiated hospital by hospital; England's commissioning decisions sit with integrated care boards; and Japanese fee-schedule items carry facility and volume conditions verified per institution. What differs across systems is not whether such variation exists but whether it is published.

3.2 Regulatory review pathways and the approval–payment interface (RQ1)

3.2.1 Review architecture and tempo. Gate 1 is anything but trivial: review tempo varies by an order of magnitude across the six systems, and for the newest pathogen diagnostics it is not a product review at all (review-pathway detail: Supplementary Material S6). In China, mandatory registration testing and clinical-evaluation demands stretch real elapsed times for Class III pathogen nucleic-acid reagents to roughly 24–60 months (Tier B) [36, 37, 38] — against multi-year EU notified-body backlogs and US review clocks paused by Additional Information holds [39, 40, 41, 42]. US panels are Class II, with real calendar medians well above user-fee goals once Additional Information holds are counted (Tier B) [39, 40]. In the EU, the shift from roughly 8–10% of IVDs requiring a notified body under the former Directive to 80–90% under the IVDR [41] has made certification the rate-limiting step: by February 2026, 19 designated bodies faced 3,723 applications against 2,318 certificates [42]. Japan's PMDA review runs near its published targets [43, 44], and England recognises CE-marked IVDs until 30 June 2030, registration remaining distinct from funding [45, 46].

For mNGS specifically, Gate 1 is de facto a laboratory-accreditation regime rather than a product review: in the United States, the vacated LDT final rule returned clinical mNGS assays to CLIA-only oversight, and no infectious-disease mNGS assay holds FDA marketing authorisation [47, 48]; in the EU, the in-house-test exemption faces a 2030 "no equivalent device" cliff [49].

Gate-1 innovation channels, where they exist, under-serve diagnostics: the IVD share of approvals under China's innovative-device channel fell from about a quarter in 2018 to about 8% by 2024 (derived from a 2018 press report [50] and annual-report product counts [51]; Tier B), no infectious-disease mNGS assay appears in the US Breakthrough Devices Program's listings as of August 2026 [52], and the EU IVDR framework establishes no equivalent expedited channel [41, 53].

3.2.2 The approval–payment interface: bridges and lags. The gates are not merely sequential but desynchronised, and the longest lags concentrate at the approval–payment interface. In the United States, the median interval from FDA authorisation to nominal Medicare coverage is 5.7 years for technologies needing a new pathway (2016–2019 premarket-approval and De Novo cohort, device-dominated; diagnostics' lags were shorter) [54, 55]; consistently, our own index-test cross-walk yields shorter diagnostics-specific medians (Gate 1→Gate 2: 0.67 years; Gate 2→Gate 3: 2.29 years; Table S5e), plausibly reflecting MolDX's technical-assessment track. The bridges built to close this gap are limited in scale or capacity-capped: FDA–CMS Parallel Review has two completions ever [56], and the Transitional Coverage for Emerging Technologies pathway is paused for new candidates as of August 2026 [57, 58]; its proposed successor, RAPID, would exclude in-vitro diagnostics from eligibility altogether [58]. France's device-listing route has a statutory 180-day target but has exceeded 300 days in practice [59]; Japan pairs the fastest benchmark (a 58-day median approval-to-listing interval for novel medicines) with a biennial fee-revision lag of up to two years [60, 61]; and China has no statutory approval-to-reimbursement linkage for diagnostics (a median 440-day lag is documented for drugs) [60]. Nowhere does Gate 1 bind under the Section 2.3.4 definition; but for metagenomic LDTs it mutates into an accreditation regime whose tempo disciplines every downstream gate.

The gate-timing cross-walk (Fig. 1) makes this sequencing measurable (full dataset in Supplementary Material S5).

(A) Median Gate 1→Gate 2 elapsed time by system (n per bar; † small-n/downward-biased medians for England and China). (B) Median Gate 2→Gate 3 elapsed time; listing and funding are the same administrative act in Japan, and in Germany and France listing confers coverage for routine-tier items (lag 0 for listed items) while novel methods face a separate evaluation track; China's gate 3 remains open-ended for most molecular tests (‡ survivorship-biased, right-censored subsample). (C) Xpert MTB/RIF: Gate-1 authorisation to first price/coverage milestone per system. (D) Share of index diagnostics censored at Gate 2 or Gate 3 per system (denominators differ: 7–9 index tests per system, Table S5). Source: gate-timing cross-walk (Supplementary Material S5); per-cell dates from primary documents.

Gate 1→Gate 2 medians ranged from under one year (United States, 0.67 years, n = 7; France, 1.7 years, n = 6) to four and a half years in Germany (4.5 years, n = 5) — though the German figure mixes three tests that entered the EBM on a single batch-coding date (1 July 2022) with Xpert MTB/RIF, for which a product-neutral tuberculosis NAAT fee item (GOP 32825) has been billable since 2008, and is therefore not directly comparable with per-item regimes — with China at roughly 3.6 years and three tests right-censored at the price gate; Japan's fused design compresses approval-to-listing to days (median 108 days excluding one outlier, n = 3). Gate 2→Gate 3 medians collapse to near zero in Japan, where listing and funding are the same administrative act, and for routine-tier listed items in Germany and France (novel methods in both face a separate evaluation track), but stretch to 2.29 years in the United States (n = 7) and remain open-ended for most Chinese molecular tests (survivorship-biased subsample, n = 3). Systems thus differ less in *whether* gates exist than in *where* elapsed time accumulates, though small samples and right-censoring make these estimates hypothesis-generating.

3.3 The double squeeze: convergent cost-containment instruments (RQ2)

Section 2.3.2 defined the **double squeeze**; this section documents its instruments and magnitudes (instrument inventory: Supplementary Material S6). The central finding is that the two jaws are archetype-independent: all six systems are exposed to both levers — the case bundle and the administered price — though in England the outpatient jaw operates through bundling rather than an explicit test-level price, and France's outpatient compression is comparatively weak (Supplementary Material S6.2).

1. **3.3.1 Inpatient bundling converting laboratories to cost centres.** When Medicare's Prospective Payment System fixed the case payment in 1983, routine inpatient testing showed "major decreases" for Medicare and non-Medicare patients alike: every additional test became a marginal cost with zero marginal revenue [15]. The same mechanism operates in all six systems: no

separate payment is made for US inpatient IVD tests [62]; Germany's G-DRG case rates cover all inpatient laboratory diagnostics [63]; France routes public-hospital testing through GHS bundles [27]; and Japan's DPC/PDPS per-diem cut acute myocardial infarction episode charges by US$1,061 (2012 evaluation) while raising readmissions [64]. China provides the largest natural experiment: by April 2025 all 393 insurance-pooling regions paid by DRG or DIP [65, 66], and causal estimates confirm the laboratory margin responds — inpatient examination-and-testing expenditure fell 19.0% in DIP pilot cities [67] and examination and consultation fees fell 23% under DRG [68] — although in one county-hospital regression-discontinuity study laboratory fees *rose* (borderline significance), plausibly substitution within constrained bundles [69].

2. **3.3.2 Outpatient price compression.** Outside the hospital, systems compress the administered price itself (Fig. 2). These instruments form part of deliberate administered-price governance that has substantially lowered patient out-of-pocket costs for high-volume tests; our analysis concerns not that programme's rationale but its differential incidence at the adoption margin of new nucleic acid diagnostics. China's VBP alliances cut headline reagent prices by 47–77% (Anhui 2021, − 47.02%; Jiangxi-led liver-function alliance, − 68%; Jiangxi-led glucose-metabolism alliance 2025, approximately − 70%; kidney-function/myocardial-enzyme alliance, approximately − 77%; 25-province immunoassay alliance, − 53.9%; 28-province tumour-marker alliance, − 52.62%), but two-level transmission confined actual manufacturer ex-factory erosion to roughly 10–20% [70,71]. The US PAMA re-based the CLFS on private-payer medians — 10%-per-year caps for 2018–2020, congressional freezes through 2021–2026, and cuts of up to 15% per year resuming in 2027 — so current rates still derive from 2016 data, and announced and realised compression must be distinguished [72]. Japan's biennial revisions cut 256 specimen-test items in FY2014 (clinical chemistry 41.4% of cut items), and the FY2026 revision trimmed automated analytes by 3–5 points while adding points for skilled microbiology [73]; Germany's EBM compresses through volume-conditioned discounts rather than headline cuts [74].

(A) Headline price reductions, selected instruments, sorted; the US PAMA entry (asterisk) is a compounded statutory cap (1 − 0.9³ = −27.1%, 2018–2020), not a realised average. (B) Transmission of headline cuts to manufacturer prices under China's volume-based procurement. (C) Japan's emergency-era COVID-19 PCR fee trajectory (points), an illustration of administrative pricing speed outside structural comparison. (D) The US PAMA statutory schedule 2018–2027: phased − 10% caps, the 2021–2026 congressional freezes, and the 2027 resumption at − 15% per year. Source: instrument-level policy documents listed in Supplementary Material S6.

Figure 2 (reproducibility package: Supplementary Material S3) makes three points the narrative can obscure: the steepest publicly announced headline compression is Chinese, clustered in a narrow − 47% to − 77% band suggesting a stable procurement reservation-price logic; headline cuts overstate manufacturer impact, because two-level transmission confines net erosion to roughly 10–20% (Panel B); and the US entry is a *cap*, not a realised average — PAMA's significance lies in its ratchet and Congress's repeated suspensions rather than its depth. Depth (China), transmission and durability (United States) should therefore be weighed separately.

3.3.3 Industry and access consequences. The squeeze's incidence is measurable in industry data, most sharply in China: of 55 A-share listed IVD companies, 44 reported revenue decline in FY2025, according to financial-press compilations of Wind data (Tier B) [75]. The United States supplies the counterpoint: Medicare Part B laboratory spending grew 5% in 2024, with genetic tests at 43% of spending on 5% of volume — utilisation and mix shift, not price, now drive CLFS growth [76]. Uniform compression thus falls hardest on high-volume routine diagnostics and on the adoption margins of new molecular tests, while aggregate effects are blunted by mix shift or setting-specific substitution [69, 76].

3.4 Innovation carve-outs as coverage with evidence development (RQ3)

1. **3.4.1 Five mechanisms, one CED-shaped family.** Five of the six systems pay, temporarily or conditionally, for innovations not yet in standard schedules (carve-out inventory: Supplementary Material S6). The five — Germany's NUB→ZE→DRG funnel, France's RIHN 2.0, the US MolDX technical assessment, England's NICE Early Value Assessment (an evaluation programme without attached funding), and China's special-case deliberation and carve-out payment (a payment channel without an evidence-generation obligation — the family's boundary case) — echo the logic of Medicare's "coverage with evidence development" [11]. Japan, where fee-schedule listing is itself the coverage decision, has no equivalent funded carve-out (its Advanced Medical Care scheme is the nearest analogue).
2. **3.4.2 Shared failure modes for diagnostics.** The family exhibits four shared failure modes for diagnostics. **First, device- and drug-shaped design**: all five were built around hospital-budget innovations or pharmaceuticals, and the consequence is exclusion at assessment — diagnostic NUB applications were near-totally rejected, and only 105 of more than 3,400 NUB methods transferred to regular payment in 2005–2020 [26, 77] (Tier B), while the operative US molecular-panel LCD expressly places mNGS outside its scope, and no affirmative Medicare policy has taken its place [25]. **Second, evidence obligations mismatched to supply**: the mechanisms demand precisely the outcome-trial evidence whose supply remains sparse [4]. **Third, value externalised across budget silos**: the payer bearing the test cost captures neither avoided antibiotic days nor transmission benefits, and pilots lapse when short-term funding ends [16, 78]. **Fourth, temporary-status instability**: NUBs persist beyond ten years unintegrated [77], legacy French acts (merged into the liste des actes hors nomenclatures, LAHN, in 2024) face an annual décote [79], and LCD scope is revisable in either direction [25]. Conditional payment thus trades one uncertainty (evidence) for another (payment continuity), to which diagnostics — whose diffusion depends on routine, protocolised use — are particularly exposed. Section 3.5 stress-tests these mechanisms against the hardest case.

3.5 Case study: molecular tuberculosis diagnostics in China

Molecular rapid tuberculosis diagnostics are the limiting case of the value–payment mismatch; China is the stress case, combining the largest documented price-and-volume compression experiment (Section 3.3) with the strongest-mandate, weakest-payment contrast for a WHO-endorsed test. WHO recommends molecular rapid diagnostics as initial tests for anyone evaluated for tuberculosis [80], and China's National Tuberculosis Control Plan (2024–2030) mandates molecular-first diagnosis at designated facilities [81], against an estimated 696,000 incident cases in 2024 [82]. China reports a WHO-recommended rapid diagnostic as the initial test for at least 80% of newly diagnosed tuberculosis, but this aggregate masks test-specific and subnational gaps [83, 84], and county-level accounts document under-use of the cartridge-based test specifically [85]. Throughout, every index test decomposes into two layers rather than a product or instrument: a first-layer amplification, signal-generation or enrichment step — thermal-cycling PCR, isothermal amplification (for example LAMP or RPA), CRISPR-based signal generation (Cas12/Cas13 collateral cleavage, typically following a brief isothermal pre-amplification), or, for sequencing-based assays, target enrichment by multiplex-PCR amplification or hybrid capture — with shotgun metagenomics amplifying nothing — and a second-layer readout, namely fluorescent probes (real-time hydrolysis-probe fluorescence or melting-curve analysis), ligation-dependent probe amplification read by fragment sizing (MLPA), or sequencing (Sanger, second- or third-generation, including shotgun metagenomic, targeted-amplicon and ribosomal-marker formats); the closed-versus-open device axis is orthogonal to both layers (Section 2.3.5 sets out the decomposition; a methods primer with per-class enzyme systems, primer and probe design, and platform attributes: Supplementary Material S11). The analysis targets the technology class rather than any single product: in China the imported index product (Xpert MTB/RIF, Cepheid — the original cartridge; import registration 2014, renewed 2017; the Ultra successor approved 2023; both tracked in Supplementary Material S5) has held Class III registration since 2014, and registration records list at least seven domestic manufacturers holding Class III registrations for tuberculosis molecular or drug-resistance nucleic-acid tests [86]. Registration, however, is not clinical equivalence: the index product's standing rests on WHO evaluation of performance across patient groups, including smear-negative and other difficult-to-diagnose presentations [80]. Domestically registered alternatives, at least seven of which hold Class III registrations, have not yet published an equivalent WHO-evaluated cross-population performance dossier — an evidential rather than regulatory gap that is narrowing as domestic validation studies accumulate [86]. Single-source procurement notices give platform exclusivity as their stated reason — the installed GeneXpert systems accept only the manufacturer's sealed cartridges, which users can neither open, interrupt mid-run nor reprogram [86]. That lock-in is a property of the cartridge design — a fully closed, no-reopening format chosen so the assay can run outside a PCR-dedicated laboratory, with reduced contamination risk, fewer operator errors and no requirement for specialist molecular staff — not of the method class: the same closed archetype exists

among domestic platforms (fully closed isothermal systems), while other domestic assays in the class run on general-purpose, user-programmable real-time PCR or isothermal-fluorescence instruments (some on a manufacturer-designated instrument), where laboratories set the amplification and detection programmes themselves, so no equivalent device lock-in arises for those. In our reading, the deeper question of whether a domestic assay could substitute for the index product is the evidential gap above, not any registration barrier. That within-class hierarchy is the evidence-supply problem of Section 4.2 in miniature. Market structure adds a second caveat: Xpert is the most widely installed single molecular platform in China's designated-tuberculosis network — used by 74.6% of laboratories in national proficiency testing — yet domestically developed assays (isothermal amplification, melting-curve, microarray and conventional real-time PCR) collectively account for the majority of testing volume, particularly at county level (Supplementary Material S7). Xpert is therefore read as the category's policy reference point, not as a proxy for the entire Chinese market; and because county-level documentation of under-use exists only for China, the case study evidences the mechanism rather than China's exceptionality in degree. Price and insurance-status detail is provided in the supplement (Xpert price detail: Supplementary Material S6; cross-system price levels for the index tests: Table S6.6).

In China, the mismatch localises to Gates 2 and 3: "equipment without a price item; a price item without insurance coverage" [21, 85]. Where provincial price items exist, their published levels illustrate the magnitude: after Guangdong created item 250403090-1N (rpoB detection) in 2024, publicly notified hospital execution prices included CN¥700 at one district hospital and CN¥650 at another, both self-paid (Supplementary Material S5, register entry S5-38); the sixth batch of national price governance capped the item at CN¥300 in 2025 [22], against a reimbursed sputum smear at roughly CN¥8 (21,85, Tier B). These are item-level prices under a product-neutral code shared by the imported assay and domestic equivalents, not product-specific tariffs; hospital execution prices are not centrally published, so the items billed, the units counted and the applicable regional standard may all differ between institutions, and these figures indicate the order of magnitude before and after the item was created rather than a national price level. What the sequence shows is that Gate 2 was an artefact of catalogue administration rather than technology cost; yet the same test class remains simultaneously insured (Xinjiang), uninsured (Tianjin, documented 2020) and provisionally excluded (Anhui) across provinces [24, 32, 33] — these provincial items are product-neutral, shared by the imported Xpert and by domestic assays such as Zeesan's melting-curve products, so the divergence is not product-specific — although routine pathogen PCR billed under long-standing generic items is typically covered, so the binding concentrates on newly created dedicated items, which enter as self-pay or are provisionally excluded pending insurance evaluation (Supplementary Material S6) — and per-case quotas expose hospitals making greater use of high-value technology to greater overage risk [85]. The 2026 national guideline for laboratory-test price items (trial) removes the price-item barrier at the national level; provincial implementation and insurance-listing follow-through remain to be observed [23, 87], so the insurance-listing gate is now binding. Elsewhere, the same technology has cleared the comparable gates: in Japan under dedicated fee-schedule items [88]; in England, NICE guidance recommends it for selected indications [89], though with no test-level price and no statutory funding mandate its passage is not comparable on the three-gate metric. For this technology class, China's insurance-listing gate is the last of the six systems to close in the documented record; with the 2026 national guideline and the 2024–2030 National Tuberculosis Control Plan, it is also the system now moving fastest to close it — because tuberculosis detection's benefits are public-health externalities while the cost lands on a hospital's fixed case payment (Section 4).

4. Discussion

4.1 Interpretation: the reimbursement gap is structural, not transitional

1. **4.1.1 Universal gates, archetypical binding constraints.** The findings extend prior comparative work, which stopped at route description [9, 10], by adding the mechanism layer: the three gates are universal, but which gate binds is archetype-typical and sequentially mobile — China's 2025–2026 reforms relocate the constraint from the price gate to insurance listing rather than abolishing it. The RQ2 finding is stronger still: the double squeeze operates identically across all four financing archetypes — a convergence more plausibly read as the common fiscal arithmetic the OECD describes [5] than as transitional policy fashion. The county-hospital counterpoint, in which laboratory fees *rose* after DRG introduction [69], qualifies this reading: volume effects are setting-dependent.
2. **4.1.2 Externality misalignment as the economic root.** We interpret the recurring pattern — National Health Service stakeholders name the operative barrier as "who pays for it, and who sees the reward" [78] — as *externality misalignment*: the benefits of rapid

molecular testing accrue outside the budget that bears the test cost, in effect a transfer-pricing failure between budgets. The mortality benefit of molecular rapid diagnostic testing materialises only when testing is coupled to antimicrobial stewardship [1]; syndromic PCR was cost-effective for stewardship outcomes but not clinical cure in intensive care [90]; and blood-culture identification panels shortened time to optimal therapy by 28.7 hours [91] — benefits accruing to pharmacy budgets, bed management and public health, domains the outcomes literature under-measures [16], while the cartridge cost lands in the laboratory silo or the DRG bundle. Stated heuristically: a laboratory silo adopts a test if and only if its fee f is at least the test's cost c, while the system optimum requires only that the sum of benefits across silos reaches c; the gap is the externality.

Put in numbers for the best-documented case — rapid blood-culture identification panels coupled to an antimicrobial stewardship programme, per 100 suspected bloodstream-infection admissions under bundled payment (the cross-silo ledger: Supplementary Material S6) — the arithmetic is unfavourable to adoption. No separate fee exists, so the laboratory silo faces roughly US$41,700 in gross panel costs (US$38,000–40,800 incremental), benchmarked to the gastrointestinal-panel CLFS rate in the absence of a published bloodstream-infection-panel rate (assumption; Table S6.5), with no offsetting revenue, and the local adoption rule fails by construction. The systemic comparison is not demonstrable on monetised terms alone — monetisable savings (≈ US$30,000 from contaminant identification) [91] fall short of panel costs — but is satisfied once natural units are counted: about 248 freed bed-days at the meta-analytic length-of-stay effect [1], and antibiotic courses optimised 28.7 hours sooner [91], with a mortality benefit that materialises only where a stewardship programme co-produces it [1] — an organisational asset appearing in no row of the laboratory's ledger, even though the payer mandates that programme as a coverage condition [25]. The benefit rows are context-dependent [90, 91]; their *location* outside the laboratory silo is not — and no single budget ever sees them jointly. Two rival explanations were weighed and set aside: pure evidence scarcity (Section 4.2) explains slow evaluation but not why systems with completed evaluations still fail to pay; and technology immaturity cannot explain why a WHO-endorsed test marketed since 2010 remained unpriced in China until 2025. The externality account is the only one that predicts both the cross-system convergence of instruments and the specific locations of the binding gates. A parallel asymmetry sits on the reference side of every evaluation: the culture benchmark against which molecular tests are assessed has its own structural ceilings — blood-culture contamination reached 12.5% in a neonatal intensive care unit before a bundling intervention, each false positive adding 3.8 hospital days and US$883; culture sensitivity after antibiotic exposure falls to 41% in pertussis; and blood cultures are positive in fewer than 50% of haematogenously disseminated and 20% of intra-abdominal candidiasis cases (Supplementary Material S9). The payer's "culture is cheaper and is the gold standard" comparison therefore misprices both sides: it omits the downstream cost of contamination, and it evaluates molecular tests against a reference that is itself structurally insensitive in the settings where molecular value concentrates (Supplementary Material S9). Stated generally, health-technology assessment convention treats the reference standard as a fixed measuring rod. For pathogen diagnostics it is not: its sensitivity varies with prior antibiotic exposure, specimen type and host immune status, and its false positives carry their own downstream costs. An assessment that does not model the reference standard's own error structure will systematically under-value the index test.

4.2 The evidence-economics mismatch

A second asymmetry compounds the first. Payers increasingly demand randomised-trial-grade clinical-utility evidence, yet the global supply of outcome trials for diagnostics remains about 37 per year [4] — structural, not transitional, because such trials are costly, under-funded by manufacturers facing compressed prices, and difficult to power on downstream outcomes. Context-dependence deepens the problem, but the contrast is instructive rather than merely cautionary: the Danish trial's primary prescribing outcome was null in a setting with already restrictive antibiotic use, while its secondary outcomes showed significantly more targeted and more adequate prescribing [92]; the Norwegian trial, designed around the judicious use of the panel, raised the proportion of patients receiving pathogen-directed treatment from 13.4% to 35.3% [93]; and US settings show stewardship-coupled mortality effects [1], so a payer can find trial-grade support for divergent coverage stances. What varies with setting is not the test's information content but the decision process that converts it into prescribing. The predictable result is diffusion without payment — the state in which a technology has cleared regulatory approval and is physically deployed in service delivery, yet no price item or coverage decision attaches to it, so utilisation is financed by institutional absorption, patient self-payment or project funding rather than by routine reimbursement. China's county hospitals received Xpert instruments years before payment followed [85] — a pre-2026 gap the national guideline is designed to close [23] — and US mNGS, despite a growing prospective evidence base [94], still lacks any affirmative Medicare coverage determination — a search of the Medicare Coverage Database in August 2026 returned no NCD or LCD addressing metagenomic sequencing, and commercial policies are similarly non-covering [48]. The same evidence base carries

a caution in the opposite direction: discrepant non-culture-positive/culture-negative results can promote inappropriate antifungal treatment and spurious reporting of hospital-acquired infections (Supplementary Material S9), so conditional payment must pair coverage with the interpretive stewardship that makes the difference clinically meaningful.

One refinement tempers the archetype reading: within each system, technology attributes modulate how hard the binding gate is to pass, through four channels — the availability of a product-registration route (metagenomic sequencing has none in most systems, so Gate 1 mutates from product review into laboratory accreditation); the difficulty of generating outcome evidence (multi-target panels resist attributing outcomes to any single target, which is why the syndromic-panel LCD demands peer-reviewed outcome evidence while routine single-plex tests inherit coverage); platform design (closed cartridges yield single-source procurement and price rigidity, whereas open-platform reagents enter competitive markets — China's 47–77% volume-based procurement cuts fell on open reagents); and target content, which fee schedules stratify directly. Holding the technology class fixed — multi-pathogen targeted detection — the schedules encode one economic regularity through four different mechanisms. The United States prices multiplex syndromic panels on a target-count ladder within each syndromic family (respiratory CPT 87631/87632/87633 at $142.63/$218.06/$416.78 for 3–5, 6–11 and 12–25 targets), so the rate rises with the number of targets. The ladder is family-specific rather than uniform: the gastrointestinal series is priced differently in its lower bands (87505 at $128.29 for 3–5 targets and 87506 at $262.99 for 6–11, against $142.63 and $218.06 respectively for respiratory), and the two series coincide only at the top band, where 87507, 87633 and the central-nervous-system code 87483 all sit at $416.78. That top band is a ceiling rather than a rung: $416.78 is a value shared by 21 CLFS codes in CY2025 Q1, including seven outside infectious disease altogether. The regularity the schedule encodes is therefore a declining marginal rate per target that reaches zero above twelve targets, not a demonstration that the pathogen set is irrelevant to price. The ladder covers only the 3-to-25-target multiplex family: single-target codes are priced independently (87635 for SARS-CoV-2 at $51.31, 87556 for M. tuberculosis at $41.68). Germany charges per pathogen with a differentiated first unit and a hard ceiling (GOP 32851: €19.90 per pathogen, €7.23 from the second service on the treatment day, with a ceiling of €85.00 for that item alone, set by ceiling item GOP 32813), placing the fixed cost on the first target and with the ceiling binding from the eleventh pathogen (ten pathogens bill €84.97). China's 2026 guideline moves in the opposite direction on the same premise, discounting by indicator count (≤ 5 indicators at 80%, ≤ 10 at 70%, more than 10 at 60%), and states the premise explicitly as the declining marginal cost of combined testing (23; S5 register entry S5-129). Japan bands by panel content under the product-neutral D023 item (963 points for panels that exclude SARS-CoV-2, 1,350 points once SARS-CoV-2 is included — listed twice, for outsourced and in-house delivery alike — 1,700 points for cerebrospinal fluid, and a separate 1,273-point item for panels carrying resistance genes in sputum or bronchoalveolar lavage fluid) [88]. Four mechanisms — tiered pricing, first-unit differentiation, volume discounting and threshold pricing — express the same proposition: the fixed component of a molecular assay is incurred once, and marginal targets cost less than the first. France states the proposition in its limiting form: above the ten-primer-pair threshold the marginal price of an additional target is zero. Japan is the exception that locates the limit of the generalisation — none of its D023 sub-bands is defined by target count at all, and the 1,350-point band exceeds the 963-point band because it includes SARS-CoV-2 rather than because it carries more targets, so panel content rather than panel size drives the Japanese rate. France prices per PCR reaction and bands at a primer-pair threshold, with a priced tier on each side (RIHN/LAHN N131 at €135 below ten primer pairs and N156 at €270 at ten or more, in the 2024 valorisations), so the French schedule encodes the same declining-marginal-target regularity. The July 2025 LAHN then withdrew the tariffs altogether ("Suppression des tarifs"), replacing them with an abatement applied to the 2024 valorisations when the MIG envelope is allocated — and it duplicated each affected code, N156 becoming V009, so that indications already assessed by the Haute Autorité de Santé escape that abatement. Because these acts remain outside the NABM nomenclature either way, the HAS assessment buys protection of the funding base rather than coverage: an explicit instance of evidence assessment purchasing payment continuity, not entitlement; China had no national test-level price before the 2026 guideline, which unifies item definitions without publishing prices; and England prices nothing at the test level (Supplementary Material S11, Tables S11.2 and S11.3). System archetype determines where the gate binds; technology determines how hard passage is. Yet pricing by target count prices test content; clinical value accrues per correct and actionable diagnosis, and the two diverge systematically wherever a negative result does not exclude disease, because the comparator's true cost is the diagnostic pathway rather than the single test (Supplementary Material S10).

4.3 Policy implications: toward diagnostic-specific carve-out design

4.3.1 Design proposal. Section 3.4 showed that all five carve-out mechanisms echo coverage-with-evidence-development logic but were shaped around drugs and devices, underperforming for diagnostics [11, 95, 96]. The externality-misalignment diagnosis implies four redesigns.

First, test-level shadow pricing and national test tariffs. Absent a test-level price signal, the laboratory's cost-centre condition is invisible and unmanageable. England's 2026/27 NHS Payment Scheme introduces the first national blended tariffs for genomic testing — initially for cancer and rare-disease genomics rather than pathogen testing [97] — and the Pathology Transformation Review recommends shadow price-per-test tariffs [98]: such tariffs convert implicit quantity constraints into an explicit, auditable price. China's 2026 national guideline performs the complementary upstream function — standardising the item definitions on which any test-level price must rest [23]; it publishes no prices itself, with provincial benchmarks to follow. A caveat bounds the tariff recommendation: where a single platform dominates, publishing prices alone does not lower them — the GeneXpert platform absorbed roughly US$252 million of public research investment, and decentralised molecular testing proved cost-effective over hub-and-spoke delivery (Supplementary Material S10) — so transparency must be paired with platform competition. A second caveat concerns what the tariff is anchored to. A rate set by target count alone would misprice the class, because the same marker costs differently to detect depending on platform: closed-cartridge assays carry single-source procurement and price rigidity, whereas open-platform reagents for the identical target entered competitive procurement and fell by 47–77% in China's volume-based rounds. Contemporaneous procurement awards qualify that picture. Among 2022–2025 notices on the national procurement platform reporting a per-test unit price, cartridge-based assays that detect M. tuberculosis and rifampicin resistance in one run cleared at CN¥258–480 per test, while open-platform reagents covering the same two readouts were procured as separate kits: in one 2025 provincial award the complex-detection kit and the rifampicin-resistance kit cleared at CN¥135 each, CN¥270 combined. The platform premium at the level of a complete rifampicin-resistance workup is therefore modest in these awards, and the open-platform advantage reported in the volume-based rounds operates on individual reagents rather than on the assembled diagnostic answer (Supplementary Material S5). Germany's schedule already encodes the distinction — €19.90 for the first pathogen against €7.23 for each additional — recognising that fixed extraction, instrument and labour costs attach to the first target rather than to each one. Class ceilings with cost-structured pricing beneath them, as in China's 2025 round (rpoB ≤ CN¥300; resistance gene ≤ CN¥130), fit this evidence better than uniform per-target rates.

Second, stewardship-linked evidence generation. Because outcome value is co-produced with antimicrobial stewardship [1], conditional payment should reimburse the test *and* the stewardship coupling, with evidence obligations tied to stewardship outcomes rather than test performance alone; RIHN 2.0's binding protocols [99] and NICE's evidence-generation plans [100] provide the scaffolding, but the funded unit must become the pathway, not the cartridge.

Third, cross-silo value accounting. Carve-out budgets and health-technology-assessment value frames should internalise externalised benefits [16, 101], recording avoided antibiotic days and bed-days to the budget that orders the test; and cost containment itself should be value-differentiated, with a safe harbour exempting diagnostics above an evidence-graded cost-effectiveness threshold from procurement and fee-cut rounds.

Fourth, pay for the decision, not only for the test. Payment reform removes an access barrier; it does not remove a selection barrier. Once a test is covered, what determines whether it generates value is who selects it and on what basis. Where clinicians do not command the operating principles and boundaries of the method classes available to them — which organisms culture cannot recover within the decision window, what a negative result can and cannot exclude, and how the choice of reference standard moves reported performance (Supplementary Material S9 and S10) — selection migrates by default to laboratory availability or vendor recommendation. Conditional payment should therefore be tied not only to coverage together with an antimicrobial stewardship programme but to diagnostic stewardship carrying a documented prescriber-competency requirement: the Norwegian trial's increase in pathogen-directed treatment (from 13.4% to 35.3%) was obtained under exactly such a judicious-use protocol [93]. Operationally, the requirement can ride on instruments that already exist: accreditation standards addressed to the ordering service rather than to the laboratory alone, indication-linked ordering sets that record the clinical question each test is meant to answer, and periodic audit of the proportion of results that change management — the same audit infrastructure antimicrobial stewardship programmes already operate.

Framed this way, diagnostic-specific payment design is not a transfer from one party to another but a realignment in which the gains are shared. When the funded unit is the diagnostic pathway rather than the cartridge, and when reimbursement is conditioned on who selects the test and on what basis, the same reform serves several interests at once: patients gain earlier pathogen-directed treatment and fewer avoidable bed-days; payers and hospitals recover the externalised value of avoided antibiotic days and shortened stays against the budget that orders the test; manufacturers gain an incentive anchored to demonstrated clinical value

rather than to procurement volume or sales promotion; and regulators and governments gain coverage decisions grounded in routine real-world utilisation evidence rather than in industry-sponsored submissions alone. The audit record that a prescriber-competency requirement generates — the clinical question each test was ordered to answer, and the proportion of results that changed management — is precisely the evidence that conditional-coverage schemes demand; where ordering clinicians produce it, professional bodies acquire an evidentiary basis for pricing and coverage deliberation independent of vendor claims. Payment that makes clinician competency a condition of reimbursement should therefore also make clinician-generated evidence an input to the coverage review that follows, closing the loop between how a test is used and how it is paid for.

The same evidence base bears on a question that grows more pressing as access widens and the commercial stakes rise: whether testing volume, once reimbursed, tracks clinical benefit. The trials reviewed here locate the mortality benefit of molecular rapid diagnostics not in testing volume as such but in testing coupled to a stewardship and ordering process that records the clinical question and the proportion of results that change management [1, 93]; tests performed outside that process appear in the ledger as revenue but not, on the available evidence, as measured patient benefit. A payment design whose funded unit is demonstrated clinical value rather than cartridge volume, and whose coverage review draws on clinician-generated utilisation evidence, is thus observed to align the reimbursed quantity with the quantity that changes care — an alignment we document as a structural property of the design, not a policy we are positioned to recommend.

Several systems already operate fragments of this design, which a diagnostic-specific scheme could extend rather than invent. The United States has attempted exactly this linkage: the Protecting Access to Medicare Act's Appropriate Use Criteria programme (PAMA Section 218(b)) was designed to make consultation of a qualified clinical decision-support mechanism a condition of Medicare payment for advanced imaging (S5-133) — its indefinite pause in the CY2024 Physician Fee Schedule final rule (S5-133), on grounds of administrative burden rather than principle, identifies the binding constraint for any prescriber-competency condition: the split between the ordering clinician whose behaviour is conditioned and the furnishing entity that bills. Japan couples payment to a stewardship process rather than to a device: the 2018 fee-schedule revision added an antimicrobial-stewardship support fee (per inpatient admission) payable to hospitals that operate a qualifying multidisciplinary stewardship team (S5-134) — a competency-and-process condition attached to reimbursement, not to a product. Germany's Erprobung provision (SGB V Section 137e, in force since 2012) (S5-135) lets the Federal Joint Committee fund a method of promising potential conditionally while structured evidence is generated — a coverage-with-evidence-development instrument whose logic, applied to the diagnostic pathway rather than to a single test, is what the design above requires. China's tiered antimicrobial-management rules have conditioned prescribing privileges on physician seniority since 2012 — special-use antimicrobials require a senior-title prescriber or expert consultation — a competency condition of exactly the kind the design proposes, already familiar to Chinese clinicians (S5-132). None of these was built for pathogen nucleic acid diagnostics; the proposal is to adapt their existing machinery to the funded unit of the diagnostic decision.

4.3.2 Country-specific implications. For **China**, the binding gate having migrated to insurance listing, the priority is a national molecular-test reimbursement pathway for WHO-endorsed NAATs building on the new price-item guideline; the special-case deliberation channel — which in 2025 processed 2.44 million DRG/DIP exception applications with an 85.1% approval rate [65] — offers an immediately available bridge for high-value molecular tests while provincial listing proceeds, with commercial insurance realistically supplementary given payouts of only 4.2–4.5% of health expenditure [102]. For the **United States**, two fixes dominate: an mNGS evidence pathway replacing the current absence of coverage policy with stewardship-coupled conditional coverage — the proposed RAPID pathway's exclusion of in-vitro diagnostics is the present instance of device-shaped design [58] — and structural repair of the PAMA market-median methodology. An inpatient add-on channel also exists (the New Technology Add-On Payment: up to 65% of a new technology's cost per case, 75% for qualifying antimicrobials), but it is drug- and device-shaped, with no diagnostic-specific track record (S5-131). For **Germany**, diagnostic-specific NUB criteria assessing pathway value rather than device novelty should end the near-total rejection pattern. For **France**, RIHN 2.0 merits export as the most faithful extant CED template; the remaining defect is the post-assessment pricing lag on the standard (droit commun/LPPR) route. For **England**, the new National Healthtech Access Programme supplies a funding-mandate route in principle — it currently covers a small number of high-impact products and does not yet extend to pathogen diagnostics — and pathogen genomics governance would be integrated into a single commissioning pathway. For **Japan**, the bidirectional revisions are the operative lesson: compression should protect stewardship-critical microbiology even as automated analytes are trimmed.

4.4 Limitations

Twelve limitations bound these conclusions. First, this is a document-based analysis without stakeholder interviews; behavioural mechanisms are inferred from documents and published qualitative work. Second, several quantitative inputs rest on medium-confidence single sources (Tier B), notably Chinese industry statistics. Third, confidence-tiering removed relevant material from main claims, including US IVD market-size estimates (US$24–54 billion, inconsistent scopes). Fourth, generalisation is bounded: England is analysed rather than the United Kingdom, subnational variation is sampled not mapped, the county-hospital counter-evidence is a single regression-discontinuity study [(69)], and the China case study reads the gates at class level without assuming equivalent validation records across registered products (Section 3.5). Fifth, no primary cost-effectiveness modelling was undertaken, and non-payment determinants of adoption are treated as confounders. Sixth, no comparable cross-country laboratory-test volume data exist, so utilisation responses could not be benchmarked. Seventh, regulatory-tempo figures rest partly on Tier B secondary syntheses and are dated snapshots. Eighth, Chinese primary documents were translated by the authors without independent translation review; all translated documents are cited with issuing body, document number and URL to permit independent re-translation, and the underlying verbatim extraction records are described in Supplementary Material S1. Ninth, public documentation is asymmetric across systems. Chinese provincial price catalogues, listing notices and procurement awards are published in full, so our Chinese evidence is correspondingly granular and current; France publishes tariffs but not the negotiations that produce them, Germany publishes NUB status lists but not decision rationales or hospital-level outcomes, England's framework prices are confidential by policy, and Japan's test volumes are available only on application (Supplementary Material S7). Gate-failure indicators therefore differ in sensitivity across systems, and conclusions resting on subnational or procurement-level granularity (Sections 3.1.3, 3.3.2, 3.5) characterise what is publicly observable; the double-squeeze symmetry is asserted at the level of instrument design, not of measured magnitudes. Tenth, searching was conducted in Chinese and English with targeted German-, French- and Japanese-language queries, so retrieval completeness may be lower for those systems' national literatures — a retrieval gap distinct from the publication gaps above. We quantify this gap rather than assert it: of 275 logged source URLs, 49 (17.8%) could not be retrieved in full, and the per-URL log with failure reasons is released with this study (Supplementary Material S12). Notably, the largest single block of failures is not linguistic but technical — cms.gov refuses programmatic retrieval, so 10 of 43 United States official URLs were unobtainable by that route (an eleventh, an OIG report, failed on host unreachability) and their content was obtained from alternative official postings or, where stated, reconstructed from indexed official PDF text. No claim rests on a source never retrieved: where a live document could not be re-retrieved in the archival round, values are carried as originally accessed and are marked in the registers; where a document was never obtained, the corresponding cell is left empty or the claim downgraded, and both are marked. Eleventh, the German analysis reads coverage through the statutory-insurance fee schedule (EBM); private insurance bills through a separate schedule (GOÄ) that we did not analyse, so the German binding-gate diagnosis applies to the statutory system that covers the large majority of the population. Twelfth, this study did not assess prescriber competency or diagnostic-stewardship implementation in any of the six systems; the competency recommendation in Section 4.3.1 is an inference from the trial evidence cited and from the performance boundaries documented in Supplementary Material S9 and S10, not a finding of this comparison.

5. Conclusion

5.1 Summary of contributions

This study set out to explain why pathogen nucleic acid diagnostics face persistently weak payment despite unusually strong cost-effectiveness evidence. It makes four contributions: an analytical framework — the three-gates × gate-sequencing model, in which the gates are universal but the binding constraint is archetype-typical and sequentially mobile; a two-dimensional account separating where the binding gate sits (system archetype) from how hard it is to pass (technology attributes); the first six-system, primary-source-verified comparative account through the mid-2026 policy frontier; and a diagnostic-specific carve-out architecture derived from the externality-misalignment diagnosis. The central finding: the reimbursement gap is structural — consistent with, and best explained by, convergent payment architectures that systematically undervalue informational technologies whose benefits accrue outside the budget that bears their cost — and is unlikely to close without payment redesign rather than further accuracy evidence.

5.2 Future research

The framework's value lies in predictions specific enough to be wrong; four are falsifiable against policies already in force. First, if China's binding gate is insurance listing rather than price, the 2026 National Guideline for Laboratory-Test Price Items should shift

molecular-test adoption in step with provincial listings, not price levels: provinces listing molecular tuberculosis NAATs should show uptake gains within one to two catalogue cycles, while provinces whose prices converge without listing should not. Second, the post-delay repricing of the US CLFS from January 2027 should move routine-test volumes before molecular coding migrates: high-volume automated analytes should show a measurable volume response within one CLFS year, whereas molecular-panel volumes respond later and only where LCD scope already permits. Third, England's 2026/27 genomic tariffs should produce the first measurable volume response in a historically price-silent system: if block funding was the binding constraint, test-level blended tariffs should raise recorded genomic-test activity even absent new evidence. Fourth, if selection capability rather than access is the residual constraint, test-level payment reform unaccompanied by a competency or stewardship requirement should raise test volumes without a commensurate rise in pathogen-directed prescribing: China's 2026 price-item guideline and England's 2026/27 genomic tariffs both create price signals without such a requirement; the testable form is a ratio — pathogen-directed prescriptions per molecular test performed — measured at provincial or regional level. If selection capability is the residual constraint, test volumes should rise within two catalogue cycles while that ratio stays flat; if access was the only constraint, the ratio should rise in step with volume. Two research needs remain: econometric isolation of DRG/DIP effects on laboratory test volumes, exploiting China's staggered rollout; and prospective evaluation of France's first RIHN 2.0 cohort across its six-year coverage horizon.

Declarations

Ethics approval and consent to participate: Not applicable. This study is a comparative analysis of publicly available policy documents and published literature; it involves no human or animal participants and no identifiable individual data.

Consent for publication: Not applicable.

Availability of data and materials: All policy documents analysed are publicly available from the sources listed in the References, cited with URLs or document numbers. The figure reproduction package (scripts and tidy source data) is provided in Supplementary Material S3; the gate-timing cross-walk dataset is provided in Supplementary Material S5. The verbatim extraction records underlying each translated or quantified claim, and the unpublished Chinese-language policy survey used as a secondary source, are available from the corresponding author on reasonable request.

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Figures

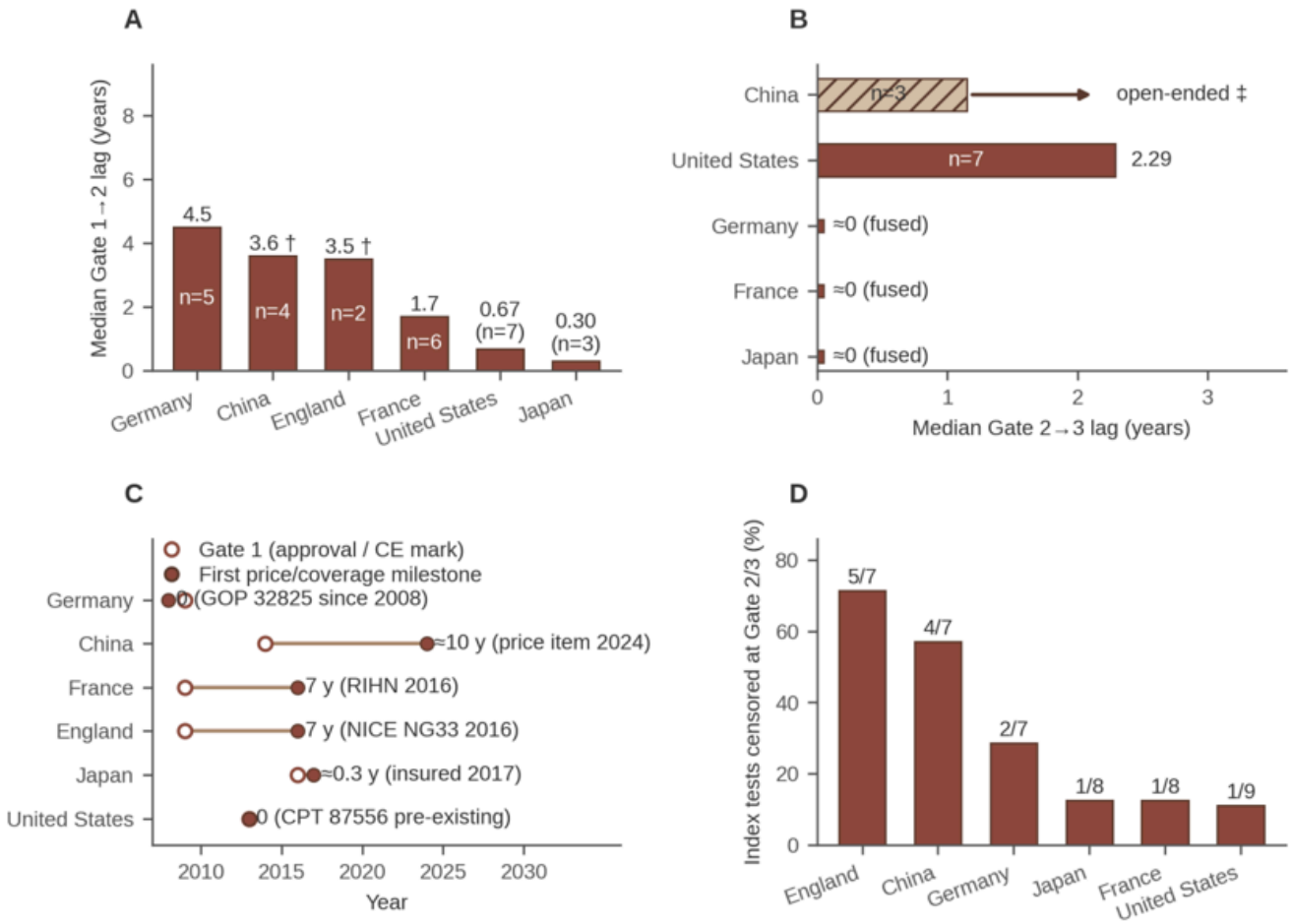


Figure 1

Gate timing across six systems.

(A) Median Gate 1 →Gate 2 elapsed time by system (n per bar; † small-n/downward-biased medians for England and China). (B) Median Gate 2→Gate 3 elapsed time; listing and funding are the same administrative act in Japan, and in Germany and France listing confers coverage for routine-tier items (lag 0 for listed items) while novel methods face a separate evaluation track; China's gate 3 remains open-ended for most molecular tests (‡ survivorship-biased, right-censored subsample). (C) Xpert MTB/RIF: Gate-1 authorisation to first price/coverage milestone per system. (D) Share of index diagnostics censored at Gate 2 or Gate 3 per system (denominators differ: 7–9 index tests per system, Table S5). Source: gate-timing cross-walk (Supplementary Material S5); per-cell dates from primary documents.

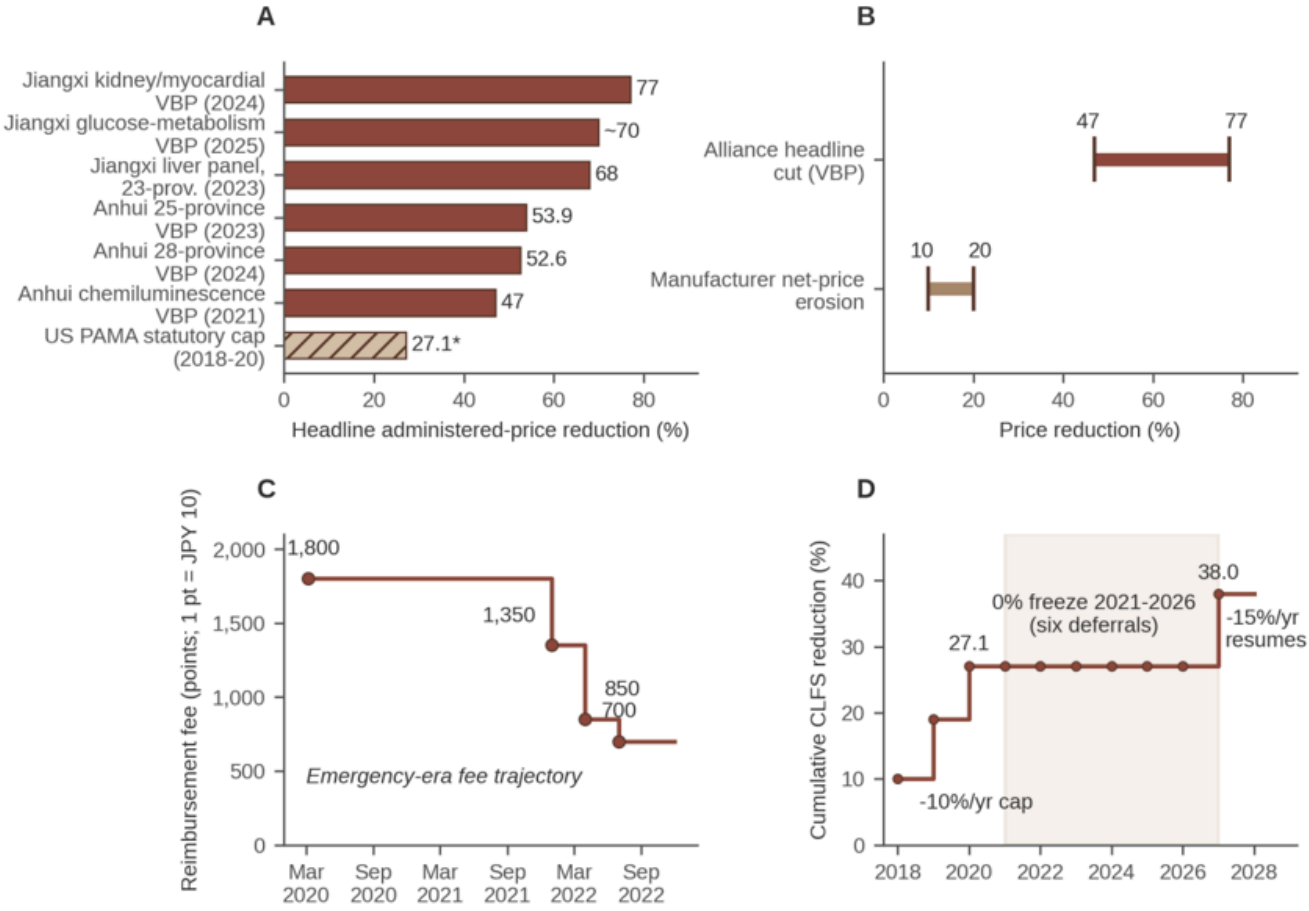


Figure 2

The double squeeze in outpatient administered pricing.

(A) Headline price reductions, selected instruments, sorted; the US PAMA entry (asterisk) is a compounded statutory cap (1−0.9³ = −27.1%, 2018–2020), not a realised average. (B) Transmission of headline cuts to manufacturer prices under China's volume-based procurement. (C) Japan's emergency-era COVID-19 PCR fee trajectory (points), an illustration of administrative pricing speed outside structural comparison. (D) The US PAMA statutory schedule 2018–2027: phased −10% caps, the 2021–2026 congressional freezes, and the 2027 resumption at −15% per year. Source: instrument-level policy documents listed in Supplementary Material S6.

Supplementary Files

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- 20260828PathogenMolDxPreprintSupplementary.pdf