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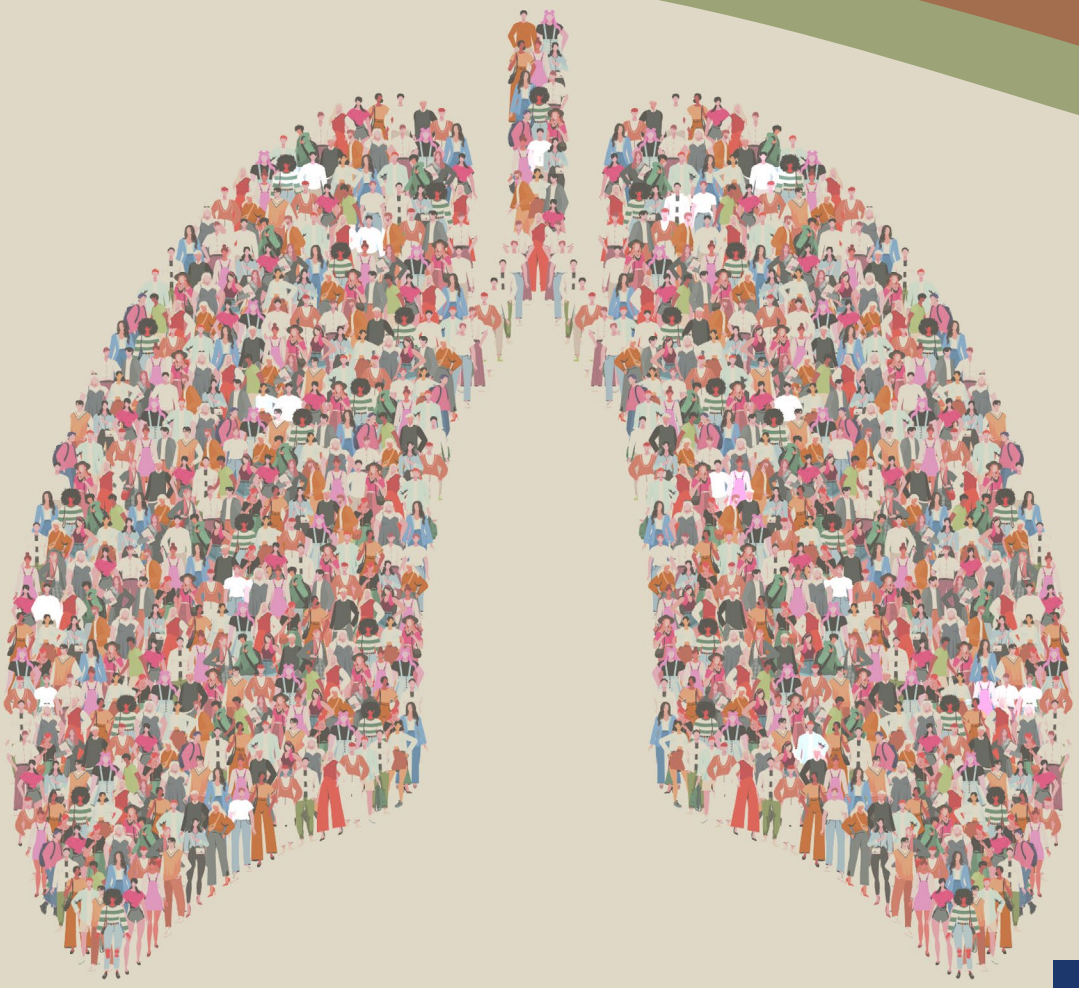
Integrating Indirect Health Benefits into Biomedical Policy: Key Reforms for Federal Agencies to Reduce Disease Transmission



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INTRODUCTION

Biomedical innovation continues to provide unprecedented opportunities to diagnose, prevent, and treat infectious disease. Infectious diseases pose harm not only to those who have been infected but may also harm those in contact with the infected individual through disease transmission. A leading set of examples is respiratory viruses like respiratory syncytial virus (RSV), influenza, and SARS-CoV-2. Diagnostics, vaccines, and therapeutics for respiratory viruses have the potential for important health benefits beyond the direct benefits to individuals who use them, by reducing risk to others of viral transmission and the consequences of infection.[1] These *indirect health benefits* are a potentially important consideration in assessing and communicating the overall impact of these products to inform individual and clinical decision-making on product use.[2] Yet despite the potential importance of effects of infectious disease products on non-users, federal agencies do not have a systematic approach to integrate consideration of such indirect benefits into regulatory and reimbursement policies.

Consequently, evidence on indirect benefits can be useful to patients, health care providers, regulators, and payers. Such evidence could be the basis of additional labeled claims related to indirect health benefits for a medical product, and in turn the basis for clinical guidelines and better information to patients to health care decision-making. More favorable coverage and payment policies for products with larger demonstrated indirect health benefits could lead to better overall health for the covered population.

There is precedent for such consideration of indirect benefits in authorization and reimbursement of medical products. For example, certain current products have labeled indications for use that primarily reflect indirect benefits to non-users, e.g., newborns who benefit from treatments administered to the mother.[3] Despite such examples, FDA approval, recommendations from CDC's ACIP, and most subsequent coverage decisions are largely based on evidence demonstrating reduction in risk of serious illness and favorable demonstrated safety profiles for individual users.[4, 5] Coverage for such preventive vaccines and therapeutics typically occurs with no copays,[6] and use of some childhood and adult vaccines is linked to quality measures and payments in Medicare[7] and Medicaid.[8] However, many treatments and diagnostic tests that may significantly reduce transmission typically require copays. Further, there is no clear regulatory pathway or special supports for demonstrating indirect benefits on top of major health benefits to individuals, or clear standards for differential coverage or payment incentives for infectious disease products that reduce the risk of serious illness complications to the user but also have a significant impact on transmission reduction.

This paper is the third in a three-part series focused on the indirect benefits of biomedical products. In this paper, we assess the authority and past actions by the U.S. Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services (CMS) to consider indirect benefits of medical products and identify regulatory and reimbursement reforms that could clarify how these benefits are considered. In turn, this could provide clearer pathways and greater incentives to develop such evidence, using the approaches described in our companion paper on generating better evidence on indirect benefits. We begin with an assessment of how FDA might support more systematic benefit-risk assessment to consider indirect benefits in market authorization and labeling decisions, including through post-market opportunities available to improve evidence related to indirect benefits and risks; and how FDA could build on past regulatory actions to provide a clearer pathway for labeled claims based on evidence of indirect benefits and encourage development of relevant products and evidence. In the subsequent section, we identify ways for CMS to build on its current authorities and past policy decisions to incorporate indirect benefits in coverage and payment policies.

Table 1 | Summary of Policy Recommendations

	Regulatory Recommendations	Statutory Recommendations
FDA	• Update the current benefit-risk guidance documents to incorporate indirect effects in premarket studies systematically, using infectious disease case examples. Examples can describe how reduced infection, duration and severity of symptoms, and (if available) viral shedding measures can all be potential surrogate markers for indirect benefits; and how impact on transmission to contacts could also be considered. • Provide guidance on studies and platforms to support real-world evidence development for indirect benefits in postmarket studies. Interventional studies with cluster randomization, observational studies and dynamic modeling can provide basis for claims of indirect benefits. • Support the development of transmission-reducing products with further category-specific guidance on demonstrating benefits for prophylactic, therapeutic, and diagnostic indications.	• Congressional authorization of future user fee agreements or appropriations to: - Require improvements in existing guidance documents to address the value of indirect benefits. - Develop interagency strategy to advance real-world evidence development to identify, evaluate, and monitor indirect benefits. - Support enhanced FDA review staff and supporting resources to help product developers incorporate better evidence of indirect benefits in their regulatory review and labeling, with user fee goals to improve incorporation of evidence on indirect benefits.
CMS	• Update existing coverage assessment guidance for infectious disease products to explicitly incorporate indirect effects as considerations for coverage and payment incentives. • Support improvements in data collection platforms to help health care organizations track the use and impact of products with potential indirect benefits in a community, e.g. in nursing homes, assisted living facilities, and hospital case reporting, using Medicare quality improvement and coverage with evidence authorities. • Revise the clinical laboratory fee schedule to reflect the additional benefits of timely screening and diagnostic test processing for tests with expected indirect benefits. • Develop and support use of products with demonstrated indirect benefits, through Medicare and Medicaid performance measures and CMS payment reforms focusing on improving population health while reducing total spending.	• Legislative direction for CMS to clarify Medicare's consideration of indirect benefits in coverage and payment decisions through: - Directing CMS to provide further guidance on inclusion of indirect benefits. - A pilot program to assess the impact of additional payment incentives for use of products with significant demonstrated indirect benefits outside of declared public health emergencies. - A collaboration to produce a platform registry to align data collection and analysis across health systems, hospitals, and public health organizations to advance the assessment of indirect benefits for Medicare beneficiaries and communities (e.g., in coordination with AHRQ or PCORnet). - Modest additional staffing and appropriations to support these activities.

U.S. Food and Drug Administration

FDA is tasked with protecting and promoting public health by ensuring the safety, efficacy, and security of drugs, biological products, and medical devices.[9] The Federal Food, Drug, and Cosmetic (FD&C) Act enables FDA to regulate the development and authorization of medical products.[10] FDA approval of new medical products is generally based on demonstrating safety and efficacy for the product recipient when used as labeled. Based on a review of the evidence, FDA determines what information is relevant to regulatory decision-making and post-market regulatory oversight.[11] FDA can, and has, considered indirect benefits and risk when approaching both product approval and post-market regulation decisions. These actions could inform a clearer pathway for the authorization and regulation of innovative products based on their indirect benefits and could be further clarified and supported through legislation.

Incorporating Indirect Benefits into Benefit-Risk Assessments

FDA has published guidance describing the factors the agency regards as relevant to its analysis of benefits and risks in light of uncertainties inevitably associated with each. This assessment is focused on evidence submitted by the product sponsor, to enable FDA's assessment of whether the benefit of use will be greater than the risk for the intended product users if the product is granted marketing authorization. While the benefit-risk assessment is focused on the product user, FDA has the ability to weigh the impact of use beyond the user in its decisions. Specifically, in the 2023 guidance document *Benefit-Risk Assessment for New Drug and Biological Products* FDA states that:

> "*In certain circumstances, FDA's benefit-risk assessment incorporates broader public health considerations for both the intended patient population and others. For example, in the review of drugs, including vaccines, to diagnose, prevent, or treat communicable diseases, risks related to disease transmission are important considerations. Similarly, for drugs identified as controlled substances, FDA's benefit-risk assessment incorporates considerations such as risks related to misuse or accidental exposure in the intended population and in other populations who may have access to the drug."*[13]

FDA has taken regulatory actions that target the indirect health risks of medical products. In response to children exhibiting serious side effects after being exposed to testosterone gel products, FDA implemented a Risk Evaluation and Mitigation Strategy (REMS) alerting prescribed users of the risks of adverse events to children inadvertently exposed to the gel and added warning labels for product use. These actions were all targeted to explicitly prevent exposure incidents and indirect risks in non-users of the medical product.[14] Similarly, FDA considered indirect risks and public health impacts in its authorization of transmucosal immediate release fentanyl (TIRF). In particular, FDA's approval decision assessed the risk of off-label use and accidental exposure in children. As a result, the products are labeled as contraindicated for nonopioid-tolerant patients, with a warning label describing their harm to children who may be inappropriately exposed.[15] In addition, FDA established a TIRF REMS program that is designed to reduce exposure risk in nonusers. More generally, FDA considers community impact (potential community harms from misuse) in its decisions involving opioid products.

Building on this precedent, FDA can provide further clarity about the regulatory oversight of approved products with indirect benefits. Indeed, there are already several examples of FDA incorporating positive public health considerations beyond the user in its regulatory decisions. FDA approved the use of a tetanus-diphtheria-pertussis (Tdap) vaccine for administration during the third trimester of pregnancy to provide post-partum protection to the neonate during their first 2 months of life.[16, 17] Tdap vaccine approvals for use in pregnancy followed a prior ACIP recommendation for women's health care providers to implement maternal Tdap vaccination programs and a broader "cocooning" strategy endorsed by ACIP to vaccinate adolescents and adults in close contact with infants.[18] The manufacturers of both vaccines developed registries to collect further safety information on use in pregnancy, and data from registries was utilized in FDA's clinical review to ensure there were no additional specific risks to use in pregnancy.[19] The clinical review memos also acknowledged the protections to the infant provided by the "cocooning" strategy. In addition, studies included on the product label demonstrate very favorable benefit-risk assessment for the neonate, who is particularly vulnerable to these viruses in their first

few months of life.[20] The Tdap approval in pregnancy demonstrated that FDA relied on substantial evidence generation that was catalyzed by a collaboration between health care providers, public health, and vaccine manufacturers.

While FDA guidance and past decisions have incorporated public health considerations, additional clarity would create stronger incentives for the development and use of products with significant indirect benefits. This may begin with clarification of guidance documents on the benefit-risk assessment process. FDA could update the aforementioned 2023 guidance document *Benefit-Risk Assessment for New Drug and Biological Products* and the 2019 guidance document for devices on *Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications*—which both already reference public health impacts, including the capacity to detect disease and prevent spread.[21] FDA could include an explicit component on how the agency approaches indirect benefits beyond the user in its assessment, using approved products for which indirect benefits were considered to establish a more complete framework like we have described in our accompanying paper. Congressional appropriations or funding through future user fee agreements can support efforts to update this guidance and achieve measurable progress on clarity about indirect benefits. Further resources, including staff, that FDA may need to integrate indirect benefits into regulatory decision-making could also be provided by congressional appropriations.

To support these efforts, FDA could collaborate with developers, other stakeholders and agencies to support a more robust evidence generation infrastructure on the indirect benefits of products (see: *Supporting Evidence Generation of Indirect Benefits and Risks for Medical Products Used for Infectious Diseases*) that reduce transmission. In the post-market setting, improving opportunities to assess indirect benefits, based on clearer guidance, further progress on electronic data sharing, and emerging platforms for real-world evidence development for indirect benefits, can advance the availability and use of products that improve infectious disease outcomes in communities. These initiatives can provide greater certainty for product developers, partners in FDA's Sentinel and BEST Initiatives, and other stakeholders to facilitate the collection of necessary post-market evidence on effectiveness.

Taken together, these efforts to update current policies would contribute to a unified framework on how FDA approaches oversight of products with indirect benefits with information collected from real-world settings.

Expanding Product Labels to Reflect Indirect Benefits

Product developers could use clarified guidance on benefit-risk assessments and a more robust evidence generation framework to develop evidence to support additional claims of indirect benefits for drugs and biologics. Existing examples of labeled claims for infectious disease products serve as a foundation for such label expansions. For example, after initial authorization of RSV vaccines for use in adolescents and the elderly, FDA subsequently approved label expansions for vaccines administered to pregnant individuals to confer post-partum protection of neonates.[22, 23]

Like the Tdap vaccine example described above, the pregnant person who receives the vaccination gets little direct benefit. Unlike the Tdap vaccine, there are no preventive measures related to vaccinating close contacts with the infant. The label expansion for use in pregnancy also occurred within a much shorter timeframe, reflecting that prelicensure studies were designed to provide a foundation for a secondary indication, in addition to the primary indication for use in older adults.

Another potential example involves building on label expansions for antiviral products for prophylaxis. For example, antiviral drugs initially approved for the treatment of influenza in adults have expanded labeled indications to include prophylaxis of influenza in all individuals older than one-year old during a community outbreak.[24, 25] The prophylactic indication was justified by additional studies performed in household settings based on increased risk of exposed individuals. Similar studies could potentially address impact on infection or complication risks in household members or other contacts who did not use the antiviral for prophylaxis, but had close contacts who did – that is, spillover benefits for non-product users. Close contacts, who do not respond well to vaccination and live with chronic diseases, are potential therapeutic candidates to substantiate claims of transmission reduction in postlicensure studies.

FDA also took steps to differentiate testing products by their individual and population-level treatment goals during the COVID-19 pandemic. According to FDA, *diagnostic tests* are used to identify infections in individuals who have reason to suspect infection – either through symptoms or close contact with an infected person. On the other hand, *screening* tests are intended for use in at-risk populations in order to identify undetected infections. Use of tests for both purposes can reduce transmission to others,[26] for example if those who test or screen positive change their behavior to reduce exposure of others and/or use therapeutics that reduce transmission. While most FDA tests for COVID-19 were approved to diagnose the virus, FDA authorized several tests explicitly for screening during the pandemic.

These product examples serve as a starting point for more systematic and comprehensive consideration of indirect benefits in regulatory decision-making frameworks. As part of updating current benefit-risk guidance generally related to indirect benefits, FDA can provide additional details and examples of how the agency might approach labeled claim expansion based on indirect benefits. This includes product-type specific guidance and examples of pre-market assessments of markers of indirect benefits (e.g., duration of symptoms, viral load) and of post-market assessments of indirect benefits in real-world studies (e.g., cluster-randomized comparisons or observational controls using similar treated/untreated households and communities).

Through cooperation with other Federal agencies, FDA may inform the development of evidence generation systems to identify, capture, evaluate, and monitor the indirect benefits of products. Through cooperative agreements, the agency can work with stakeholders across the landscape of post-market pharmacovigilance to support evidence generation on indirect benefits, building off the FDA's Sentinel and BEST initiatives. In collaboration with the Centers for Disease Control and Prevention, FDA could provide clarity about how data from (CDC) initiatives to expand use of automated electronic data reporting from health care organizations and laboratories could be used to support label information on the impact of product use on community spread.[27]

Illustration: Extending FDA Policies to Address Respiratory Virus Threats

Respiratory viruses like RSV, influenza, and COVID-19 have posed major public health threats. Clearer FDA policies on the population health impact of products that address these conditions not only for individuals but beyond the user could have a significant impact on their development and use. Such benefit-risk guidance extensions could address label expansion of preventive, therapeutic, and diagnostic medical products on the basis of markers or direct evidence of a reduction in disease transmission for the non-user. FDA support of a more robust evidence generation structure can also help product developers implement studies that generate relevant evidence. FDA's 2023 benefit-risk guidance identifies risks related to disease transmission as valuable considerations for decision-making on products to prevent, treat or diagnose communicable diseases. However, there is no explicit focus on benefits related to disease transmission factoring into the public health considerations for regulatory decision-making. Product- or category-specific guidance on the benefits to reduce transmission for each of the three categories—preventive, therapeutic, and diagnostic—can facilitate label expansions that highlight indirect benefits. Some examples are as follows:

- **Preventive:** A label for a vaccine, monoclonal antibody, or a prophylactic product for prevention of complications from a respiratory infection typically states that product use can reduce the likelihood of serious respiratory disease complications when administered in advance to that individual. Further FDA guidance may support the design of a post-market study demonstrating how vaccination of schoolchildren results in reduced disease transmission in related community settings.[28] This type of study can enable a label expansion to include evidence that use by an individual reduces viral shedding and/or viral load, and/or has additional evidence of significant benefits for reducing infection or complication risks in close contacts of the user. As noted in our companion white paper, biomarkers like viral load can be validated to stand in as surrogate endpoints, in place of clinical outcomes [Canter et al.]. Both serological and clinical outcomes would be needed to justify claims of transmission reduction.

- **Therapeutic:** A label for a drug antiviral or biologic monoclonal antibody typically states that product use can reduce the duration or severity of symptoms of respiratory viral infection in an individual. Further guidance may facilitate a post-market study demonstrating how rapid treatment with an antiviral drug or monoclonal antibody to residents of congregate living facilities or households impacted transmission within this community. The resulting label expansion would then add a stronger evidence-based claim that treatment of an infected individual can reduce viral shedding and/or viral load, and/or has additional evidence of significant benefits for reducing community disease spread. Like with potential preventive label expansions, therapeutic labels could expand based on serological and clinical outcomes. Guidance could also clarify how studies can distinguish between the direct benefit of reducing transmission to an immunocompromised or individual living with a chronic disease and the indirect benefit of reducing transmission to a broader community.
- **Diagnostic:** A label for a diagnostic test for a viral respiratory infection typically states that product use can reliably determine the presence of a respiratory viral infection in an individual. Further guidance could inform a post-market study showing how screening tests in a hospital wing reduced transmission within the local community surrounding the hospital more widely. FDA could describe how this evidence could also be the basis for a claim of benefits to others in the community in addition to those tested. Label expansion could include an evidence-based explicit claim that diagnosis of an infected individual or use of a test in screening an at-risk population reduces the risk of infection or severe respiratory complications in other members of the community.

Centers for Medicare and Medicaid Services

With a growing market of infectious disease products with potentially important indirect health benefits, coverage and reimbursement policies could take further steps to recognize and account for such benefits, in turn providing incentives to support the development of such products and their effective voluntary use to increase population health benefits. Medicare beneficiaries are at relatively high risk for complications of respiratory infections. CMS policy reforms may also be adopted by Medicaid programs and private payers who also cover populations at risk for respiratory virus complications. Consequently, CMS plays an important role in enabling the development and uptake of products with indirect benefits.

Title XVII of the Social Security Act lays out parameters for Medicare coverage and payment.[29] CMS considers items or services for Medicare coverage if they fall under at least one benefit category as defined in the Act, and are reasonable and necessary for the diagnosis or treatment of illness or injury, or to improve the functioning of a malformed body member.[30] This language has been traditionally interpreted to mean that the product must show evidence of a direct therapeutic benefit exceeding risks for the affected beneficiary under conditions of actual use – not benefits to others.

As a result of more recent legislation, including the Affordable Care Act, Medicare must cover preventive services if they are reasonable and necessary for the prevention or early detection of an illness or disability, and have an "A" or "B" grade of evidence of direct health benefit as assessed by the U.S. Preventive Services Task Force (USPSTF).[31] Notably, the USPSTF is not bound by any specific requirements regarding the evidence framework they must use for their recommendations, such as whether they must exclusively consider direct benefits. Instead, the USPSTF has some reasonable scope to define the evidentiary framework used to support its recommendations.

Incorporating Indirect Benefits into Coverage Decisions

Most products are incorporated routinely into Medicare coverage under local coverage determinations (LCDs). A product that raises new or complex considerations can trigger a national coverage assessments (NCA) with a more complete analysis and public comment period leading to a national coverage determination (NCD) for the product. In these processes, the agency has shown consideration for the public health impact of products. For example, in its NCA for sexually transmitted infections (STI) screenings, the agency highlighted the public health benefit of reducing STI transmission as a result of identifying infected beneficiaries, which contributed to its decision to cover screenings under the preventive services benefit category.[32] The recent NCD for coverage of pre-exposure prophylaxis (PrEP) against HIV infection reflected CMS' determination of the direct benefit to at-risk individuals, but CMS also recognized evidence of indirect benefits through reducing transmission to others who may not undergo prophylaxis. Specifically, the NCD notes that antiretroviral therapy, the treatment used as part of PrEP, has been demonstrated to reduce the risk of HIV transmission.[33]

CMS can build on these coverage decisions to develop a more systematic process for considering indirect benefits in coverage assessments. As a starting point, CMS could update the 2024 *National Coverage Analysis Evidence Review* guidance document to address how indirect benefits and public health impact may be included. Updating this guidance could also help clarify evidence generation expectations for manufacturers as it relates to indirect benefits and streamline coverage decisions for products with large indirect benefits. Congressional action and appropriations can spur CMS to update guidance.

Clarifying Reimbursement Flexibilities to Address Public Health Impacts

CMS has demonstrated flexibilities in reimbursement when faced with disease outbreaks, particularly in regional or national public health emergencies. During the COVID-19 pandemic in 2020, CMS rapidly adapted its coverage, coding, and payment structures in ways that protected beneficiaries from both infection and transmission of the virus, for example by enabling telehealth- and home- and community-based services to reduce infection risk with direct contact.[34, 35] This was achieved through emergency authority waivers enabled by the Public Health Emergency declaration, as well as statutory changes, new regulations, and agency enforcement discretion. In addition, supported by timely legislative action, CMS quickly established coding and payment rates with no cost-sharing for authorized COVID-19 vaccines even before they arrived to market.[36] The agency also established coverage with no cost-sharing for therapeutics and clinical diagnostics in order to maximize access to novel products during the PHE.[37, 38] After the PHE ended, CMS continued to facilitate access to these products with sustained coverage and no cost-sharing through the end of 2024.[39] While eliminating cost sharing and procuring vaccines at scale made it easier for beneficiaries to access medical products to protect themselves from COVID-19, this increased uptake also likely impacted those around these beneficiaries, as their exposure to COVID-19 and subsequent risk of infection was lowered.

To support greater access to products with both direct benefits and indirect benefits during disease spread, CMS also established differential payment across treatment modalities. In 2021, Medicare began providing an additional payment amount (nearly double the standard payment) to providers who administered in-home COVID-19 vaccines for patients with certain medical conditions and clinical, socioeconomic, or geographic barriers to reaching clinical care.[40] Beginning in 2020, CMS also established add-on payments for labs using high throughput technology to more rapidly run COVID-19 diagnostic tests and rewarded rapid, 2-day testing turnaround.[41] CMS noted that these efforts were expected to contribute to transmission reduction, protecting those beyond the test user – including providing both indirect health benefits to others, as well as non-health benefits to health care worker burden and health care system capacity by reducing the patient load on hospitals and health care systems.

CMS' rapid actions during the COVID-19 PHE, and other actions related to coverage of products that reduce infectious disease spread, highlight the agency's willingness to enact policies to enable access to products that provide or are likely to provide important

indirect benefits beyond their direct benefits to Medicare beneficiaries. CMS and Congress can build on this precedent by identifying opportunities outside of PHE-authority to pilot and incorporate more limited, predictable coverage and reimbursement incentives for products with significant demonstrated indirect benefits. For example, CMS can establish an add-on financial incentive or support for health care organizations that engage beneficiaries in decisions to use a covered product that is expected to reduce infection spread and health system case burden. Congressional appropriations and support for additional staffing can support such policies to be established for rapid triggering in times or areas with significant outbreaks or high risk of disease spread. Enshrining a more predictable coverage and reimbursement pathway would in turn facilitate greater development of and access to products, good evidence on indirect benefits and better contain disease transmission to avoid larger outbreaks.

Promoting More Timely and Less Burdensome Information on Disease Spread – and Evidence on Indirect Benefits

Under the Medicare and Medicaid programs, health care organizations must comply with conditions of participation (CoPs) and conditions for coverage (CfCs) to receive payments for items and services. This includes establishing programs that have a public health impact on both Medicare and non-Medicare patients—including hospital-wide programs for the surveillance, prevention, and control of infectious disease as well as antibiotic stewardship.[42] Currently, hospitals and facilities participating in Medicare programs have to provide reports on major respiratory infections, emergency department visits, and admissions. Justification for these reporting requirements stems from the necessity for local public health authorities, hospitals, and communities to understand their risks and potentially disruptive outbreaks. In the event of a declared PHE, CMS can require hospitals to report additional relevant data. Further policy steps could make these activities, which have important implications for reducing infectious disease spread, both less burdensome and more likely to reduce spread in the communities served by the health care organizations subject to COPs.

By making such case data easier to report through electronic health record standards (e.g. USCDI/TEFCA), and by building on current CDC infrastructure support to enable such health data to be routinely used to support local case tracking, CMS could advance the use of a more automated and accurate reporting infrastructure on local disease spread. This can inform effective use of products with indirect benefits across the impacted community. Congressional appropriation and direction can facilitate collaboration to produce a platform registry to align data collection and analysis across health systems, hospitals, and public health organizations. Coordination with the Agency for Healthcare Research and Quality and the National Patient-Centered Clinical Research Network can advance the assessment of indirect benefits for Medicare beneficiaries and communities. These steps would better inform individual decisions about the voluntary use of such products, as some individuals' decisions may be influenced by the opportunity to benefit their close contacts and their community. These data can also be used to assess indirect benefits from use of products with individual benefits. CMS financial incentives for timely and accurate infectious disease detection, or for advancing the use of interoperable data and standards for improving care, can accelerate such routine case data collection (e.g., as an activity qualifying for a Quality Improvement bonus).

Promoting Better Population Health in Care Delivery

As part of a larger shift towards high-value, accountable care, CMS has increasingly incorporated population health outcomes in its payment models. For example, CMS has integrated population health measures into reporting programs. Physicians serving Medicare beneficiaries must generally participate in the Quality Payment Program (QPP), which aims to reward providers for high-quality, patient-centered care. The QPP Merit-based Incentive Payment System (MIPS) includes key population health performance measures including use of screening for influenza vaccination, vaccination for children and teenagers, and STI screening and testing.[43] Amidst a proliferation in quality-performance programs and questions about clinical meaningfulness and applicability

of potential measures, CMS has proposed a universal foundation of quality measures to align measurement efforts and reduce provider burden. This foundation incorporates population health measures relevant to reducing the burden of major infectious disease threats. As CMS takes further steps to advance the goals of reliable performance measurement and improvement to lower reporting burden, the agency could establish or modify existing measures to reflect both preventive health benefits and indirect benefits. For example, as outlined in a Duke-Margolis paper on hepatitis C elimination, in order to support increased hepatitis C care, screening and treatment measures could be added to the Healthcare Effectiveness Data and Information Set measure set, and CMS could establish a pathway to implement hepatitis C screening and treatment measures through automated electronic health data reporting, reflecting the benefit to individuals as well as reduced hepatitis C transmission. These efforts could support increased use across Medicaid payment programs and for commercial payers as well.[44]

In conjunction with the development of measures and incentives for direct and indirect population health benefits, CMS has also prioritized a long-term strategy to move away from fee-for-service (FFS) payments to alternative, person-based payments, to enable greater and more flexible support for improvements in care quality and efficiency, with greater provider accountability for both individual and population-level health improvements while reducing total costs of care. In such models, medical practices or health care organizations may receive a partially or fully capitated per-member per-month payment to support the patient's care for that time period. Infrastructure supports for increased use of products with significant indirect benefits within these models – e.g., through data sharing that supports tracking and addressing gaps in use of such products – would align well with the model goals of improved population health outcomes and reducing costly complications.

Illustration: Extending CMS Policies to Address Respiratory Virus Threats

Coverage and payment guidance for infectious disease products can more systematically and explicitly describe how reimbursement decisions will reflect evidence on indirect benefits. There are a number of promising avenues to continue work that fulfills the agency's goals for improving the health of covered beneficiaries. Examples of product-specific scenarios include:

- **Incorporating indirect benefits into coverage assessments:** A number of therapeutics are in development for respiratory infections that may have a greater indirect benefit (i.e., reduced transmission) compared to currently available products.[45] CMS could develop guidance that clarifies how the indirect benefits of products will impact coverage and payment. Without such clarification, LCDs or NCDs based on direct benefits only, or based on a less predictable approach to incorporating indirect benefits, may result in more limited access and less population health impact, especially during seasonal outbreaks or infectious disease emergencies.

- **Establishing innovative payment mechanisms:** The Center for Medicare and Medicaid Innovation can implement a pilot model for flu and/or other major respiratory infections that incorporates updated performance measures related to the use of vaccines, therapeutics, and diagnostics with indirect benefits into its quality payment incentives, as described above. Because FFS models do not have total population accountability, additional financial support for providers who engage their patients in considering use of such products can have an impact on population health extending beyond the patients they serve. This kind of pilot program can also incorporate incentives to establish vaccination or diagnostic programs that better reach beneficiaries and utilize test to treat or other rapid turnaround techniques. Similarly, while partially or fully capitated payment models encourage the use of products that reduce costly downstream complications for an accountable provider's beneficiaries, performance measures and incentives reflecting the broader community benefit would more fully align with CMS's population health goals.

- **Reducing health care burden:** In order to appropriately deploy vaccines, therapeutics, and diagnostics to improve population health outcomes while reducing clinician burden, CMS could establish a program that supports key "use cases" for applying current electronic health record data standards to report on respiratory virus cases and the use of vaccines, therapeutics, and diagnostics that have important indirect benefits. Such incentives would have administrative benefits in terms of reduced public health reporting burden related to infectious diseases, and in terms of increasing the availability of timely and reliable information on viral respiratory outbreaks and opportunities to contain them, in turn helping health care organizations target their limited resources and avoid overburdening emergency rooms and hospitals. These measures and aggregated data could also support performance measures and financial incentives, providing quality improvement payments aligned with data sharing with local public health organizations and across health care organizations in the community. CDC could take complementary steps to support public health data interoperability building on its recent infrastructure payments.[46] This type of platform can also support health systems and hospitals to meet enhanced reporting and compliance requirements during a PHE.

CONCLUSION: ACCELERATING PROGRESS

Previous FDA and CMS regulatory and legal actions have used existing authorities to consider population health outcomes including indirect benefits in regulatory and reimbursement decision-making. However, there are opportunities for clearer and more significant steps to integrate indirect benefits into regulatory and reimbursement policies, as part of a coordinated policy strategy that better aligns limited resources at CMS, FDA, and other public health agencies. While FDA and CMS can take further steps in approaching the reforms outlined above, additional legislation could both clarify these authorities and assure that agency activities are advancing indirect health benefits for Americans as efficiently as possible. Maximizing the impact of reforms will also require improving data infrastructure and evidence generated on indirect benefits [Canter et al.]. This is a time of unprecedented opportunities to develop and inform voluntary use products to reduce the burden of infectious diseases – both through their direct benefits for individuals who choose to use them, and through a better understanding of indirect benefits that may also impact individual decisions about these products. A scalable and sustainable infrastructure that can generate better evidence and support informed use of such products will have important population health benefits, and increase the impact of activities undertaken by FDA, CMS, as well as their public and private partners and communities to reduce the burden of infectious diseases.

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