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STAKEHOLDER SUMMIT. Coverage from the AJMC® gathering of 4 community oncology leaders, who discussed what implementing the Enhancing Oncology Model might look like in everyday practice and what features they would change, [SP506](#).

NCCN PATHWAYS. Roy Beveridge, MD, of Avalere Health discusses the importance of clinical pathways in selecting therapies in non-small cell lung cancer, and the use of pathways and guidelines from the National Comprehensive Cancer Network (NCCN), [SP512](#).

IVBM. Full coverage from our Institute for Value-Based Medicine® (IVBM) sessions with Oncology Consultants of Houston, Rocky Mountain Cancer Centers, Astera Cancer Care of New Jersey, and Vanderbilt-Ingram Cancer Center, [SP516-SP531](#).

DRUG PRICING COMPLEXITY. Brian Corvino, MBA, of Deloitte Consulting, LLP, offered the Community Oncology Alliance Payer Exchange Summit an overview of how the surge of innovation in oncology and resulting drug approvals have dominated the biopharmaceutical sector, [SP542](#).

NEW TO NASHVILLE. Our exclusive coverage from the inaugural OneOncology Physician Leadership Conference in Nashville, Tennessee, featured policy highlights from former Obama administration official Kavita Patel, MD, MS, and Adam Boehler, the former director of the Center for Medicare and Medicaid Innovation, [SP554-SP556](#).

THERAPEUTIC ADVANCES

Data Sharing From Cancer Drug Trials Falls Short of Promises, Study Authors Say

Mary Caffrey

THE PRECISION MEDICINE ERA promises treatments for cancer and other diseases will be increasingly tailored to a patient's individual traits. That may mean finding therapies that target certain genes or proteins or using data to learn which regimens work best given a patient's sex, ethnicity, age, or other factors.

As study results are reported, some answers seem clear; others, less so. Results of a study published in May found that women in cancer clinical trials are far more likely than men to experience severe adverse events (AEs) from drug toxicity.¹ Meanwhile, investigators of a study published in 2021 asked whether different pharmacokinetic responses were due to ethnic differences or to factors such as age, diet, and other medicines patients were taking.²

One thing is certain: answering these questions requires more data, not less. And that's why investigators from Australia sounded the alarm with results from an audit published in the September issue of *JAMA Oncology*. They found that individual participant data (IPD) from 55% of the cancer clinical trials that led to FDA approvals over a 10-year period are not available to independent investigators, despite a 2014 pledge from the pharmaceutical industry to improve data transparency.³

Lead author and PhD candidate Natansh D. Modi, BPharm; and senior author Ashley M. Hopkins, PhD, both of the College of Medicine and Public Health at Flinders University in Adelaide, Australia, told *Evidence-Based Oncology™ (EBO)* in an interview how the audit was triggered by their individual frustrations in seeking trial data for other projects.

INTERVIEW

COA's Bo Gamble: Slowing Down, but Not Stepping Away From Bringing Quality to Cancer Care

Interview by Mary Caffrey

BO GAMBLE, THE LONGTIME DIRECTOR of strategic practice initiatives at the Community Oncology Alliance (COA) and a go-to person for all things value-based care, will soon step down from his full-time role. Gamble was honored on October 24, 2022, at the COA Payer Exchange Summit in Tysons Corner, Virginia, for his service to the organization and his work to bring transformation to cancer care.

Gamble, who joined COA full-time in May 2011, will be transitioning to part-time status on January 1, 2023, when he will begin mentoring 2 new staff members taking on COA initiatives. Gamble will also work with the American Society of Clinical Oncology (ASCO) to implement the Oncology Medical Home (OMH) ASCO Patient-Centered Cancer Care Certification (APC4) program, a joint project of ASCO and COA.¹ Gamble helped develop the program using OMH standards and a systemic evidence review; the review panel toured cancer centers to evaluate how well they met the standards.

COMMENTARY

PBM Fees Put the "GER" in Danger for Specialty Pharmacies

Darrell L. Willyard, PharmD; and Alexis V. Fanshier, BA

SHOULD MEDICALLY INTEGRATED specialty pharmacies (MIPs) be forced to lose money in order to serve their patients? What if a pharmacy would lose more than \$10,000 by filling a single prescription? Many MIPs face this situation because of a direct and indirect remuneration (DIR) fee known as a generic effective rate (GER).

Data Sharing From Cancer Drug Trials Falls Short of Promises, Study Authors Say

MARY CAFFREY

CONTINUED FROM COVER

Although the authors say data availability has improved, some meta-analyses are impossible because data for certain top-selling drugs are off limits. Their paper pointed specifically to nivolumab (Opdivo), pembrolizumab (Keytruda), and pomalidomide (Pomalyst). The audit found that 90% of the trial data for these 3 therapies were unavailable. The authors noted that this trio of therapies generated \$30 billion in revenue in 2020.⁴

The top reasons given when trial sponsors were asked why IPD were ineligible for sharing was that the trial was ongoing (53%), or that the trial was complete but the IPD were still under embargo (21%). In their paper and during the *EBO* interview, Modi and Hopkins rejected these reasons, stating that, given the level of activity in cancer drug development, sharing anonymized IPD is essential for robust research on newer anticancer medicines.

“The concerning aspect of what we found in our study was that some of the most-used medicines—those having the most money spent on their use—were found to have the least transparency in the data,” Hopkins said. “It is a little bit concerning that when medicine seems to be a high-profit kind of medicine, it hasn’t been set up in a way to share that data.”

This fact is of concern to philanthropic groups that Hopkins works with because when drugs are new it may be too early for these entities to find real-world, postmarketing evidence to guide decision-making. But the greater concern with IPD sharing is that evidence be available for secondary analyses and to design new trials, he said.

Support for the audit came from author fellowships or grants from Cancer Council Australia and the National Health and Medical Research Foundation. Two coauthors on the audit reported unrelated research support from Pfizer.

Multiple Requests for Data Status

The audit stemmed from Hopkins’ 2018 research on data availability.⁵ Attempts to gain access were met with statements that IPD were ineligible for release, which Hopkins noted was in direct conflict with the companies’ stated policies.

Modi’s research involved the use of artificial intelligence in treating patients with breast cancer—another project that required requests for clinical trial data. “What we were getting in responses was, ‘These data are not eligible to share.’ And then we said, ‘Hold on, this doesn’t really match your data-sharing policies,’” he said.

In the interview, Modi described audit methods, which first required identifying all anticancer medicines approved by the FDA between January 1, 2011, and June 30, 2021. Using product labels accessed through the National Institutes of Health DailyMed database, the authors compiled a list of all clinical trials with results that were used in the approval process for the therapies. This resulted in a list of 304 trials for 115 different therapies. All trials were registered on ClinicalTrials.gov.

Trial start and completion dates were of interest because the authors noted those that started after January 1, 2014. This was the effective date of an agreement on transparency for IPD, which was developed jointly by industry trade groups, the Pharmaceutical Research and Manufacturers of America (PhRMA) and the European Federation of Pharmaceutical Industries and

Associations (EFPIA).⁶ Of the 304 trials in the audit, the authors noted that 140 (46%) had a start date before January 1, 2014.

“Less than 3 years had passed since the results summary was added to the product label for 136 (45%) of the trials, 3 to 7 years for 126 (41%) trials, and more than 7 years for 42 (14%) trials,” the authors wrote.³

Among the companies involved, the authors found that 24 belong to 1 or both signatories to the 2014 transparency pledge, 19 have published an IPD policy on their website or a third-party source, and 21 lack a published IPD policy.

Modi then described the painstaking process of contacting all the trial sponsors to learn IPD eligibility. Of the 304 industry-sponsored trials in the audit, IPD sharing eligibility was publicly available for 64 trials (21%). For the remaining trials, Modi contacted the sponsor to determine the status. He created a cadence of reaching out every 30 days until he received a response. In some cases, the drug was no longer owned by the initial trial sponsor, which created delays. In the end, 9 trials (3%) sponsored by 8 different companies offered no response on the eligibility status of the trial data.

The contacts themselves were straightforward, Modi explained. “Our email is just asking them, ‘[Are these] data eligible to share or not? And if not, just give us a reason,’” he said. “The median response time was 42 days because they took their time until I followed up, then followed up again.”

Variation Among Companies

Amid some frustration, there was good news. The authors found the IPD were eligible for sharing from 136 trials, involving 60 anticancer drugs and data from more than 70,000 patients. Data were available from more than 50% of the trials for atezolizumab (Tecentriq), abiraterone (Zytiga), enzalutamide (Xtandi), ibrutinib (Imbruvica), osimertinib (Tagrisso), palbociclib (Ibrance), and pertuzumab (Perjeta).

“Furthermore, 5 of the top 20 pharmaceutical companies by revenue (Amgen, AstraZeneca, Boehringer Ingelheim, Pfizer, and Sanofi) indicated that more than 75% of their sampled oncology trials were eligible for IPD sharing,” the authors wrote. These achievements, they wrote, are a direct result of the 2014 data sharing principles “and are a beacon of hope to one of the least trusted industries in the world.”³

In their paper and in the interview, the authors called on regulatory agencies and journal editors to take stronger stands in support of data sharing. Three specific recommendations are:

- Pharmaceutical sponsors should join PhMRA and/or EFPIA and establish a data sharing policy;
- Sponsors should establish an IPD sharing process external to the company, recognizing there may be conflicts of interest; and
- Enact a policy that states “all IPD underlying results presented in a product label will be immediately available for sharing.” This element is designed to remove extended embargo periods and ensure that registration of product triggers availability of clinical data.³

Hopkins said changes are needed to promote research to improve patient care. A major reason for requesting trial data, »



MODI

Natansh D. Modi, BPharm, and PhD candidate, Flinders University, Australia.



HOPKINS

Ashley M. Hopkins, PhD, senior research fellow, College of Medicine and Public Health, Flinders University, Australia.

he said, is to allow systemic evaluation of data in search of signals related race or sex. A second reason is to address variability in the quality of data provided, Hopkins said.

“Some companies put in a lot of care with the data that they provide. And they’re also transparent as to what data [were] collected throughout the entire trial—you can see that in the data dictionary,” Hopkins said. With other companies, “they don’t give the data dictionary and they redact a lot of the clinical data,” he said.

For investigators looking to study signals into differences in rates of AEs by race or sex, the way these data are reported matters a lot, he said. With the current emphasis on reducing disparities in

cancer care, it would seem to matter more than ever how these data are shared. Today, some companies do a very good job in this area, Hopkins said, but others do not.

“So that’s the next step—trying to set standards around actual data provision,” he said. ♦

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COMMENTARY

PBM Fees Put the “GER” in Danger for Specialty Pharmacies

DARRELL L. WILLYARD, PHARM.D.; AND ALEXIS V. FANSHIER, BA



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CONTINUED FROM COVER

This article will discuss the real-world consequences of GER fees within specialty pharmacies, specifically oral oncology pharmacies. It is important to note that other pharmacies dispensing high-cost generics also may be affected.

Pharmacy benefit managers (PBMs) began as intermediaries between insurers and providers.¹ In recent years, mergers and acquisitions have led to PBMs being under the same roof with insurers, specialty pharmacies, and, in some cases, provider services. Three PBMs (Express Scripts, CVS Caremark, and OptumRX) control approximately 89% of the market.² All 3 PBMs also own specialty pharmacies, making it lucrative for them to keep prescriptions within the pharmacies they control.

PBMs and MIPs often struggle over which entity should provide pharmacy care for patients. MIPs are specialty pharmacies embedded in the patient’s medical clinic that offer several advantages over PBM-owned specialty pharmacies.^{3,4} PBM pharmacies may need assistance from providers to obtain necessary information when filling specialty prescriptions, which can delay patient care. MIPs have access to the patient’s chart, allowing them to easily retrieve needed information such as the appropriate *International Classification of Diseases, Tenth Revision* codes, allergies, past medical history, and patient demographics. The physician’s office is easily accessible to the MIP for collaboration and order clarification. Often, the patient may meet directly with the pharmacist for face-to-face education or to provide signatures for needed grants. MIPs are skilled at working with patients to obtain free drugs from the manufacturer when needed. This service is often not offered by other specialty pharmacies.

PBMs typically mandate that their commercially insured patients use the PBM’s specialty pharmacy.^{5,6} CMS oversees

Medicare and allows patients to choose their specialty pharmacy. However, PBMs may prevent Medicare patients’ migration to other pharmacies through low-paying contracts or high DIR fees.⁷ Nebulous contracts and high DIR fees may keep MIPs from contracting with PBMs, which prevents the MIP from filling prescriptions for PBM-insured patients.

Between 2010 and 2020, retroactive DIR fees increased by more than 100,000%.⁸ DIR fees are charged by PBMs outside of administration fees and are often collected after the point of sale (POS) and do not reflect the pharmacy’s actual reimbursement at the time of dispensing. Traditionally, DIR fees are based on so-called pharmacy performance metrics.⁹ DIRs have recoupment fees of up to 15% of the adjudicated price paid to the pharmacy for dispensing a prescription. PBMs develop and manage specific criteria used to score the contracted pharmacy.¹⁰

The scoring process varies from insurer to insurer and may include unachievable goals for specialty pharmacies focused on dispensing oncology medications. Unrealistic goals may include placing adherence ratings suitable for chronic diseases, such as type 2 diabetes or hyperlipidemia, on high-cost oncology drugs. Cancer drugs often require temporary discontinuation of treatment due to the adverse effect profile unique to that class of drugs and cancer disease state. For instance, pancytopenia is a common adverse drug reaction in many oral chemotherapy agents. In this example, the MIP prescriber may temporarily discontinue the patient’s oncolytic until their pancytopenia is resolved. However, PBMs may interpret this as nonadherence and increase DIR penalties.

Increasingly, PBM contracts are incorporating GER fees. These fees are not based on pharmacy performance metrics but instead are calculated on a drug’s maximum allowable cost, wholesale acquisition cost, or average wholesale price (AWP).¹¹ PBMs may

FIGURE. Example of Pharmacy Cost vs Pharmacy Payment

R _x cost	$\$25,000 \times 60\% = \$15,000$
R _x payment	$\$25,000 \times 15\% \text{ (AWP} - 85\%) = \$3,750$
Loss to pharmacy:	\$11,250

contract with an entire network of pharmacies to pay a cumulative GER across generics dispensed by network pharmacies. GERs based on AWP may pay as low as AWP minus 85% to 89%.¹² Although this may be appropriate for older, more competitive generic products, it does not work for all generics, including many cancer medications. AWP prices and the cost for generic drugs may be similar when the generic is first released but they tend to separate over time as the actual cost for older generic drugs continues to fall. Generic medications with actual costs exceeding 10% to 15% of their AWP will cause the pharmacy to lose money with this type of contract.

For example, a new generic version of sorafenib originally came to market with an AWP of more than \$25,000 for a month's supply. The actual cost of the drug was as high as 60% of the AWP when it was first released. If a PBM pays the pharmacy at AWP minus 85%, the pharmacy could lose more than \$11,000 each time the drug is dispensed (**Figure**).

In this example, the pharmacy would lose \$11,250 each time this prescription was dispensed. Although dispensing the brand-name drug is an option and may remain profitable, the PBM may mandate the pharmacy to dispense the generic medication unless the prescriber or patient requests explicitly otherwise. Pharmacies losing money to GER fees may become more prevalent as more high-cost oncology drugs become generic.¹

GER fees may occur at the POS or, more commonly, as a retroactive "take back" fee.^{5,6} POS recoupments allow pharmacies to identify financial losses when dispensing prescriptions. Retroactive GER fees may remain hidden at POS, allowing the PBM to claw back money later as single or multiple DIR recoupment(s). This may go unrecognized by the pharmacy initially. Reconciled GER rates may not occur until the end of the year when the pharmacy receives a report called a *true-up*.^{6,13}

Contracts between the MIP and the PBM may be directly negotiated between the 2 entities or, more often, may be controlled by a pharmacy services administrative organization (PSAO). PSAOs negotiate pharmacy network contracts and perform various office operations for pharmacies. PSAOs' primary customers, and those they are most familiar with, are usually small chains or independently owned pharmacies.¹³ As oncology specialty pharmacies are an even smaller niche, PSAOs may not consider tailoring their contracts to this specialty. The role of PSAOs is to protect pharmacies from unreasonable takebacks. MIPs that dispense oncology medications should work closely with their PSAO when contracting to identify required benchmarking and unreasonable metrics. The PSAO should be able to identify and communicate potentially harmful GER contracts for the specialty pharmacy.^{13,14}

The contractual agreement between PBM and PSAO can involve stipulations regarding DIR fees potentially hidden in confusing language that could mislead the pharmacy's understanding of reconciliations.^{13,15} This lack of transparency can be detrimental both to MIPs and their patients. It can drive specialty pharmacies to leave the contract with the PBM for financial reasons, pushing patients to go to cumbersome and less-accessible specialty pharmacies. Pharmacies discovering unreasonable GER fees should immediately contact their PSAO to discuss options for improved transparency. The pharmacy also could consider contacting the PBM about reasonable alternatives, such as addendums, which would exclude new generic drugs to market from the high GER rates.¹³

Generic effective rate (GER) fees may occur at the point of service (POS) or, more commonly, as a retroactive "take back" fee.... Retroactive GER fees may remain hidden at POS, allowing the PBM to claw back money later as a single or multiple direct or indirect recoupment.

GER fees may be harmful to both patients and pharmacies. Patients may pay excessive co-payments if GER fees are adjudicated after POS. PBMs may take back thousands of dollars on a prescription that a patient has already purchased. The true-up potentially could have decreased the purchase price of the prescription, which would have also reduced the patient's co-pay. In response, several states have enacted laws effectively eliminating post-POS GER fees.¹⁶ Additionally, CMS issued a final rule eliminating retroactive DIR fees in Medicare Part D plans beginning in 2024. Although this will not eliminate DIR or GER fees, this will move all DIR fees to POS. By eliminating true-ups, pharmacies can effectively determine actual prescription payments to avoid financially toxic contracts. CMS also would benefit from the lower prescription price at POS.⁸

MIPs are embedded in oncology medical clinics, allowing for effective patient care in collaboration with various health care disciplines. MIPs have had to contend with growing DIR fees shrinking the pharmacy's profit margins for several years, but new GER fees potentially could deal the final blow to MIPs' survival. MIP pharmacies could lose more than \$10,000 per prescription when dispensing newly marketed high-cost generics. These fees may be hidden for an extended period, leading to financial devastation for smaller MIPs once discovered. Worst of all, these fees may make MIPs unable to contract with PBMs, forcing the pharmacy's patients to rely on PBM-owned pharmacies and delay life-saving oncology medications. New laws will prevent

these hidden fees in the future, but will they come soon enough to save MIPs? The livelihood of MIPs, and in turn patient care, is of the essence. ♦

AUTHOR INFORMATION

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