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

Supplementary Material

This document contains Supplementary Material S1–S10 referenced in the main text. S1 expands the verification protocol summarised in Methods Section 2.4; S2 operationalises the binding-gate classification rule of Section 2.3.4 underlying Table 2; S3 provides the full reproducibility package for Figure 2; S4 records the archival justification for not using natural-geographic or demographic covariates; S5 provides the gate-timing cross-walk dataset underpinning Section 3.2.2; S6 contains the extended instrument and mechanism inventories moved from the main text for length compliance; S7 audits public data availability and product representativeness underlying Section 2.2; S8 documents the home and point-of-care regulatory boundary referenced in Section 2.2.

S1. Verification protocol — operational details

S1.1 The verbatim-excerpt rule

Every quantitative claim entering the manuscript — prices, fee points, procurement-round magnitudes, application and approval statistics, expenditure shares — was first anchored to a verbatim source excerpt. Two investigators independently extracted the relevant passage from the underlying statute, fee schedule, coverage decision, procurement announcement or peer-reviewed article and recorded it together with the document's issuing body, date and locator (article, table or page). A claim was not admitted into the manuscript as a paraphrase alone: the extraction record had to contain the source's own wording or figures, so that each number in the text can be re-traced to the exact sentence or table cell from which it derives. The verbatim-excerpt rule applies equally to primary documents and to the single secondary source used in this study, an upstream Chinese-language policy report (Global Health-Insurance and Reimbursement Policy Survey for In Vitro Diagnostic Kits, August 2026, unpublished; reference 19), whose claims were never carried into the manuscript without independent verification against primary documents.

S1.2 Two-stage verification workflow

Verification followed a two-stage protocol.

Stage 1 — independent extraction. Two investigators independently extracted verbatim source excerpts for each quantitative claim, each working from the primary documents assigned to their extraction stream (for example, National Healthcare Security Administration and provincial notices for China; the CMS Medicare Coverage Database and Clinical Laboratory Fee Schedule rulemaking for the United States; G-BA, InEK and KBV documentation for Germany; HAS opinions, Journal Officiel texts and UNCAM decisions for France; NHS England and NICE documents for England; MHLW fee schedules and Chuikyo records for Japan). Each extraction produced a claim–excerpt pair with full source metadata.

Stage 2 — cross-verification and conflict resolution. A second review stage cross-verified all claims across extraction streams, checking (i) that the verbatim excerpt supported the claim as worded, (ii) that the claim's scope, year and accounting basis matched the excerpt, and (iii) that no other stream held a conflicting figure for the same quantity. Conflicts were resolved against primary sources, privileging primary documents over secondary reportage: where the upstream report and a primary procurement announcement disagreed, the primary announcement's figure was adopted and the discrepancy recorded. Only claims surviving both stages entered the manuscript; claims that could not be stabilised were excluded or demoted to a flagged range under the confidence-tier rules below.

S1.3 Confidence-tier definitions

Facts were tiered by confidence according to Table S1. These confidence tiers (A high / B medium / C low) are distinct from the source-quality tiers used in the manuscript's tables (T1, peer-reviewed or primary official sources; T2, reputable secondary sources); tables flag both where relevant.

Table S1. Confidence-tier definitions and treatment in the manuscript.

Tier	Definition	Treatment in the manuscript
Tier A (high)	Corroborated by at least two independent sources tracing to primary documents	May be asserted directly
Tier B (medium)	Single authoritative source	Reported with an explicit source-basis note
Tier C (low)	Low-confidence or internally inconsistent estimates	Excluded from main claims, or reported only as a flagged range

Examples of tier assignment in the manuscript: the German NUB integration statistic (105 of more than 3,400 methods, 2005–2020) rests on a single peer-reviewed source and is reported as Tier B with a source-basis note; the Chinese industry statistics (Wind/IQVIA-derived) and some procurement-round magnitudes reported through professional press are likewise Tier B; US IVD market-size estimates spanning US$24–54 billion with inconsistent scopes are Tier C and were excluded from main claims entirely.

S1.4 Worked conflict-resolution example: the VBP price-cut magnitude

The protocol's conflict-resolution rule is illustrated by the treatment of Chinese in-vitro-diagnostic volume-based procurement (VBP) price cuts. The upstream secondary report estimated VBP price cuts of approximately "20–30%". Cross-verification in Stage 2 found this estimate contradicted by primary procurement announcements, which document headline alliance-level cuts of 47–77%: the Anhui chemiluminescence negotiation (August 2021), −47.02%; the Jiangxi-led 23-province liver-function biochemistry alliance, −68% (official figure; results December 2022, executed 1 July 2023); the Anhui-led 25-province chemiluminescence/immunoassay alliance, −53.9% (2023); the 28-province tumour-marker/thyroid alliance, −52.62%, with a maximum observed product-level cut of −84.25% (December 2024); and the kidney-function/myocardial-enzyme alliance, approximately −77% (opened March 2024; Hunan execution notice November 2024) (references 70, 71). The secondary estimate was superseded: the manuscript reports the primary-source range of 47.02–77% and does not carry the "20–30%" figure. The apparent gap between the two numbers was not silently harmonised but explained in the text: two-level price transmission through the multi-tier distributor system means distributors absorb most of the

administered-price reduction through margin compression, so manufacturer ex-factory net prices erode only roughly 10–20% — a quantity distinct from the alliance-level headline cut, and one that a lower-end estimate such as "20–30%" plausibly conflates with the headline. Both quantities are therefore reported, each with its own basis, rather than averaged or reconciled into a single figure.

S2. Binding-gate classification rules and Table 2 evidence mapping

S2.1 Classification rules (restating Methods Section 2.3.4)

A gate is classified as *binding* when an approved technology observably stalls at that step, evidenced by at least one of three indicator types:

- **Indicator 1 — documented absence of a price item or listing:** approved tests lack a billable price item, code or listing in the relevant catalogue, so the test cannot be charged or commissioned.
- **Indicator 2 — measurable application or rejection statistics:** the channel that governs the gate generates quantifiable application, approval or rejection data demonstrating that technologies stall there.
- **Indicator 3 — explicit exclusionary policy text:** the operative policy document contains text that conditions, restricts or excludes coverage of the technology class.

These indicators make the binding-gate diagnosis auditable against primary documents rather than impressionistic. With only six systems, the diagnosis is hypothesis-generating, not statistically identified: the manuscript claims systematic association between financing archetype and binding gate, not causal identification.

S2.2 Per-system evidence mapping (supporting manuscript Table 2)

Table S2 maps each of the six systems' three gates to the single most diagnostic piece of evidence underpinning the classification. Citation convention: parenthesised numbers (1)–(102) refer to the manuscript's reference list; numbers prefixed S (S1)–(S85) refer to the Supplementary references list at the end of this document. A gate shown as non-binding is passable in our disease area, though not trivially so for metagenomic laboratory-developed tests under the EU IVDR Article 5(5) in-house regime (references 20, 49).

Table S2. Binding-gate evidence mapping, six systems × three gates. Key evidence per cell; citation numbers refer to the manuscript's reference list.

System	Gate 1 (regulatory)	Gate 2 (price/code)	Gate 3 (coverage/funding)
China	NMPA registration attainable for index tests; not the binding constraint (Indicator — none)	Indicator 1: documented absence of price items — leading TB clinicians: new molecular tests "have no price item, and without a price item hospitals cannot charge" (21); national catalogue 2026 now dismantling the gate (23)	Indicator 3: Anhui 2025 implementation notice states the newly priced TB resistance-gene test is "for the time being not included in basic-insurance payment" (24); cross-province divergence — listed in Xinjiang, uninsured in Tianjin (32,33)
United	FDA clearance or	CPT/PLA codes and CLFS/PAMA	Indicators 2+3: LCD L38988 conditions

System	Gate 1 (regulatory)	Gate 2 (price/code)	Gate 3 (coverage/funding)
States	CLIA LDT status passable; clearance explicitly does not entail Medicare coverage [25]	pricing administratively available — coding is not the bottleneck [25]	outpatient coverage on peer-reviewed outcome evidence, restricts expanded panels, bars repeats within 14 days and explicitly excludes mNGS [25]; clinical-utility lack is the most cited denial reason [S1]
Germany	CE marking under IVDR; Article 5(5) tightens in-house tests [20]	EBM points available (chapters 32/11/19); statutory outpatient "ban with reservation of permission" shifts constraint onward [26]	Indicator 2: diagnostic NUB applications "almost exclusively rejected"; all companion-diagnostic NUB applications rejected until 2020 [26]; 105 of more than 3,400 methods integrated into regular payment 2005–2020 (2.6% per source; the stated denominator implies ~3.1%) [77]
France	CE marking under IVDR	Indicator 1: NABM listing is the legal precondition for reimbursement (Code de la sécurité sociale art. L.162-1-7) [27]; 92nd NABM version, 985 acts [27]	Indicator 1: UNCAM tariff-setting lagged favourable HAS opinions by years — documented for EGFR, BRAF, KRAS/NRAS testing [9,28]; Gate 2/3 sequencing failure
England	UKCA/CE marking	Indicator 1 (structural): no routine test-level prices — block/aligned payment and incentive flows; first national genomic-test tariffs introduced by the NHS Payment Scheme 2026/27 (released 2 April 2026, in effect 1 April 2026)	Indicator 3: NICE Diagnostics Assessment Programme recommendations carry no statutory funding mandate, so positive guidance does not compel local funding [29]; pathogen genomics excluded from the NGTD under UKHSA remit [30]
Japan	PMDA approval	Gates 2 and 3 fused: fee-schedule listing simultaneously sets the price and confers coverage; balance-billing prohibited, so an unlisted test cannot be reimbursed	Indicator 3: cancer gene panels insured from June 2019 at 56,000 points but facility-gated to designated cancer-genome hospitals with mandatory C-CAT data submission and once-per-patient billing [31] — the gate binds through facility and volume conditions, not price

S3. Figure reproducibility package

Figure 2 (manuscript Section 3.3) shows the double squeeze in outpatient administered pricing in four panels: (A) headline price reductions sorted by magnitude; (B) transmission of headline cuts to manufacturer prices under China's volume-based procurement (VBP); (C) Japan's emergency-era COVID-19 PCR fee trajectory; (D) the US PAMA statutory schedule 2018–2027. Figure 1 (manuscript Section 3.2) shows gate timing across the six systems in four panels ((A) Gate 1→Gate 2 median lags; (B) Gate 2→Gate 3 lags; (C) Xpert MTB/RIF Gate-1→first-milestone dumbbells; (D) share of index diagnostics censored per system). This section provides derivation notes (S3.1), the Figure 2 source data (S3.2), the full rendering script (S3.3) and environment and rerun instructions (S3.4). Companion files shipped in the submission package: fig2_data.csv and fig2_script.py (Figure 2), fig1_data.csv and fig1_script.py (Figure 1; its underlying cross-walk dataset is given in full in Section S5). Outputs: ivd_paper_fig1_new.png/.tiff and ivd_paper_fig2.png/.tiff (174.2 mm, 300 dpi; 2057 × 1559 px) plus 85 mm single-column variants (1003 × 2669 px, panels stacked).

S3.1 Derivation notes

Panel A values. All Panel A bars are one-off realised alliance-average cuts from China IVD VBP rounds, except the US PAMA entry, which is a statutory cap (see below). Bars are sorted in descending order of magnitude; the US entry is marked with an asterisk and a hatched, lighter-shade bar to distinguish a cap from a realised average. The maximum observed product-level cut in the Anhui 28-province round (−84.25%) is retained in the source data's source_ref field but is not plotted, because Panel A shows averages and caps only.

PAMA compounding: the −27.1% entry. The Protecting Access to Medicare Act (PAMA, 2014) phased in Clinical Laboratory Fee Schedule cuts with a statutory reduction cap of 10% per year for CY2018–2020. Compounding three consecutive 10% reductions: $1 - 0.9^3 = 0.271$, i.e. −27.1%. This is a statutory cap on the phase-in, not a realised average reduction: a 0% freeze applied during 2021–2026 through repeated congressional interventions, and a 15% annual cap resumes in CY2027. Panel D plots this full statutory schedule as a step chart (cumulative reduction: 10% by 2019, 19% by 2020, 27.1% by 2021, held to 2026, then resuming to approximately 38% by 2029 at −15% per year).

Panel C (Japan COVID-19 PCR fee) inclusion note. Japan's COVID-19 PCR fee fell from 1,800 points at insurance listing (6 March 2020) to 700 points (July 2022): $(1800 - 700)/1800 = 0.6111$, i.e. −61.1%. The series is plotted as its own clearly-labelled panel because it is an emergency-era fee trajectory, not a structural payment-reform comparator; it must not be read as cross-country evidence of structural compression.

Panel B — two-level price transmission (China IVD VBP). The alliance-level headline cut range is 47–77%, the span of the realised alliance averages in Panel A. Manufacturer ex-factory net price erosion is approximately 10–20%, based on industry and analyst estimates for China IVD manufacturers post-VBP: the multi-tier distributor system buffers manufacturers from the full headline cut, so ex-factory net prices erode far less than administered terminal prices.

Source-precision policy. Values are shown as stated in the cited sources. Source-stated approximate magnitudes are shown as whole numbers (77 for "approximately 77%"; 68 for the official NHSA-quoted figure; the trade-press 68.64% variant was not used). One decimal is retained where sources state exact precision (53.9, 52.6, 47.0 displayed as 47). Full-precision source values (47.02, 52.62, 68.64) are retained in this note and in the source references.

S3.2 Source data (fig2_data.csv, rendered as a table)

The full tidy source dataset behind Figure 2 is given in Table S3.

Table S3. Source data for Figure 2 (tidy format).

panel	series	item	date_or_year	value	unit	approx_flag	source_ref
A	headline_reduction	Jiangxi kidney/myocardial VBP	2024	77	pct	approx	Jiangxi-led kidney-function/myocardial-enzyme alliance VBP (opened Mar 2024); average cut approx. 77% as stated in source
A	headline_reduction	Jiangxi glucose-metabolism VBP	2025	70	pct	approx	Jiangxi-led glucose/lipid-metabolism biochemistry alliance VBP (2025); average cut approx. 70% as stated in source
A	headline_reduction	Jiangxi liver panel 23-province VBP	2023	68	pct	approx	Jiangxi-led 23-province liver-function biochemistry VBP (results Dec 2022, executed 1 Jul 2023); average cut 68% (official NHSA-quoted figure)
A	headline_reduction	Anhui 25-province VBP	2023	53.9	pct	exact	Anhui-led 25-province chemiluminescence/immunoassay VBP result announcement

panel	series	item	date_or_year	value	unit	approx_flag	source_ref
							(2023); average cut 53.9%
A	headline_reduction	Anhui 28-province VBP	2024	52.6	pct	exact	Anhui-led 28-province tumour-marker/thyroid VBP result announcement (2024); average cut 52.6%
A	headline_reduction	Anhui chemiluminescence VBP	2021	47	pct	approx	Anhui Provincial Healthcare Security Administration chemiluminescence reagent VBP negotiation (Aug 2021); average cut approx. 47%
A	headline_reduction	US PAMA CLFS statutory cap	2018-2020	27.1	pct	exact	Protecting Access to Medicare Act (2014) CLFS reform: 10% annual reduction cap 2018-2020 compounded ($1-0.9^3 = 0.271$); statutory cap, not an observed realised cut (hatched)
B	alliance_headline_cut	Alliance headline VBP cut lower bound	2021-2025	47	pct	approx	Span of realised alliance average cuts across the six China IVD VBP rounds in Panel A (lower bound)
B	alliance_headline_cut	Alliance headline VBP cut upper bound	2021-2025	77	pct	approx	Span of realised alliance average cuts across the six China IVD VBP rounds in Panel A (upper bound)
B	manufacturer_net_erosion	Manufacturer net-price erosion lower bound	2021-2025	10	pct	approx	Industry/analyst estimates of manufacturer ex-factory net price erosion after distributor-margin buffering (lower bound)
B	manufacturer_net_erosion	Manufacturer net-price erosion upper bound	2021-2025	20	pct	approx	Industry/analyst estimates of manufacturer ex-factory net price erosion after distributor-margin buffering (upper bound)
C	japan_covid_pcr_fee	COVID-19 NAAT fee (D023)	2020-03-06	1800	points	exact	MHLW insurance listing of SARS-CoV-2 NAAT at 1,800 points (Mar 2020); 1 point = 10 JPY
C	japan_covid_pcr_fee	COVID-19 NAAT fee (D023)	2021-12-31	1350	points	exact	MHLW fee revision reducing SARS-CoV-2 NAAT fee to 1,350 points (effective 31 Dec 2021)
C	japan_covid_pcr_fee	COVID-19 NAAT fee (D023)	2022-04-01	850	points	exact	FY2022 fee-schedule revision reducing SARS-CoV-2 NAAT fee to 850 points (Apr 2022)
C	japan_covid_pcr_fee	COVID-19 NAAT fee (D023)	2022-07-01	700	points	exact	MHLW fee revision reducing SARS-CoV-2 NAAT fee to 700 points (Jul 2022)
D	pama_clfs_schedule	Cumulative CLFS reduction	2018	10.0	pct	exact	PAMA statutory 10% annual reduction cap, year 1 (compounded)
D	pama_clfs_schedule	Cumulative CLFS reduction	2019	19.0	pct	exact	PAMA statutory 10% annual reduction cap, year 2 ($1-0.9^2$)
D	pama_clfs_schedule	Cumulative CLFS reduction	2020	27.1	pct	exact	PAMA statutory 10% annual reduction cap, year 3 ($1-0.9^3$); phase-in cap period ends
D	pama_clfs_schedule	Cumulative CLFS reduction	2021	27.1	pct	exact	Congressional deferral of CLFS cuts (1st of six);

panel	series	item	date_or_year	value	unit	approx_flag	source_ref
		freeze					schedule frozen at 2020 level
D	pama_clfs_schedule	Cumulative CLFS reduction freeze	2022	27.1	pct	exact	Congressional deferral of CLFS cuts (2nd of six)
D	pama_clfs_schedule	Cumulative CLFS reduction freeze	2023	27.1	pct	exact	Congressional deferral of CLFS cuts (3rd of six)
D	pama_clfs_schedule	Cumulative CLFS reduction freeze	2024	27.1	pct	exact	Congressional deferral of CLFS cuts (4th of six)
D	pama_clfs_schedule	Cumulative CLFS reduction freeze	2025	27.1	pct	exact	Congressional deferral of CLFS cuts (5th of six)
D	pama_clfs_schedule	Cumulative CLFS reduction freeze	2026	27.1	pct	exact	Congressional deferral of CLFS cuts (6th of six); end of freeze
D	pama_clfs_schedule	Cumulative CLFS reduction	2027	38.0	pct	exact	Statutory 15% annual reduction cap resumes 2027 ($1-0.9^3\times0.85 = 0.380$)

S3.3 Rendering script (fig2_script.py, full listing)

```
#!/usr/bin/env python3
# -*- coding: utf-8 -*-
"""
fig2_script.py — Reproduces Figure 2 ("Double-squeeze instruments", panels A-D)
for the global IVD reimbursement manuscript.

Input : fig2_data.csv (same directory as this script)
Output: ivd_paper_fig2.png / .tiff (174.2 mm, 300 dpi) and
        ivd_paper_fig2_85mm.png / .tiff (85 mm, 300 dpi, stacked),
        written to the parent directory of this script.

Tested library versions:
    Python 3.11 | matplotlib 3.10.3 | pandas 2.3.2 | numpy 2.2.5
"""
from pathlib import Path
import numpy as np
import pandas as pd
import matplotlib
matplotlib.use("Agg")
import matplotlib.pyplot as plt
import matplotlib.dates as mdates

# ---------------------------------------------------------------- style ----
CLAY = ['#A9886B', '#C2A98E', '#8C4A3C', '#9C7B5E', '#7D6A55', '#D3BEA6', '#5A3A2E']
plt.rcParams.update({
    'font.family': 'Liberation Sans',
    'font.size': 8,
    'axes.grid': False,            # HARD RULE: no gridlines anywhere
    'text.color': '#333333',
    'axes.labelcolor': '#333333',
    'axes.edgecolor': '#555555',
    'axes.linewidth': 0.8,
    'xtick.color': '#555555', 'ytick.color': '#555555',
    'xtick.labelcolor': '#555555', 'ytick.labelcolor': '#555555',
    'xtick.labelsize': 8, 'ytick.labelsize': 8,
    'axes.labelsize': 8,
    'legend.fontsize': 8,
    'legend.frameon': False,
    'axes.unicode_minus': False,
    'figure.dpi': 300, 'savefig.dpi': 300,
})
MM = 1 / 25.4
HERE = Path(__file__).resolve().parent
OUT = HERE.parent
DATA = HERE / 'fig2_data.csv'

def tag(ax, letter):
    ax.text(-0.02, 1.10, letter, transform=ax.transAxes, fontsize=10,
            fontweight='bold', color='#333333', ha='right', va='bottom')
```

```
def despine(ax):
    ax.spines['top'].set_visible(False)
    ax.spines['right'].set_visible(False)

# ---------------------------------------------------------------- panels ---
def panel_a(ax, df, compact=False):
    d = df[df.panel == 'A'].copy()
    labels = {
        'Jiangxi kidney/myocardial VBP': 'Jiangxi kidney/myocardial\nVBP (2024)',
        'Jiangxi glucose-metabolism VBP': 'Jiangxi glucose-metabolism\nVBP (2025)',
        'Jiangxi liver panel 23-province VBP': 'Jiangxi liver panel,\n23-prov. (2023)',
        'Anhui 25-province VBP': 'Anhui 25-province\nVBP (2023)',
        'Anhui 28-province VBP': 'Anhui 28-province\nVBP (2024)',
        'Anhui chemiluminescence VBP': 'Anhui chemiluminescence\nVBP (2021)',
        'US PAMA CLFS statutory cap': 'US PAMA statutory cap\n(2018-20)',
    }
    d = d.sort_values('value', ascending=True).reset_index(drop=True)
    y = np.arange(len(d))
    for i, r in d.iterrows():
        is_pama = 'PAMA' in r['item']
        ax.barh(i, r['value'], height=0.62,
                color=CLAY[2] if not is_pama else CLAY[5],
                edgecolor='#5A3A2E', linewidth=0.7,
                hatch='///' if is_pama else None)
        if 'PAMA' in r['item']:
            lab = f"{r['value']:.1f}*"
        elif 'glucose' in r['item']:
            lab = f"~{r['value']:.0f}"
        elif r['value'] == int(r['value']):
            lab = f"{r['value']:.0f}"
        else:
            lab = f"{r['value']:.1f}"
        ax.text(r['value'] + 1.2, i, lab, va='center', ha='left', fontsize=8,
                color='#333333')
    ax.set_yticks(y)
    ax.set_yticklabels([labels[i] for i in d['item']], fontsize=8)
    ax.set_xlim(0, 92)
    ax.set_xlabel('Headline price reduction (%)' if compact else
                  'Headline administered-price reduction (%)')
    despine(ax)
    tag(ax, 'A')

def panel_b(ax, df):
    d = df[df.panel == 'B']
    lo_a = d[(d.series == 'alliance_headline_cut') & d.item.str.contains('lower')].value.iloc[0]
    hi_a = d[(d.series == 'alliance_headline_cut') & d.item.str.contains('upper')].value.iloc[0]
    lo_m = d[(d.series == 'manufacturer_net_erosion') & d.item.str.contains('lower')].value.iloc[0]
    hi_m = d[(d.series == 'manufacturer_net_erosion') & d.item.str.contains('upper')].value.iloc[0]
    rows = [('Alliance headline\ncut (VBP)', lo_a, hi_a, 1, CLAY[2]),
            ('Manufacturer net-price\nerosion', lo_m, hi_m, 0, CLAY[0])]
    for name, lo, hi, yy, col in rows:
        ax.plot([lo, hi], [yy, yy], color=col, lw=5, solid_capstyle='butt', zorder=2)
        for x in (lo, hi):  # end ticks
            ax.plot([x, x], [yy - 0.16, yy + 0.16], color='#5A3A2E', lw=1.4, zorder=3)
        ax.text(lo - 1.5, yy + 0.24, f"{lo:.0f}", ha='center', fontsize=8, color='#333333')
        ax.text(hi + 1.5, yy + 0.24, f"{hi:.0f}", ha='center', fontsize=8, color='#333333')
    ax.set_yticks([1, 0])
    ax.set_yticklabels([r[0] for r in rows], fontsize=8)
    ax.set_ylim(-0.65, 1.75)
    ax.set_xlim(0, 92)
    ax.set_xlabel('Price reduction (%)')
    despine(ax)
    tag(ax, 'B')

def panel_c(ax, df):
    d = df[df.panel == 'C'].copy()
    d['date'] = pd.to_datetime(d['date_or_year'])
    d = d.sort_values('date')
    end = pd.Timestamp('2022-12-01')
    xs = list(d['date']) + [end]
    ys = list(d['value']) + [d['value'].iloc[-1]]
    ax.plot(xs, ys, drawstyle='steps-post', color=CLAY[2], lw=1.6, zorder=2)
    ax.plot(d['date'], d['value'], 'o', color=CLAY[2], ms=4.5,
            markeredgecolor='#5A3A2E', markeredgewidth=0.6, zorder=3)
    offsets = {'2020-03-06': (2, 9), '2021-12-31': (-16, 9),
               '2022-04-01': (14, 9), '2022-07-01': (0, 9)}
    for _, r in d.iterrows():
        dx, dy = offsets[r['date_or_year']]
        ax.annotate(f"{int(r['value']):,}", (r['date'], r['value']),
                    xytext=(dx, dy), textcoords='offset points',
                    ha='center', fontsize=8, color='#333333')
    ax.text(pd.Timestamp('2020-03-01'), 420, 'Emergency-era fee trajectory',
```

```
            fontsize=8, color='#333333', style='italic', ha='left')
    ax.set_xlim(pd.Timestamp('2020-01-01'), pd.Timestamp('2023-02-01'))
    ax.set_ylim(0, 2100)
    ax.set_yticks([0, 500, 1000, 1500, 2000])
    ax.set_yticklabels(['0', '500', '1,000', '1,500', '2,000'])
    ax.xaxis.set_major_locator(mdates.MonthLocator(bymonth=(3, 9)))
    ax.xaxis.set_major_formatter(mdates.DateFormatter('%b\n%Y'))
    ax.set_ylabel('Reimbursement fee (points; 1 pt = JPY 10)')
    despine(ax)
    tag(ax, 'C')

def panel_d(ax, df, compact=False):
    d = df[df.panel == 'D'].copy().sort_values('date_or_year')
    yrs = d['date_or_year'].astype(int).to_numpy()
    val = d['value'].to_numpy()
    xs = list(yrs) + [2028]
    ys = list(val) + [val[-1]]
    ax.axvspan(2021, 2027, color=CLAY[5], alpha=0.22, zorder=1)
    ax.plot(xs, ys, drawstyle='steps-post', color=CLAY[2], lw=1.6, zorder=3)
    ax.plot(yrs, val, 'o', color=CLAY[2], ms=3.5,
            markeredgecolor='#5A3A2E', markeredgewidth=0.5, zorder=4)
    ax.text(2018.6, 5.5, '-10%/yr cap', fontsize=8, color='#333333', ha='left')
    freeze_txt = '0% freeze 2021-2026\n(six deferrals)'
    ax.text(2023.5, 31.5, freeze_txt,
            fontsize=8, color='#333333', ha='center', va='bottom')
    ax.text(2027.2, 32.5, '-15%/yr\nresumes', fontsize=8, color='#333333',
            ha='left', va='center')
    ax.text(2020.0, 29.5, '27.1', fontsize=8, color='#333333', ha='center')
    ax.text(2027.0, 40.2, '38.0', fontsize=8, color='#333333', ha='center')
    ax.set_xlim(2017.6, 2029.2)
    ax.set_ylim(0, 47)
    ax.set_xticks([2018, 2020, 2022, 2024, 2026, 2028])
    ax.set_ylabel('Cumulative CLFS reduction (%)')
    despine(ax)
    tag(ax, 'D')

def run_panels(axes, df, compact=False):
    panel_a(axes[0], df, compact=compact)
    panel_b(axes[1], df)
    panel_c(axes[2], df)
    panel_d(axes[3], df, compact=compact)

def save(fig, stem):
    fig.savefig(OUT / f'{stem}.png')
    fig.savefig(OUT / f'{stem}.tiff', pil_kwargs={'compression': 'tiff_lzw'})

def main():
    df = pd.read_csv(DATA)
    # ---- 174.2 mm two-column version (2 x 2) ----
    fig, axes = plt.subplots(2, 2, figsize=(174.2 * MM, 132 * MM))
    fig.subplots_adjust(left=0.215, right=0.985, top=0.90, bottom=0.115,
                        wspace=0.45, hspace=0.52)
    run_panels(axes.flat, df)
    save(fig, 'ivd_paper_fig2')
    plt.close(fig)
    # ---- 85 mm single-column version (stacked) ----
    fig, axes = plt.subplots(4, 1, figsize=(85.0 * MM, 226 * MM))
    fig.subplots_adjust(left=0.455, right=0.965, top=0.975, bottom=0.05,
                        hspace=0.62)
    run_panels(axes.flat, df, compact=True)
    save(fig, 'ivd_paper_fig2_85mm')
    plt.close(fig)
    print('Figure 2 written to', OUT)

if __name__ == '__main__':
    main()
```

The companion script fig1_script.py (with fig1_data.csv) renders Figure 1 by the same conventions and is shipped in the submission package; its underlying per-test dates are documented in Section S5.

S3.4 Environment and rerun command

The figures were rendered with Python 3.11, matplotlib 3.10.3, pandas 2.3.2 and numpy 2.2.5 (Pillow for TIFF export), using the Liberation Sans typeface. To reproduce, place each script beside its data file and run:

```
cd supplement
python3 fig2_script.py
python3 fig1_script.py
```

The scripts write ivd_paper_fig1_new.png/.tiff and ivd_paper_fig1_new_85mm.png/.tiff, and ivd_paper_fig2.png/.tiff and ivd_paper_fig2_85mm.png/.tiff respectively, into their parent directory.

S4. Scope decision note: non-use of natural-geographic and demographic covariates

This study is a policy-institution comparison: its explanatory variables are payment architectures — the instruments that occupy the three reimbursement gates (regulatory approval, price/code assignment, coverage decision) and the cost-containment and carve-out mechanisms that act upon them. Natural-geographic and demographic covariates — ethnicity, altitude, ocean currents and similar natural or demographic geographic data — have no identifiable causal mechanism linking them to payment-gate behaviour: neither the binding-gate diagnosis nor the double-squeeze mechanism operates through population composition or physical geography, and no pathway is known or plausible by which such variables would alter the statutes, fee schedules, coverage decisions or procurement rounds that constitute the study's observations. These variables were therefore considered and not used; their inclusion would introduce noise without a defensible identification rationale in a six-system, most-different-systems design.

The only geographic dimension relevant to the research questions is *subnational jurisdictional variation* in payment institutions — Chinese provinces' divergent insurance-listing decisions, German hospital-level negotiation of innovation payments, and US Medicare Administrative Contractor coverage — and this dimension is analysed in Section 3.1.3 of the manuscript, where it is treated as a second-order access inequality superimposed on the national architecture rather than as a covariate.

Finally, the study is a policy-document analysis: it performs no patient-level case identification and applies no diagnostic or clinical coding algorithms to case records. Consequently, no case-identification rules, coding rules or patient-level inclusion/exclusion criteria apply, and none are reported.

A companion scope decision concerns the test menu. Routine single-plex respiratory NAATs — influenza A/B, Mycoplasma pneumoniae, and similar long-established targets — are retained as the no-binding-gate tier of class (i) rather than excluded: they are long-listed, low-priced and covered in every system studied, and that uniformity is itself informative. They serve as the negative control for the gate analysis, demonstrating that the binding gates identified in this study act on newly created dedicated items rather than on molecular testing as such. They are not traced through the gate-timing cross-walk, because no gate transition is recorded for them. The same holds for the legacy single-plex tier of tuberculosis testing (smear, culture, conventional PCR), which anchors the price comparison in Section 3.5 but is not itself a policy frontier. The index technologies were chosen at the innovation frontier, where the gates actually bind: a WHO-endorsed tuberculosis NAAT class, syndromic multiplex panels, and metagenomic sequencing. The routine tier they are benchmarked against is documented in Section S7.3.

S5. Gate-timing cross-walk dataset

S5.1 Design note

The cross-walk is a structured dataset indexing representative pathogen nucleic acid diagnostics — tuberculosis nucleic-acid tests (Xpert MTB/RIF and its domestic analogues), syndromic multiplex panels (respiratory, gastrointestinal, meningitis/encephalitis, pneumonia), metagenomic next-generation sequencing (mNGS), a representative COVID-19 NAAT and, where informative, parallel-review or oncology reference tests — against the three reimbursement gates of the main-text framework (Gate 1, regulatory approval; Gate 2, price/code assignment; Gate 3, coverage/funding) across the four regulatory jurisdictions studied at document level (United States; China; Germany, France and England; Japan). Every cell records a decision date or status transcribed from the primary document cited in the source key; nothing was estimated silently. Censoring conventions: a cell is marked "censored" where a gate was never reached as of August 2026, and "none" where a documented search found no instrument; medians and ranges are computed on complete (dated, uncensored) cells only. Descriptive statistics derived from this dataset are reported in main-text Section 3.2.2.

S5.2 Cross-walk tables

Dates are transcribed exactly as given in the underlying gate-timeline files. Cells whose evidence was flagged carry "(approx.)" (approximate or indirect evidence) or "(unpinned)" (no decision-day date could be pinned to a primary document). For Japan, Gates 2 and 3 are institutionally fused — the fee-schedule listing simultaneously sets the price and confers coverage — so Gate 3 cells record the fusion.

Table S5a. Gate-timing cross-walk, United States. Gate 1 = FDA authorisation or LDT status; Gate 2 = CPT/PLA code assignment (earliest applicable code) and CMS CLFS price; Gate 3 = coverage decision (NCD/LCD/commercial policy, or explicit non-coverage).

Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
Xpert MTB/RIF (Cepheid)	2013-07-25 — De Novo granted (K131706)	CPT 87556 pre-existed; no new code needed; CLFS national limit $47.80 (CY2016)	none — no test-specific NCD/LCD; de-facto covered as a CLFS lab test	S5-1, S5-2, S5-3, S5-10, S5-13
FilmArray Respiratory Panel (RP/RP2/RP2.1)	2011-02-17 — 510(k) K103175; RP2 510(k) 2017-05-30; RP2.1 De Novo DEN200031 granted 2021-03-17	CPT 87633 effective 2013-01-01 (approx.); CLFS $567.75 (CY2016); PLA 0202U (RP2.1) 2020, effective date unpinned	2022-04-17 — MolDX LCD L39003 original effective date	S5-4, S5-5, S5-6, S5-9, S5-10, S5-13, S5-14
FilmArray GI panel	2014-05-02 — 510(k) K140407	CPT 87507 effective 2015-01-01 (approx.); CLFS $567.75 (CY2016)	2022-04-17 — LCD L39003	S5-7, S5-9, S5-10, S5-13, S5-14
FilmArray Meningitis/Encephalitis (ME) panel	2015-10-08 — De Novo DEN150013 granted	CPT 87483 effective 2017-01-01 (approx.; first CLFS appearance CY2017, $571.72)	2022-04-17 — LCD L39003	S5-8, S5-11, S5-13, S5-14
FilmArray Pneumonia panel	2018-11-09 — 510(k) K180966	PLA 0151U effective 2020-01-01; contractor-gapfilled in first CLFS year; deleted 2022-04-01	2022-04-17 — LCD L39003	S5-12, S5-13, S5-14, S5-15
mNGS (UCSF CSF mNGS	LDT — no FDA	Karius PLA 0152U effective	censored — no NCD, no	S5-13, S5-

Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
/ Karius Test)	authorisation as of Aug 2026; UCSF clinical launch ~2016-06 (approx.); Karius commercial availability ~2017 (approx.)	2020-04-01 (approx.); CSF-mNGS PLA 0323U effective 2022-07-01 (approx.); UCSF has no dedicated code (billed as CPT 87999)	affirmative Medicare LCD; explicit commercial non-coverage (Anthem LAB.00050; Aetna CPB 1008)	16, S5-17, S5-18, S5-19, S5-20
Cologuard (Parallel-Review reference)	2014-08-11 — PMA P130017 approval	HCPCS G0464 effective 2015-01-01 ($492.72); CPT 81528 effective 2016-01-01 ($508.87)	2014-10-09 — NCD 210.3 decision memo (proposed on the FDA approval date — Parallel Review)	S5-10, S5-13, S5-21, S5-22, S5-23
FoundationOne CDx (Parallel-Review reference)	2017-11-30 — PMA P170019 approval	PLA 0037U in use by Q1 2018 (unpinned); CMS ADLT $3,500 from 2018-07-01	2018-03-16 — NCD 90.2 final decision (proposed on the FDA approval date)	S5-13, S5-24, S5-25, S5-26
COVID-19 NAAT (CDC 2019-nCoV / Labcorp RT-PCR)	2020-02-04 — CDC EUA; 2020-03-16 — Labcorp EUA (first commercial-lab EUA)	CPT 87635 effective 2020-03-13; CLFS rate set April 2020 (day unpinned)	2020-03-18 — FFCRA s.6001 mandated first-dollar coverage; Medicare covered from PHE start	S5-13, S5-27, S5-28, S5-29

Table S5b. Gate-timing cross-walk, China. Gate 1 = NMPA registration; Gate 2 = medical-service price item (provincial or national); Gate 3 = basic medical-insurance listing. Registration numbers are romanised (e.g., Guo Xie Zhu Zhun 2021 No. 3400256); original Chinese certificate text is not reproduced.

Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
Xpert MTB/RIF (Cepheid, imported)	2014-02-26 — Guo Shi Yao Jian Xie (Jin) Zi 2014 No. 3401153; renewed as Guo Xie Zhu Jin 2017 No. 3406215	2024 — earliest independent provincial price item identified in the retrievable public record (Guangdong, Yue Yi Bao Fa 2024 No. 19, item 250403090-1N, product-neutral, market-priced/self-paid, hospital execution from 2024-12) (approx.); 2025-09/10 sixth-batch national price governance cut price to ~CN¥300 (Shanghai from 2025-10-15); in the retrievable public record, provincial price items were largely absent before 2024 and procurement ran through single-source routes; institution-level pricing records are not centrally published and absence of a retrievable item is not evidence that the test was unavailable or unpriced locally	partial listing: Xinjiang 2019 (Xin Yi Bao 2019 No. 86); Liaoning 2023 (Liao Yi Bao Fa 2023 No. 10); explicitly fully self-paid in Guangdong and most provinces; censored elsewhere	S5-30, S5-31, S5-32, S5-37, S5-38, S5-39, S5-40, S5-41, S5-42
Xpert MTB/RIF Ultra (Cepheid)	2023-03-07 — Guo Xie Zhu Jin 2023 No. 3400073	censored — no independent price item; billed under the pre-existing TB molecular-testing items	censored — covered only where TB molecular-testing insurance policies apply (Xinjiang 2019; Liaoning 2023)	S5-33, S5-41
Domestic TB resistance-gene NAATs (Zeesan, Yaneng, Chuanglan and others)	2013-01-21 — first domestic certificate (Zeesan rifampicin-resistance kit, Guo Shi Yao Jian Xie (Zhun) Zi 2013 No. 3400100); later: Yaneng 2015, Chuanglan 2022-10-18, Zeesan MeltPro MDR 2024-04-26	Xinjiang catalogue included the item by 2019 (unpinned); Guangdong item 250403090-2N at CN¥240, self-paid (2024); Hainan tiered prices from 2025-10-15; sixth-batch 2025 governance down-adjusted	Xinjiang 2019; Liaoning 2023 (drug-resistant TB chronic-disease package); most provinces not listed — Hubei TB Control Plan 2025–2030 still calls for creating codes and reimbursement; censored elsewhere	S5-34, S5-35, S5-36, S5-37, S5-38, S5-39, S5-40, S5-43

Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
Respiratory syndromic multiplex panel — Sansure six-pathogen respiratory NAAT kit	2021-04-14 — Guo Xie Zhu Zhun 2021 No. 3400256 (influenza A/B, RSV, adenovirus, rhinovirus, M. pneumoniae); bacterial six-panel 2022; further three-plex certificates 2025-08-25	censored — no independent price item; billed under single-target items; several provinces cap respiratory-virus NAAT billing at six items, and the April 2025 national "minimum necessary" notice requires unbundling	censored — outpatient multiplex generally self-paid; inpatient bundled under DRG/DIP cost control; 2025–2026 test-bundle governance tightened further	S5-44, S5-45, S5-46, S5-47, S5-48, S5-49
mNGS pathogen testing (Genskey and others; hospital LDT)	2024-09-02 — Genskey 2019-nCoV sequencing kit (first mNGS-method class III kit, Guo Xie Zhu Zhun 2024 No. 3401661) plus analysis software; hospital mNGS LDT services long had no registration pathway	Long no price item — billed under legacy "DNA sequencing" items or self-priced; 2025-12-19 national pathology pricing-item guideline first creates a high-throughput-sequencing item; 2026-08 laboratory-medicine pricing-item guideline (formal version): mNGS billed per test, provincial price caps	2026-04 — Qinghai first province to include MPS high-throughput sequencing in class-B insurance (public-notice stage) (approx.); Chongqing/Anhui price-standardisation only; censored in all other provinces	S5-50, S5-51, S5-52, S5-53, S5-54, S5-55, S5-56
COVID-19 NAAT	2020-01-26 — emergency approval, first four certificates (Zhijiang Guo Xie Zhu Zhun 2020 No. 3400057 et al.); two further certificates 2020-01-28 (Daan, Sansure)	~2020-02 — provincial temporary price items under expedited procedure (approx.); documented: Liaoning 2020-04-11, Anhui 2020-04-20 (CN¥220/person-time), Beijing 180 to CN¥120 (2020-06-25); successive cuts to CN¥15 single / CN¥3 pooled by 2022	2020-05-06 — Hubei temporary class-B inclusion (E Yi Bao Fa 2020 No. 25); 2020-06-19 — NHSA national directive (Yi Bao Ban Fa 2020 No. 30) to include in provincial catalogues; temporary policies withdrawn after January 2023	S5-57, S5-58, S5-59, S5-60, S5-61, S5-62, S5-63
Six-/nine-item respiratory NAAT panels (Berjie, Wantai)	Berjie six-item kit 2021-09 (Guo Xie Zhu Zhun 2021 No. 3400567); Wantai nine-item kit 2025-08-25 (Guo Xie Zhu Zhun 2025 No. 3401726)	censored — no province has created a dedicated price item (none found as of 2026-08); same six-item cap and unbundling constraints as the Sansure panel	censored — no provincial insurance listing of respiratory multiplex panels found (none found as of 2026-08)	S5-47, S5-48, S5-49, S5-64, S5-65, S5-66

Table S5c. Gate-timing cross-walk, Germany, France and England (combined). Gate 1 = CE marking (IVDD/IVDR) or in-house/health-institution status; Gate 2 = coding/listing milestone (EBM GOP in Germany; NABM code/RIHN listing in France; NHS tariff, NICE or NGTD milestone in England); Gate 3 = coverage/funding milestone (GKV/DRG/NUB/ZE in Germany; NABM/RIHN funding in France; NGTD listing or commissioning in England).

Country	Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
Germany	Xpert MTB/RIF	2009-04 — CE-IVD mark	pre-existing product-neutral item — GOP 32825 (MTC-complex NAAT, €61.40) billable since 2008-01-01 (DKGEv key table); the Bewertungsausschuss decision of 15 Jun 2022 (effective 2022-07-01) re-formulated (Neufassung) the existing microbiology NAAT catalogue rather than creating these items	EBM listing = GKV ambulatory coverage (lag 0 by construction); inpatient absorbed in G-DRG; no dedicated G-BA decision found (none)	S5-67, S5-68, S5-69
Germany	FilmArray Respiratory Panel	CE-IVD and commercially available in Europe by Sep 2013 (approx.)	2022-07-01 — GOP 32851 (respiratory pathogens; €19.90 first pathogen, €7.23 each additional; capped by GOP 32813, €85)	EBM = GKV coverage; inpatient via G-DRG	S5-68, S5-69, S5-70

Country	Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
Germany	FilmArray GI panel	CE-IVD anticipated late spring 2014 (approx.)	2022-07-01 — GOP 32853 (acute GI infection pathogens); capped by GOP 32814 (€85)	EBM = GKV coverage; inpatient via G-DRG	S5-69, S5-71
Germany	FilmArray ME panel	2016-01-26 — CE marked	censored — no dedicated EBM GOP for CSF multiplex panels; CNS pathogens billable only via single-pathogen GOPs	inpatient within G-DRG; no NUB identified (none)	S5-72
Germany	QIAstat-Dx respiratory/GI panels	2018-01 — CE-IVD (IVDD); IVDR certification 2024-09-26	2022-07-01 — generic GOPs 32851/32853 apply to QIAstat-Dx cartridges	EBM = GKV coverage; inpatient via G-DRG	S5-69, S5-73, S5-74
Germany	mNGS infectious-disease testing	in-house/health-institution tests (IVDD Art. 1(5)/IVDR Art. 5(5) exemption); no CE-marked product	censored — no EBM GOP for mNGS	censored — no NUB/ZE listing verified for mNGS pathogen diagnostics (not evidenced)	S5-75, S5-76
Germany	COVID-19 NAAT	2020-01/02 — in-house assays, then CE-marked kits (approx.)	late Jan 2020 — GOP 32816 introduced at €59 (approx.); successively devalued (€19.90 from 2023-04-01)	Hospital ZE under s.26(2) KHG (SARS-CoV-2 testing supplement; renewed 2023-05-01 at €30.40); GOP 32816 billed extrabudgetary	S5-77, S5-78, S5-79, S5-80
France	Xpert MTB/RIF	2009-04 — CE-IVD mark	NABM acte 4102 (mycobacteria molecular diagnosis, B 250); long-standing code, first listing date unpinned	NABM listing = Assurance Maladie reimbursement (60% standard; 100% ALD); lag 0 by construction	S5-81, S5-82
France	FilmArray Respiratory Panel	CE-IVD by Sep 2013 (approx.)	Not in NABM as a panel; RIHN N156 (multiplex PCR 10+ primer pairs, BHN 1000 = €270) from RIHN V2016 (2016-01-01)	RIHN listing = funding act via MERRI G03 / mission specifique (instruction 2015/258; renewed instruction 2025/135); still hors-nomenclature in 2024–2025	S5-83, S5-84, S5-85, S5-86, S5-87
France	FilmArray GI panel	CE-IVD ~2014 (approx.)	Not in NABM; RIHN N156 from 2016-01	RIHN = funding (as above)	S5-71, S5-84, S5-86
France	FilmArray ME panel	2016-01-26 — CE marked	Not in NABM (single-plex CSF codes 4504–4507 exist); RIHN N156 explicitly cited for the ME panel; BCID2 costed at €270 under N156	RIHN = funding (as above), from V2016 onward	S5-84, S5-88, S5-89
France	QIAstat-Dx respiratory/GI panels	2018-01 — CE-IVD (IVDD); IVDR 2024-09-26	Not in NABM as a panel; RIHN N156 pre-existing	RIHN N156 hospital-funding pathway	S5-73, S5-74, S5-84
France	mNGS infectious-disease testing	in-house, research framework (Fourgeaud et al., Lancet Microbe 2024)	censored — no NABM code	censored — no dedicated reimbursement identified (research-funded)	S5-90
France	COVID-19 NAAT	in-house/CE-marked assays Feb–Mar 2020 (approx.)	NABM acte 5271 — arrete of 2020-05-12; reference tariff B 160 by arrete of 2020-12-12 with turnaround-time bonus/malus	NABM listing = 100% coverage during the pandemic; lag 0 by construction	S5-91, S5-92, S5-93
France	Respiratory quadriplex (Flu	CE-marked quadriplex kits	2026-01-30 — HAS recommendation reserving quadriplex PCR to the	Recommendation and hospital-only listing	S5-94, S5-95,

Country	Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
	A/B + RSV + SARS-CoV-2)	since ~2021 (approx.)	hospital setting; NABM inscription restricted to hospital laboratories	concurrent (lag 0); community-lab access contested (FBM, 2026-03-17)	S5-96, S5-97
England	Xpert MTB/RIF	2009-04 — CE-IVD mark	2016-01-13 — NICE NG33 published (recommends rapid TB NAAT and rifampicin-resistance NAAT); no NHS national tariff (none)	not on NGTD; routine TB WGS service launched 2017-03; NAAT delivered through the NHS/PHE TB laboratory network (position statement Jul 2013)	S5-98, S5-99, S5-100, S5-101
England	FilmArray Respiratory Panel	CE-IVD by Sep 2013 (approx.)	censored — no NHS tariff; no NICE diagnostics guidance; local hospital adoption only	censored — not on NGTD; local commissioning only	S5-70
England	FilmArray GI panel	CE-IVD ~2014 (approx.)	censored — as above	censored — as above	S5-71
England	FilmArray ME panel	2016-01-26 — CE marked	censored — no NHS tariff/NGTD listing (NICE NG240, Mar 2024, recommends CSF PCR but is not a listing instrument)	censored	S5-72
England	QIAstat-Dx respiratory/GI panels	2018-01 — CE-IVD (IVDD); IVDR 2024-09-26 (GB accepts CE under transitional rules)	censored — no tariff/NGTD	censored	S5-73, S5-74
England	mNGS infectious-disease testing	in-house/health-institution status (UKAS-accredited LDTs in reference laboratories)	censored — no NHS tariff	censored — not routinely commissioned; research/service-evaluation use	S5-76
England	COVID-19 NAAT	in-house PHE assays Jan 2020; CE-marked commercial assays from Mar 2020	2020-05-27 — NHS Test and Trace launched across England (centrally funded, free PCR); no tariff — national programme funding via DHSC	centralised commissioning: NHS Test and Trace / UKHSA laboratory network (incl. Lighthouse labs); not NGTD	S5-102, S5-103

Table S5d. Gate-timing cross-walk, Japan. Gate 1 = PMDA review outcome / MHLW marketing approval or certification; Gate 2 = national health-insurance listing date plus fee-schedule points and reimbursement category (E1 existing item, E2 existing item/new method, E3 new item); Gate 3 is fused with Gate 2 (listing simultaneously sets price and confers coverage). Japanese document and item names are romanised or translated; approval numbers are transcribed as Latin text.

Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
Xpert MTB/RIF (Cepheid / Danaher)	2016-09 (month-level; approval no. 22800AMX0067300; exact day unpinned)	2017-01-01 — interim listing under existing D023 items: TB-group NAAT 410 points + rifampicin-resistance gene detection 850 points (E1; no facility gate; the D023 items are product-neutral, not Xpert-specific). NB: a "June 2017" date in some project material corresponds to a different fee item; 2017-01-01 used	fused with Gate 2 — same listing event	S5-104, S5-105, S5-106, S5-107
cobas MTB-RIF/INH (Roche Diagnostics)	not publicly retrieved (approval no. pattern suggests FY2022; must precede the	2023-02-01 — new item, simultaneous rifampicin- and isoniazid-resistance gene detection, 963 points (E3); Chuikyo 536th	fused with Gate 2	S5-108, S5-109, S5-110

Index test	Gate 1 (date/status)	Gate 2 (date/status)	Gate 3 (date/status)	Source key
	2023-01-18 Chuikyo decision) (unpinned)	general meeting 2023-01-18		
FilmArray Respiratory Panel 2.1 (bioMerieux)	2020-06-02 — MHLW approval (partial-change approval adding SARS-CoV-2)	2020-08-01 — multiplex NAAT item incl. SARS-CoV-2, 1,800 points (1,350 without specimen transport), facility-gated; Chuikyo 2020-07-22	fused with Gate 2 (lag 60 days)	S5-111, S5-112, S5-113
FilmArray Respiratory Panel (original 20-target)	not publicly retrieved (2019; certification via registered certification body) (unpinned)	2019-11-01 — new fee item under D023 (sub-bands -022/-023 in the MHLW procedure master), virus/bacteria multi-item simultaneous NAAT: 963 points for panels without SARS-CoV-2 (D023-022); panels including it (RP2.1 from 2020-08) bill 1,350 points (D023-023) (E3; facility-gated to ICU/emergency-admission categories)	fused with Gate 2	S5-113, S5-114, S5-115
FilmArray ME panel	not publicly retrieved (at or before Sep 2022) (unpinned)	2022-10-01 — new item, multiplex NAAT (CSF), 1,700 points (E3); Chuikyo 528th general meeting 2022-09-14. NB: some trackers state Sep 2022; 2022-10-01 used	fused with Gate 2	S5-116, S5-117, S5-118
BioFire Pneumonia Panel	FY2021 (approval no. 30300EZX00084000; day unpinned); Japan sales start 2022-03-15	2026-02-01 — new item, multi-item simultaneous NAAT and drug-resistance-gene detection, 1,273 points (E3; facility-gated); Chuikyo 2026-01-23	fused with Gate 2 (approval-to-listing lag ~49–55 months)	S5-119, S5-120, S5-121
Syndromic multiplex NAAT fee item (1,273 points, facility-gated)	fee-schedule construct, not a single product	2026-02-01 — same event as the BioFire Pneumonia Panel row (D023 item created; E3)	fused with Gate 2	S5-120, S5-121, S5-122
mNGS pathogen testing	no PMDA-approved commercial IVD for pathogen mNGS as of Aug 2026	censored — no insurance listing; research/self-paid only; advanced-medical-care (senshin iryo) entry strategies reported	censored	S5-122, S5-123
COVID-19 NAAT	not applicable as a single event (listing-led emergency pathway; individual kit approvals followed from spring 2020)	2020-03-06 — D023 SARS-CoV-2 NAAT, 1,800 points (1,350 without specimen transport; E1 item extension; no facility gate)	fused with Gate 2	S5-124
NCC Oncopanel (contrast case)	2018-12-25 — approval no. 23000BZX00398000 under the sakigake priority-review scheme	2019-06-01 — new item, cancer gene-panel test, 56,000 points (E3; facility-gated to designated cancer-genome hospitals); Chuikyo 2019-05-29	fused with Gate 2 (lag 158 days)	S5-125, S5-126, S5-127

S5-128. Wugang Municipal Hospital of Traditional Chinese Medicine. Hospital price list: pathogen RNA fluorescent quantitative PCR CN¥68 per test, pathogen DNA fluorescent quantitative PCR CN¥47.9 per test, both Class A (fully covered) insurance items [in Chinese]. Originally at: http://zgwg.gov.cn/contents/41390/353939.html (link dead as of 2026-11; values as accessed 2026-08, Tier B). Corroborating published hospital price list with the same generic items: Feicheng City People's Hospital item list [in Chinese]. http://www.feicheng.gov.cn/module/download/downfile.jsp?classid=0&filename=dced46cc951347beae809080a9c82752.pdf S5-129. National Healthcare Security Administration. Interpretation article for the laboratory-test price-item guideline (trial) ('收官之作！检验类立项指南正式发布'), 2026-08-14: multiplex combined testing discounted by indicator count (≤5 indicators at 80%, ≤10 at 70%, >10 at 60% per item), on the stated premise of declining marginal cost of combined testing [in Chinese]. https://www.nhsa.gov.cn/art/2026/8/14/art_14_21764.html. S5-130. China Government Procurement Network (ccgp.gov.cn) and provincial procurement platforms, tuberculosis nucleic-acid testing award and single-source notices, 2022–2025. Per-test unit prices were extracted only where a notice states one

and names the analyte, and are compared only within matched readouts. Cartridge-based assays detecting M. tuberculosis together with rifampicin resistance in a single run: Xpert MTB/RIF CN¥258 (Shanghai 2025-05) and CN¥319.6 (Shanghai 2022-12); Xpert MTB/RIF Ultra CN¥480 (Shanghai 2025-05 and 2022-12) and CN¥400 (Shanxi 2025-01). Open-platform domestic reagents separate the two readouts into distinct kits: in the Heilongjiang 2025-05 award the complex-detection kit and the rifampicin-resistance melting-curve kit each cleared at CN¥135, CN¥270 for both; a Guizhou 2025-04 budget-derived figure for an rpoB detection-and-mutation kit was CN¥200. Earlier drafts of this note reported a 2.3-fold median gap between a cartridge group and an open-platform group. That comparison is withdrawn: three of the five records then assigned to the open-platform group do not test rifampicin resistance (CN¥140 is a fluoroquinolone-resistance kit, CN¥35 is detection only without resistance testing, and CN¥145 is a combined quotation across five drug resistances), so the groups were not matched on analyte. Xpert XDR awards (CN¥859.8–867.5) are likewise excluded as they cover a different drug panel. Awards quoted per kit, per budget line or per box without a stated test count are excluded throughout. A ceiling-price quotation (Hunan 2023-08, CN¥247.2) is likewise excluded because a posted ceiling is not a clearing price. Full notice texts and a 177-row product-level index are archived in the evidence library accompanying this manuscript [in Chinese]. S5-131. US Code of Federal Regulations, 42 CFR §412.87–412.88 (New Technology Add-On Payment: additional payment beyond the DRG; the lesser of 65% of the technology's cost or 65% of the excess of case cost over the DRG payment; 75% for Qualified Infectious Disease Product / Limited-Population-Pathway antimicrobials). https://www.ecfr.gov/current/title-42/section-412.88. S5-132. Ministry of Health (China). Measures for the Clinical Management of Antimicrobial Drugs (MOH Decree No. 84, 2012): tiered antimicrobial management (unrestricted / restricted / special-use), special-use agents requiring a senior-title prescriber or expert consultation [in Chinese]. https://www.moj.gov.cn/pub/sfbgw/flfggz/flfggzbmgz/201207/t20120705_145157.html. S5-133. US Congress. Protecting Access to Medicare Act of 2014, §218(b) (appropriate-use criteria for advanced imaging); CMS. CY2024 Physician Fee Schedule final rule (AUC programme paused and its regulations rescinded, effective 2024-01-01; the stated grounds were claims-reporting burden and data integrity, not the principle). https://www.hklaw.com/en/insights/publications/2023/11/cms-issues-cy-2024-medicare-physician-fee-schedule-final-rule. S5-134. Ministry of Health, Labour and Welfare (Japan). 2018 fee-schedule revision: antimicrobial-stewardship support fee (抗菌薬適正使用支援加算), payable per inpatient admission to hospitals operating a qualifying multidisciplinary stewardship team [in Japanese]. https://www.mhlw.go.jp/content/12404000/000583841.pdf. S5-135. Sozialgesetzbuch Fünftes Buch, §137e (Erprobung neuer Untersuchungs- und Behandlungsmethoden; introduced 2012): where the Federal Joint Committee finds a method potentially necessary but its benefit not yet sufficiently proven, it must commission a time-limited trial under the sickness funds while evidence is generated [in German]. https://www.gesetze-im-internet.de/sgb_5/__137e.html.

S5.3 Lag statistics

Table S5e consolidates the per-system gate-lag statistics computed from the dated cells of Tables S5a–S5d. Lags are expressed in years (days/365.25) except for Japan, where the fused gate structure

makes days the natural unit. All medians and ranges are computed on complete cells only; censoring is reported separately, and the China Gate 2-to-Gate 3 figure is explicitly survivorship-biased.

Table S5e. Gate-lag statistics by system, computed on complete (dated, uncensored) cells only.

System	Gate 1 to Gate 2: median (range; n)	Gate 2 to Gate 3: median (range; n)	Censoring and structural notes
United States	0.67 y (0.09–1.87; n = 7)	2.29 y (−0.23–9.29; n = 7)	Xpert MTB/RIF excluded from both lags (code pre-existed; no policy decision); mNGS censored at Gate 3 (commercial non-coverage). Negative lower bound reflects Parallel Review: Cologuard's NCD (2014-10-09) preceded its first code (2015-01-01)
China	~3.6 y (0–10.3; n = 4)	~0.3 y (0–0.3; n = 3) — survivorship-biased (cells where Gate 3 actually occurred)	3 tests censored at Gate 2 (Sansure six-pathogen panel, Wantai nine-item panel, Xpert Ultra); most novel tests are also censored at Gate 3 ("price item without insurance" equilibrium); censoring biases both medians downward
Germany	~4.5 y (0–10.3; n = 5; 3 of 5 approximate; NB: three of the five dated Gate-2 events share a single batch date, 2022-07-01 — the 596th Bewertungsausschuss batch-coding decision — while Xpert's Gate 2 is the pre-existing product-neutral TB NAAT item GOP 32825, billable since 2008-01-01; the median therefore mixes batch-event distance with a pre-existing item, not per-test processing time)	0 by construction for listed routine-tier items (n = 5) — EBM listing confers GKV ambulatory coverage; novel or high-risk methods face a separate evaluation track not captured by this metric	ME panel and mNGS censored at Gate 2; inpatient tests absorbed in G-DRG without dated events; NUB/ZE channel used only for COVID-19 (2020–2023)
France	~1.7 y (0–4.9; n = 6; 4 of 6 approximate)	0 by construction for the listing act itself (n = 7; n exceeds the Gate 1→2 sample because one observation is dated at listing but not at Gate 1); the HAS-opinion-to-tariff lag occurs upstream of listing and is not captured by this metric	mNGS censored; the operative lag is RIHN (derogatory hospital funding, N156 from 2016) to NABM droit-commun inscription, which stayed closed ~10 y and opened only in restricted hospital-only quadriplex form on 2026-01-30
England	~3.5 y (0.3–6.8; n = 2)	centralised commissioning — no sequential listing-to-funding step exists for these diagnostics	Gate 2 censored for most syndromic panels (no NHS national tariff mechanism; NGTD does not cover these tests); dated gates exist only for NICE-recommended TB NAAT (NG33, 2016) and the centralised COVID-19 programme (2020)
Japan	approval-to-listing ~108–133 d (range 60–1,677 d incl. the BioFire Pneumonia Panel outlier; n = 4; excluding the outlier: median 108 d, range 60–158 d, n = 3)	fused gates — listing is a single dated event; no Gate 2-to-Gate 3 interval exists	mNGS censored (never listed); three further tests (cobas, RP original, ME) are bounded at zero because approval dates were not publicly retrieved; COVID-19 NAAT followed a listing-led emergency pathway with no Gate 1 event

S5.4 Source list

Numbering convention: the references below are numbered S5-1 to S5-127 and are local to Section S5; they are not the manuscript's citation numbers. The list merges the Vancouver source lists of the four gate-timeline files (United States, China, Germany/France/England, Japan), deduplicated; Chinese- and Japanese-language sources are given with romanised issuing bodies and English-translated titles, with document and registration numbers transcribed as Latin text. All URLs were accessed August 2026.

United States

S5-1. US FDA. De Novo classification order, Xpert MTB/RIF Assay (K131706), July 25, 2013. https://www.accessdata.fda.gov/cdrh_docs/pdf13/K131706.pdf.

S5-2. Cepheid. Cepheid receives FDA market authorization for Xpert MTB/RIF [press release]. July 25, 2013. https://cepheid.mediaroom.com/2013-07-25-Cepheid-Receives-FDA-Market-Authorization-for-Xpert-MTB-RIF.

S5-3. CDC. Revised device labeling for the Cepheid Xpert MTB/RIF assay for detecting Mycobacterium tuberculosis. MMWR 2015;64(7):193. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6407a8.htm.

S5-4. US FDA. 510(k) Premarket Notification database: K103175, FilmArray Respiratory Panel (RP), Idaho Technology — decision date 02/17/2011. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?id=K103175.

S5-5. US FDA. FDA permits marketing of first SARS-CoV-2 diagnostic test using traditional premarket review process [BioFire RP2.1, De Novo DEN200031] [news release]. March 17, 2021. https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-sars-cov-2-diagnostic-test-using-traditional-premarket-review-process ; De Novo letter: https://www.accessdata.fda.gov/cdrh_docs/pdf20/DEN200031.pdf ; EUA (EUA200521, authorized May 2020) revocation: https://www.fda.gov/media/146766/download.

S5-6. bioMerieux/BioFire Diagnostics press-release archive (RP2 FDA clearance June 1, 2017; RP2.1 EUA May 4, 2020; RP2.1 De Novo March 18, 2021). https://www.biofiredx.com/media/press-releases/.

S5-7. US FDA. 510(k) database: K140407, FilmArray Gastrointestinal (GI) Panel — decision date 05/02/2014. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?id=K140407.

S5-8. US FDA. De Novo classification order, FilmArray Meningitis/Encephalitis (ME) Panel (DEN150013), October 8, 2015. https://www.accessdata.fda.gov/cdrh_docs/pdf15/DEN150013.pdf ; FDA press release Oct 8, 2015 (archived): http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm466360.htm; bioMerieux press release, October 9, 2015: https://www.biomerieux.com/us/en/journalists/press-releases/biofire-diagnostics-receives-de-novo-clearance-fda-filmarrayr-meningitisencephalitis-panel.html.

S5-9. Blue Cross Blue Shield of Kansas. Molecular diagnosis of respiratory/GI infections — medical policy revision history documenting CPT 87631–87633 "effective 01-01-2013" and CPT

87505–87507 "effective January 1, 2015". https://www.bcbsks.com (medical policy library; accessed via policy PDF).

S5-10. CMS. CY2016 Clinical Diagnostic Laboratory Fee Schedule (16CLAB.zip; national limitation amounts: 87633/87507 $567.75; 87556 $47.80; 81528 $508.87; 87483 absent). https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/16CLAB.zip. Values as originally accessed; this archive was not re-retrievable in the 2026-11 archival round (cms.gov refuses programmatic access).

S5-11. CMS. CY2017 CLFS (17CLAB.zip; 87483 "Cns dna amp probe type 12-25", national limit $571.72 — first CLFS appearance, i.e., code effective 1/1/2017). https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/17CLAB.zip. Values as originally accessed; this archive was not re-retrievable in the 2026-11 archival round (cms.gov refuses programmatic access).

S5-12. CMS. CY2020 Q4 CLFS (20clabq4.zip; PLA codes 0151U/0152U/0202U shown as contractor-priced "L/$0.00" in first cycle; 0037U $3,500; 81528 $508.87). https://www.cms.gov/files/zip/20clabq4.zip. Values as originally accessed; this archive was not re-retrievable in the 2026-11 archival round (cms.gov refuses programmatic access).

S5-13. CMS. CY2025 Q1 CLFS (25clabq1.zip; 87556 $41.68; 87631 $142.63; 87632 $218.06; 87633 $416.78; 87507 $416.78; 87483 $416.78; 81528 $508.87; 0037U $3,500.00; 0152U $2,126.20; 0323U $2,126.20; 0202U $416.78; 87635 $51.31). https://www.cms.gov/files/zip/25clabq1.zip.

S5-14. CMS Medicare Coverage Database. LCD L39003 — MolDX: Molecular Syndromic Panels for Infectious Disease Pathogen Identification Testing (original effective date 04/17/2022; source proposed LCD DL39003; billing article A58761). https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39003.

S5-15. Federal Register / CMS CY2020 IPPS final rule (technology add-on context noting PLA 0151U published October 1, 2019, effective January 1, 2020). 84 FR 42044 (Aug 16, 2019). https://www.federalregister.gov.

S5-16. Schlaberg R, Chiu CY, Miller S, et al. Validation of metagenomic next-generation sequencing tests for universal pathogen detection (UCSF CLIA-lab mNGS validation; clinical availability from mid-2016). Arch Pathol Lab Med. 2017;141(6):776-786. https://pubmed.ncbi.nlm.nih.gov/28169558/.

S5-17. Blauwkamp TA, Thair S, Rosen MJ, et al. Analytical and clinical validation of a microbial cell-free DNA sequencing test (Karius Test) for infectious disease. Nat Microbiol. 2019;4:663-674. https://pubmed.ncbi.nlm.nih.gov/30833797/.

S5-18. AMA / CPT PLA code list (mindxsciences mirror): 0152U (Karius Test) — descriptor revision effective January 1, 2021 (code in existence by 2020); 0100U deletion effective April 1, 2021. https://mindxsciences.com/docs/cpt-pla-codes-short.pdf.

S5-19. Discoveries in Health Policy. CMS CY2023 CLFS crosswalk meeting notes: PLA 0323U (CSF metagenomics, Johns Hopkins) crosswalked to Karius 0152U (September 2022). https://www.discoveriesinhealthpolicy.com/2022/09/.

S5-20. Anthem (Carelon) medical policy LAB.00050 — Metagenomic Sequencing for Infectious Disease in the Outpatient Setting: investigational and not medically necessary, all indications (publish 01/06/2026; last review 11/06/2025; predecessor GENE.00053 ~2021). https://www.anthem.com/medpolicies/abc/active/mp_pw_e002725..html; Aetna CPB 1008 — Infectious Diseases: Selected Tests (Karius Test and CNS mNGS experimental/investigational/unproven; last reviewed 01/14/2026). https://www.aetna.com/cpb/medical/data/1000_1099/1008.html.

S5-21. US FDA. PMA database: P130017, Cologuard (Exact Sciences) — approval August 11, 2014. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P130017 ; FDA news release Aug 11, 2014.

S5-22. CMS. Decision Memo for Screening for Colorectal Cancer — Stool DNA Testing (CAG-00440N), October 9, 2014; NCD 210.3. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=277.

S5-23. Clinical Lab Products / CLP. CMS finalizes CY2015 CLFS: HCPCS G0464 (Cologuard) at $492.72 via crosswalk (finalized November 2014). https://www.clpmag.com.

S5-24. US FDA. PMA database: P170019, FoundationOne CDx (Foundation Medicine) — decision date 11/30/2017. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P170019.

S5-25. CMS. Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R), March 16, 2018; NCD 90.2. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=296.

S5-26. Foundation Medicine. Foundation Medicine receives new ADLT status for FoundationOne CDx from CMS [press release; $3,500 rate under HCPCS 0037U from July 1, 2018]. May 21, 2018. https://www.foundationmedicine.com/press-releases/.

S5-27. US FDA. Emergency Use Authorization: CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel (EUA issued February 4, 2020); Labcorp COVID-19 RT-PCR Test (EUA issued March 16, 2020). FDA EUA archive/historical EUA page. https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/historical-information-about-device-emergency-use-authorizations.

S5-28. AMA. CPT code 87635 — expedited publication for SARS-CoV-2 nucleic acid detection, effective March 13, 2020. https://www.ama-assn.org/press-center/press-releases/ama-announces-new-cpt-code-covid-19-testing.

S5-29. US Congress. Families First Coronavirus Response Act, Pub. L. 116-127 s.6001 (March 18, 2020); CMS. COVID-19 CLFS payment determinations (~$51.31 per 87635/U0002; U0001 $35.92), April 2020; 87635 remained $51.31; the CY2021 figure of $75.00 applies to the high-throughput codes

U0003/U0004 (reduced from $100). https://www.cms.gov/medicare/payment/fee-schedules/clinical-laboratory-fee-schedule-clfs.

China

S5-30. Vedeng Medical (reproducing the NMPA database). Mycobacterium tuberculosis rpoB gene and mutation detection kit (real-time fluorescent PCR) (trade name Xpert MTB/RIF), import registration Guo Shi Yao Jian Xie (Jin) Zi 2014 No. 3401153, approval date 2014-02-26. https://www.vedeng.com/zhucezheng/jk/129642.html.

S5-31. National Medical Products Administration (NMPA). Medical device recall event report form (Cepheid; renewal registration Guo Xie Zhu Jin 2017 No. 3406215). https://www.nmpa.gov.cn/directory/web/nmpa/images/1668418676877049983.pdf.

S5-32. Beijing Center for Disease Control and Prevention. Award announcement for MDR-TB testing reagent procurement (single-source Xpert reagents, CN¥220 per test). 2023-09-13. Originally at: http://www.ccgp-beijing.gov.cn/xxgg/sjzfcggg/sjzbjggg/t20230913_1533711.html (link dead as of 2026-11; content as accessed at original access date, Tier B); Jiangsu CDC award announcement (CN¥209 per test), 2023-09-06. https://www.chinabidding.com/bidDetail/256090843-BidResult.html.

S5-33. Yaozh Data (reproducing NMPA). Xpert MTB/RIF Ultra, import registration Guo Xie Zhu Jin 2023 No. 3400073, approval date 2023-03-07. https://dbadminmaster.yaozh.com/jinkoujixie/7322034630000002.html.

S5-34. Qgyyzs Pharmaceutical Network (reproducing NMPA). Zeesan (Xiamen) M. tuberculosis rifampicin-resistance mutation detection kit, Guo Shi Yao Jian Xie (Zhun) Zi 2013 No. 3400100 (2013-01-21); renewal Guo Xie Zhu Zhun 2017 No. 3400497 (2017-03-16). https://shuju.qgyyzs.net/gcylqx/details23718alHPk48yzA54588.html.

S5-35. Yaneng Bio. M. tuberculosis resistance mutation gene detection kit (PCR-reverse dot blot), Guo Xie Zhu Zhun 2015 No. 3400356. https://www.yanengbio.com/product/mycobacteria.html.

S5-36. Wuxu Data (reproducing NMPA). Zeesan MeltPro MDR (RIF+INH), Guo Xie Zhu Zhun 2024 No. 3400763, approval date 2024-04-26. https://www.wuxuwang.com/qixiecn/e303b71d-288c-11ef-91cf-0a7966a5a76e ; Fujian Provincial Medical Products Administration: priority-review approval 2024-05-09. https://yjj.scjgj.fujian.gov.cn/zwgk/xwdt/sjdt1/202405/t20240509_6445686.htm.

S5-37. Xinjiang Uygur Autonomous Region Healthcare Security Bureau. Notice on including 10 tuberculosis diagnosis-and-treatment items in the basic-insurance payment scope (Xin Yi Bao 2019 No. 86, 2019). https://ylbzj.xinjiang.gov.cn/ylbzj/mlgkyyfw/202011/b881bfd121db47de9c7c032e0ec71ffc.shtml (accessed 2026 Nov); issuance year confirmed by the bureau's reply to a People's Congress proposal, 2025-07-02. http://ylbzj.xinjiang.gov.cn/ylbzj/mlgkjyta/202507/5658fa1354054092a865de8d7a26d9f4.shtml.

S5-38. Shenzhen Bao'an District People's Hospital. Public notice of new medical-service item prices (Yue Yi Bao Fa 2024 No. 19; item 250403090-1N, CN¥700 per item, executed 2024-12-02). 2024-11-25. https://www.bawjxt.net/szsbaqrmyy/jyzn/wjgs/content/post_1427277.html; Guangzhou

Huadu District People's Hospital notice (fully self-paid), 2025-03-06. http://www.hdhosp.com/info/1208/6772.htm; Guangzhou Chest Hospital notice (items 250403090-1N at CN¥650 and 250403090-2N at CN¥240, fully self-paid, executed 2025-02-12). https://www.xkyy.com.cn/info/1731/9441.htm (notice listing; price table in linked PDF).

S5-39. Shenzhen Bao'an Songgang People's Hospital. Pricing guide: TB resistance-gene detection 250403090-2N at CN¥130; rpoB detection 250403090-1N at CN¥300 (after the 2025 price governance). https://www.bawjxt.net/sgrmyy/en/guide/pricing/content/post_1739102.html.

S5-40. Liaoning Provincial People's Government. Liao Yi Bao Fa 2023 No. 10, notice on improving the province's outpatient chronic/special-disease benefit policy (including rpoB gene and rifampicin-resistance rapid testing). https://www.ln.gov.cn/web/zwgkx/lnsrmzfgb/2023n/zk/zk9/bmwj/2023080208540079992/.

S5-41. Hebei Provincial Healthcare Security Bureau. Notice on adjusting prices of selected medical-service items (Ji Yi Bao Han 2025 No. 87, sixth batch of price-standardisation governance, reducing rpoB testing and three other items). 2025-09-19. https://www.duyaonet.com/News/Detail/D2752D4C-7C57-41ED-B7ED-D97E2BFD60A6 ; Shanghai Healthcare Security Bureau/Health Commission price-cut notice (CN¥300 per test, effective 2025-10-15), report: http://www.cn-witmed.com/list/5/17097..html; Guangdong Healthcare Security Bureau, Yue Yi Bao Han 2025 No. 205: http://www.jieyang.gov.cn/jyybj/attachment/0/155/155995/972540.pdf.

S5-42. Changsha Hospital of Traditional Chinese Medicine. Outsourced-testing price list: M. tuberculosis and rifampicin-resistance detection (Xpert MTB/RIF), price code 250501048, CN¥661. 2024-09-02. https://m.vedeng.com/zhaobiao/detail-500788104.html.

S5-43. Hubei Provincial Health Commission. Hubei Tuberculosis Control Plan (2025–2030) (requiring item codes and prices for TB resistance testing and their inclusion in reimbursement). 2025-12. http://wjw.hubei.gov.cn/zfxxgk/zc/gkwj/ybxwj/202605/t20260529_5946473.shtml.

S5-44. CLS.cn / STAR Market Daily. Sansure Biotech's six-item respiratory multiplex assay approved (six-pathogen respiratory NAAT kit, 2021-04-14). https://m.cls.cn/detail/727362.

S5-45. Sansure Biotech. Registration-certificate announcement (Guo Xie Zhu Zhun 2021 No. 3400256). 2021-04-14. https://www.sansure.com.cn/gsyw/info.aspx?itemid=1107 ; VBDATA news flash including the registration number. https://www.vbdata.cn/newsDetail/54e8877e9cfb11eb8cb700163e0cb09b.

S5-46. Gansu government-procurement negotiation quotation detail (Sansure six-item respiratory bacterial panel, Guo Xie Zhu Zhun 2022 No. 3400597; six-item pathogen kit, Guo Xie Zhu Zhun 2021 No. 3400256). 2023-05. https://attach.gsei.com.cn/uploadfile/20230510120145831.pdf.

S5-47. Xiaojudeng Network (iivd.net). Respiratory multiplex testing: big bundles inside small bundles — why? (insurance cost control, six-item caps, "unbundle everything that can be unbundled"). 2026-04-21. https://www.iivd.net/article-44725-1.html.

S5-48. Xiaojudeng Network. The dilemma of molecular respiratory multiplex testing (April 2025 National Health Commission notice on further standardising testing in medical institutions; Beijing

2025 order-set advice: respiratory pathogen NAAT not exceeding six items). 2025-10-10. https://www.iivd.net/portal.php?mod=view&aid=42783.

S5-49. Second Affiliated Hospital of Guangzhou Medical University. Procurement documents (Guangdong prices: 13-item respiratory pathogen NAAT at CN¥220.8, etc., 2024). https://m.cgwenjian.com/view/file/202503180001608724.

S5-50. Yaozh Data (reproducing NMPA). Genskey Medical 2019-nCoV NAAT kit (reversible-terminator sequencing method), Guo Xie Zhu Zhun 2024 No. 3401661, approval date 2024-09-02. https://db.yaozh.com/jixie/7647686890000000.html.

S5-51. Pharnexcloud / Genskey Medical. China's first mNGS-method COVID-19 kit and companion software approved as class III (Guo Xie Zhu Zhun 2024 No. 3401661 / Guo Xie Zhu Zhun 2024 No. 3211580). https://www.pharnexcloud.com/zixun/yytrz_18307.

S5-52. iPathology News. Qinghai moves first: NGS enters medical insurance, capped at 9,800 (Qinghai public notice adjusting 419 medical-service price items, NGS at CN¥1,980 per panel, class-B insurance; NHSA Guideline for Pricing Items of Pathology Medical Services (Trial), 2025-12-19). 2026-04-10. https://news.ipathology.cn/article/6754.html.

S5-53. Economic Information Daily. BGI/MGI: payer-side milestone — Qinghai first includes MPS in class-B insurance; Chongqing/Anhui consultation drafts. 2026-04-30. http://www.jjckb.cn/20260430/a64dacae1106450ba4e73d3baafba32a/c.html.

S5-54. Xiaojudeng Network. Laboratory-medicine pricing-item guideline formally issued: mNGS billed per test, tNGS priced per 50-pathogen panel. 2026-08-14. https://www.iivd.net/article-46117-1.html.

S5-55. Darui Medical. Guangdong unified NGS pricing implemented (implementation of the Guideline for Pricing Items of Pathology Medical Services (Trial)). 2026-06-22. http://daruidiag.com/xyzx/info.aspx?itemid=385.

S5-56. Anhui Fuyang hospital outsourced-testing tender (Anhui item GLBW8000, pathogen metagenomic detection, first-batch 2024 provincial trial-price filing at CN¥2,000). 2024-11-29. https://ah.bidcenter.com.cn/diqucontent-320665845-1.html.

S5-57. Innomd (reproducing the NMPA emergency-approval list). Regulator approved 37 COVID-19 testing products: Zhijiang Guo Xie Zhu Zhun 2020 No. 3400057 and three further certificates approved 2020-01-26; Daan No. 3400063 and Sansure No. 3400064 approved 2020-01-28. https://m.innomd.org/article/5eb8b52407bace0521ec7493.html.

S5-58. Liaoning Provincial Healthcare Security Bureau. Notice on temporarily establishing COVID-19-related testing price items (Liao Yi Bao 2020 No. 32, 2020-04-11). https://ybj.ln.gov.cn/ybj/zxzx/tzgg/2DF8747B00324F3D92CFB093185B8FE4/index.shtml.

S5-59. Anhui Provincial People's Government. Wan Yi Bao Mi 2020 No. 49: COVID-19 NAAT at CN¥220 per person-time, partial-payment class (2020-04-20). https://www.ah.gov.cn/szf/zfgb/8333381.html.

S5-60. Hubei Provincial Healthcare Security Bureau. E Yi Bao Fa 2020 No. 25: temporary inclusion of NAAT/antibody testing in the insurance catalogue under class-B management during the epidemic (effective 2020-05-06); E Yi Bao Fa 2020 No. 23, temporary new price items. https://ybj.hubei.gov.cn/zfxxgk/zc/qtzdgkwj/gkwj/202005/P020200505639389395108.pdf.

S5-61. Beijing Municipal Healthcare Security Bureau. Jing Yi Bao Fa 2020 No. 22 policy interpretation: NAAT price reduced from 180 to CN¥120 per test (effective 2020-06-25). https://ybj.beijing.gov.cn/zwgk/2024zcjd/202406/t20240614_3712599.html.

S5-62. cn-healthcare.com. NHSA Yi Bao Ban Fa 2020 No. 30 (2020-06-19): NAAT/antibody testing to be included in provincial medical-insurance diagnosis-and-treatment catalogues. https://www.cn-healthcare.com/article/20210824/content-559217.html.

S5-63. cn-healthcare.com. National summary of insurance-agency price cuts (NAAT prices reduced to below CN¥80). 2021-01-29. https://www.cn-healthcare.com/articlewm/20210129/content-1185780.html.

S5-64. National Medical Products Administration (NMPA). 2025-08-26 medical-device approval-document delivery notice: Wantai nine-item respiratory pathogen NAAT kit, Guo Xie Zhu Zhun 2025 No. 3401726, approval date 2025-08-25. https://www.nmpa.gov.cn/zwfw/sdxx/sdxxylqx/qxpjfb/20250826153202198.html.

S5-65. PR Newswire Asia. Wantai Bio's "nine-item respiratory pathogen NAAT kit" approved. 2025-09-02. https://www.prnasia.com/story/501790-1.shtml.

S5-66. cn-healthcare.com. The market battle for upper/lower respiratory multiplex testing (Berjie six-item, Guo Xie Zhu Zhun 2021 No. 3400567; Zhuocheng Huisheng six-plex, 2021 No. 3400026; Zhongzhi seven-item, 2015 No. 3401469). https://www.cn-healthcare.com/articlewm/20220514/content-1355096.html.

Germany, France, England

S5-67. Shinnick TM, et al. Evaluation of the Cepheid Xpert MTB/RIF assay. PMC5875728. "In April 2009, Xpert MTB/RIF received Conformite Europeenne marking as an in vitro diagnostic medical device." Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5875728/.

S5-68. Deutsches Aerzteblatt. Beschluss des Bewertungsausschusses nach s.87 Abs. 1 Satz 1 SGB V in seiner 596. Sitzung am 15. Juni 2022 zur Aenderung des Einheitlichen Bewertungsmassstabes (EBM). Available from: https://www.aerzteblatt.de/archiv/beschluss-des-bewertungsausschusses-nach-87-abs-1-satz-1-sgb-v-in-seiner-596-sitzung-am-15-juni-2022-zur-aenderung-des-einheitlichen-bewertungsmassstabes-ebm-135c62e1-ce1c-455d-b41a-9968a35ad1eb.

S5-69. KVHB Bremen. Neue Leistungen in Mikrobiologischer Diagnostik abrechenbar (GOP 32851–32853, effective 1 Jul 2022). 6 Jul 2022. Available from: https://www.kvhb.de/praxen/nachrichten/detail/neue-leistungen-in-mikrobiologischer-diagnostik-abrechenbar.

S5-70. GenomeWeb via inknowvation.com. bioMerieux to Acquire BioFire Diagnostics for $450M Plus Debt (RP "also has CE marking and is commercially available in Europe"; FDA clearance

May 2011). Sep 2013. Available from: https://www.inknowvation.com/sbir/story/biom%C3%A3%C2%A9rieux-acquire-biofire-diagnostics-450m-plus-debt.

S5-71. BioFire Diagnostics. Press release: BioFire's FilmArray Gastrointestinal Panel Receives FDA Clearance (CE IVD marking anticipated late spring 2014). 5 May 2014. Available from: https://www.biofiredx.com/wp-content/uploads/2016/03/PRESS_RELEASE-BioFire_**s_FilmArray**_Gastrointestinal_Panel_Receives_FDA_Clearance_05052014.pdf.

S5-72. BioFire Diagnostics. Press release archive: "BioFire's FilmArray Meningitis/Encephalitis Panel gets CE marked", 26 Jan 2016. Available from: https://www.biofiredx.com/media/press-releases/.

S5-73. Inside Precision Medicine. Qiagen Wins FDA Clearance for QIAstat-Dx Syndromic Testing System, Respiratory Panel (CE-IVD marking January 2018; EU launch April 2018). 20 May 2019. Available from: https://www.insideprecisionmedicine.com/news-and-features/qiagen-wins-fda-clearances-for-qiastat-dx-syndromic-testing-system-respiratory-panel/.

S5-74. QIAGEN. QIAGEN receives European IVDR certification for QIAstat-Dx syndromic testing instruments and assays. Venlo, 26 Sep 2024. Available from: https://corporate.qiagen.com/English/newsroom/press-releases/press-release-details/2024/QIAGEN-receives-European-IVDR-certification-for-QIAstat-Dx-syndromic-testing-instruments-and-assays/default.aspx.

S5-75. Inspiring-health / AOK. NUB procedure documentation (InEK status definitions; s.6 Abs. 2 KHEntgG). Available from: https://www.inspiring-health.de/de/glossarbegriff/nub-antrag.html and https://www.aok.de/gp/krankenhaus/verguetung-drg/nub.

S5-76. Brown JR, et al. Encephalitis diagnosis using metagenomics: applications of NGS for undiagnosed encephalitis (in-house status evidence, DE/FR/UK laboratories; cf. UK encephalitis mNGS literature, e.g., Morfopoulou S, et al.). PMC7112567. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7112567/.

S5-77. Aerzte Zeitung. PCR-Test auf SARS-CoV-2 nach GOP 32816 wird zum 1. Juli deutlich abgewertet ("Bei Einfuehrung der neuen Leistung Ende Januar 2020 war der Test noch mit 59 Euro bewertet"). 23 May 2022. Available from: https://www.aerztezeitung.de/Wirtschaft/PCR-Test-auf-SARS-CoV-2-nach-GOP-32816-wird-zum-1-Juli-deutlich-abgewertet-429285.html.

S5-78. Deutsches Aerzteblatt. Erweiterter Bewertungsausschuss senkt Verguetung fuer PCR-Tests ab (GOP 32816: €39.40 to €35 from 1 Jul 2021). 26 May 2021. Available from: https://www.aerzteblatt.de/news/erweiterter-bewertungsausschuss-senkt-verguetung-fuer-pcr-tests-ab-0cc2d7a8-6c10-488e-8155-3fe6a9433c26.

S5-79. Gelbe Liste. Verguetung fuer PCR-Test auf SARS-CoV-2 wird gesenkt (€19.90 from 1 Apr 2023; €59 at introduction "Anfang 2020"). 13 Mar 2023. Available from: https://www.gelbe-liste.de/nachrichten/pcr-test-verguetung-april-2023.

S5-80. Deutsche Krankenhausgesellschaft. Vereinbarung nach s.26 Abs. 2 KHG (Zusatzentgelt SARS-CoV-2 testing; successor agreement from 1 May 2023, €30.40). Available from:

https://www.dkgev.de/themen/finanzierung-leistungskataloge/covid-19/vereinbarung-nach-26-abs-2-khg/.

S5-81. Arrete ministeriel n. 96-209 du 2 mai 1996 (Monaco; mirror of NABM ch. 16): acte 4102 "Diagnostic direct d'infection a mycobacteries dans les tissus et le liquide cephalorachidien : recherche d'ADN par hybridation moleculaire avec ou sans amplification ... B 250"; acte 4101 B 150. Available from: https://legimonaco.mc/tnc/arrete-ministeriel/1996/05-02-96-209@2024.09.21.

S5-82. Magnolia / NABM overview (NABM structure: code, designation, coefficient B; point value €0.25). Available from: https://www.magnolia.fr/mutuelle-sante/assurance-maladie/nomenclature-actes-biologie-medicale.

S5-83. Syndicat des Biologistes (SDB). NABM : la cotation du test PCR de la grippe publiee au JO (arrete du 28 dec. 2020; acte influenza RT-PCR B 60; COVID RT-PCR B 160 after arrete du 12 dec. 2020). 5 Jan 2021. Available from: https://sdbio.eu/2021/01/05/nabm-la-cotation-du-test-de-la-grippe-publiee-au-journal-officiel/.

S5-84. DGOS. Referentiel des actes innovants hors nomenclatures (RIHN), Version 2016, validity 01/01/2016–31/12/2016: "N156 — PCR classique ou temps reel qualitative multiplex pour 10 couples d'amorces ou plus (ADN/ARN) — AHC/BHN 1000 — €270". Available from: https://emploi.fhf.fr/sites/default/files/documents/R%C3%A9f%C3%A9rentiel%20des%20actes%20innovants%20hors%20nomenclatures%20%28RIHN%29%20%20Version%202016.xlsx.

S5-85. Ministere de la Sante. RIHN 2.0 : un soutien renouvele a l'innovation (instruction DGOS/PF4/2015/258 du 31 juillet 2015; decret n. 2024-290 du 29 mars 2024; arrete du 25 nov. 2024; LAHN 2024). Available from: https://sante.gouv.fr/soins-et-maladies/qualite-securite-et-pertinence-des-soins/biologie-medicale/rihn.

S5-86. Bulletin officiel. Instruction n. DGS/PP1/DGOS/FIP1/DSS/1B/2025/135 du 16 octobre 2025 relative aux actes de biologie medicale et d'anatomopathologie hors nomenclature (LAHN = merged RIHN+LC since 2024). Available from: https://bulletins-officiels.social.gouv.fr/instruction-ndeg-dgspp1dgosfip1dss1b2025135-du-16-octobre-2025-relative-aux-actes-de-biologie-medicale-et-danatomopathologie-hors-nomenclature-eligibles-au-financement-au-titre-des-missions-specifiques-aux-regles-de-facturation-de-ces-actes-et-aux.

S5-87. CH Brive. Panel multiplex meningo-encephalite (PCR): "Code NABM VZV: 4507... Code RIHN : N156". Available from: https://ch-brive.manuelprelevement.fr/DetailNew.aspx?id=A1050.

S5-88. Universite d'Angers thesis. Evaluation du panel FilmArray BioFire BCID2 ("le cout d'un test avec le panel FilmArray BioFire BCID2 est de 270 euros (N156 RIHN)"). Available from: https://dune.univ-angers.fr/system/files/depots/19012878/2021MCEM14285/14285F.pdf.

S5-89. Cairn/RBM. L'approche diagnostique syndromique en microbiologie (RIHN ch. 14-2, code N156 "PCR classique en multiplex"). Available from: https://shs.cairn.info/article/RBM_346_0021/pdf?lang=fr.

S5-90. Fourgeaud J, Regnault B, Ok V, et al. Performance of clinical metagenomics in France: a prospective observational study. Lancet Microbe. 2024;5(1):e52–e61. doi:10.1016/S2666-5247(23)00244-6.

S5-91. ARS PACA. Conditions d'utilisation des tests de diagnostic du SARS-CoV-2 ("Acte 5271 : examens de detection du genome du SARS-CoV-2 par les techniques d'amplification genique ... Cf. Arrete du 12 mai 2020"; acte 4274 antigenique arrete du 16 oct. 2020; B 160 per arrete du 12 dec. 2020). Available from: https://www.paca.ars.sante.fr/media/71348/download.

S5-92. Biologiste365. Les tests antigeniques inscrits a la nomenclature (antigen B 36; CE-marking requirement). Available from: https://www.biologiste365.fr/3566-les-tests-antigeniques-inscrits-a-la-nomenclature/.

S5-93. Biologiste365. Prise en charge du diagnostic simultane de la Covid-19 et de la grippe (combined test reimbursable only during co-circulation). 5 Jan 2021. Available from: https://www.biologiste365.fr/3674-prise-en-charge-du-diagnostic-simultane-de-la-covid-19-et-de-la-grippe/.

S5-94. Federation de Biologie Medicale via SDB. Acces au diagnostic respiratoire ("recommandation publiee le 30 janvier 2026 par la HAS, qui reserve l'utilisation des tests PCR quadriplex (Grippe A/B, VRS, SARS-CoV-2) au seul milieu hospitalier"). 17 Mar 2026. Available from: https://sdbio.eu/2026/03/17/acces-au-diagnostic-respiratoire-la-fbm-appelle-a-renforcer-la-coordination-entre-la-ville-et-lhopital/.

S5-95. Le Quotidien du Medecin. PCR grippe/Covid/VRS : les biologistes demandent le remboursement en ville. 17 Mar 2026. Available from: https://www.lequotidiendumedecin.fr/actu-medicale/sante-publique/pcr-grippecovidvrs-les-biologistes-demandent-le-remboursement-en-ville.

S5-96. HAS. Rapport d'evaluation: Interet des TAAN multiplex dans la prise en charge medicale des infections des voies respiratoires superieures (TAAN quadriplex = Influenza A/B + RSV + SARS-CoV-2). Jan 2026. Available from: https://has-sante.fr/jcms/p_3845949/fr/interet-des-techniques-d-amplification-des-acides-nucleiques-taan-multiplex-dans-la-prise-en-charge-medicale-des-infections-des-voies-respiratoires-superieures-rapport-d-evaluation.

S5-97. HAS. Rapport TAAN infections respiratoires basses (volet diagnostic), Dec 2024; SFM/ANRS-MIE indications quadriplex/multiplex, v2 21 Feb 2025. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2024-12/rapport_taan_irb_vd.pdf and https://www.sfm-microbiologie.org/wp-content/uploads/2025/03/SFM_ANRS-MIE-Indic-4plx_mplx-respi-_-v2-21022025.pdf.

S5-98. NICE. Tuberculosis. NICE guideline NG33. Published 13 Jan 2016; last updated 16 Feb 2024 (rapid diagnostic NAAT for M. tuberculosis complex; rapid rifampicin-resistance NAAT recommendations). Available from: https://www.nice.org.uk/guidance/ng33.

S5-99. Walker T, et al. Tuberculosis is changing (PHE routine WGS service launch, March 2017). Lancet Infect Dis 2017. Available from: https://ora.ox.ac.uk/objects/uuid:fb621df0-d244-4544-8b88-63a64bce1047/files/m3efde8851fb9fc2c761350d90d9d0a1b.

S5-100. Genomics England. Whole Genome Sequencing to diagnose TB (PHE announcement). 29 Mar 2017. Available from: https://www.genomicsengland.co.uk/news/whole-genome-sequencing-diagnose-tb.

S5-101. Public Health England. Position statement: direct molecular testing for tuberculosis in England, Scotland and Wales. Jul 2013 (cited in J Infect 2017; Scottish evaluation). Available from: https://www.sciencedirect.com/science/article/pii/S0163445317300543.

S5-102. Harding-Edgar L, et al. Test and trace strategy has overlooked importance of clinical input ("18th May: Anyone in UK with symptoms able to apply for a test... 27th May: Test and Trace launched across England"). J R Soc Med 2020. PMC7686522. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7686522/.

S5-103. Wikipedia (chronology cross-checked to gov.uk). NHS Test and Trace. Available from: https://en.wikipedia.org/wiki/NHS_Test_and_Trace.

Japan

S5-104. National Center for Global Health and Medicine (NCGM). Kokusai Tenkai Nyumon ("Introduction to international expansion") booklet (Xpert MTB/RIF Japan approval September 2016). https://www.ncgm.go.jp/ (booklet PDF, retrieved via search Aug 2026).

S5-105. Falco Biosystems. Insurance-listing information (entry 45-063: M. tuberculosis-group NAAT, listed Heisei 29-01-01). https://www.falco.co.jp/business/cl_02_info4.html.

S5-106. Japanese Society of Laboratory Medicine (JSLM). Insurance-listed test list ("applicable from January 2017: M. tuberculosis-group NAAT, published in vol. 65 no. 3"; "applicable from November 2019: virus/bacteria multi-item simultaneous NAAT"). https://www.jslm.org/.

S5-107. Nikkei Medical. Pulmonary tuberculosis (guideline series, 2022-05-19; noting Xpert MTB/RIF insurance listing in 2017 and cobas MTB-RIF/INH listing in 2023). https://medical.nikkeibp.co.jp/leaf/all/series/guideline/202205/574926.html.

S5-108. Ministry of Health, Labour and Welfare (MHLW). 536th Chuikyo (Central Social Insurance Medical Council) General Meeting, 2023-01-18, material Sou-2-2 "Insurance coverage of clinical laboratory tests (listing planned for February 2023)". https://www.mhlw.go.jp/content/12404000/001039378.pdf ; agenda: https://www.mhlw.go.jp/stf/shingi2/0000212500_00173.html.

S5-109. Roche Diagnostics K.K. Launch of "cobas MTB-RIF/INH" (media release, 2023-03-06; "the test was newly insured as a new item effective 1 February"). https://www.roche-diagnostics.jp/ja/media/releases/2023_3_6.html (canonical: https://www.roche-diagnostics.jp/media/releases/2023-3-6)

S5-110. Medical Online. cobas MTB-RIF/INH insurance coverage (2023-03-06). https://www.medicalonline.jp/news/detail?id=10105.

S5-111. Ministry of Health, Labour and Welfare (MHLW). Approval information for in vitro diagnostics related to COVID-19 (FilmArray Respiratory Panel 2.1, approval date 2020-06-02). https://www.mhlw.go.jp/stf/newpage_11331.html (successor page; the originally cited URL now redirects to an unrelated leaflet list) (COVID-19 IVD approval list page, retrieved Aug 2026).

S5-112. m3.com Iryo Ishin. "Simultaneous testing for COVID-19 and influenza now possible" (2020-07-22; RP2.1 at 1,800 points, 1,350 without specimen transport, insured from August). https://www.m3.com/news/iryoishin/801326.

S5-113. Japan Institute for Health Security (JIHS / Infectious Disease Information Center). RSV topics document RS_20251022.pdf (2019 FilmArray Respiratory Panel insurance coverage; 2020 RP2.1 coverage; facility-requirement details). https://id-info.jihs.go.jp/relevant/vaccine/topics/140/RS_20251022.pdf ; MHLW version: https://www.mhlw.go.jp/content/10900000/001583668.pdf.

S5-114. GemMed (Global Health Consulting Japan). "New test identifying 20 respiratory pathogens with high accuracy in a short time to be insured from November — MHLW" (2019-11-05; 963 points computed by bundled reference). https://gemmed.ghc-j.com/?p=30254.

S5-115. Japanese Society of Infectious Diseases. Kansenshogaku Zasshi (Journal of the Japanese Society of Infectious Diseases) vol. 94 (2020-05-20; records FilmArray Respiratory Panel insurance listing in November 2019). http://journal.kansensho.or.jp/Disp?pdf=0940030317.pdf.

S5-116. Ministry of Health, Labour and Welfare (MHLW). 528th Chuikyo General Meeting (2022-09-14), material "Insurance coverage of clinical laboratory tests (listing planned for October 2022)" (FilmArray ME panel, E3, 1,700 points). https://www.mhlw.go.jp/content/12404000/000989563.pdf (528th Chuikyo, 2022-09-14, material sou-1-2; the originally cited meeting-page URL now resolves to the 363rd meeting) (meeting material; retrieved Aug 2026).

S5-117. Daiichi Kishimoto. Insurance-listed test tracker (virus/bacteria multi-item simultaneous NAAT (CSF), applicable Reiwa 4-10-01). https://www.daiichikishimoto.co.jp/.

S5-118. Kyorin University MedicalBridge. FilmArray ME panel 2022 insurance-coverage information (September/October 2022 discrepancy; resolved to 2022-10-01). https://www.kyorin-u.ac.jp/.

S5-119. bioMerieux Japan K.K. "New product BioFire Pneumonia Panel launch notice" (bMXLCL22101, March 2022; approval no. 30300EZX00084000; sales start 2022-03-15). https://www.biomerieux-jp.net/wp/wp-content/uploads/2022/03/bMXLCL22101_BioFirePN.pdf.

S5-120. MTJ ONE (Jiho Medical Press). "Insurance coverage approved for three clinical-laboratory products; listing on 1 February" (2026-01-30; Chuikyo 2026-01-23; 1,273 points). https://mtj.jiho.jp/news/system/2343.

S5-121. bioMerieux Japan product-bulletin notices. "BioFire Pneumonia Panel insurance-coverage notice" (2026-02-05); "BioFire Pneumonia Panel sales start" (2022-03-15). https://www.biomerieux-jp.net/news.

S5-122. Japan Association of Certified Laboratory Medicine Physicians (JACLaP). D023 microbial nucleic-acid identification/quantification insurance-listing information (virus/bacteria NAAT and drug-resistance-gene multi-item simultaneous detection, 1,273 points, newly established Reiwa 8-02-01; cobas MTB-RIF/INH, 963 points, E3). https://jaclap.org/2238/category1/.

S5-123. Microbes, Infection and Chemotherapy (via ScienceDirect). Pathogen detection by multiplex PCR in Japanese patients (2025-09-04; "insurance coverage remains limited" — pre-listing pneumonia-panel era; mNGS not reimbursed). https://www.sciencedirect.com/science/article/pii/S2212534525001212.

S5-124. m3.com Iryo Ishin. SARS-CoV-2 NAAT insurance coverage from 6 March at 1,800 points (article of 2020-03-05). https://www.m3.com/news/iryoishin/ (retrieved Aug 2026).

S5-125. National Cancer Center (NCC). Press release: NCC Oncopanel marketing approval obtained (2018-12-25; approval no. 23000BZX00398000; sakigake priority-review designation scheme). https://www.sysmex.co.jp/en/news/2018/181225.html.

S5-126. PanCAN Japan / pancreatic-cancer patient association. Cancer gene-panel test insurance listing, 2019-06-01, at 56,000 points (Chuikyo 2019-05-29). https://www.pancan.jp/.

S5-127. Beckman Coulter K.K. Xpert MTB/RIF ("Cepheid") product page (marketing approval no. 22800AMX0067300). https://www.beckmancoulter.co.jp/dx/product/molecular-diagnostics/Xpert_MTB_RIF/.

S6. Extended results and country detail

This section contains the instrument and mechanism inventories moved from the main text for length compliance (main-text Sections 3.2–4.1 carry the analytical narrative and pointers to these tables). Citation numbers refer to the main manuscript's reference list.

S6.1 Regulatory review pathways (from main-text Section 3.2)

Table S6.1. Regulatory review of pathogen nucleic acid diagnostics: architecture, tempo, and Gate-1 innovation channels, six systems.

System	Review body & pathway for nucleic acid diagnostics	Statutory/target tempo	Observed tempo	Gate-1 innovation channel (diagnostic track record)
China	NMPA/CMDE; Class III registration for pathogen NAATs (36)	90 working days technical review (37)	~24–60 months elapsed (Tier B) (38)	Innovation/priority channels; IVD share fell 24%→~8% (2018→2024) (50)
United States	FDA; Class II via 510(k); first-of-type De Novo (39)	90/150 FDA days (510(k)/De Novo) (40)	approximately 151 and 372 calendar days (Tier B) (40)	Breakthrough Devices; no infectious mNGS authorised (52)
Germany	EU IVDR notified bodies; mostly Class C (S2)	No statutory deadline; transition milestones (49)	13–18 months certification (42)	None; IVDR transition relief only
France	EU IVDR notified bodies; Class C/D as Germany	No statutory deadline; transition milestones (49)	13–18 months certification (42)	None at Gate 1; RIHN operates at Gate 3
England	MHRA registration; CE-mark reliance (UK MDR 2002) (45)	None; CE recognised to 30 June 2030 (45)	Administrative registration; CE-defined	IDAP pilot; 4 of 8 products IVDs (S3)
Japan	PMDA review plus MHLW approval (Class III) (43)	12 months standard; 7 months ordinary (targets) (43)	~12 months standard / 7.3–8.4 months priority (actuals, 80th percentile; Tier B) (44)	Sakigake ('forerunner') designation; conditional early approval (2026) (S4,S5)

Note. Tempo figures are statutory targets unless stated; observed-tempo entries are Tier B where based on secondary syntheses. Target categories (standard/ordinary) and actual-performance categories (standard/priority-reviewed) follow PMDA reporting conventions.

Table S6.1 warrants three observations. First, nominal stringency does not map onto elapsed time: the United States combines the lightest pathway classification with mid-range calendar performance, whereas Japan pairs the most demanding formal architecture with the most predictable clock — resourcing and clock-stop rules matter more than pathway labels. Second, the EU's notified-body bottleneck is a capacity phenomenon, not a statutory one: the applications-to-certificates ratio implies a structural backlog that transition extensions manage rather than resolve [42]. Third, observed tempo describes conventional NAAT products and understates divergence at the frontier: the first mNGS-based Class III kit reached the Chinese market only in September 2024 [S6], and the established QIAstat-Dx platform required multi-year IVDR transition effort before certification in 2024 [S7].

For mNGS specifically, Gate 1 is de facto a laboratory-accreditation regime rather than a product review. In the United States, the May 2024 LDT final rule was vacated in full in *ACLA v. FDA* (March 2025) and rescinded in September 2025, returning clinical mNGS assays to CLIA-only oversight; as of 2026 no infectious-disease mNGS assay holds FDA marketing authorisation [47,48]. In the EU, Article 5(5) permits in-house tests within health institutions, but the "no equivalent device" justification faces a 2030 cliff [49] where more than 83% of specialised haematology-laboratory tests are in-house [S8]; a December 2025 Commission proposal would delete that condition for IVDs (proposal only) [S9]. England's health-institution exemption operates on similar logic [S10].

Innovation channels at Gate 1 and their diagnostic track record.

Every system except the two EU-regulated cases (Germany and France) operates a Gate-1 innovation channel that mirrors the Gate-3 carve-outs of Section 3.4 in design and limitations. China's special review procedure for innovative medical devices (chuangxin yiliao qixie tebie shencha chengxu, 2014) approved 54 devices by end-2018, 13 of them IVDs (24%), and 315 by 2024 with the IVD share down to about 8% [50,51], for a documented time saving of only ~83 days; the 2016 priority-review procedure has repeatedly admitted TB NAAT kits [S11,S12], and the emergency channel approved the first COVID-19 NAATs in January 2020, some within four days [S13]. Thin diagnostic uptake is partly designed in: China's channel requires domestic-first products with Chinese invention patents, and the US Breakthrough programme demands superiority over alternatives, device-shaped eligibility hurdles that informational diagnostics rarely clear.

The US Breakthrough Devices Program shows the same asymmetry at larger scale: 1,284 designations against 198 marketing authorisations as of March 2026 [52], with infectious-disease mNGS assays designated (UCSF/Delve Bio, August 2023 [S14]; the Karius Test, May 2024 [S15]) but none yet authorised. Japan's sakigake ('forerunner') designation produced its flagship IVD, the National Cancer Center (NCC) Oncopanel (approved December 2018, insured June 2019) [S4,S16], and conditional approval was extended to IVDs by a March 2026 notification, with no IVD approvals reported as of August 2026 [S5]; England's Innovative Devices Access Pathway (IDAP) pilot selected eight products in February 2024, four of them IVDs [S3].

The EU, conspicuously, has no Gate-1 innovation channel, and the IVDR's deterrent record is measurable: EU-first launches by large IVD firms fell by 40% [53], 53% of German manufacturers surveyed in 2025 reported cutting research and development [S17], niche pathogen tests have been discontinued since 2022 [S18], and bioMérieux filed its latest gastrointestinal panels with the FDA *before* IVDR submission [S19].

The approval–payment interface: bridges and lags.

Extending main-text Section 3.2.2 with the underlying statistics: the 5.7-year median approval-to-coverage interval rests on a premarket-approval and De Novo cohort of n = 64 (2016–2019; diagnostics' lags were shorter, plausibly aided by the MolDX programme), in which fewer than 30% of technologies achieved coverage within three years [54,55]. The bridges built to close this gap are limited in scale, capacity-capped, or suspended. FDA–CMS Parallel Review has attracted 97 requests but only two completions ever, Cologuard (2014) and FoundationOne CDx (2017), both diagnostics, with National Coverage Determinations (NCDs) finalised 2–3.5 months after approval [56]. The Transitional Coverage for Emerging Technologies (TCET) pathway (finalised August 2024; ≤5 breakthrough devices per year) is paused for new candidates as of 11 August 2026 [57,58]; its proposed successor, RAPID, remains a proposal (Tier B) [58].

France illustrates statutory–actual divergence: LPPR has a statutory 180-day processing target but has exceeded 300 days in practice (parliamentary record, 2016) [59], while RIHN 2.0 is arguably the most IVD-tailored bridge in this study, pairing a ≤75-day HAS evaluation with a ≤60-day ministry decision within a six-year funded evidence-development window [S20,S21]. Japan combines the fastest drug benchmark (a 58-day median approval-to-listing interval, the shortest of five countries studied [60]) with an administratively parallel diagnostic route: the insurance-listing application (hoken tekiyo kibosho) may proceed alongside PMDA review, and E1 listing follows roughly 20 days after acceptance [61], although new-technology (C2) fees are set only at biennial revisions, building in a lag of up to two years [61]. The interface still produced a lag of roughly nine years for the first FilmArray panel (US-cleared 2011; insured August 2020, a COVID-era listing) [S22], against Xpert MTB/RIF's roughly four-month interval (approved September 2016; insured January 2017) [S23].

China lacks any statutory linkage: one five-country analysis describes marketing authorisation and reimbursement assessment as "separate procedures with no overlap", and median drug time-to-reimbursement is 440 days against 58 in Japan, 197 in France and 322 in the United Kingdom [60]. The 2025 NHSA measures for innovative drugs introduce point-to-point guidance upon NMPA filing acceptance; whether an analogous arrangement will extend to IVDs has not been announced [S24], but the first commercial-insurance innovation catalogue (CHIIDL, December 2025, 19 products) excludes devices and IVDs entirely [S25], and Beijing's carve-out payment batches tie relief to products approved within the preceding three years [S26].

These interface findings reinforce the binding-gate diagnosis. Xpert MTB/RIF cleared China's Gate 1 in 2014 [S27], yet the subsequent decade of stalled price and coverage progress documented above confirms that early approval did not secure access; conversely, at least seven domestic TB NAAT manufacturers now hold NMPA registrations, while single-source procurement notices justify sole-sourcing on platform exclusivity — the installed GeneXpert systems accept only the manufacturer's

sealed, non-user-programmable cartridges [86]. Nowhere does Gate 1 bind under the Section 2.3.4 definition; but for novel metagenomic LDTs it mutates into an accreditation regime whose tempo disciplines every downstream gate.

A cross-walk of gate-to-gate elapsed times makes this sequencing measurable (full dataset in Supplementary Material S5). Gate 1→Gate 2 medians ranged from under one year (United States, 0.67 years, n = 7) and France (1.7 years, n = 6) to four and a half years (Germany, 4.5 years, n = 5), with China at roughly 3.6 years and three tests right-censored at the price gate; Japan's fused design compresses its approval-to-listing interval to days (median 108 days excluding the pneumonia-panel outlier, n = 3); Gate 2→Gate 3 medians collapse to near zero wherever listing and funding are the same administrative act (Germany, France, Japan), but stretch to 2.29 years in the United States (n = 7, a sample mixing Parallel-Review and emergency cases with FilmArray panels, whose own lags run 2.3–9.3 years) and remain open-ended for most Chinese molecular tests (survivorship-biased subsample, n = 3). The binding gate is thereby measurable rather than rhetorical: systems differ less in *whether* gates exist than in *where* elapsed time accumulates, though small samples and right-censoring make these estimates hypothesis-generating.

S6.2 Double-squeeze instruments and evidence (from main-text Section 3.3)

Table S6.2. Double-squeeze instrument inventory: inpatient bundling and outpatient price compression across six systems, with verified magnitudes.

Instrument	Jurisdiction	Mechanism	Magnitude and date	Source-tier note
IPPS/MS-DRG bundling	United States	Fixed case payment absorbs all inpatient tests	"No separate payment made for IVD tests in the inpatient setting" (1983–) [62]	T1 statute; wording via SEC-filed disclosure (T2)
G-DRG case flat rate	Germany	Case rate covers the "entire scope" of necessary treatment	All inpatient laboratory diagnostics bundled; Zusatzentgelt the narrow exception [63]	T1 (Federal Ministry of Health)
GHS bundles	France	DRG payment for public-hospital inpatients	NABM tariffs inapplicable inside GHS [27]	T1 (IGAS–IGF 2025)
DPC/PDPS per-diem	Japan	Inclusive per-day rate for acute care	Acute myocardial infarction charges −US$1,061; length of stay −2.29 d; readmission OR 1.37 (2012 evaluation) [64]	T1 peer-reviewed
DRG/DIP case payment	China	all 393 pooling regions covered by April 2025 (191 DRG + 200 DIP; Tianjin and Shanghai run both)	DIP: −19.0% inpatient testing expenditure (DID) [67]; DRG: −23% examination fees, out-of-pocket +8% [68]; county RDD: lab fees rose [69]	T1 peer-reviewed; RDD single-source (T2)
HRG block contracts / aligned payment and incentive (API) blended payment	England	Inpatient bundled payment with no routine outpatient test-level tariff to compress (global budgets; only unbundled items such as community-diagnostic-centre point-of-care tests (POCTs) carry fixed prices)	Structural (no test-level price); block contracts 2020–2022 (pandemic-era); aligned payment and incentive successor from 2022/23	Tier B
PAMA CLFS repricing	United States	Rates = volume-weighted private-payer median	10%/yr caps 2018–2020; 0% freeze 2021–2026; 15%/yr cap from CY2027; repeated delays [72]	T1 (CMS; GAO-19-67) [S28]
IVD VBP alliances	China	Inter-provincial volume-based reagent procurement	−47.02% (2021); −68% (2023); ~−77% (2024); −53.9% (25-	T1 provincial bureaus; T2 press for

Instrument	Jurisdiction	Mechanism	Magnitude and date	Source-tier note
			province 2023); −52.62% (28-province 2024); ~−70% (glucose-metabolism alliance, January 2025) [70,71]	some rounds
Fee-schedule cuts	Japan	Biennial point reductions	FY2014: 256 items (chemistry 41.4% of items); COVID-19 PCR 1,800→700 pts, −61.1% (2020–2022) [73]	T1 (MHLW/Chuikyo)
Bidirectional revision	Japan	Schedule steered up for skilled work, down for automation	+15 pts microscopy/culture; −3 to −5 pts automated analytes (2024/2026) [73]	T1 schedule tables; T2 professional digests
EBM volume steering	Germany	Vorwegabzug deductions, Laborquote, efficiency bonuses	Chapter-32 laboratory paid at 89% of regional fee scale (Berlin, 2021) [74]	T1 (KBV/regional association)

Source tiers: T1 = peer-reviewed or primary official document; T2 = reputable secondary. Confidence tiers per Section 2.4.

Table S6.2 shows that the squeeze is structurally symmetrical across archetypes: four of the six systems operate an instrument of each jaw; England structurally lacks an outpatient test-level price signal (its block and aligned-payment model is best read as bundling subsuming price compression, not as a counterexample), and France's outpatient compression is comparatively weak. Outpatient instruments differ in *form* (Table S6.2) but not in direction. Magnitudes diverge sharply: China's procurement rounds (−47% to −77%) exceed anything in the OECD repertoire precisely because they target the reagent input rather than the service fee, whereas PAMA's caps and Japan's point cuts operate in single digits annually.

One qualification matters: statutory design can be repeatedly suspended: congressional delays mean current CLFS rates still derive from 2016 private-payer data, so announced and realised compression must be distinguished. Figure 2 quantifies the cross-instrument magnitudes.

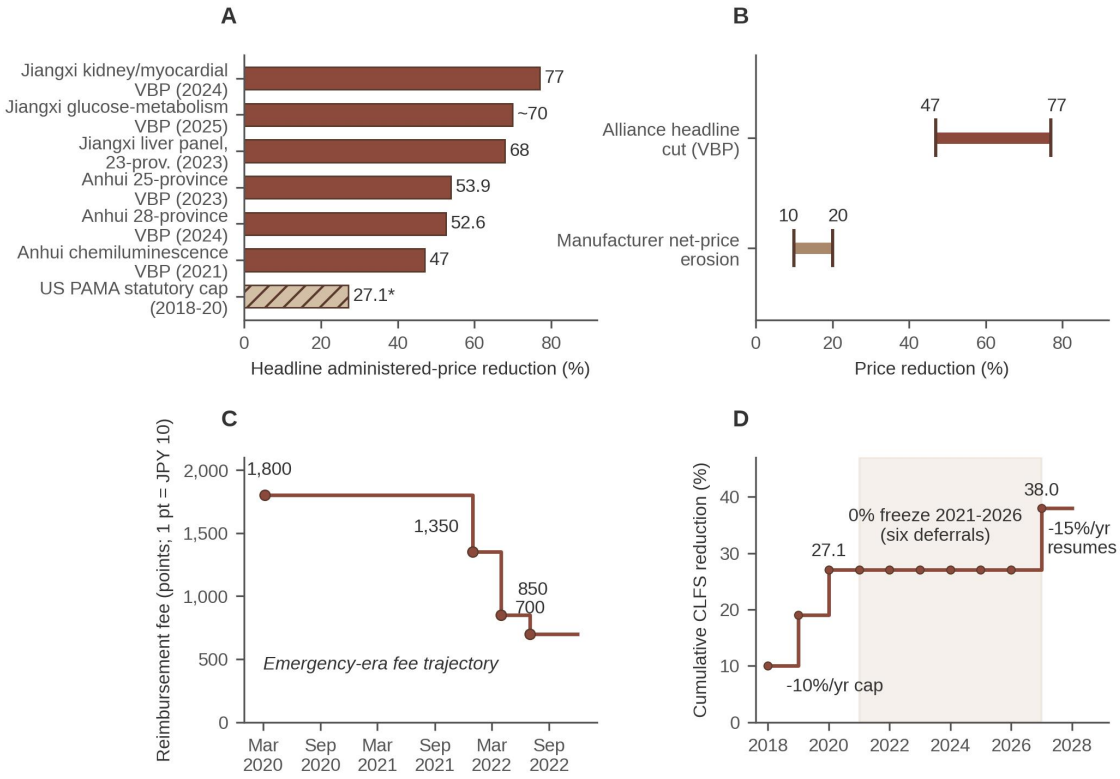


Figure 2. Outpatient administered-price compression for laboratory and IVD payment, selected instruments. *(A) Headline price reductions, selected instruments, sorted; the US PAMA entry (asterisk) is a compounded statutory cap (1−0.9³ = −27.1%, 2018–2020), not a realised average. (B) Transmission of 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 Table S6.2.*

Figure 2 (reproducibility package: Supplementary Material S3) makes three points the instrument-by-instrument narrative can obscure. First, the steepest publicly announced headline compression is Chinese: four of the five deepest bars in Panel A are VBP rounds, all within a narrow −47% to −77% band, suggesting a stable procurement reservation-price logic rather than progressively deeper cuts. Second, Panel B shows that headline cuts overstate manufacturer impact: two-level transmission confines manufacturer net erosion to roughly 10–20%, a quantity distinct from the alliance-level headline and not to be conflated with it. Third, the US bar is the smallest and is a *cap*, not a realised average: PAMA's significance lies less in its depth than in its ratchet and in Congress's six suspensions of even this modest compression. Panels C and D isolate two trajectories that sit outside the structural comparison — Japan's emergency-era COVID-19 PCR fee path and the US statutory PAMA schedule. Cross-instrument comparison should therefore weigh depth (China), transmission (Panel B) and durability (United States) separately rather than ranking systems on headline percentages alone.

Industry and access consequences.

The squeeze's incidence is now measurable in industry and access data, most sharply in China: of 55 A-share listed IVD companies, 44 reported revenue decline and 37 net-profit decline in FY2025, and sector revenue fell 14.5% year-on-year in Q1–Q3 2025 (Wind data via financial press; Tier B) [75].

Because the decline partially reflects evaporated COVID-19 testing revenue, these figures corroborate the squeeze's direction rather than isolating its incidence.

Market-size estimates diverge by scope but agree in direction: the China IVD Industry Annual Report (2025 edition) estimates the 2025 market at approximately CN¥108 billion, −10% versus 2024, reversing pre-2022 double-digit growth (Tier B) [75]. Inside hospitals, laboratory-medicine researchers document departmental restructuring under DRG toward pathway-integrated, cost-justified test menus [S29], and listed-company annual reports describe the laboratory's conversion from "profit centre" to "cost centre", with reagent selection shifting toward lower-priced domestic manufacturers (Tier B) [75].

The US experience supplies the heterogeneity counterpoint: Medicare Part B laboratory spending reached US$8.4 billion in 2024 (+5% year-on-year), with genetic tests accounting for 43% of spending on only 5% of volume (up from 18% in 2018), even as non-genetic spending fell from US$6.3 billion to US$4.8 billion [76]: utilisation, not price, now drives CLFS growth. This fits the model's core RQ2 prediction: uniform compression falls hardest on high-volume routine diagnostics and on the adoption margins of new molecular tests that must displace them, while aggregate effects are blunted by mix shift (United States) or offset by setting-specific substitution (China's county hospitals) [69,76]. The squeeze is real, convergent and mechanism-identical, but its access consequences are mediated by market structure and hospital tier (Section 3.5).

Table S6.6. Documented price levels for the index tests across the six systems (most recent documented value; local currency and units as published).

Test	China	United States	Germany	France	England	Japan
Xpert MTB/RIF (TB NAAT)	No national test-level price item before the 2026 guideline (trial); provincial items where created, e.g. Guangdong 250403090-1N (rpoB detection, product-neutral): CN¥700 and CN¥650 at two publicly notifying district hospitals, self-paid (2024; S5-38), reduced to ~CN¥300 by the 2025 sixth-batch governance (22, S5-39). A point-of-care price of ~CN¥760 is reported for 2024 (media-documented; Tier B) [21,85]	CLFS CPT 87556: $47.80 (CY2016) → $41.68 (CY2025 Q1) — single cartridge reporting TB plus rifampicin resistance; no separate resistance payment exists (S5-10, S5-13)	dedicated outpatient TB-NAAT GOP 32825 (€61.40) in place since 2008; microbiology NAAT catalogue re-formulated (Neufassung) 1 July 2022 (S5-68, S5-69)	NABM acte 4102 = B 250; B value €0.27 until Jan 2023, €0.26 from Feb 2023 and €0.25 from 15 Jan 2024 → ≈€62.50 current (S5-81)	none — no routine test-level prices exist	410 points (JP¥4,100) for TB-group NAAT under the product-neutral D023 item, under which Xpert was listed in 2017; rifampicin-resistance detection is a separate 850-point item (JP¥8,500) with no separately billed US counterpart; cobas MTB-RIF/INH is billed under the product-neutral item for simultaneous rifampicin and isoniazid resistance-gene detection (code 160235850, D023-022, 963 points), a separate entry from the 963-point multiplex item in the same sub-band (88; S5)
FilmArray Respiratory Panel (RP/RP2.1)	no dedicated price item	CLFS CPT 87633: $567.75 (CY2016) → $416.78 (CY2025	GOP 32851 (from 1 July 2022): €19.90 first pathogen	panel priced via constituent NABM acts	none	RP2.1: billed under the product-neutral 1,350-point sub-band (D023-023), whose

Test	China	United States	Germany	France	England	Japan
		Q1) (S5-10, S5-13)	+ €7.23 each additional (S5-68, S5-69)			official full name specifies SARS-CoV-2 inclusion, listed as two entries by delivery route (outsourced/in-house); 1,350 points = JP¥13,500 (S5-104)
FilmArray ME panel (CSF)	approved 2022; no dedicated price item	—	no dedicated GOP — CNS multiplex not billable as a panel (S5-72)	—	none	1,700 points = JP¥17,000 (2022) (S5-116)
COVID-19 NAAT (emergency-era reference)	successive provincial caps to CN¥15 single / CN¥3 pooled by 2022 (S5)	$51.31 per test (87635; CY2021–2025) (S5-13)	GOP 32816: €59 (Jan 2020) → €19.90 (from Apr 2023) (S5-77, S5-78)	NABM actes priced during emergency	none	1,800 → 1,350 → 850 → 700 points (2020–2022) (73) → 650 points (FY2026 revision) (88)
mNGS (pathogen)	~CN¥3,000–4,000 per test, self-pay hospital send-out; national price item created in the 2026 catalogue (trial) (S5)	~$3,000 per sample for UCSF's CSF mNGS (2024); other CLIA laboratory-developed-test providers quote ~$1,000–2,500; no CLFS code (S43)	none	none	none	none

Note. Values are shown in local currency and local units exactly as published (CN¥ = Chinese yuan; JP¥ = Japanese yen; 1 Japanese fee-schedule point = JP¥10; the French tariff is the B-coefficient times the B value, which stood at €0.27 until January 2023 and declined to €0.26 (February 2023) and €0.25 (from 15 January 2024)). Deliberately no exchange-rate conversion: The China column reports item-level prices where provincial items exist; a nationally uniform test-level price framework was established only by the 2026 guideline (trial). The table's purpose is to show each test's price position within its own system — the levels on which the compression instruments of Section 3.3 operate — not cross-country affordability, which would require purchasing-power adjustment. Empty cells ("none") are findings, not missing data: they mark systems where no test-level price exists for that product.

S6.3 Innovation carve-outs (from main-text Section 3.4)

Five-mechanism inventory with the 2024–2026 policy frontier.

Five of the six systems pay, temporarily or conditionally, for innovations not yet in standard schedules (Table S6.3). They form a family echoing the logic of Medicare's "coverage with evidence development": time-limited payment tied to evidence generation, resolving into routine coverage, repricing, or exit (11). Japan, where fee-schedule listing is itself the coverage decision, has no equivalent.

Germany: NUB → ZE → DRG. Hospitals, not manufacturers, apply annually to InEK for temporary, extrabudgetary NUB fees (legal basis and window: Table S6.3). For 2026, 326 of 1,084 requested methods (~30%) received Status 1, permission to negotiate hospital-by-hospital with sickness

funds while creating no tariff [S30]. The intended pathway runs NUB Status 1 → OPS (operation and procedure) code with mandatory data collection → negotiable then fixed Zusatzentgelt (ZE) → dedicated DRG, yet only 105 of more than 3,400 NUB methods transferred to regular payment in 2005–2020 (2.6% per source; the stated denominator implies approximately 3.1%), and some NUBs persist beyond ten years [77]. Diagnostic applications were "almost exclusively rejected" (all companion diagnostics until 2020); a §31 KHG reform making InEK legally accountable now renders decisions contestable [26].

France: RIHN 1.0 → RIHN 2.0. RIHN 2.0 (LFSS 2023 art. 51 and its 2024 implementing texts; Table S6.3) is the family's most faithful CED design: an applicant files a binding clinical or medico-economic data-collection protocol via the HAS EVActe platform (CEDiag opinion ≤75 days; ministry decision ≤60 days), and coverage runs six years, renewable once, exiting to the NABM/CCAM nomenclatures after HAS assessment of expected service (SA) and its improvement (ASA) [99]. It replaces RIHN 1.0 (2015), whose closed MERRI G03 envelope (€521.5 million in 2024) paid only approximately 50% of declared activity; its 616-act stock entered the LAHN (liste des actes hors nomenclatures) in 2024 under a 20%-per-year décote from 2025, subsequently moderated to 10% [79].

First decisions: favourable HAS opinions for VisioCyt Bladder (June 2025) and NOVAGRAY RILA Breast (September 2025, after two 2020 rejections) [S31]; the first ministerial inclusion (decision dated March 2026, announced April 2026; code R001; €253 cap), whose initial restriction to the 2,000-patient study population was partially suspended by the Conseil d'État in June 2026, and an UNCAM decision (2 June 2026) completed the first RIHN→NABM transitions: four codes, two next-generation sequencing (NGS) panels [S32] (single-source: ministry/Journal officiel texts as reported by MTRC and APMnews; Tier B).

United States: MolDX technical assessment. MolDX operationalises CED through ex ante assessment, not time-limited payment: tests lacking FDA-cleared intended uses register in the DEX Diagnostics Exchange for a Z-code and undergo Technical Assessment (TA) against analytic validity, clinical validity and clinical utility (AV/CV/CU); FDA clearance establishes validity only, not Medicare coverage [S33]. Coverage terms appear in Local Coverage Determinations (LCDs): the L38988 family (2022; revised July 2025, companion LCDs re-revised through June 2026) covers syndromic panels on restrictive terms (outpatient-only; targeted versus expanded panel tiers; specialist ordering; a 14-day repeat bar) and explicitly excludes mNGS [25]; clinical-utility lack is the most cited denial reason [S1].

England: NICE Early Value Assessment. The NICE EVA (interim statement PMG39, December 2022) issues conditional early-use recommendations with evidence-generation plans and fixed reassessment; the diagnostic record is mixed: the Genedrive MT-RNR1 point-of-care test was conditionally recommended (HTE6), urinary-tract-infection point-of-care tests were not (HTE7) [100]. From July 2025 the diagnostics, medical-technology and interventional-procedures programmes merged into one HealthTech programme applying lifecycle cost-effectiveness evaluation; the National Healthtech Access Programme (NHAP), launched February 2026, adds a medicines-style funding-mandate route, consequential because NICE diagnostics guidance historically carried none [S34].

China: special-case deliberation (teli danyi) / carve-out payment (chuwai zhifu). China's DRG/DIP 2.0 scheme institutionalised special-case deliberation, case-level exceptions capped at 5% of

DRG or 5‰ (0.5%) of DIP discharges, and encouraged carve-out payment for new drugs and technologies; in 2025, 2.071 million of 2.435 million applications were approved (85.1%; approximately CN¥61.26 billion) [65]. Beijing's second batch (29 items, 2026–2028) sets cost thresholds (at least twice the group average; more than 50% new-technology share); both channels are drug/consumable-shaped (22 drugs, 5 consumables, 2 procedures), and diagnostic-specific use remains limited [65].

Table S6.3. Innovation carve-out and coverage-with-evidence-development mechanisms in five systems: legal basis, duration, evidence obligation and diagnostic track record (status mid-2026).

Mechanism	Jurisdiction	Legal–institutional basis	Duration & renewal	Evidence obligation	Diagnostic track record
NUB → ZE → DRG	Germany	§6 Abs. 2 KHEntgG; annual InEK window (early Sept–31 Oct); Status 1–4; hospital applicants	One-year, hospital-specific extrabudgetary fees; annual re-application	Status 1 permits payer negotiation (no tariff set); mandatory OPS-code data collection; no formal outcomes protocol	326/1,084 methods Status 1 (2026, ≈30%) [S30]; 105 of >3,400 methods integrated 2005–2020 [77]; diagnostics near-totally rejected; all companion diagnostics rejected until 2020; some NUBs persist >10 years [26,77]
RIHN 1.0 → RIHN 2.0	France	LFSS 2023 art. 51 → CSS L.162-1-24 → Décret 2024-290 → Arrêté 25 Nov 2024; MERRI G03 envelope	Six years, renewable once; legacy LAHN stock under 20%/yr décote from 2025	Binding clinical/medico-economic protocol via HAS EVActe; CEDiag opinion ≤75 days; ministry decision ≤60 days; exit via SA/ASA to NABM/CCAM	RIHN 1.0 paid ~50% of declared activity; 616-act stock [79]; first decisions 2025–2026 (VisioCyt R001, €253 cap; NOVAGRAY) [S31,S32]; first RIHN→NABM transitions 2 Jun 2026 [S32]
MolDX technical assessment	United States	Medicare "reasonable and necessary" standard; DEX Z-code registration; contractor LCDs	Continuous; LCD scope revisable	ACCE-based TA (AV/CV/CU); 15-day documentation window; clinical utility must be demonstrated in peer-reviewed literature	LCD L38988: outpatient-only, targeted ≤5 vs expanded ≥6 panels, specialist ordering, 14-day repeat rule; mNGS explicitly excluded [25]; clinical-utility lack is the top denial reason [S1]
NICE EVA → HealthTech	England	PMG39 (Dec 2022); single HealthTech programme from 14 Jul 2025	Fixed conditional period, then routine-use reassessment	Published evidence-generation plans; lifecycle cost-effectiveness for all technologies	HTE6 (Genedrive) conditionally recommended; HTE7 (UTI point-of-care tests) not recommended [100]; diagnostics guidance carried no statutory funding mandate; NHAP launched February 2026 [S34]
Special-case deliberation (teli danyi) / carve-out payment (chuwai zhifu)	China	NHSA General Office Document [2024] No. 9 (DRG/DIP 2.0); Beijing Municipal Healthcare Security Bureau Document [2025] No. 22	Case-by-case (≤5% of DRG / ≤5‰ (0.5%) of DIP discharges); Beijing batch 2 covers 2026–2028	None formalised; cost thresholds (Beijing: ≥2× group average cost; ≥50% new-technology cost share)	2.071 million cases approved 2025 (85.1%; CN¥61.26 billion) [65] (special-case deliberation statistics: Tier B, single official source); drug/consumable-dominated; diagnostic-specific use limited [65]

Note. 2026-frontier French entries (16 April 2026 inclusion; 2 June 2026 RIHN→NABM transitions) rest on single-source ministry/Journal officiel texts as reported by MTRC and APMnews, April–June 2026 (Tier B). Source tiers: T1 = peer-reviewed or primary official document; T2 = reputable secondary. Confidence tiers per Section 2.4.

Three contrasts emerge: only France requires a binding outcomes protocol (Germany demands coding data; MolDX demands utility evidence ex ante); exit discipline diverges (France engineered exits; Germany's 105-method record is a transition few complete; China's route has volume without evidence linkage); and conditional status is revisable in both directions, as the 2025 L38988 revision and the litigation of France's first inclusion show. Temporary payment resolves uncertainty only partially and slowly. A supranational layer now looms above these national Gate-3 processes: the European Union's Health Technology Assessment Regulation (Regulation (EU) 2021/2282) begins joint clinical assessments for high-risk devices from 2026, which may add a shared evidence layer above national coverage decisions, although proposal-stage coverage details remain national [49].

Shared failure modes for diagnostics.

The five mechanisms exhibit four shared failure modes for diagnostics. **First, device- and drug-shaped design.** All five were built around hospital-budget innovations or pharmaceuticals assessed one technology at a time: Germany's funnel is drug- and device-dominated [S30], China's batches enumerate drugs and consumables [65], and MolDX assesses utility test-by-test where diagnostic value is informational and realised only downstream; the consequence is exclusion at assessment, as near-total rejection of diagnostic NUBs [26] and mNGS's exclusion from the only US molecular-panel LCD [25] show. **Second, evidence obligations mismatched to supply.** The global supply of outcome trials remains the sparse flow documented in Section 1.1 [4], yet the mechanisms demand precisely such evidence, MolDX ex ante [S33,S1] and France via financed protocols, as NOVAGRAY's two rejections illustrate [S31].

Third, value externalised across budget silos. The payer bearing the test cost — the laboratory, the DRG bundle, the special-case quota — captures neither avoided antibiotic days, shorter stays nor transmission benefits; NHS stakeholders name "who pays for it, and who sees the reward" as the operative barrier, with pilots discontinued when short-term funding ends [78], and the outcomes literature under-measures the economic and societal domains where benefits sit [16]. **Fourth, temporary-status instability.** NUBs persist beyond ten years unintegrated [77], LAHN acts face an annual décote absent re-evaluation [79], and LCD scope is revisable either way, as the 2025 L38988 revision shows [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: Xpert MTB/RIF, a WHO-endorsed test with the field's strongest cost-effectiveness evidence, inside China's now well-established double-squeeze configuration.

S6.4 Molecular tuberculosis diagnostics in China (from main-text Section 3.5)

Table S6.4 summarises prices, insurance status and evidence sources for the index test class in China.

Table S6.4. Molecular tuberculosis diagnostics in China: prices, insurance status and evidence sources.

Item	Indicative price	Insurance status	Evidence source
Sputum smear microscopy	~CN¥8 per slide	Reimbursed; free (with chest X-ray) at designated TB clinics	Caixin Weekly 2024 [85]
rpoB detection — provincial price item 250403090-1N (product-neutral; billed by the imported assay and domestic equivalents alike)	CN¥700 / CN¥650 at two publicly notifying Guangdong district hospitals, self-paid (2024); ~CN¥300 after the 2025 sixth-batch governance	Self-paid market-priced item; insurance listing decided provincially	Hospital price notices (S5-38, S5-39); governance notice [22]
Xpert MTB/RIF (imported index product) — reported point-of-care price	~CN¥760 per test (2024, media-documented; Tier B)	Province-dependent; self-pay in many localities	Caixin Weekly 2024 [85]
Domestically registered TB molecular / drug-resistance NAATs (technology class)	Set by provincial price-item catalogues	Class III registrations held by at least seven domestic manufacturers; single-source procurement notices state platform exclusivity (sealed, non-user-programmable cartridge systems) as their reason [86]; in our reading, whether a domestic assay could substitute is an evidence gap (no equivalent WHO-evaluated cross-population performance dossier published to date; no comparable published validation record), not a registration gap	Registration and procurement records [86]; WHO evaluation scope [80]
Drug-resistance gene tests (isoniazid, fluoroquinolone)	CN¥300 per item	Province-dependent	Caixin Weekly 2024 [85]
TB molecular tests after the sixth batch of national price governance (2025)	National caps ~CN¥100–300 (e.g., rpoB ≤CN¥300; resistance gene ≤CN¥130)	Prices standardised; insurance listing still provincial (Anhui provisionally excluded)	Provincial notices 2025 [22,24]

First, before provincial items existed the gap between a reimbursed smear and an item-priced molecular test spanned roughly two orders of magnitude on the published figures, prohibitive for a disease concentrated among low-income groups. Second, administrative price governance cut the catalogue-price ratio to roughly 12–37-fold in the 2025 rounds, showing that Gate 2 was an artefact of catalogue administration rather than technology cost; and because smear microscopy is free at designated clinics, the patient-facing price ratio in non-reimbursing areas is effectively unbounded. Third, the same test class is simultaneously insured (Xinjiang, ten items, 2019), uninsured (Tianjin's Hain line-probe assay, CN¥500) and provisionally excluded (Anhui, 2025) across provinces [24,32,33]: Gate 3, not performance, determines access. The provincial items are product-neutral — they name targets and methods, not products — so the imported Xpert and domestic assays (including Zeesan's melting-curve products) are billed under the same items, and the divergence is not product-specific. Note that the default differs by item vintage: routine pathogen PCR billed under long-standing generic items is typically Class A (fully covered) — a county-hospital price list shows pathogen RNA/DNA PCR at CN¥68 and CN¥47.9, both Class A (S5-128) — whereas newly created dedicated items enter as self-pay (Guangdong, 2024) or are provisionally excluded pending insurance evaluation (Anhui, 2025). Hospitals facing a catalogue price below cost may also resort to market-adjusted self-pricing, whose insurance treatment varies by locality and is not systematically documented. In practice, hospitals without a dedicated price item often bill molecular tests through generic proxy items (per-gene or pathogen nucleic-acid catch-alls), with the item applied varying by institution; the national reform's

own rationale documents regional catalogues ranging from about 4,000–5,000 to more than 20,000 items, with identical item names carrying different content across provinces [87]. Even where listed, the double squeeze deters use: under per-case quotas, hospitals using more high-value technology face greater overage risk, a Beijing Chest Hospital clinician reports [85]. The NHSA's 2026 national laboratory-test pricing catalogue (trial) [87] removes the price-item barrier at the national level; provincial implementation and insurance-listing follow-through remain to be observed, so the insurance-listing gate is now binding.

Cross-national echo: closing the coverage gap in China.

The same technology has cleared the comparable gates elsewhere (cf. Table 1): dedicated outpatient fee items for tuberculosis NAATs exist on the US CLFS, the German EBM and the French NABM; Japan reimburses tuberculosis NAAT at 410 points and rifampicin-resistance detection at 850 points (Chuikyo fee-schedule documentation; Tier B) [88]; and England's NICE guideline NG33 recommends rapid NAATs for the *M. tuberculosis* complex on primary specimens [89] — although England has no test-level price and NICE guidance carries no funding mandate, so its passage is not comparable on the three-gate metric. Among the six systems, China shows the widest publicly documented gap between device deployment and payment — a statement bounded by the documentation asymmetry of Section 4.4 — and a gap its 2025–2026 pricing reforms and the 2024–2030 National Tuberculosis Control Plan are now explicitly designed to close. The misalignment is archetypal: tuberculosis detection's benefits (averted transmission, avoided resistance amplification) are public-health externalities, while the cost lands on a hospital's fixed case payment (Section 4).

S6.5 The cross-silo ledger (from main-text Section 4.1)

Table S6.5. A cross-silo ledger for 100 suspected bloodstream-infection admissions under bundled inpatient payment (illustrative, published parameters).

Silo (pays / benefits)	Ledger line	Quantity per 100 admissions	Status (Verified / Assumption)
Laboratory budget (pays; cost absorbed into the MS-DRG bundle)	Gross price of the rapid molecular panel at the GI-panel CLFS proxy (a price proxy — directionally overestimates cost by roughly threefold)	≈US$41,700 per 100 panels (US$417 each); incremental versus conventional workup ≈US$38,000–40,800 (US$9–37 per test)	Assumption (GI-panel CLFS benchmark [91]); Verified only for the DRG-bundling mechanism
Pharmacy budget (benefits; does not pay)	Faster optimisation and de-escalation of antibiotic therapy	−28.7 h median time to optimal therapy (43.4 vs 72.1 h); −19.0 h to anti-MRSA de-escalation [91]	Verified
Inpatient bed budget (benefits; does not pay)	Avoided bed-days (not monetised)	−2.48 days length of stay per patient → ≈248 bed-days freed [1]; null in the single implementation cohort [91]	Verified (meta-analytic average, not a guaranteed local effect)
System / public health (benefits; pays only via global budgets)	Contaminant-identification savings; ICU-cost and mortality effects	≈US$30,000 saved via CoNS-contaminant identification [91]; −£7,802 per ICU episode on the stewardship endpoint only, confidence interval crossing zero [90]; mortality OR 0.66 only with ASP [1]	Verified (mortality ASP-conditional; ICU estimate from a different setting and non-significant)
Stewardship programme (ASP) (co-produces the benefit; unfunded by the laboratory fee)	Organisational precondition for the Rows 2–4 benefits	Coverage requires an ASP equipped for 24-hour tailoring of antimicrobial therapy [25]; the ASP's cost appears in no row of the laboratory's ledger	Verified

Two features of Table S6.5 matter more than any single magnitude. First, the benefit rows are context-dependent — the INHALE saving is endpoint-dependent and from UK intensive care [90], and the implementation cohort found no length-of-stay or mortality difference [91] — but their *location*, outside the laboratory silo, is not. Second, Row 5 shows that the payer itself recognises value as co-produced: LCD L38988 mandates a stewardship team as a coverage condition [25], yet no payment mechanism funds it. The ledger thus reads as the transfer-pricing failure in miniature: every row is individually published and verified, yet no single budget ever sees them jointly.

S7. Data availability and product representativeness

S7.1 Data-availability audit

A document-based comparison is bounded by what each system publishes. We audited public data availability for six data classes in each of the six systems, recording each cell as published in full, partially published (aggregated, scattered, paywalled or not machine-readable), not published, not generated by the institution, or available only on application.

Table S7.1. Public data availability by data class and system.

Data class	China	United States	Germany	France	England	Japan
Price catalogues / fee schedules	Full	Full	Full	Full	Not generated (no routine test-level prices)	Full
Coverage decisions, with rationale	Full (provincial notices)	Full (NCD/LCD)	Partial (NUB status lists published without rationales)	Full (HAS opinions)	Full (NICE guidance)	Full (Chuikyo records)
Procurement awards and prices	Full (public tender notices)	Partial (federal public; commercial contracts confidential)	Partial (public tenders; hospital-level supplementary-payment outcomes not published)	Partial (public tenders; CHAB negotiations confidential)	Partial (notices public; framework prices confidential by policy) [S35]	Not published
Regulatory review statistics	Partial (annual reports; per-product elapsed times reconstructed)	Full (FDA databases; MDUFA reports)	Partial (notified-body surveys)	Partial	Partial	Full (PMDA review reports)
Test-utilisation volumes	Not published officially (commercial databases paywalled)	Full (Medicare Part B, by code)	On application (Forschungsdatenzentrum)	Partial (aggregated statistics)	Partial (monthly diagnostics activity; no per-test pathology volumes)	On application (NDB custom tabulations)
Provider-level charging practice	Partial (statutory price display; online practice varies)	Partial (chargemasters are not transaction prices)	Not published	Not published	Not published	Partial (facility notifications scattered across eight regional

Data class	China	United States	Germany	France	England	Japan
						bureaus)

Three structural readings follow. First, the national decision layer is symmetric: all six systems publish price catalogues and coverage decisions in full text, so the binding-gate diagnosis (Table 2) rests on low-bias evidence. Second, asymmetry concentrates in the execution layer — procurement prices, utilisation volumes and provider-level charging — where China's statutory publication requirements make its evidence the most granular, while equivalent failure modes in France (listing delays negotiated behind closed doors) and Germany (hospital-level NUB negotiation failures) leave no public trace. Third, England's empty price cell is not missing data but a finding: the institution does not generate routine test-level prices. Throughout, we distinguish retrieval gaps (public documents not located) from publication gaps (data classes a system does not generate or publish); "no evidence of a barrier" is never read as "evidence of no barrier" in systems with publication gaps.

S7.2 Product representativeness cross-check

The three index technologies are reference points, not market proxies. We cross-checked their position against national guidelines, consensus statements and market evidence in each system.

Table S7.2. Guideline status and market position of the index technologies by system.

Technology	China	United States	Germany	France	England	Japan
Tuberculosis NAAT	Guidelines product-neutral [S36]; GeneXpert used by 74.6% of laboratories in national proficiency testing [S37, S38]; domestic isothermal, melting-curve, microarray and qPCR assays from at least seven registered manufacturers collectively account for the majority of testing volume [86]	Guideline-named (Xpert MTB/RIF; CDC/ATS/IDSA) [S45]	Product-neutral S2k guidelines; GeneXpert and GenoType (Hain/Bruker) platforms both in routine laboratory use [S46]	Product-neutral (ERS/ECDC standards); no product-specific national guideline	NICE NG33 recommends rapid NAATs in defined scenarios [89]	Product-neutral; domestic platforms (TRC, Loopamp, cobas) dominate; Xpert insured 2017, cobas MTB-RIF/INH 2023 [S42]
Syndromic multiplex panels	Meningitis/encephalitis panel approved 2022; domestic panels dominate volume	IDSA class-level endorsement; segment leader reports ~70% multiplex share and 26,750 installed systems [S39]; closest multiplex competitor >3,500 installed [S40]	Meningitis guideline recommends multiplex panels; adult pneumonia guideline conservative	Multiplex panels integrated into standard practice texts; domestic manufacturer	Product-neutral; NICE declined to distinguish single- from multiplex PCR	FilmArray ME panel insured 2022; respiratory panel 2025
mNGS	Multiple national expert consensuses; first Class III registration 2024 [S5]; central-laboratory send-out model	CLIA laboratory-developed-test services (e.g., Karius, used in >400 hospitals) [S41]; no society guideline recommendation	No national guideline; research-level	No national guideline; research-level	NHS metagenomics network pilots	No national guideline

The comparison throughout is by technology class, not by identical product: the specific registered products in each system, with registration or accession numbers, are tracked individually in Section S5.

The asymmetries in Table S7.2 are themselves findings. China's tuberculosis NAAT market pairs the leading imported platform with a larger domestic assay ecosystem — a dual structure without parallel in the other five systems — so Section 3.5 reads Xpert as the category's policy reference point, not as a proxy for the entire Chinese market. The syndromic-panel exemplar leads its multiplex segment but not the larger single-plex volume. And mNGS has formal consensus status mainly in China; elsewhere it diffuses as a laboratory service. None of this alters the gate analysis, which binds at the level of the technology class in every system.

S7.3 Routine-tier baseline: established respiratory NAATs

The index technologies sit at the innovation frontier by design; the routine tier supplies the baseline against which "binding" is defined. Established single-plex respiratory NAATs pass all three gates in every system, and their payment position is unremarkable precisely because they are old, cheap and validated.

Table S7.3. Routine-tier respiratory NAATs: baseline payment status by system.

System	Routine single-plex NAATs (influenza A/B, M. pneumoniae, RSV)	Multiplex respiratory panels	Point-of-care NAAT
China	Long-listed in provincial catalogues as single-target items (e.g., Guangdong 13-item respiratory NAAT cap CN¥220.8, 2024)	No dedicated price item; billed under single-target items, with several provinces capping respiratory-virus billing at six items and the 2025 national "minimum-necessary" notice requiring unbundling [S5]	No waived-testing pathway; NAATs are laboratory-based Class III products
United States	Long covered under the CLFS; multiplex respiratory panels priced on a target-count ladder (CPT 87631 $142.63; 87632 $218.06; 87633 $416.78, CY2025) (S5-13)	Same ladder; MolDX LCDs condition panel coverage on outcome evidence [25]	CLIA-waived NAATs approved through the waiver pathway (Abbott ID NOW, the first CLIA-waived molecular platform, 2015; Roche cobas Liat, 2015) [S44]
Germany	Single-target GOPs in EBM chapter 32	GOP 32853 from 1 July 2022: €19.90 first pathogen + €7.23 each additional (S5-68, S5-69)	No separate POCT tier; EBM covers practice laboratories
France	Single-target NABM acts	Panels priced via constituent acts; RIHN covers innovation	Centralised laboratory biology is the default model
England	No test-level prices; commissioned within pathology networks	Same	Same
Japan	Single-target NAAT items in the fee schedule; FilmArray RP2.1 insured 2025 under the product-neutral 1,350-point sub-band D023-023 (JP¥13,500; the sub-band's official full name specifies SARS-CoV-2 inclusion) (S5-104)	Same	Limited; listing follows the laboratory-fee model

Two readings matter for the main text. First, the three gates bind selectively: the routine tier passes everywhere, so the binding-gate diagnosis is a property of the innovation frontier, not of the test menu as a whole. Second, even the semi-routine multiplex tier is gate-blocked in China — respiratory panels approved since 2021 still lack a dedicated price item and are billed through capped single-target proxies — which is exactly the improvised proxy-billing equilibrium described in Section 3.1.2. The maturity gradient also answers a scope question: Xpert MTB/RIF (CE 2010; FDA 2013) anchors the mature end and is not the innovation frontier; the case study's point is that even a WHO-endorsed mature technology remained gate-blocked in China until the 2025–2026 reforms.

S8. Home and point-of-care testing: regulatory frameworks

S8.1 The self-test / self-collection distinction

Regulators draw a sharp line between *self-testing* — a lay person performing any part of the assay (adding reagents, running the device, reading the result) — and *self-collection for laboratory analysis*, in which the lay person only collects, seals and preserves the specimen. The former requires product approval with an explicit self-test indication and lay-user evidence; the latter is not self-testing and follows a lighter path: the specimen receptacle is regulated as a low-risk device, and compliance rests on the analysing laboratory's accreditation [S55].

S8.2 Home-use approvals by system

Table S8.1. Home-use diagnostic approvals and self-collection examples.

System	Self-test product approvals	Home NAAT self-test?	Self-collection-for-laboratory examples
United States	Flowflex COVID-19 Antigen Home Test — first OTC rapid-antigen 510(k) [S47]; Lucira COVID-19 & Flu Home Test — first OTC home-use molecular test [S48]; Cepheid Xpert Xpress is CLIA-waived POCT, not home use	Yes, one exception: Lucira (LAMP-based)	Cologuard (PMA P130017) home stool collection with central-lab analysis [S49]; BD Onclarity HPV self-collection in clinical settings [S50]; Teal Wand first at-home self-collection device [S51]; Waters/BD Onclarity at-home kit [S52]; Pixel by Labcorp COVID self-collection [S53]
England	MHRA registration plus Approved Body certification for self-test IVDs; COVID products additionally require CTDA performance review [S59]	None	freetesting.hiv self-collected blood samples returned to accredited labs; NHS HPV self-sampling kits in the national screening programme [S58]
European Union	IVDR Annex IX 5.1 requires a lay-user study for self-testing devices; Germany's BfArM issues special lay-person approvals [S56]; France's autotest VIH was CE-marked for HIV self-testing in 2015 [S57]	None identified	Specimen receptacles are Class A devices under MDCG 2020-16 r3 [S55]; HPV self-sampling embedded in several national screening programmes
Japan	Only six product categories approved for OTC self-testing (urine glucose, urine protein, pregnancy, ovulation, COVID antigen, COVID+flu antigen) [S60]; HIV self-testing not approved	None identified	Demecal home blood-collection kit, approved as a controlled medical device [S61]
China	COVID antigen self-testing opened by the 2022 application scheme [S62]; HIV urine and saliva self-tests approved; **no home NAAT self-test approved** [S65]	None identified	JD Daojia / Meituan home-sampling services analysed by third-party or hospital laboratories [S64]

S8.3 Self-paid door-to-door sampling services

Table S8.2. Self-paid home-sampling services compared.

Service	Model	Price (as reported)	Compliance anchor
JD Daojia quick test (China)	Order online → nurse/courier home sampling → third-party or hospital laboratory → electronic report	Community group-buy CN¥69.9 per person; nurse home sampling CN¥176–188; 16-plex CN¥323–328; Ditan Hospital triple test CN¥256 + CN¥99 home-service fee	"Internet + nursing" framework [S63]: licensed institutions and registered nurses perform sampling; the platform is an information intermediary only
Meituan home quick test (China)	Courier collects the self-collected swab → third-party laboratory → online result	CN¥69.9 introductory; CN¥99–188 standard	Same framework [S63, S64]
Quest Mobile	Mobile phlebotomist home	$55–79 in-home convenience fee	State phlebotomy rules; CLIA-

Service	Model	Price (as reported)	Compliance anchor
(US)	collection → Quest laboratory		certified laboratory [S53]
Getlabs for Labcorp (US)	Full-time collector home visit → Labcorp patient-service centres	From $25	Same [S54]
NHS HPV self-sampling (England)	Postal self-sampling kit → NHS laboratory	Free (DHSC-funded)	National screening programme with UKAS-accredited laboratories [S58]
Demecal (Japan)	Self-collected finger-prick blood by post → registered laboratory	Self-paid	Collection kit approved as a controlled medical device [S61]

S8.4 Compliance determination logic

A home or door-to-door testing service is compliant only when four layers hold simultaneously: (i) the product is approved with an intended use covering lay users (self-test indication, or specimen-receptacle status for collection-only kits); (ii) the lay person's role is correctly classified (performing the assay = self-testing; collecting a specimen = not self-testing); (iii) the analysing laboratory holds the relevant accreditation (CLIA, UKAS/CQC, NMPA-licensed institution, or registered Japanese health laboratory); and (iv) sales and service delivery follow local rules (US state phlebotomy and direct-access-testing restrictions; China's online-sales and internet-nursing rules; EU online-service provisions; Japan's OTC-pharmacist requirement). Home-use NAAT self-tests are essentially absent outside the United States, so home NAAT is delivered through self-collection with central laboratory analysis in every system compared here.

S9. Structural limitations of the culture reference standard

Payers often evaluate molecular tests against culture as the reference standard. This section documents, with peer-reviewed sources, that the reference standard itself has structural performance ceilings — and that its costs are externalised in the opposite direction to the molecular tests'.

Table S9.1. Documented limitations of the culture reference standard.

Limitation	Evidence	Source
Blood-culture contamination is common and costly: 12.5% contamination in a neonatal ICU before a bundling intervention (3.8% after), each false positive adding 3.8 hospital days and US$883; 14 avoided contaminations saved 54 hospital days and US$12,549.60	NICU bundle study, 320 procedures	[S66]
Culture fails after antibiotics — the dominant real-world pathway: culture sensitivity was 41% against PCR in pertussis, and "conventional cultures are insensitive and of limited utility after antibiotic exposure"	5-year pertussis study, 104 PCR-positive submissions	[S67]
Legionella culture remains the gold standard but is slow and requires special media; PCR is highly sensitive and detects multiple serogroups	Legionellosis review	[S68]
Urinary antigen tests target only L. pneumophila serogroup 1, which accounts for 70–80% of cases in Europe and the United States — non-SG1 serogroups and L. longbeachae are systematically missed by design	Five-assay comparison, 81 urine samples	[S69]
Blood cultures are positive in <50% of haematogenously disseminated and <20% of intra-abdominal candidiasis; T2Candida reaches ~90% sensitivity / 98% specificity for candidemia	Non-culture diagnostics review	[S70]
Aspergillus culture remains foundational (viability, species identification, susceptibility testing) but with limited sensitivity and long turnaround; non-culture methods add sensitivity, early detection and resistance-mutation identification — a division of labour, not a substitution	Aspergillosis laboratory-diagnostics review	[S71]

Limitation	Evidence	Source
In immunocompromised patients with negative microscopy, PCP PCR achieved 93.1% sensitivity and 98.7% specificity (PPV 96.4%, NPV 97.1%)	96-patient immunocompromised cohort	(S72)

The honest caveat runs the other way: discrepant non-culture-positive/culture-negative results can promote inappropriate antifungal treatment and spurious reporting of hospital-acquired infections, so conditional payment must pair coverage with interpretive stewardship (S70).

S10. Clinical questions that culture, antigen detection and serology cannot answer

S9 documented the performance ceilings of the reference standard. This section documents the converse: the specific diagnostic questions for which molecular methods are not a more expensive alternative but the only method that returns an answer within the treatment-decision window. The index technologies of this study (syndromic panels, mNGS, Xpert MTB/RIF) sit on axes 1, 2 and 4.

Table S10.1. Diagnostic questions answerable only by molecular methods.

Axis	Evidence	Source
1. Slow-growing and fastidious organisms — culture is unavailable at the decision point. *Mycoplasma pneumoniae* has a doubling time of approximately 6 hours, is not cultured routinely in clinical laboratories, and results take weeks when attempted.	Clinical review	(S73)
2. Paucibacillary disease — smear and culture sensitivity collapses. In smear-negative, culture-positive pulmonary tuberculosis, Xpert Ultra summary sensitivity was 80%. In extrapulmonary tuberculosis, Xpert sensitivity against culture varies by specimen from 31% (pleural tissue) to 97% (bone or joint fluid), while specificity is ≥98% in most specimen types. In paediatric extrapulmonary tuberculosis (8 studies, 652 specimens), pooled sensitivity was 71% (95% CI 0.63–0.79) and specificity 97% (0.95–0.99); by specimen, lymph node 80% (0.70–0.88)/94% (0.89–0.97) versus cerebrospinal fluid 42% (0.22–0.63)/99% (0.95–1.00).	Cochrane reviews; paediatric meta-analysis	(S74), (S75), (S76)
2b. Paucibacillary disease in the immunocompromised host. Where respiratory microscopy is negative, *Pneumocystis jirovecii* PCR achieved 93.1% sensitivity and 98.7% specificity (PPV 96.4%, NPV 97.1%).	96-patient immunocompromised cohort	(S72)
3. Delayed antibody kinetics — serology post-dates the treatment decision. Serological confirmation of *M. pneumoniae* requires paired sera collected 2–3 weeks apart demonstrating a fourfold titre rise; early-illness false negatives are common. Serology answers whether a patient has been infected, not what to treat now.	Reference review	(S77)
4. Sub-species characterisation — no non-molecular method returns this information. Macrolide resistance in *M. pneumoniae* is determined by point substitutions at A2063G/A2064G in 23S rRNA domain V; phenotypic susceptibility testing is impractical because of slow growth, so molecular detection identifies organism and resistance genotype in the same actionable time window. The genotype carries clinical consequence: in A2063G-mutant infection, age and hypoalbuminaemia independently predicted pulmonary consolidation.	Diagnostic-stewardship review; paediatric cohort	(S78), (S79)

Table S10.2. The antigen-detection ceiling.

Antigen tests are the usual low-cost comparator in payer assessments. Two limitations are structural rather than incremental — a sensitivity ceiling, and a coverage gap by design (the latter documented for *Legionella* in Table S9.1).

Test	Pooled sensitivity	Note	Source
Rapid influenza diagnostic tests	**62.3%**	Children 66.6% versus adults 53.9%; influenza A 64.6% exceeds influenza B	(S80)
RSV rapid antigen detection	**80%** (specificity 97%)	Children 81% versus adults 29%. Sensitivity is lowest when RT-PCR is the reference standard (74%) and highest against immunofluorescence (88%), P<0.05	(S81)

Test	Pooled sensitivity	Note	Source
Paediatric RSV, multiplex versus singleplex RT-PCR	**96%**	Multiplex format does not sacrifice sensitivity relative to single-target PCR	(S82)

The reference-standard dependency in the RSV data is methodologically consequential for payers: accuracy studies that do not use RT-PCR as the reference systematically overstate antigen test performance, and health-technology assessments that pool such studies inherit the overstatement.

Implication for the measurement unit. Payers price per test; clinical value accrues per correct and actionable diagnosis. The two diverge systematically where a negative result does not exclude disease — the paediatric, extrapulmonary and smear-negative populations above — because the true comparator cost is the diagnostic pathway, not the single test. The item-level prices reported in main-text Section 3.5 — CN¥700 and CN¥650 for the product-neutral rpoB item at two publicly notifying hospitals in 2024, against a reimbursed smear at roughly CN¥8 (S5-38) — hold on a per-test basis; on a per-correct-diagnosis basis in these populations, the smear arm must carry the cost of the subsequent work-up its negative result cannot avert.

Platform dependence and the limits of price transparency. The tariff recommendations in Section 4.3.1 assume that publishing test-level prices makes rationing visible; but where a single platform dominates, transparency alone does not lower prices. The GeneXpert platform absorbed approximately US$252 million of public research investment across its development (S83); and in head-to-head cost-effectiveness comparisons, decentralised molecular testing outperformed hub-and-spoke delivery — in Mozambique, treatment initiation within seven days cost US$853 per patient at hubs versus US$690 with decentralised placement, and the increment per additional patient started on treatment within seven days was US$403 (Tanzania: US$580) (S84); extended cost-effectiveness analysis reaches the same direction (S85).

S11. Method classes and platform attributes: a primer

This primer fixes the class definitions used in the main text (Sections 2.3 and 3.5). It is definitional only — textbook-standard method descriptions with no new empirical claims; products referenced are tracked in the S5 register. Every test decomposes into two layers: a first-layer amplification, signal-generation or enrichment step (thermal-cycling PCR; isothermal amplification such as LAMP or RPA; CRISPR-based signal generation; or, for sequencing-based assays, target enrichment by multiplex-PCR amplification or hybrid capture — shotgun metagenomics amplifying nothing) and a second-layer readout (fluorescent probes — real-time hydrolysis-probe fluorescence or melting-curve analysis; ligation-dependent probe amplification read by fragment sizing, i.e. MLPA; or sequencing). The closed/open device axis is orthogonal to both layers.

Table S11.1. Method classes for pathogen nucleic-acid detection: principle, chemistry and platform attributes.

Method class	Reaction principle / enzyme system	Primers and detection chemistry	Platform attributes	Position in this study
Real-time fluorescent PCR (hydrolysis-	Thermostable Taq polymerase with thermal cycling (denaturation–annealing–extension)	Primer pair plus a dual-labelled probe (5′ reporter, 3′ quencher);	General-purpose qPCR instruments; user-programmable;	Syndromic multiplex panels; the

Method class	Reaction principle / enzyme system	Primers and detection chemistry	Platform attributes	Position in this study
probe, TaqMan)		Taq 5′→3′ exonuclease hydrolyses the probe during extension, releasing fluorescence	open-format workflow requires a PCR-grade laboratory	routine single-plex tier; some domestic TB NAATs
Multiplex panel implementation routes	The same amplification chemistry delivered in different physical formats: (a) mixed multiplex PCR in one tube with probe panels; (b) parallel single-plex amplifications in separate wells or chambers (array / multi-chamber cartridge; FilmArray is a closed pouch with two-stage nested multiplex PCR and array readout); (c) MLPA — ligation-dependent probe panels with universal-primer amplification, a second-layer readout by fragment sizing; (d) multiplex isothermal amplification	Probe panels per target; MLPA uses ligated universal-primer probes	Open qPCR instruments or closed multi-chamber pouches/cartridges — both exist	Syndromic panels (FilmArray RP, QIAstat, domestic six/nine-item kits)
Melting-curve PCR (e.g., MeltPro)	Taq PCR followed by post-amplification melting analysis	Melting-temperature (Tm) shifts of probe–target hybrids read point mutations (e.g., rpoB, katG) directly — resistance genotyping without sequencing	Same open qPCR instruments with a melting module; user-programmable	Domestic TB drug-resistance assays (S5 register)
Isothermal amplification (LAMP, RPA, ERA)	Strand-displacing polymerase (e.g., Bst) or a recombinase-assisted system operating at a constant 37–65 °C; no thermal cycling	4–6 primers recognising 6–8 target regions (LAMP) or recombinase–primer complexes (RPA); readout by fluorescent probe, turbidity or colour	Open isothermal-fluorescence instruments (user-programmable) or dedicated closed cartridges — both exist	Domestic rapid TB and M. pneumoniae assays
Closed-cartridge real-time fluorescent PCR (semi-nested)	Semi-nested real-time PCR with fluorescently labelled probes (e.g., molecular beacons) — methodologically a fluorescent PCR, not an isothermal method	Extraction, amplification and detection integrated in a sealed cartridge; users cannot open it, interrupt the run or reprogram it	Dedicated instrument only; Xpert MTB/RIF and Ultra are the index *products* of this class, not the class name	
Shotgun metagenomic sequencing (mNGS)	Unbiased library of all nucleic acids in the specimen, high-throughput sequencing, bioinformatic alignment	No target primers	Sequencer plus bioinformatics pipeline; centralised laboratory service	The mNGS case
Targeted sequencing (tNGS)	Multiplex-PCR or hybrid-capture enrichment of target pathogens, then sequencing	Target-specific primer panels or capture probes	Sequencer plus pipeline	mNGS-adjacent; noted in S5/S7
Ribosomal-marker amplicon sequencing (16S/18S/ITS)	Universal primers on hypervariable regions (bacterial 16S, most often the V3–V4 region; 18S/ITS for fungi/parasites)	Universal primers plus sequencing	Sequencer; community profiling, not routine clinical quantitation	Context only; not tracked
Other formats (not tracked)	Digital PCR (limiting-dilution absolute quantification); CRISPR-based signal generation (Cas12/Cas13 collateral cleavage, a first-layer chemistry typically following a short isothermal pre-amplification)	Various	Various	Out of scope

The closed/open axis is independent of method. The dominant carryover-contamination risk in open PCR is aerosolised amplicon: opening a tube after amplification can seed false positives in

subsequent runs, which is why open formats require separated laboratory areas and unidirectional workflow. Fully closed formats retain amplicons permanently, so the assay can run outside a PCR-dedicated laboratory with reduced contamination risk, fewer operator errors and no specialist molecular staff. That rationale is shared by imported (Xpert) and domestic (fully closed isothermal) platforms alike; qPCR, isothermal and CRISPR chemistries can each be built in either open or closed formats.

Table S11.2. Technology attributes and observed gate outcomes.

Technology class	Gate 1 form and difficulty	Outcome-evidence difficulty	Typical paying budget	Observed binding gate (this study)
Routine single-plex PCR	Product registration; straightforward	Low (mature evidence base)	Outpatient fee schedule; default Class-A coverage for established items in China	Largely unobstructed
Syndromic multiplex PCR panel	Product registration; moderate	High — outcomes hard to attribute to any single target	Tiered outpatient fees (US target-count tiers; Japan multi-item items)	United States evidence gate (MolDX LCD)
Closed-cartridge real-time PCR rapid NAAT	Product registration plus dedicated instrument	Low (WHO-endorsed, mature cost-effectiveness record)	Public-health programmes plus outpatient items	China price gate, then insurance listing
mNGS	No product route in most systems; laboratory-accreditation regime instead	High	Inpatient bundle / self-pay / send-out laboratory service	Coverage decision (US non-coverage; China national price item created 2026)
tNGS	Emerging registration route	Moderate	A national price item exists under the 2026 guideline; the announcement publishes no rate (the per-50-pathogen figure circulated in trade press is not in the official text)	Under observation

Table S11.3. Pricing rules for the same technology classes across six systems: code level, official item name, clinical use and the unit on which the price is set.

System	Item code	Code level	Official item name	Clinical use	Pricing unit	Price	Evidence tier
United States	CPT 87631 / 87632 / 87633	National code, national rate	Respiratory virus, multiplex amplified probe technique, 3–5 / 6–11 / 12–25 targets	Multi-pathogen targeted respiratory detection	Target-count ladder (three bands, 3–25 targets); single-target codes are priced outside the ladder (87635 SARS-CoV-2 $51.31; 87556 M. tuberculosis $41.68) and the top band is flat	$142.63 / $218.06 / $416.78 (CLFS 2025 Q1)	A — CMS CLFS file, verified
United States	CPT 87507	National code, national rate	Gastrointestinal pathogen, multiplex amplified probe technique, 12–25 targets	Multi-pathogen targeted GI detection	Separate GI ladder; coincides with the respiratory ladder only at the top band	$416.78 — equal to 87633 and to the CNS code 87483, but the lower bands of the two	A — CMS CLFS file, verified

System	Item code	Code level	Official item name	Clinical use	Pricing unit	Price	Evidence tier
						ladders differ (GI 87505 $128.29 and 87506 $262.99 against respiratory $142.63 and $218.06), so the equality marks the ceiling of the ladder rather than pathogen-set neutrality	
Germany	GOP 32851 (ceiling GOP 32813)	National code, national rate	Indication-specific direct nucleic-acid pathogen detection, acute respiratory infection	Multi-pathogen targeted respiratory detection	Per pathogen: first + each additional, with a ceiling	€19.90 per pathogen; from the second service of GOP 32851 on the same treatment day, €7.23 per pathogen; ceiling €85.00 for GOP 32851 alone (ceiling item GOP 32813), not yet reached at ten pathogens (19.90 + 7.23 × 9 = 84.97) and binding from the eleventh (92.20). The decision states the ceiling as a bare amount and specifies no reference period for it	A — KVHB notice and 596th Bewertungsausschuss decision, verified
Germany	GOP 32853 (ceiling GOP 32814)	National code, national rate	Indication-specific direct nucleic-acid pathogen detection, acute gastrointestinal infection	Multi-pathogen targeted GI detection	Per pathogen, with a ceiling	€19.90 per pathogen; €7.23 per pathogen from the second service of GOP 32853 on the same treatment	A — KVHB notice, verified

System	Item code	Code level	Official item name	Clinical use	Pricing unit	Price	Evidence tier
						day; ceiling €85.00 for GOP 32853 alone (ceiling item GOP 32814), stated without a reference period	
Germany	GOP 32825	National code, national rate	MTC-complex NAAT	Single-pathogen detection (M. tuberculosis complex)	Per item	€61.40, billable since 2008	A — 596th Bewertungsausschuss decision, verified
France	RIHN/LAHN N156 (sister code V009 for HAS-assessed indications)	National code on a derogatory hors-nomenclature list; hospital funding, not a reimbursement tariff	Conventional or real-time qualitative multiplex PCR for 10 or more primer pairs (DNA/RNA)	Multi-pathogen targeted detection	Per PCR reaction ("par réaction PCR"), banded at 10 primer pairs (below the band: N131 qualitative, N155 quantitative)	No tariff published in the July 2025 LAHN: the 2025 list suppressed all item valorisations ("Suppression des tarifs"); €270 is the 2024 valorisation, carried in the 2025 file only as the "Valorisation maximale V2024" column of the modification log	A for item name, pricing unit, V009 duplication and tariff suppression (all verified in the LAHN 2025 primary file); B for the €270 figure itself, which the 2025 file records only as a superseded 2024 value
France	NABM acte 4102	National code, tariff = B coefficient × B letter-key value (€0.25 from 15 January 2024)	Mycobacteria molecular diagnosis	Single-pathogen detection (mycobacteria)	Per act	B 250	B — as recorded in S5-81, S5-82; not independently re-verified
Japan	D023-006	National code, national points	Influenza / Mycoplasma / RS virus nucleic acid detection	Single-pathogen detection (three pathogens share one band)	Per item, product-neutral	291 points each	A — MHLW procedure masters_20260501.csv, verified
Japan	D023-014	National code, national points	M. tuberculosis complex nucleic acid detection	Single-pathogen detection	Per item, product-neutral	410 points	A — MHLW master, verified
Japan	D023-021	National code,	M.	Resistance	Per item,	850 points	A — MHLW

System	Item code	Code level	Official item name	Clinical use	Pricing unit	Price	Evidence tier
		national points	tuberculosis complex rifampicin-resistance gene detection	variant as a separate item	product-neutral		master, verified
Japan	D023-022	National code, national points	Virus/bacteria multi-item simultaneous NAAT, SARS-CoV-2 NOT included; the same sub-band also carries M. tuberculosis rifampicin + isoniazid simultaneous resistance-gene detection	Multi-pathogen targeted detection	Band by panel content	963 points	A — MHLW master full-name field, verified
Japan	D023-022	National code, national points	Virus/bacteria nucleic acid AND drug-resistance-gene multi-item simultaneous detection, restricted by specimen type (sputum / bronchoalveolar lavage fluid)	Multi-pathogen targeted detection with resistance genes	Band by panel content and specimen type	1,273 points	A — MHLW master full-name field, verified
Japan	D023-023	National code, national points	Virus/bacteria multi-item simultaneous NAAT INCLUDING SARS-CoV-2 detection, listed as two entries by delivery route: outsourced (kensa itaku) and in-house (kensa itaku igai)	Multi-pathogen targeted detection including SARS-CoV-2	Band by panel content (SARS-CoV-2 included), with parallel entries for delivery route	1,350 points for both entries	A — MHLW master full-name field, verified
Japan	D023-024	National code, national points	Virus/bacteria multi-item simultaneous NAAT (cerebrospinal fluid)	Multi-pathogen targeted detection, CSF	Band by sub-item; this sub-band also carries a bacterial nucleic-acid plus resistance-gene item with no specimen restriction	1,700 points	A — MHLW master, verified

System	Item code	Code level	Official item name	Clinical use	Pricing unit	Price	Evidence tier
China	250403090-1N	PROVINCIAL code (Guangdong, Yue Yi Bao Fa 2024 No. 19); no national price code published	rpoB detection (product-neutral)	Single-pathogen resistance variant	Item-level; provincial execution	Sixth-batch national cap ≤CN¥300; resistance gene ≤CN¥130; two hospitals executed CN¥700 and CN¥650 (2024, self-paid)	B — provincial notices
China	2026 Guideline (662 main items, 114 surcharges, 7 extensions)	National ITEM DEFINITIONS; no national price code or rate published	National Guideline for Laboratory-Test Price Items (trial)	Establishes item scope and pricing unit	Per ci (one-to-one: the item covers a single specified analyte or one complete test run) or per xiang (one-to-many: each enumerated sub-analyte counts as one xiang) — but the Guideline expressly exempts "gene-testing and a small number of other price items" from this convention, and the announcement does not state what unit applies to them. Combined-testing (lianjian) discount by analyte count: ≤5 at 80%, ≤10 at 70%, >10 at 60%. Method-level differences are compensated through named surcharges rather than separate	Publishes no prices	A — NHSA announcement, verified

System	Item code	Code level	Official item name	Clinical use	Pricing unit	Price	Evidence tier
					main items		
England	—	No test-level code	No test-level price item	—	No test-level price	—	B — as recorded in S5; no NHS Payment Scheme document in the source pack

Note. Prices are not comparable across systems and the Price column should not be read as a cross-system price comparison: the entries differ in kind as well as in currency. They include national payment rates (United States), outpatient fee-schedule values (Germany), superseded hospital-funding valorisations (France, 2024), fee-schedule points at JP¥10 per point (Japan), and national caps and individual hospital execution prices (China); exchange rates, bundling conventions and insurance structures differ throughout. The comparable objects are the code level and the pricing unit. US descriptors and rates are taken verbatim from the CMS Clinical Laboratory Fee Schedule 2025 Q1 file (S5-13), and Japanese item names and points from the MHLW procedure master s_20260501.csv; both were re-verified against the primary files for this table. German rows were re-verified against the KV Bremen notice implementing the 596th Bewertungsausschuss decision (1 July 2022) and the decision text itself; that check corrected a ceiling-code error carried in earlier drafts, in which GOP 32813 was attached to the gastrointestinal item: 32813 is the ceiling for GOP 32851 (respiratory) and 32814 for GOP 32853 (gastrointestinal), both €85.00. Three further points of German billing mechanics are documented in the decision text and are easily misread. First, each ceiling is attached to a single fee item rather than to the respiratory, sexually transmitted and gastrointestinal items as a group, and the decision attaches no reference period to these ceilings, so we do not state one. Second, GOP 32852 is the exception to that pattern, sharing a €40.00 ceiling with GOP 32800 (herpes simplex virus nucleic-acid detection in immunodeficient patients). Third, the decision expresses both tiers in the same unit, "je Erreger" (per pathogen), and triggers the lower tier "ab der 2. Leistung am Behandlungstag": because GOP 32851 is itself valued per pathogen, the second service on a treatment day is the second pathogen billed under that item, so the tier turns on the count of pathogens billed that day, not on how many panels were physically run. French rows were re-verified against the official LAHN table (July 2025 version). The three values recorded for the French B letter-key are a time series rather than a discrepancy: €0.27 before 2023, €0.26 from February 2023 (avenant 11) and €0.25 from 15 January 2024 (avenant 12), the current value. Two French sources could not be retrieved directly and are carried at their original citation: the Monaco mirror of NABM acte 4102 and the 2016 RIHN reference list. One structural difference is visible in the code-level column: the United States, Germany, France and Japan each attach a national price or point value to a national code, whereas China's 2026 guideline unifies item definitions without publishing a national price code or rate, leaving code assignment and pricing to provinces. China therefore has no national base price against which its multiplex discount schedule operates. This reflects a division of competence between two layers rather than a single incomplete one: the 2026 guideline standardises item definitions, pricing units and discount rules nationally, while price-level calculation is assigned to the provinces. A separate clause permits (not directs) provincial authorities, when setting prices, to take the diagnosis-related technical value of a test into account in the price level; it concerns the pricing of diagnostic reporting, not the allocation of pricing competence. The

empty cells record design choices, not missing data. England prices nothing at the test level. These cells are left empty rather than imputed.

S12. Search and retrieval record

All web-based (non-journal) sources cited in this study were retrieved programmatically and archived. Every URL was logged with retrieval status, byte count and, where retrieval failed, the failure reason.

Table S12.1. Retrieval outcomes by source group.

Source group	Retrieved in full	Host-blocked	Dead link (404 / dead domain)	Article-level record only	Total
China official	45	1	3	0	49
United States official	28	11	0	4	43
Germany / France / EU	16	0	0	0	16
England / Japan / WHO	22	0	0	0	22
Vendor / think tank / press	115	17	5	8	145
Total	**226**	**29**	**8**	**12**	**275**

Retrieval rate: 226/275 = 82.2%.

Host-blocked is not absent. The 29 host-blocked URLs mark failures of the retrieval method, not evidence about whether the document exists; manual browser access is likely to succeed for most. The largest concentration is cms.gov (10 URLs: CLFS archives, LCD and NCD pages), which refuses programmatic access; one further US official item (an OIG report on oig.hhs.gov) failed on host unreachability and its content was recovered from the indexed official PDF text with corroborating coverage. The remaining 17 are vendor, think-tank and press sources behind Cloudflare challenges, login walls or paywalls.

Dead links [8] are annotated in the registers as "link dead as of 2026-11; values as accessed" with an alternative source where one exists.

Article-level only [12]: the retrieval returned a report *about* the document rather than the document itself; these sources are Tier B by construction.

Failures concentrated in the United States, not China. China official: 45/49 retrieved (91.8%); US official: 28/43 (65.1%); Germany/France/EU + England/Japan/WHO: 38/38 (100%). The asymmetry is technical (cms.gov's hard block), not a difference in how much the systems publish.

The full per-URL log (status, bytes, failure reason) accompanies this study in the evidence archive.

Supplementary references

S1. Peabody JW, Shimkhada R, Tong KB, Zubiller MB. New thinking on clinical utility: hard lessons for molecular diagnostics. Am J Manag Care. 2014;20[9]:750–6. PMID: 25365750. Available from: https://pubmed.ncbi.nlm.nih.gov/25365750/ (accessed 2026 Aug). S2. MedDeviceGuide. EU IVDR classification rules guide. 2026. Available from: https://meddeviceguide.com/blog/ivdr-classification-rules-guide (accessed 2026 Aug). S3. Medicines and Healthcare products Regulatory

Agency. The Innovative Devices Access Pathway (IDAP): pilot phase. London: MHRA/GOV.UK; 2024. Available from: https://www.gov.uk/government/publications/the-innovative-devices-access-pathway-idap (accessed 2026 Aug). S4. Pharmaceuticals and Medical Devices Agency. Sakigake review designation system: designated products list [in Japanese]. Tokyo: PMDA; 2026. Available from: https://www.pmda.go.jp/review-services/drug-reviews/0003.html (accessed 2026 Aug). S5. Ministry of Health, Labour and Welfare. Handling of conditional approval for medical devices and in-vitro diagnostics (Notification Iyakuki-Shin No. 0331-23) [in Japanese]. Tokyo: MHLW; 2026 Mar 31. Available from: https://www.mhlw.go.jp/web/t_doc?dataId=00tc9969&dataType=1&pageNo=1 (accessed 2026 Aug). S6. Pharnexcloud. Genskey Medical SARS-CoV-2 mNGS sequencing kit and software approved as Class III (registration nos. 20243401661/20243211580) [in Chinese]. 2024 Sept. Available from: https://www.pharnexcloud.com/zixun/yytrz_18307 (accessed 2026 Aug). S7. QIAGEN. QIAGEN receives European IVDR certification for QIAstat-Dx syndromic testing instruments and assays [press release]. Hilden: QIAGEN; 2024 Sept 26. Available from: https://corporate.qiagen.com/English/newsroom/press-releases/press-release-details/2024/QIAGEN-receives-European-IVDR-certification-for-QIAstat-Dx-syndromic-testing-instruments-and-assays/default.aspx (accessed 2026 Aug). S8. Lubbers BR, Dombrink I, Kalina T, Hofmans M, Bruun MS, Stanworth SJ, et al. Experience with IVDR implementation in three diagnostic laboratories. HemaSphere. 2023;7(4):e865. doi:10.1097/HS9.0000000000000865. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9995097/ (accessed 2026 Aug). S9. European Commission. Commission staff working document SWD(2025) 1050 and Council ST-16919-2025-ADD-2: targeted revision of the MDR/IVDR (Article 5(5) simplifications for IVDs). Brussels: European Commission; 2025. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52025SC1050 (accessed 2026 Aug). S10. Regulatory Affairs News. UK MHRA medical device guidance: health institution exemption conditions. 2025. Available from: https://www.regulatoryaffairsnews.com/post/uk-mhra-med-dev-guidances-legal-requirements-for-specific-medical-products-and-the-health-instituti (accessed 2026 Aug). S11. Dongwu Securities. Research report on the CFDA public consultation on the special approval procedure for innovative medical devices (revised draft) [in Chinese]. 2018. Available from: http://qccdata.qichacha.com/ReportData/PDF/203b7f3eead18503ce2c32b86fdb4455.pdf (accessed 2026 Aug). S12. Center for Medical Device Evaluation (CMDE), NMPA. Priority-approval application review results public notice (2025 No. 2) [in Chinese]. 2025 Feb 6. Available from: https://www.cmde.org.cn/xwdt/zxyw/ (accessed 2026 Aug). S13. National Health Commission. Transcript of the State Council joint prevention-and-control press conference, 3 February 2020 [in Chinese]. 2020-02-03. Available from: https://www.nhc.gov.cn/xcs/fkdt/202002/3b721c0120cf498f8568872032fa97ac.shtml (accessed 2026 Aug). S14. Tan JK, Servellita V, Stryke D, Kelly E, Streithorst J, Sumimoto N, et al. Laboratory validation of a clinical metagenomic next-generation sequencing assay for respiratory virus detection and discovery. Nat Commun. 2024. Available from: https://pubmed.ncbi.nlm.nih.gov/39532844/ (accessed 2026 Aug). S15. Karius, Inc. Karius Test receives FDA breakthrough device designation to aid in the diagnosis of infectious disease [press release]. Redwood City: Karius; 2024 May 16. Available from: https://kariusdx.com/resources/press-releases/karius-test-r-receives-fda-breakthrough-

device-designation-to-aid-in-the-diagnosis-of-infectious-disease (accessed 2026 Aug). S16. AnswersNews. Sakigake review designation system: list of designated products and development status [in Japanese]. 2021 Jul 5. Available from: https://answers.and-pro.jp/pharmanews/17132/ (accessed 2026 Aug). S17. VDGH, BVMed, Medical Mountains, SPECTARIS. MDR and IVDR slow innovation: new industry survey shows need for action [press release, in German]. Berlin: VDGH; 2025 Oct. Available from: https://www.vdgh.de/presse/pressemitteilungen/details/mdr-und-ivdr-bremsen-innovationen-neue-branchenumfrage-zeigt-handlungsbedarf-fuer-wettbewerbsfaehigkeit-und-versorgungssicherheit/ (accessed 2026 Aug). S18. Coste A, Egli A, Schrenzel J, Nickel B, Zbinden A, Lienhard R, et al. IVDR: analysis of the social, economic, and practical consequences of the application of an ordinance of the in vitro diagnostic ordinance in Switzerland. Diagnostics (Basel). 2023;13(18):2910. doi:10.3390/diagnostics13182910. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10529212/ (accessed 2026 Aug). S19. bioMérieux. bioMérieux submits 510(k) to US FDA for the latest versions of the BIOFIRE FILMARRAY gastrointestinal panels [press release]. Marcy-l'Étoile: bioMérieux; 2026. Available from: https://www.biomerieux.com/us/en/journalists/press-releases/FDA-submission-GI-panels.html (accessed 2026 Aug). S20. Ministère de la Santé. RIHN 2.0 official page (référencement des actes innovants hors nomenclature) [in French]. Paris: Ministère de la Santé; 2025. Available from: https://sante.gouv.fr/soins-et-maladies/qualite-securite-et-pertinence-des-soins/biologie-medicale/rihn (accessed 2026 Aug). S21. MSD Connect. RIHN 2.0 and equitable access to innovative diagnostic tests in oncology [in French]. 2025. Available from: https://www.msdconnect.fr/therapeutic-areas/pilote/articles-publications/rihn-2-0-acces-equitable-tests-diagnostiques-oncologie/ (accessed 2026 Aug). S22. m3.com. Simultaneous testing for COVID-19 and influenza now possible [in Japanese]. 2020 Jul 22. Available from: https://www.m3.com/news/iryoishin/801326 (accessed 2026 Aug); Falco Biosystems insurance-listing tracker [in Japanese]. Available from: https://www.falco.co.jp/business/cl_02_info4.html (accessed 2026 Aug). S23. National Center for Global Health and Medicine. Introduction to international expansion of medical care for enterprises [in Japanese]. Tokyo: NCGM; 2022. Available from: https://kyokuhp.ncgm.go.jp/activity/internal/consult/access_delivery_book.pdf (accessed 2026 Aug). S24. National Healthcare Security Administration; National Health Commission. Several measures to support high-quality development of innovative drugs (30 June 2025) [in Chinese]. Beijing: NHSA; 2025. Available from: https://policy.mofcom.gov.cn/claw/clawContent.shtml?id=103179 (accessed 2026 Aug). S25. National Healthcare Security Administration. Basic medical-insurance drug catalogue and commercial health-insurance innovative drug catalogue (first CHIIDL, 19 drugs) [in Chinese]. Beijing: NHSA; 2025 Dec 7. Available from: https://www.nhsa.gov.cn/art/2025/12/7/art_14_18972.html (accessed 2026 Aug). S26. Cailianshe. Beijing Medical Insurance Bureau trials carve-out payment for new drugs and new technologies [in Chinese]. 2022. Available from: https://www.cls.cn/detail/xk/966db78e2a4c29cde394c08151fe67e1 (accessed 2026 Aug). S27. Vedeng Medical (NMPA registration data). Xpert MTB/RIF registration certificate Guo Shi Yao Jian Xie (Jin) Zi 2014 No. 3401153 [in Chinese]. Available from: https://www.vedeng.com/zhucezheng/jk/129642.html (accessed 2026 Aug). S28. US Government Accountability Office. Medicare Laboratory Tests: Implementation of New Rates May Lead to Billions

in Excess Payments (GAO-19-67). Washington, DC: GAO; 2018. https://www.gao.gov/products/gao-19-67. S29. Dong W, Zhang J, Wang R, et al. Impact of DRG payment reform on laboratory-department test items [in Chinese]. International Journal of Laboratory Medicine. 2026 (online ahead of print). Available from: http://www.gjjyyxzz.com/gjjyyxzz/article/abstract/G20260420015 (accessed 2026 Aug). S30. Bundesministerium der Justiz. §6 KHEntgG (Krankenhausentgeltgesetz), statutory text. Available from: https://www.buzer.de/gesetz/507/v335618-2026-01-01.htm (accessed 2026 Aug); AOK. Neue Untersuchungs- und Behandlungsmethoden in der Somatik (NUB process; 2026 statistics). Available from: https://www.aok.de/gp/krankenhaus/verguetung-drg/nub (accessed 2026 Aug). S31. HAS. Avis n°2025.0027/AC/SEAP du 5 juin 2025 (VisioCyt® Bladder). https://www.has-sante.fr/jcms/p_3609098/fr/avis-n2025-0027-ac-seap-du-5-juin-2025-du-college-de-la-has-relatif-a-la-prise-en-charge-derogatoire-de-l-acte-de-cytologie-urinaire-digitalisee-et-assistee-par-intelligence-artificielle-impliquant-le-dispositif-medical-de-diagnostic-in-vitro-visiocyt-bladder-en-application-de-l-article-l-162-1-24-du-css; HAS. Avis n°2025.0046/AC/SEAP du 25 septembre 2025 (NOVAGRAY RILA Breast). https://www.has-sante.fr/jcms/p_3687752/fr/avis-n2025-0046-ac-seap-du-25-septembre-2025-du-college-de-la-has-relatif-a-la-prise-en-charge-derogatoire-du-test-novagray-rila-breast-en-application-de-l-article-l-162-1-24-du-css. S32. MTRC. The first IVD device included for coverage under the renewed RIHN 2.0 framework in France. 24 Apr 2026. https://mtrconsult.com/news/first-ivd-device-included-coverage-under-renewed-rihn-20-framework-france; APMnews. Conseil d'État partial suspension of VisioCyt coverage restriction. 18 June 2026. https://www.apmnews.com/depeche/0/437999/; MTRC. NABM update sets regular reimbursement for two NGS panels in France. 2 June 2026. https://mtrconsult.com/news/france. S33. XiFin. Cracking the Code: Mastering Z-Codes for Molecular and Genetic Tests. 2023-08-18. https://www.xifin.com/resource/blog-post/cracking-the-code-mastering-z-codes-for-molecular-and-genetic-tests/. S34. MTRC. NICE implemented a new HealthTech program in England. 17 Jul 2025. https://mtrconsult.com/news/nice-implemented-new-healthtech-program-england; Costello Medical. Opinions on the NICE HealthTech Programme Consultation. 7 Feb 2025. https://www.costellomedical.com/what-we-do/medtech/nice-healthtech-programme-consultation/; Hardian Health. How NICE is changing HealthTech adoption in NHS. 20 Apr 2026. https://www.hardianhealth.com/insights/nice-healthtech-nhs-adoption. S35. NHS England. Policy statement on access to the NHS England Medicines Procurement and Supply Chain (MPSC) framework prices. 2024-01-01. https://www.england.nhs.uk/long-read/policy-statement-on-access-to-the-nhs-england-medicines-procurement-and-supply-chain-mpsc-framework-prices/. S36. National Center for Tuberculosis Control and Prevention, China CDC. China tuberculosis prevention and control technical specifications (2020 edition) [in Chinese]. 2020. https://www.chinacdc.cn/jkyj/crb2/yl/fjh/jswj_fjh/202410/P020241010432930570191.pdf. S37. Du J, Shu W, Liu Y, Wang Y, Zhan Y, Yu K, et al. Multicenter feasibility study to assess external quality panels for molecular diagnostics for tuberculosis in China. Eur J Clin Microbiol Infect Dis. 2020;39(2):339–343. doi:10.1007/s10096-019-03730-9. S38. Ou X, Xia H, Wang S, Zhao B, Fan J, Song Y, et al. National proficiency testing of molecular diagnostics for tuberculosis and drug resistance detection — China, 2014–2019. China CDC Wkly. 2021;3(12):247–251. doi:10.46234/ccdcw2021.072. S39. bioMérieux. Universal Registration Document 2025 (BIOFIRE multiplex segment share and

installed base). Marcy-l'Étoile: bioMérieux; 2026. https://www.biomerieux.com (investor relations). S40. Qiagen. QIAstat-Dx receives approval in India (cumulative installed base >3,500 systems by end-2022) [press release]. 2024. https://s28.q4cdn.com/. S41. Karius, Inc. The Karius Test (clinical evidence and hospital adoption) [company information]. 2026. https://kariusdx.com. S42. Nikkei Medical. Pulmonary tuberculosis (guideline series; Xpert MTB/RIF insurance listing 2017, cobas MTB-RIF/INH listing 2023) [in Japanese]. 2022-05-19. https://medical.nikkeibp.co.jp/leaf/all/series/guideline/202205/574926.html.

S43. Benoit P, Brazer N, de Lorenzi-Tognon M, Kelly E, Servellita V, Oseguera M, et al. Seven-year performance of a clinical metagenomic next-generation sequencing test for diagnosis of central nervous system infections. Nat Med. 2024;30(12). doi:10.1038/s41591-024-03275-1. Available from: https://escholarship.org/uc/item/0fp8x3gp; cost review: https://pmc.ncbi.nlm.nih.gov/articles/PMC12658282/. S44. Zhang JY, Bender AT, Boyle DS, Drain PK, Posner JD. Current state of commercial point-of-care nucleic acid tests for infectious diseases. Analyst. 2021;146(8):2449–2462. doi:10.1039/d0an01988g. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8139840/ (Abbott ID NOW first CLIA-waived molecular platform, 2015; Roche cobas Liat waiver, 2015). S45. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention clinical practice guidelines: diagnosis of tuberculosis in adults and children. Clin Infect Dis. 2017;64(2):111–115. Available from: https://www.idsociety.org/practice-guideline/diagnosis-of-tb-in-adults-and-children/. S46. The diagnostic performance of the GenoType MTBDRplus version 2 line probe assay is equivalent to that of the Xpert MTB/RIF assay (routine high-throughput laboratory comparison). Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC3486209/. S47. ACON Laboratories. Flowflex COVID-19 Antigen Home Test — FDA 510(k) K230828 (first OTC rapid-antigen 510(k) clearance). 2023-11. https://www.510kdatabase.net/k230828/. S48. Lucira Health. Lucira COVID-19 & Flu Home Test — first OTC home-use molecular test authorisation (RT-LAMP). https://xtalks.com/lucira-gets-fda-authorization-for-first-otc-at-home-test-for-covid-19-and-flu-3395/. S49. Exact Sciences. Cologuard — FDA premarket approval P130017 (at-home stool-DNA collection with central-laboratory analysis). 2014. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p130017. S50. Becton Dickinson. Onclarity HPV Assay — PMA supplement P160037/S017 (self-collection in clinical settings, 2024). https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160037. S51. Teal Health. Teal Wand — first FDA-authorised at-home self-collection device for cervical-cancer screening (2025). https://www.factmr.com/report/self-sampling-cervical-kits-market. S52. Waters / Becton Dickinson. Onclarity HPV Self-Collection Kit — FDA clearance for at-home self-collection (2026). https://www.cancernetwork.com/view/fda-clears-at-home-hpv-self-collection-kit-to-expand-cervical-cancer-screening-access. S53. Quest Diagnostics. Quest Mobile — mobile phlebotomy service enabling at-home specimen collection (2023; in-home collection fee). https://www.prnewswire.com/news-releases/quest-diagnostics-launches-mobile-phlebotomy-service-enabling-convenient-at-home-specimen-collection-in-the-united-states-301983447.html. S54. Getlabs / Labcorp. Home diagnostic test collection service (2022; convenience fee from $25). https://www.biospace.com/labcorp-launches-convenient-home-diagnostic-test-collection-service-in-

collaboration-with-getlabs. S55. European Commission / MDCG. Guidance document MDCG 2020-16 rev. 3 (distinction between self-testing devices and specimen-receptacle devices). 2024. https://info.qbdgroup.com/en/regulatory-updates/new-mdcg-2020-16-revision-3-guidance-documents-released. S56. Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM). Sonderzulassung for lay-person COVID-19 antigen self-tests (first approvals 2021-02-24). https://www.pharmazeutische-zeitung.de/bfarm-laesst-die-ersten-selbsttests-zu-123996/. S57. AAZ. autotest VIH — CE 0459 mark for HIV self-testing (2015). https://www.prnewswire.co.uk/news-releases/autotest-vih-hiv-self-test-has-received-the-ce-0459-mark-501788991.html. S58. NHS England / DHSC. HIV self-sampling service freetesting.hiv; NHS HPV self-sampling kits in the national screening programme (2021 announcement; 2025 rollout). https://www.england.nhs.uk/2021/02/nhs-gives-women-hpv-home-testing-kits-to-cut-cancer-deaths/; https://www.noclor.nhs.uk/news-events/research-leads-roll-out-home-testing-kits-lifesaving-checks-against-cervical-cancer. S59. UK Government. Medical Devices (Coronavirus Test Device Approvals) Regulations 2021 (UKIA 2021/95). https://www.legislation.gov.uk/ukia/2021/95/pdfs/ukia_20210095_en.pdf. S60. Japan Self-Medication Industry Association. General-use (OTC) test products list. https://www.jsmi.jp/special/switch/kensa/index.html; MBL. GLINE-2019-nCoV Ag kit (general-use) OTC launch. 2022. https://www.jsr.co.jp/news/2022/20221212.html. S61. Demecal. Home blood-collection kit (MHLW approval 22600BZX00362000). https://demecal.shop/. S62. State Council Joint Prevention-and-Control Mechanism. Application scheme for COVID-19 antigen testing (trial), 2022 (No. 21); full scheme, 2022 (No. 118) [in Chinese]. https://www.nhc.gov.cn/yzygj/c100068/202203/1cebdf0216754716b465083fac707009.shtml; https://www.chinanews.com.cn/gn/2022/12-08/9910753.shtml. S63. State Food and Drug Administration. Measures for the supervision of online medical-device sales (Order No. 38), 2018 [in Chinese]. https://www.gov.cn/gongbao/content/2018/content_5277700.htm; National Health Commission. Notice on the "Internet + Nursing Services" pilot (Guo Wei Ban Yi Han [2019] No. 80) [in Chinese]. https://www.gov.cn/zhengce/zhengceku/2019-10/08/content_5436955.htm. S64. Caixin. JD Daojia quick test and Ditan Hospital home-sampling service pricing (2025-12-04) [in Chinese]. https://www.caixin.com/2025-12-04/102389534.html; Caixin Weekly. Meituan home quick-test service (2024-12-21) [in Chinese]. https://weekly.caixin.com/2024-12-21/102270601.html. S65. Medical Device Blue Book (November 2023): no home NAAT self-test product approved by NMPA [in Chinese]. https://www.toutiao.com/article/7299024591152874047/. S66. Çalkavur Ş, Kalkanlı OH, Ketenci T, Kavas N, Yılmaz Çelebi M, Bayram A, et al. Effectiveness of a blood culture bundle in reducing contamination rates in a neonatal intensive care unit. Turk J Pediatr. 2025. doi:10.24953/turkjpediatr.2025.5613. PMID: 40466670. S67. DeVincenzo JP, Guyton C, Rea H, Elmore E, Patel S, Wynn L, et al. Molecular detection and quantification of pertussis and correlation with clinical outcomes in children. Diagn Microbiol Infect Dis. 2013. doi:10.1016/j.diagmicrobio.2012.12.015. PMID: 23490009. S68. Ma J, Dong T, Li F, He C, Li B, Liu Z. Legionellosis: global epidemiology and current perspectives on diagnosis and treatment. Infect Drug Resist. 2026. doi:10.2147/IDR.S603565. PMCID: PMC13075499. S69. Azzato F, Elieh L, Brizuela R, Hor E, Raios K, Williams E, et al. Performance assessment of five Legionella urinary antigen tests for Legionella pneumophila and Legionella longbeachae. Pathology. 2026.

doi:10.1016/j.pathol.2026.05.001. PMID: 42471296. S70. Clancy CJ, Nguyen MH. Non-culture diagnostics for invasive candidiasis: promise and unintended consequences. J Fungi (Basel). 2018;4(1):27. doi:10.3390/jof4010027. PMCID: PMC5872330. S71. Tomazin R, Matos T. Laboratory diagnostics of aspergillosis: present state and future directions. J Fungi (Basel). 2026;12(5):379. doi:10.3390/jof12050379. PMCID: PMC13208596. S72. Abramovich T, Korem M, Kuint R, Michael-Gayego A, Moran-Gilad J, Olshtain-Pops K. The role of polymerase chain reaction (PCR) and quantification cycle values in the diagnosis of Pneumocystis jirovecii pneumonia. J Fungi (Basel). 2025;11(8):557. doi:10.3390/jof11080557. PMCID: PMC12387715. S73. Mycoplasma pneumoniae respiratory tract infections in children: when and how to diagnose and treat. Breathe (Sheff). 2025;21(4):250046. doi:10.1183/20734735.0046-2025. PMCID: PMC12519950. S74. Horne DJ, Zifodya JS, Shapiro AE, Church EC, Kreniske JS, Kay AW, et al. Xpert MTB/RIF Ultra assay for pulmonary tuberculosis and rifampicin resistance in adults and adolescents. Cochrane Database Syst Rev. 2025;CD009593.pub6. doi:10.1002/14651858.CD009593.pub6. PMCID: PMC12305759. S75. Kohli M, Schiller I, Dendukuri N, Dheda K, Denkinger CM, Schumacher SG, et al. Xpert MTB/RIF assay for extrapulmonary tuberculosis and rifampicin resistance. Cochrane Database Syst Rev. 2018;CD012768.pub2. doi:10.1002/14651858.CD012768.pub2. PMCID: PMC6513199. S76. Xpert MTB/RIF assay for diagnosis of extrapulmonary tuberculosis in children: a systematic review and meta-analysis. BMC Infect Dis. 2020;20:9. doi:10.1186/s12879-019-4745-1. PMCID: PMC6945699. S77. Waites KB, Talkington DF. Epidemiology, clinical manifestations, pathogenesis and laboratory detection of Mycoplasma pneumoniae infections. FEMS Microbiol Rev. 2008;32(6):956–73. PMID: 18754792. S78. Reporting macrolide-resistant Mycoplasma pneumoniae: a diagnostic obligation? J Clin Microbiol. 2026. PMCID: PMC13556224. S79. Age and hypoalbuminemia independently predict pulmonary consolidation in children with 23S rRNA A2063G-mutant Mycoplasma pneumoniae infection. Front Pediatr. 2026;14:1773231. doi:10.3389/fped.2026.1773231. PMCID: PMC13233452. S80. Chartrand C, Leeflang MMG, Minion J, Brewer T, Pai M. Accuracy of rapid influenza diagnostic tests: a meta-analysis. Ann Intern Med. 2012;156(7):500–11. PMID: 22371850. S81. Chartrand C, Tremblay N, Renaud C, Papenburg J. Diagnostic accuracy of rapid antigen detection tests for respiratory syncytial virus infection: systematic review and meta-analysis. J Clin Microbiol. 2015;53(12):3738–49. PMCID: PMC4652120. S82. Pediatric respiratory syncytial virus diagnostic testing performance: a systematic review and meta-analysis. J Infect Dis. 2023;228(11):1516–27. PMCID: PMC10681870. S83. Public research investment in the development of the GeneXpert platform (approximately US$252 million across documented grants). PLoS One. 2021. PMID: 34464413. S84. Decentralised versus hub-and-spoke molecular tuberculosis diagnostics: cost per patient started on treatment within seven days (Mozambique US$853 hub versus US$690 decentralised; Tanzania US$596 versus US$592; increment per additional patient US$403 / US$580). PLOS Glob Public Health. 2025. PMID: 40446169. S85. Extended cost-effectiveness analysis of decentralised tuberculosis diagnostics. BMJ Glob Health. 2025. PMID: 41260888.