WHITE PAPER

The Gross-to-Net Squeeze:

How Physician-Led Patient Education Reduces GTN Erosion and Recovers Net Revenue at Scale

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For Pharma Commercial Operations, Patient Services, and Market Access Teams

ABSTRACT

The pharmaceutical industry's gross-to-net (GTN) challenge is widely understood as a contracting and pricing problem — one fought at the rebate table with PBMs and payers. But a $356 billion annual gap between list and net revenue cannot be closed by negotiation alone. A significant and systematically overlooked contributor to GTN erosion is patient abandonment: prescriptions that are written, rebate obligations that are triggered, and drugs that are never taken. This white paper presents a demand-side GTN optimization framework and demonstrates how physician-led patient education — delivered at scale via Hoot Health's platform — directly reduces abandonment, accelerates treatment initiation, and recovers net revenue that contracting strategies alone cannot capture.

What Is Gross-to-Net? Understanding the Fundamental Problem

The gross-to-net problem is one of the most consequential — and least understood — dynamics in the entire U.S. drug pricing system. At its core, it is the gap between what a drug officially costs (the list price) and what a manufacturer actually receives after all the discounts, rebates, fees, and deductions are stripped away.

THE GROSS-TO-NET FORMULA

Gross Revenue (WAC List Price) − Rebates − Discounts − Chargebacks − Fees − Returns = **Net Revenue**

The problem is not just accounting complexity. It is that the gap between those two numbers has grown so large that it is distorting drug pricing, warping incentives across the entire supply chain, and — most painfully — falling hardest on patients and manufacturers alike.

How the System Works — and How It Broke

The key players driving this gap are Pharmacy Benefit Managers (PBMs) — middlemen who manage drug benefits on behalf of insurers and employers. PBMs leverage large numbers of patients to secure drug manufacturer discounts, but their increasingly opaque practices distort pricing and premiums, including by incentivizing higher list prices for rebate maximization.

THE PERVERSE PBM INCENTIVE LOOP

1	Manufacturers set a high list price (WAC) to create room for rebate negotiation.
2	PBMs negotiate large rebates in exchange for preferred formulary placement — the right for a drug to be recommended to patients.
3	PBMs retain a portion of those rebates as profit, creating a direct incentive to maximize rebate size.
4	Manufacturers raise list prices further to fund even larger rebates to maintain their formulary position.
5	Patients — whose copays are based on list price, not net price — pay more out of pocket despite manufacturers receiving less.

The real driver of the GTN bubble was not high launch prices — it was the pharmaceutical industry's ability to raise drug prices year after year, enabled by loopholes in PBM contracts. PBMs often profited from list price increases through price increase rebates, which incentivized drugmakers to raise prices within negotiated thresholds, contributing to widespread inflation in drug costs.

How Big Is This Problem? The Numbers

The scale of the GTN problem is genuinely staggering — and it has grown relentlessly for over a decade.

$356B
GTN reductions for all brand-name drugs in 2024 — larger than the GDP of most countries

47%
Average discount rate reported by Janssen across its portfolio (2018 Transparency Report)

43.7%
Average discount rate reported by Merck in its 2019 U.S. Pricing Transparency Report

In 2024, drugmakers sold their products for roughly half of the list price. Gross-to-net differences in price changes ranged from -12.8% to +6.3% across the nine largest manufacturers. KPMG has observed average GTN ratios of 55% across pharma SKUs, with up to 35% of products entirely unprofitable after discounts are applied.

Real-World Examples: The GTN Problem in Practice

DRUG / COMPANY	THE SITUATION	THE GTN REALITY	THE LESSON
Remicade (J&J)	Blockbuster biologic facing biosimilar competition from 2016 onward	List-to-net discount of 54% as of January 2020 — discount increased 27 percentage points between 2016 and 2020 alone	Biosimilar competition forces ever-deeper rebates, compressing net revenue even as list price holds steady
Daraprim (Turing)	Martin Shkreli raised price 5,000% — from $13.50 to $750 per pill overnight	Annual treatment cost went from under $5,000 to nearly $275,000. Drug remained broadly covered through PBM open-enrollment loopholes	The same PBM infrastructure that enables rebate inflation also enabled one of the most notorious price hikes in pharma history

DRUG / COMPANY	THE SITUATION	THE GTN REALITY	THE LESSON
Insulin (Sanofi et al.)	List prices for insulin attracted intense public and political scrutiny over rising drug costs	Sanofi characterized the criticism as misleading — net prices were actually falling, making insulin less expensive for payers	List price theater vs. net price reality — patients paid high copays based on list price while manufacturers cited falling net prices
Specialty Biologics (RA/MS)	Drugs for rheumatoid arthritis, multiple sclerosis, and oncology face maximum PBM leverage due to competition	These categories carry the largest GTN gaps in the industry — discounts and rebates routinely exceed 40-50% of list price	The more competitive the therapeutic area, the deeper the required rebate — and the wider the GTN gap

Who Gets Hurt Most?

The cruelest irony of the GTN bubble is that the people it harms most are the patients the system is ostensibly designed to serve. Patients are still fully or partially exposed to the undiscounted list price of their prescriptions — paying coinsurance based on WAC, not net price. Plans routinely shift out-of-pocket costs to patients with chronic conditions who utilize highly rebated prescriptions.

Pharmaceuticals are the only part of the U.S. healthcare system in which the difference between list and net prices is monetized as rebates and redistributed via intermediaries to payers — rather than passed directly to patients at the pharmacy counter.

KEY INSIGHT

The gross-to-net problem is a shadow pricing system built on top of the official one. List prices are theater. Net prices are reality. And the $356 billion annual gap between them funds a complex ecosystem of intermediaries while leaving patients exposed to artificially inflated out-of-pocket costs — and manufacturers facing products that are technically unprofitable despite high sticker prices.

The Gross-to-Net Problem: A Brief for Commercial Operations Leaders

For pharmaceutical commercial operations and patient services teams, gross-to-net (GTN) management has become one of the defining financial challenges of the decade. The GTN ratio — the difference between a drug's Wholesale Acquisition Cost (WAC) and the net revenue a manufacturer actually retains after rebates, discounts, chargebacks, and mandatory program deductions — has reached historic levels of erosion.

$356B
Total brand-name GTN reductions in 2024(Drug Channels Institute)

55%
Average GTN ratio across pharma SKUs (KPMG)

35%
of pharma SKUs unprofitable due to discount pressure (KPMG)

The drivers of this erosion are well-documented: PBM rebate demands, Medicaid mandatory rebate obligations, 340B program pricing, formulary access concessions, and distribution fees. Commercial operations teams spend enormous resources modeling, forecasting, and negotiating these variables.

What is far less discussed — and far less acted upon — is the demand-side contribution to GTN erosion: the revenue that disappears not because of a rebate, but because a patient never initiated therapy, or abandoned it before generating meaningful net revenue.

KEY INSIGHT

Every patient who abandons therapy after a prescription is written represents gross revenue that was never converted to net revenue — a rebate obligation potentially triggered with zero commercial return.

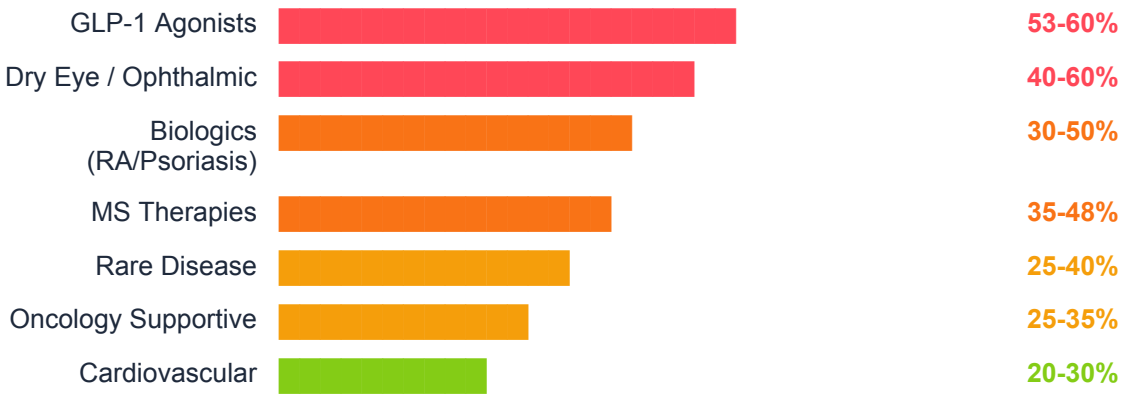
FIGURE 1: The Growing GTN Bubble — Annual Gross-to-Net Reductions (Brand-Name Drugs)

Source: Drug Channels Institute 2025 Economic Report on U.S. Pharmacies and Pharmacy Benefit Managers. Bar scale indexed to 2024 peak of $356B.

The Hidden GTN Driver: Patient Abandonment

In the standard GTN model, manufacturers focus on the spread between WAC and net realized revenue from drugs that are dispensed. But there is a pre-dispensing loss layer that rarely appears in GTN analyses: prescription abandonment at the point of initiation.

FIGURE 2: Year-1 Patient Abandonment / Discontinuation Rates by Therapeutic Area



Sources: JAMA Cardiology (GLP-1), peer-reviewed adherence literature by therapeutic area. Ranges reflect published study variation.

FIGURE 3: Annual Revenue at Risk from Abandonment — Per 100,000 New Prescriptions

THERAPEUTIC AREA	LIST PRICE ($/month)	AVG NET ($/month)	YEAR-1 ABANDONMENT	MONTHS LOST per 100K Rxs	NET REVENUE AT RISK
GLP-1 Agonists	$1,000	$450	57%	3.4M months	**$1.53B**
Biologics (RA)	$3,500	$1,400	42%	5.0M months	**$7.04B**
Dry Eye (Specialty)	$600	$270	50%	3.0M months	**$810M**
Rare Disease	$8,000	$3,200	33%	4.0M months	**$12.8B**
MS Therapies	$7,000	$2,800	44%	5.3M months	**$14.8B**
Cardiovascular	$400	$180	25%	1.5M months	**$270M**

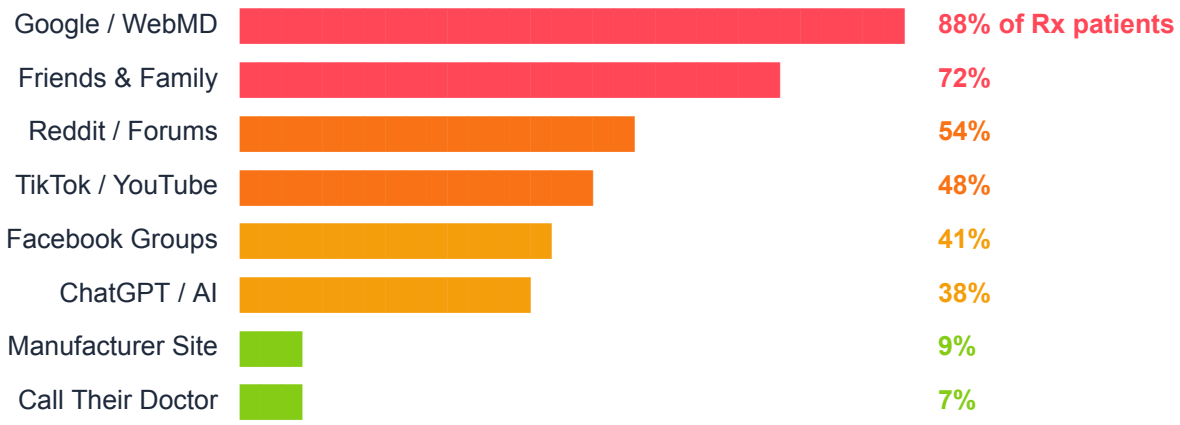
Note: Net revenue at risk calculated as (abandonment rate × avg months abandoned × net revenue/month × 100,000 patients). Illustrative model using published abandonment ranges.

The Root Cause: Patient Confusion at the Point of Care

Why do patients abandon therapy at such high rates? The answer is rarely purely financial. Research consistently shows that the primary drivers of non-initiation and early discontinuation are confusion, fear, and the absence of physician reinforcement after the clinical visit.

The average physician consultation is 7 minutes. Patients leave with fragments of information — and then self-educate through unreliable channels. The physician's voice, the most trusted source for treatment decisions, disappears the moment the patient walks out the door.

FIGURE 4: Where Patients Research Their Prescription After Leaving the Clinic



Source: Health information seeking behavior research (Pew Research Health, JAMA Internal Medicine). Values illustrative of published research ranges.

THE TRUST GAP

Patients trust their physician above all other sources — yet only 7% call their doctor when confused post-visit. The rest turn to sources with no accountability for adherence outcomes. Hoot bridges this gap by delivering the physician's own voice directly to the patient's phone.

The Hoot Solution: Physician-Led Patient Education as a GTN Strategy

Hoot Health is an AI-powered patient education platform that extends the physician's voice beyond the clinical visit through automated, personalized video content delivered via SMS and email. Built on the insight that patients trust their doctor above all other sources, Hoot delivers physician-recorded (or AI-generated physician avatar) content at the precise moments when patients are most vulnerable to confusion, hesitation, and abandonment.

The Five GTN Impact Mechanisms

#	MECHANISM	GTN LEVER	REVENUE IMPACT
1	Reduce Pre-Fill Abandonment	Initiation rate improvement	Converts written Rx to first fill — recovers 100% of at-risk gross revenue per non-initiating patient
2	Accelerate Treatment Start	Revenue timing (cash flow)	7x faster initiation — earlier net revenue recognition, reduces margin compression from fixed rebate obligations
3	Improve 12-Month Adherence	Revenue volume (LTV)	3x adherence benchmark — each retained patient generates 4-9 additional months of net revenue vs. baseline
4	Reduce Product Returns	Return/waste reduction	Lower confusion-driven abandonment = fewer mid-supply returns = cleaner GTN deductions
5	Formulary Differentiation	Reduce rebate concession depth	Outcomes data shifts payer negotiations — adherence value offsets formulary rebate requirements over time

Figure 5: Hoot's five GTN impact mechanisms and the commercial lever each activates.

Modeling the GTN Impact: A Framework for Commercial Operations

Commercial operations and finance teams require a quantifiable model for evaluating any GTN optimization investment. The tables below provide a multi-scenario framework across brand sizes and net revenue levels.

FIGURE 6: Core GTN Recovery Model — Baseline vs. Hoot (100K Annual Prescriptions, $500/mo Net)

VARIABLE	BASELINE (NO HOOT)	WITH HOOT
Annual new prescriptions	100,000	100,000
Year-1 abandonment rate	55%	38% (−15% recovery)
Net revenue per patient/month	$500	$500
Avg months on therapy (Year 1)	5.4 months	7.7 months
Net revenue per retained patient	$2,700	$3,850
Total net revenue (Year 1)	$121.5M	**$173.3M**
Incremental net revenue recovered	—	**+$51.8M**

Figure 6: Conservative model assuming 15% patient recovery rate. Hoot's 3x adherence benchmark implies larger impact at higher-abandonment brands.

FIGURE 7: Net Revenue Recovery Scenarios by Brand Size and Price Point

SCENARIO	ANNUAL Rxs	NET REV/mo	ABANDON RATE	PATIENTS RECOVERED (15%)	AVG MONTHS ADDED	NET REV RECOVERED
GLP-1 Mid-Brand	100K	$450	57%	8,550	+4.5 mo	**$17.3M**
Biologic (RA)	50K	$1,400	42%	3,150	+5.2 mo	**$22.9M**
Dry Eye Specialty	200K	$270	50%	15,000	+3.8 mo	**$15.4M**
Rare Disease	10K	$3,200	33%	495	+6.0 mo	**$9.5M**
MS Therapy	25K	$2,800	44%	1,650	+5.5 mo	**$25.4M**
Large GLP-1 (Ozempic-scale)	1M	$450	57%	85,500	+4.5 mo	**$173.1M**

Figure 7: Illustrative scenarios using conservative 15% patient recovery assumption and published abandonment rates. Actual impact varies by brand, therapeutic area, and program maturity.

FIGURE 8: Projected Net Revenue Recovery by Scenario ($ Millions)

Figure 8: Bar scale indexed to Large GLP-1 scenario at $173.1M. All scenarios based on 15% patient recovery rate with conservative adherence assumptions.

The GTN Waterfall: Where Revenue Disappears — and Where Hoot Intervenes

The following waterfall table traces the journey of $1 billion in gross pharmaceutical revenue to final net revenue — and identifies precisely where Hoot's platform creates intervention value.

FIGURE 9: GTN Revenue Waterfall — $1B Gross Revenue Brand

REVENUE LAYER	DEDUCTION TYPE	BASELINE AMOUNT	WITH HOOT	HOOT IMPACT
Gross Revenue (WAC)	Starting point	**$1,000M**	$1,000M	Baseline
PBM/Commercial Rebates	Contractual	−$270M	−$270M	No change*
Medicaid Mandatory Rebates	Statutory	−$150M	−$147M	−$3M benefit
340B Program Discounts	Statutory	−$80M	−$80M	Minimal change
Distribution / Chargeback Fees	Operational	−$40M	−$39M	−$1M benefit
Product Returns (Abandonment)	Avoidable	−$35M	−$24M	−$11M benefit
Pre-Fill Abandonment Loss	Avoidable	−$120M	−$78M	−$42M benefit
Early Discontinuation Loss	Avoidable	−$105M	−$70M	−$35M benefit
NET REVENUE RETAINED	After all deductions	**$200M**	**$289M**	**+$89M (44.5%)**

*Figure 9: Illustrative waterfall for a $1B gross revenue brand. Hoot impacts the avoidable deductions (highlighted). *Commercial rebates not reduced by Hoot but formulary differentiation strategy may reduce long-term rebate depth.*

Strategic Fit: Where Hoot Creates the Greatest GTN Leverage

Not all brands face equivalent GTN risk from patient abandonment. Hoot's GTN optimization impact is greatest in therapeutic contexts with high list prices, complex initiation, and chronic therapy requirements.

FIGURE 10: GTN Optimization Fit Score by Therapeutic Area

THERAPEUTIC AREA	HIGH LIST PRICE	COMPLEX INITIATION	CHRONIC (12+ mo)	HIGH COMPETITION	STRONG REBATE PRESSURE	HOOT FIT SCORE
GLP-1 / Metabolic	●●●	●●●	●●●	●●●	●●●	★★★★★
Biologics (RA/Psoriasis)	●●●	●●●	●●●	●●●	●●●	★★★★★
Rare Disease	●●●	●●●	●●	●	●●●	★★★★☆
MS / Neurology	●●●	●●●	●●●	●●	●●●	★★★★☆
Dry Eye / Ophthalmic	●●	●●●	●●●	●●	●●	★★★★☆
Oncology Supportive	●●●	●●●	●●	●	●●	★★★☆☆
Cardiovascular	●	●	●●●	●●●	●●	★★★☆☆

Figure 10: Relative fit scoring across GTN optimization criteria. ●●● = high impact factor; ★★★★★ = strongest Hoot GTN leverage.

Hoot vs. Traditional Patient Support: The ROI Comparison

Pharmaceutical companies currently invest billions annually in patient support programs. The question for commercial operations leaders is not whether to invest in patient support — it is which investments produce measurable GTN outcomes.

FIGURE 11: Patient Support Program Comparison — GTN Impact and ROI

PROGRAM TYPE	ANNUAL COST RANGE	PHYSICIAN VOICE	INITIATION LIFT	ADHERENCE LIFT	FORMULARY VALUE	NET REVENUE ROI
HOOT HEALTH	$150K–$350K	✓ Direct	High	3x Benchmark	Strong	**40:1–80:1**
Hub / Nurse Educator	$2M–$15M	Indirect	Moderate	Moderate	Moderate	8:1–15:1
Copay Card Program	$5M–$50M	None	High	Low	Low	5:1–12:1
Digital Adherence App	$1M–$5M	None	Low	Moderate	Low	3:1–8:1
Call Center / PSP	$3M–$20M	Indirect	Low	Low	Low	2:1–6:1
Patient Brochures/ Print	$500K–$2M	None	Minimal	Minimal	None	1:1–2:1

Figure 11: Comparative assessment of patient support program types on key GTN metrics. ROI estimates based on industry benchmarks and Hoot platform performance data.

THE HOOT DIFFERENCE

Pharma patient services programs often measure success by program enrollment and outbound contact rates. Hoot measures success by prescription fill rates, 30/60/90-day refill completion, and physician-reported patient confidence — the metrics that directly translate to GTN outcomes.

Implementation: How Pharma Companies Partner with Hoot

Hoot Health works with pharmaceutical manufacturers through two primary partnership models, each designed to fit different commercial structures and brand lifecycle stages.

FIGURE 12: Hoot Pharma Partnership Models

PROGRAM	CONTENT TYPE	DEPLOYMENT	LAUNCH TIME	PRICE RANGE	BEST FOR
Branded PatientEducation Program	MRL-reviewed physician video	Hoot physician network + patient SMS/email	60–90 days	$150K–$350K/yr	Brands with active patient services investment
Medical AffairsContent Deployment	Existing approved video content	Hoot delivery infrastructure	30–45 days	$75K–$200K/yr	Brands with strong medical affairs content

Figure 12: Hoot pharma partnership structures. Custom pricing available for multi-brand and enterprise agreements.

Conclusion: The Next Frontier of GTN Optimization

The pharmaceutical industry has spent a decade trying to manage the gross-to-net bubble through contracting strategy. The result is a $356 billion annual gap that continues to grow despite sophisticated rebate modeling, payer negotiation, and formulary access investment.

The missing dimension is the patient. Every dollar of list price that is never converted to a dispensed, adherent prescription is a dollar of gross revenue that disappears before GTN calculations even begin. This pre-revenue abandonment is not a clinical problem or a patient services problem. It is a commercial problem — and it requires a commercial solution.

Hoot Health provides that solution by deploying the most trusted voice in healthcare — the prescribing physician — at the moments when patients are most likely to abandon therapy. The result is measurable improvement in initiation rates, adherence, and long-term net revenue per patient.

For pharma commercial operations leaders, patient services directors, and market access teams searching for new approaches to the gross-to-net challenge, Hoot Health represents a fundamentally different kind of intervention — one that creates net revenue by protecting it, before it is lost.

Request a Patient Confusion Audit for Your Brand

Hoot Health offers complimentary Patient Confusion Audits for pharma commercial and patient services teams. We map your current patient journey, identify the highest-value abandonment intervention points, and model the potential net revenue recovery for your specific brand.

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HOOT HEALTH

Physician-Led Patient Education. Delivered Automatically. At Scale.