HEADING UPSTREAM
Can U.S. healthcare address the social determinants of health?

PLUS
DRUGS IN THE PIPELINE
Atopic dermatitis

FORMULARY DEVELOPMENT
Humira biosimilars

AND
CHRONIC DISEASE
Hepatitis C

INDUSTRY ANALYSIS
The Transparency in Coverage rule

Behind the future of telehealth
How **adherent** and **persistent** are your members living with MS to their treatment regimen?

**Indications**
OCREVUS is indicated for the treatment of:
- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults.

**Contraindications**
OCREVUS is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening infusion reaction to OCREVUS.

**Warnings and Precautions**
**Infusion Reactions:**
Management recommendations for infusion reactions depend on the type and severity of the reaction. Permanently discontinue OCREVUS if a life-threatening or disabling infusion reaction occurs.

**Infections:**
Delay OCREVUS administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment with OCREVUS and after discontinuation, until B-cell repletion.

**Reduction in Immunoglobulins:**
Monitor the level of immunoglobulins at the beginning of treatment. Monitor during and after discontinuation of treatment with OCREVUS, until B-cell repletion, and especially when recurrent serious infections are suspected. Consider discontinuing OCREVUS in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

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M-US-00013429(v1.0) 12/21
Genentech analyzed 2 years of data to determine patient adherence and persistence across several DMTs\(^1,2\)

**Objective:** Evaluate adherence and persistence with OCREVUS compared with other DMTs for the treatment of MS in a retrospective cohort study of 1710 patients from the IBM MarketScan US Commercial and Medicare claims database for the period between April 1, 2016 and December 31, 2019.

**Primary outcomes measured**

<table>
<thead>
<tr>
<th>Adherence</th>
<th>Persistence</th>
</tr>
</thead>
<tbody>
<tr>
<td>In this study, adherence was calculated based on proportion of days covered (PDC), with ≥80% considered adherent to the DMT initiated.</td>
<td>In this study, persistence was measured based on switch to another DMT or gap in index DMT coverage of ≥60 days at any time during the evaluation period.</td>
</tr>
</tbody>
</table>

**Routes of administration (ROA) analyzed\(^2\)**

- **31%** OCREVUS infusions
- **41%** Orals
- **21%** Self-injectables
- **7%** Other infusions

**Malignancies:**
An increased risk of malignancy, including breast cancer, may exist with OCREVUS.

**Most Common Adverse Reactions**

**RMS:** The most common adverse reactions (≥10% and >REBIF): upper respiratory tract infections and infusion reactions.

**PPMS:** The most common adverse reactions (≥10% and >placebo): upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

**For additional safety information, please see accompanying Brief Summary of full Prescribing Information.**

**INTENDED FOR DISTRIBUTION ONLY TO MANAGED CARE CUSTOMERS, INCLUDING FORMULARY DECISION MAKERS.**

These HCEI materials were prepared pursuant to FD&C Act Sec. 502(a) standards. They are intended solely for use by payers, formulary committees, or other similar entities with knowledge and expertise in the area of healthcare economic analysis to facilitate drug selection decisions for coverage or reimbursement. These materials are not intended to be used by healthcare practitioners for the purpose of making individual patient prescribing decisions.

**References:**
OCREVUS® (ocrelizumab) injection, for intravenous use

Brief Summary of Full Prescribing Information

1 INDICATIONS AND USAGE

OCREVUS is indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults

2 CONTRAINDICATIONS

- OCREVUS is contraindicated in patients with:
- Active HBV infection
- [see Warnings and Precautions (5.2)]
- A history of life-threatening infusion reactions to OCREVUS [see Warnings and Precautions (5.9)]

3 WARNINGS AND PRECAUTIONS

5.1 Infusion Reactions

OCREVUS can cause infusion reactions, which can include pruritus, rash, urticaria, erythema, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngitis, or laryngitis events associated with head and neck pain, jaw pain, headache, dyspnea, nausea, tachycardia, and anaphylaxis. In multiple sclerosis (MS) clinical trials, the incidence of infusion reactions in OCREVUS-treated patients (who received methylprednisolone or an equivalent steroid) and possibly other pre-medication to reduce the risk of infusion reactions prior to each infusion was 0% to 40%, with the highest incidence with the first infusion. There were no fatal infusion reactions, but 0.3% of OCREVUS-treated MS patients experienced infusion reactions that were serious, some requiring hospitalization. Observe patients with OCREVUS for infusion reactions during the infusion and for at least one hour after completion of the infusion. Inform patients that infusion reactions can occur at any time.

Reduction of the Risk of Infusion Reactions and Managing Infusion Reactions

- Administer pre-medication (e.g., methylprednisolone or an equivalent corticosteroid), and an antihistamine and antipyretic (e.g., acetaminophen) may also be considered.
- Monitor the patient for evidence of infusion reactions depending on the type and severity of the reaction. For life-threatening infusion reactions, immediately and permanently stop OCREVUS and administer appropriate supportive treatment. For less severe infusion reactions, may consider temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

5.2 Infections

A higher proportion of OCREVUS-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of OCREVUS-treated patients experienced infections compared to 52% of REBIF-treated patients. In the PPSMS trial, 70% of OCREVUS-treated patients experienced one or more infections compared to 68% of placebo-treated patients. OCREVUS was associated with an increased risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections (see Adverse Reactions (6.1)). OCREVUS was not associated with an increased risk of serious infections in MS patients. Delay OCREVUS administration in patients with an active infection until the infection is resolved.

Respiratory Tract Infections

A higher proportion of OCREVUS-treated patients experienced respiratory tract infections compared to patients taking REBIF or placebo. In RMS trials, 40% of OCREVUS-treated patients experienced upper respiratory tract infections compared to 33% of REBIF-treated patients, and 8% of OCREVUS-treated patients experienced lower respiratory tract infections compared to 4% of REBIF-treated patients. In the PPSMS trial, 49% of OCREVUS-treated patients experienced upper respiratory tract infections compared to 43% of patients on placebo and 15% of OCREVUS-treated patients experienced lower respiratory tract infections compared to 9% of patients on placebo. The infections were predominantly mild to moderate and consisted mostly of upper respiratory tract infections and bronchitis.

Herpes

In active-controlled (RMS) clinical trials, herpes infections were reported more frequently in OCREVUS-treated patients than in REBIF-treated patients, including herpes zoster (2.1% vs. 1.0%), herpes simplex (0.7% vs. 0.1%), oral herpes (3.0% vs. 2.2%), genital herpes (0.1% vs. 0%), and herpes virus infection (0.1% vs. 0%). Infections were predominantly mild to moderate in severity. In the placebo-controlled (PPSMS) clinical trial, oral herpes was reported more frequently in the OCREVUS-treated patients than in the patients on placebo (2.7% vs 0.8%). Serious cases of infections caused by herpes simplex virus and varicella zoster virus, including central nervous system infections (encephalitis and meningo), intracranial infections, and disseminated infections have been reported in the postmarketing setting in multiple sclerosis patients receiving OCREVUS. Serious herpes virus infections may occur at any time in patients treated with OCREVUS. Some cases were life-threatening.

If serious herpes infections occur, OCREVUS should be discontinued or withheld until the infection has resolved, and appropriate treatment should be administered (see Patient Counseling Information (17)).

Progressive Multifocal Leuкоencephalopathy (PML)

PML is an opportunistic viral infection of the brain caused by the John Cunningham (JC) virus that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. Although no cases of PML were identified in OCREVUS clinical trials, JC virus infection resulting in PML has been observed in patients treated with other anti-CD20 antibodies and other MS therapies and has been associated with some risk factors (e.g., immunocompromised patients, polytherapy with immunosuppressants). At the first sign or symptom suggestive of PML, withhold OCREVUS and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and consciousness leading to confusion and personality changes.

Hepatitis B Virus (HBV) Reactivation

Hepatitis B reactivation has been reported in MS patients treated with OCREVUS in the postmarketing setting. Fulminating hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with OCREVUS. Do not administer OCREVUS to patients with active HBV confirmed by positive results for HBsAg and anti-HB antibodies. For patients who are negative for surface antigen (HBsAg) and positive for HB core antibody [anti-HBc] or are carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment.

Possible Increased Risk of Immunosuppressant Effects with Other Immunosuppressants

When initiating OCREVUS after an immunosuppressive therapy or initiating an immunosuppressive therapy, consider the potential increased immunosuppressive effects (see Drug Interactions (7.1)). OCREVUS has not been studied in combination with other MS therapies.

4 VACCINATIONS

Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of OCREVUS for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of OCREVUS for non-live vaccines. OCREVUS may interfere with the immune response to live vaccines. The safety of immunization with live or live-attenuated vaccines following OCREVUS therapy has not been studied, and vaccination with live-attenuated or live vaccines is not recommended during treatment and until B-cell depletion.

5.3 Reduction in Immunoglobulins

As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with OCREVUS treatment. The pooled data of OCREVUS clinical studies (RMS and PPSMS) and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of immunoglobulin G (IgG), IgM, and IgA and increased rates of serious infections. Monitor the levels of quantitative serum immunoglobulins during OCREVUS treatment and after discontinuation of treatment, until B-cell repletion, and especially in the setting of recurrent serious infections. Consider discontinuing OCREVUS therapy in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins [see Adverse Reactions (6.1)].

5.4 Malignancies

An increased risk of malignancy with OCREVUS may exist. In controlled trials, malignancies, including breast cancer, occurred more frequently in OCREVUS-treated patients. Breast cancer occurred in 6 of 781 females treated with OCREVUS and none of 648 females treated with REBIF or placebo. Patients should follow standard breast cancer screening guidelines.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Infusion Reactions [see Warnings and Precautions (5.1)]
- Infections [see Warnings and Precautions (5.2)]
- Reduction in Immunoglobulins [see Warnings and Precautions (5.3)]
- Malignancies [see Warnings and Precautions (5.4)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The safety of OCREVUS has been evaluated in 1311 patients across MS clinical studies, which included 825 patients in active-controlled clinical trials in patients with relapsing forms of MS (RMS) and 486 patients in a placebo-controlled study in patients with primary progressive MS (PPSMS).

Adverse Reactions in Patients in Relapsing Forms of MS

In active-controlled clinical trials (Study 1 and Study 2), 825 patients with RMS received OCREVUS 600 mg intravenously every 24 weeks (initial treatment was given as two separate 300 mg infusions at Weeks 0 and 2). The overall exposure in the 48-month controlled treatment period was 1488 patient-years. The most common adverse reactions in RMS (incidence ≥ 10%) were upper respiratory infections and infusion reactions. Table 2 summarizes the adverse reactions that occurred in RMS trials (Study 1 and Study 2).

Table 2 Adverse Reactions in Adult Patients with RMS with an Incidence of at least 5% for OCREVUS and Higher than REBIF

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>OCREVUS 600 mg IV Every 24 Weeksa</th>
<th>REBIF 44 mg SQ 3 Times per Weekb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infections</td>
<td>40</td>
<td>33</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>34</td>
<td>10</td>
</tr>
<tr>
<td>Depression</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Lower respiratory tract infections</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Back pain</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Herpes virus-associated infections</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

aThe first dose was given as two separate 300 mg infusions at Weeks 0 and 2.

Adverse Reactions in Patients with Primary Progressive MS

In a placebo-controlled clinical trial (Study 3), a total of 486 patients with PPSMS received one course of OCREVUS (600 mg of OCREVUS administered as two 300 mg infusions twice a week) given intravenously every 24 weeks and 239 patients received placebo intravenously. The overall exposure in the controlled treatment period was 1419 patient-years, with median treatment duration of 3 years.

The most common adverse reactions in the PPSMS trial (incidence ≥ 10%) were upper respiratory tract infections, skin infections, and lower respiratory tract infections. Table 3 summarizes the adverse reactions that occurred in the PPSMS trial (Study 3).
Attenuated or live vaccines is not recommended during treatment and until B-cell repletion. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody, OCREVUS to patients with active HBV confirmed by positive results for HBsAg and anti-HB tests. Reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV monitoring in multiple sclerosis patients receiving OCREVUS. Serious herpes virus infections may occur at any time after initiating OCREVUS and Higher than REBIF experienced one or more infections compared to 68% of patients in a control group. Respiratory Tract Infections [see Warnings and Precautions (5.4)].

5.2 Infections
Respiratory Tract Infections, infusion reactions, skin infections, and lower respiratory tract infections, skin infections, and herpes-related infections have been reported more frequently in OCREVUS-treated patients. In RMS trials (Study 1 and Study 2). Decreased Neutrophil Levels In the PPMs clinical trial (Study 3), decreased neutrophil counts occurred in 13% of OCREVUS-treated patients compared to 10% in placebo patients. The majority of the decreased neutrophil counts were only observed once for a given patient treated with OCREVUS and were between LLN - 1.5 x 10^9 and 1.0 x 10^9. Overall, 1% of the patients in the OCREVUS group had neutrophil counts less than 1.0 x 10^9 and these were not associated with an infection.

6.2 Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. Immunogenicity data are highly dependent on the sensitivity and specificity of the test methods used. Additionally, the observed incidence of a positive result in a test method may be influenced by several factors, including sample handling, timing of sample collection, drug interference, concomitant medication, and the underlying disease. Therefore, comparison of the incidence of antibodies to OCREVUS with the incidence of antibodies to other products may be misleading. Patients in MS trials (Study 1, Study 2, and Study 3) were treated at multiple time points (baseline and every 8 months post-treatment for the duration of the trial) for anti-drug antibodies (ADAs). Out of 1311 patients treated with OCREVUS, 12 (1%) tested positive for ADAs, of which 2 patients tested positive for neutralizing antibodies. These data are not adequate to assess the impact of ADAs on the safety and efficacy of OCREVUS.

6.3 Postmarketing Experience
The following adverse reactions have been identified during postapproval use of OCREVUS. Benefits of OCREVUS are reported voluntarily by patients and are not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Serious herpes infections have been identified during postapproval use of OCREVUS (see Warnings and Precautions (5.2)).

7 DRUG INTERACTIONS
7.1 Immunosuppressive or Immune-Modulating Therapies
The concomitant use of OCREVUS and other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids, is expected to increase the risk of immunosuppression. Consider the risk of additive immune system effects when coadministering immunosuppressive therapies with OCREVUS. When switching from drugs with prolonged immune effects, such as cladribine, fingolimod, natalizumab, tenofovir, or mitoxantrone, consider the duration and mode of action of these drugs because of additive immunosuppressive effects when initiating OCREVUS (see Warnings and Precautions (5.2)).

7.2 Vaccinations
A Phase 3b randomized, open-label study examined the concomitant use of OCREVUS and several non-live vaccines in adults 18-55 years of age with relapsing forms of MS (68 subjects undergoing treatment with OCREVUS at the time of vaccination and 34 subjects unvaccinated at the time of vaccination). OCREVUS administered concomitantly to OCREVUS attenuated antibody responses to tetanus toxoid-containing vaccine, pneumococcal polysaccharide, pneumococcal conjugate vaccines, and seasonal influenza vaccine. The impact of the observed attenuation on vaccine effectiveness in this patient population is unknown. The safety and effectiveness of live or live-attenuated vaccines administered concomitantly with OCREVUS have not been assessed (see Warnings and Precautions (5.2)).

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category C
There is a pregnancy exposure registry that monitors pregnancy and fetal/neonatal infant outcomes exposed to OCREVUS during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-837-872-4370 or visiting www.ocreveruspregnancyregistry.com.

8.2 Lactation
OCREVUS is a humanized monoclonal antibody of an immunoglobulin G1 subtype and immunoglobulins are known to cross the placental barrier. There are no adequate data on the developmental risk associated with use of OCREVUS in pregnant women. Herd transient peripheral B-cell depletion and lymphopenia was reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. B-cell levels in infants following maternal exposure to OCREVUS have not been studied in clinical trials. The potential duration of B-cell depletion in such infants, and the impact of B-cell depletion on vaccine safety and effectiveness, is unknown (see Warnings and Precautions (5.2)).

8.3 Females and Males of Reproductive Potential
Women of childbearing potential should use effective contraception while receiving OCREVUS and for 6 months after the last infusion of OCREVUS.

8.4 Pediatric Use
Safety and effectiveness of OCREVUS in pediatric patients have not been established.

8.5 Geriatric Use
Clinical studies of OCREVUS did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

17 PATIENT COUNSELING INFORMATION
Advising patients to take the FDA-approved patient labeling (Medication Guide).

8.6 Adverse Reactions
Inform patients about the signs and symptoms of infusion reactions, and that infusion reactions can occur up to 24 hours after infusion. Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion reactions (see Warnings and Precautions (5.1)).

Infusion Reactions
Advise patients to contact their healthcare provider for any signs of infection during treatment or after the last dose. Signs include fever, chills, constant cough, or signs of herpes such as cold sores, shingles, or genital sores (see Warnings and Precautions (5.1)).

Infections
Advise patients to complete any required live or live-attenuated vaccinations at least 4 weeks prior to initiation of OCREVUS. Administration of live-attenuated or live vaccines is not recommended during treatment with OCREVUS and until B-cell repletion.

Vaccinations
Advise patients to complete any required live or live-attenuated vaccinations at least 4 weeks and, whenever possible, non-live vaccinations at 2 weeks prior to initiation of OCREVUS. Administration of live-attenuated or live vaccines is not recommended during treatment with OCREVUS and until B-cell recovery (see Warnings and Precautions (5.2)).

Contraception
Advise patients that an increased risk of malignancy, including breast cancer, may exist with OCREVUS. Advise patients that they should follow standard breast cancer screening guidelines (see Warnings and Precautions (5.2)).

pregnancy
Instruct patients that if they are pregnant or plan to become pregnant while taking OCREVUS they should inform their healthcare provider (see Use in Specific Populations (8.1)). Encourage patients to enroll in the OCREVUS Pregnancy Registry if they become pregnant while taking OCREVUS (see Use in Specific Populations (8.1)).

OCREVUS® [ocrelizumab]
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Table 3 Adverse Reactions in Adult Patients with PPMS with an Incidence of at Least 5% for OCREVUS and Higher than Placebo

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Study 3</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCREVUS 600 mg IV Every 24 Weeks*</td>
<td>(n=436)</td>
<td>(n=239)</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>42</td>
<td>26</td>
</tr>
<tr>
<td>Skin infections</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Lower respiratory tract infections</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Cough</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Herpes virus associated infections</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

*One dose of OCREVUS (400 mg administered as two 300 mg infusions two weeks apart)
Realistic expectations about SDOH

Social determinants of health (SDOH) are a trending topic in U.S. healthcare. But as Timothy Kelley discusses in the cover story of this issue of Managed Healthcare Executive®, the idea that our health has causes outside the typical boundaries of healthcare is hardly new — and actually kind of obvious.

Where we live, what we do for a living, the food we eat and the air we breathe are all factors in a complicated, multifactorial equation that can produce an “answer” of good health and long life or one burdened by illness and cut short. There are other factors, of course, such as inherited tendencies. But study after study has shown that the SDOH factors in the equation have large coefficients. They are, in fact, determinative. We ignore them at our peril.

What is new is the spotlight that has been trained on SDOH. The uneven effects of the COVID-19 pandemic are partly responsible. The murder of George Floyd in 2020 layered in a powerful consideration of race and racism.

Awareness is almost always a necessary starting point for addressing a problem. But it will never get you across the finish line. The efforts that people in U.S. healthcare are making to address SDOH are as varied as the SDOH themselves.

Healthcare runs on data, and as Margaret Murray, M.P.A., CEO of the Association for Community Affiliated Plans and a member of Managed Healthcare Executive’s editorial advisory board, points out in our cover story, there has been a lack of data on race and ethnicity that needs to be corrected.

U.S. healthcare also runs on billing codes, and the creation of Z codes for nonmedical conditions (e.g., homelessness or the death of a spouse) in the ICD-10 coding system may aim some resources toward addressing SDOH.

Clinicians are stretched thin and there are good reasons not to put even more on their plates. Let physicians be physicians, not social workers. Fuller and more robust integration of healthcare workers trained to deal with SDOH in a culturally competent way is one way to go. The “on the other hand” is that physicians and nurses cannot be allowed to have tunnel vision. “If I’m prescribing a medicine a patient can’t afford and there are cheaper alternatives, that’s just bad medicine,” Laura Gottlieb, M.D., M.P.H., a professor of family and community medicine at the University of California, San Francisco, told Kelley.

Realistic expectations are important. Expecting healthcare to solve SDOH is a setup for failure. But healthcare that takes SDOH into account and begins to address them is better healthcare.
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TARPEYO™ (budesonide) delayed release capsules is designed to deliver treatment to an area of the ileum to target mucosal B cells, which are responsible for the production of galactose-deficient IgA1 antibodies, causing immunoglobulin A Nephropathy (IgAN).1,2,4

*Drug release is initiated in the ileum by the pH-dependent disintegration of the enteric coat.1,3

**Designated to deploy in the ileum**

**FDA approved to reduce proteinuria in IgA Nephropathy1**

**Indication**
TARPEYO™ (budesonide) delayed release capsules is a corticosteroid indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g. This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

**Important Safety Information**

**Contraindications:** TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis, have occurred with other budesonide formulations.

**Warnings and Precautions**

**Hypercorticism and adrenal axis suppression:** When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy (see Dosing and Administration) or switching between corticosteroids, monitor for signs of adrenal axis suppression. Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

**Risks of immunosuppression:** Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressive doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection; untreated fungal, bacterial, systemic viral, or parasitic infections; or ocular herpes simplex. Avoid exposure to active, easily transmitted infections (e.g., chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.
Designed to deploy in the ileum\(^1,2,4\):
- Designed to deliver treatment to the area of the ileum, including the Peyer’s patches, where mucosal B cells are located
- Mucosal B cells express glucocorticoid receptors and produce galactose-deficient IgA1 antibodies, causing IgAN
- Through anti-inflammatory and immunosuppressive effects at the glucocorticoid receptor, TARPEYO can modulate B cell numbers and activity

Statistically significant reduction in UPCR with TARPEYO plus RASI vs RASI alone at 9 months\(^5\):
- **Primary endpoint:** Significant reduction (34%) in UPCR from baseline was achieved in the TARPEYO plus renin-angiotensin system inhibitor (RASI)-treated group (n=97) vs 5% with RASI alone (n=102) at 9 months\(^6\)
  - After 3 months of observational follow-up, a 53% reduction from baseline in UPCR was seen in the TARPEYO plus RASI-treated group (n=97) vs 9% with RASI alone (n=102)\(^6\)

Additional data presented beyond the primary endpoint of 9 months should be interpreted cautiously.

\(\text{eGFR data with TARPEYO plus RASI vs RASI alone at 9 months}\):
- **Secondary endpoint:** At 9 months, absolute change in eGFR was -0.6 mL/min/1.73 m\(^2\) with TARPEYO plus RASI (n=97) vs -4.0 mL/min/1.73 m\(^2\) with RASI alone (n=102)\(^7,8\)

These interim secondary endpoint data were not prospectively controlled for multiplicity and need cautious interpretation. The clinical significance of these results is unknown. Confirmatory clinical trial results are required to draw any conclusions. It has not been established whether TARPEYO has demonstrated a benefit in slowing kidney function decline in patients with IgAN.\(^9\)

Demonstrated safety profile
- 57% of patients in the TARPEYO plus RASI-treated group reported adverse reactions vs 73% of patients on RASI alone\(^1,2,3\)
- In clinical studies, the most common adverse reactions of TARPEYO plus RASI (occurring in ≥10% of patients treated with TARPEYO plus RASI and at a higher incidence than RASI alone) were hypertension, peripheral edema, muscle spasms, and acne\(^1,4,5\)
- Incidence of serious adverse events with TARPEYO plus RASI vs RASI alone (11% vs 5%)\(^6\)
- Incidence of adverse events leading to treatment discontinuation of TARPEYO plus RASI vs RASI alone (9% vs 1%)\(^8\)
- The safety profile is generally consistent with the well-established safety profile of the active ingredient, budesonide\(^2\)

**Study Design:** NeFliArd is an ongoing, phase 3, randomized, double-blind, multicenter study to evaluate the efficacy and safety of TARPEYO 16 mg/day vs placebo in patients with primary IgAN as an addition to optimized RAS blockade therapy. Part A of the study (n=199) included a 9-month blinded treatment period and a 3-month follow-up period. The primary endpoint was UPCR at 9 months; eGFR was a secondary endpoint. Part B, a confirmatory validation study in which no treatment will be administered, will assess eGFR over 2 years.\(^3,4\)

\(^1\)It has not been established to what extent the efficacy of TARPEYO is mediated via local effects in the ileum vs systemic effects.\(^1\)
\(^2\)≥5% reduction (95% CI, 16-42) in UPCR with TARPEYO plus RASI vs RASI alone (P=0.0001).\(^3,4\)
\(^3\)All patients with a UPCR/eGFR reading regardless of use of probiotic medication at 9 months and 12 months.\(^1,3\)
\(^4\)Adjusted geometric least squares mean ratio of UPCR relative to baseline were based on a longitudinal repeated measures model.\(^1\)
\(^5\)49% reduction (95% CI, 37-58) in UPCR with TARPEYO plus RASI vs RASI alone.\(^2\)
\(^6\)Absolute changes derived from geometric least square mean ratios using the pooled baseline geometric mean.\(^3\)
\(^7\)The estimate of the ratio of geometric mean ratio of UPCR relative to baseline comparing TARPEYO 16 mg plus RASI with RASI alone was reported as percentage reduction along with the respective 95% confidence interval from the longitudinal repeated measures model and P-values.\(^1\)

**Learn more about how TARPEYO works at TARPEYOhcp.com**

**Warnings and Precautions** (cont’d)

Other corticosteroid effects: TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataracts, a family history of diabetes or glaucoma, or with any other condition in which corticosteroids may have unwanted effects.

Adverse reactions in clinical studies, the most common adverse reactions with TARPEYO (occurring in ≥5% of TARPEYO patients and ≥3% higher than placebo) were hypertension (16%), peripheral edema (14%), muscle spasms (13%), acne (11%), dermatitis (7%), weight increase (6%), face edema (6%), dyspepsia (5%), fatigue (5%), and hirsutism (5%).

**Drug interactions:** Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors, such as ketoconazole,itraconazole,ritonavir,indinavir,saquinavir,erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

**Use in specific populations**

**Pregnancy:** The available data from published case series, epidemiological studies, and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgAN. Infants exposed to in utero corticosteroids, including budesonide, are at risk for hypothalamic-pituitary-adrenal axis suppression.

**References:**
1. TARPEYO. Prescribing Information. Calliditas Therapeutics AB; 2021.
6. Primary endpoint: Significant reduction (34%) in UPCR from baseline was achieved in the TARPEYO plus RASI-treated group (n=97) vs 5% with RASI alone (n=102) at 9 months.
7. Secondary endpoint: At 9 months, absolute change in eGFR was -0.6 mL/min/1.73 m\(^2\) with TARPEYO plus RASI (n=97) vs -4.0 mL/min/1.73 m\(^2\) with RASI alone (n=102).
8. These interim secondary endpoint data were not prospectively controlled for multiplicity and need cautious interpretation. The clinical significance of these results is unknown. Confirmatory clinical trial results are required to draw any conclusions. It has not been established whether TARPEYO has demonstrated a benefit in slowing kidney function decline in patients with IgAN.
9. The safety profile is generally consistent with the well-established safety profile of the active ingredient, budesonide.

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TARPEYO™ (budesonide) delayed release capsules
Brief Summary of Prescribing Information

4 CONTRAINDICATIONS
TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis have occurred with other budesonide formulations.

5 WARNINGS AND PRECAUTIONS

5.1 Hypercorticism and Adrenal Axis Suppression
When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy (see Dosing and Administration (2)) or switching between corticosteroids, monitor for signs of adrenal axis suppression. Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure of oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B) (see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)).

5.2 Risks of Immunosuppression
Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressant doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection, untreated fungal, bacterial, systemic viral or parasitic infections, or ocular herpes simplex. Avoid exposure to active, easily-transmitted infections (e.g., chickenpox, measles). Corticosteroid therapy may decrease the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations, supplementation with a systemic corticosteroid is recommended. How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, consider therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIg). If exposed to measles, consider prophylaxis with pooled intramuscular immunoglobulin (IG). If chickenpox develops, consider treatment with antiviral agents.

5.3 Other Corticosteroid Effects
TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma or cataracts, or with a family history of diabetes or glaucoma, or with any other condition where corticosteroids may have unwanted effects.

6 ADVERSE REACTIONS
The following clinically significant adverse reactions are described elsewhere in the labeling:
- Hypercorticism and adrenal suppression [see Warnings and Precautions (5.1)]
- Risks of immunosuppression [see Warnings and Precautions (5.2)]
- Other corticosteroid effects [see Warnings and Precautions (5.3)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety of TARPEYO has been evaluated in a randomized controlled study in 197 patients. The most common adverse reactions reported in greater than or equal to 5% of TARPEYO-treated patients are listed in Table 1. The majority of adverse reactions were mild or moderate in severity.

Table 1: Reported adverse reactions occurring in greater than or equal to 5% of TARPEYO treated patients, and greater than or equal to 2% higher than Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TARPEYO 24 mg (N=97)</th>
<th>Placebo (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Patients with any Adverse Reaction</td>
<td>94 (97)</td>
<td>73 (73)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (16)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>14 (14)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Muscle spasm</td>
<td>13 (13)</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Acne</td>
<td>11 (11)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>7 (7)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Weight increased</td>
<td>7 (7)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Syncope</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fever</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>5 (5)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5 (5)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Most adverse reactions that occurred at a greater incidence for TARPEYO compared to placebo were consistent with hypercortisolism.

7 DRUG INTERACTIONS

7.1 Interaction with CYP3A4 Inhibitors
Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors; e.g. ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary The available data from published case series, epidemiological studies and reviews of oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgA Nephropathy. Infants exposed to in-utero corticosteroids, including budesonide, are at risk for hyypoaldrenism (see Clinical Considerations). In animal reproduction studies with pregnant rats and rabbits, administration of subcutaneous budesonide during
organogenesis at doses approximately 0.3 times or 0.03 times, respectively, the maximum recommended human dose (MRHD), resulted in increased fetal loss, decreased pup weights, and skeletal abnormalities. Maternal toxicity was observed in both rats and rabbits at these dose levels (see Data). The estimated background risk of major birth defects and miscarriage of the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations Disease-Associated Maternal and/or Embryo/Fetal Risk IgA nephropathy in pregnancy is associated with adverse maternal outcomes, including increased rates of cesarean section, pregnancy-induced hypertension, pre-eclampsia and preterm delivery, and adverse fetal/neonatal outcomes, including stillbirth and low birth weight. Fetal/Neonatal Adverse Reactions Hypoadrenalism may occur in infants born to mothers receiving corticosteroids during pregnancy. Infants should be carefully observed for signs of hypoadrenalism, such as poor feeding, irritability, weakness, and vomiting, and managed accordingly (see Warnings and Precautions 5.1).

Data Animal Data Budenoside was teratogenic and embryo-lethal in rabbits and rats. In an embryo-fetal development study in pregnant rats dosed subcutaneously with budenoside during the period of organogenesis on gestation days 6 to 15 there were effects on fetal development and survival at subcutaneous doses up to approximately 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose (MRHD) on a body surface area basis). In an embryo-fetal development study in pregnant rabbits dosed during the period of organogenesis on gestation days 6 to 18, there was an increase in maternal abortion, and effects on fetal development and reduction in litter weights at subcutaneous doses from approximately 25 mcg/kg (approximately 0.03 times the MRHD on a body surface area basis).

Maternal toxicity, including reduction in body weight gain, was observed at subcutaneous doses of 5 mcg/kg in rabbits (approximately 0.006 times the maximum recommended human dose on a body surface area basis) and 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose on a body surface area basis). In a peri- and post-natal development study, subcutaneous treatment of pregnant rats with budenoside during the period from Day 15 post coitum to Day 21 post partum, budenoside had no effects on delivery, but did have an effect on growth and development of offspring. In addition, offspring survival was reduced and surviving offspring had decreased mean body weights at birth and during lactation at exposures ≥ 0.012 times the MRHD (on a mg/m² basis at maternal subcutaneous doses of 20 mcg/kg/day and higher). These findings occurred in the presence of maternal toxicity.

8.2 Lactation Risk Summary Breastfeeding is not expected to result in significant exposure of the infant to TARPEYO. Lactation studies have not been conducted with oral budenoside, including TARPEYO, and no information is available on the effects of the drug on the breastfed infant or the effects of the drug on milk production. One published study reports that budenoside is present in human milk following maternal inhalation of budenoside (see Data). Routine monitoring of linear growth in infants is recommended with chronic use of budenoside in the nursing mother. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for TARPEYO and any potential adverse effects on the breastfed infant from TARPEYO, or from the underlying maternal condition.

Data One published study reports that budenoside is present in human milk following maternal inhalation of budenoside, which resulted in infant doses approximately 0.3% to 1% of the maternal weight-adjusted dosage and a milk to plasma ratio was approximately 0.5. Budenoside was not detected in plasma, and no adverse events were noted in the breastfed infants following maternal use of inhaled budenoside. Assuming a daily average milk intake of about 150 mL/kg/day and a milk to plasma ratio of 0.5, the estimated oral dose of budenoside for a 5-kg infant is expected to be less than 2 mcg/day for a maternal dose of 16 mg TARPEYO. Assuming 100% bio-availability in the infant this is about 0.1% of the maternal dose and about 3% of the highest inhaled dose used clinically for asthma in infants.

8.4 Pediatric Use The safety and efficacy of TARPEYO in pediatric patients have not been established.

8.5 Geriatric Use Clinical studies of TARPEYO did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Hepatic Impairment Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to budenoside (see Warnings and Precautions 5.1) and Clinical Pharmacology (12.3). Avoid use in patients with severe hepatic impairments (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

10 OVERDOSAGE Reports of acute toxicity and/or death following overdosage of corticosteroids are rare. In the event of acute overdosage, no specific antidote is available. Treatment consists of supportive and symptomatic therapy.

Please see Full Prescribing Information for TARPEYO at TARPEYOhcp.com TARPEYO is a registered trademark of Calliditas Therapeutics AB, or its affiliates. © Calliditas Therapeutics AB All rights reserved. 4/22 US-NEF-2100056-A
Mission
Managed Healthcare Executive provides healthcare executives at health plans and provider organizations with analysis, insights and strategies to pursue value-driven solutions.
How did you get into healthcare policy research?

You know, somebody asked me today, “Why did (you) get into healthcare policy?” I think the major reason is I get really frustrated very easily. As a doc in the healthcare system, you’re constantly facing barriers like “Why can’t I do that?” “Why is that there?” “Why do I have to discharge patients early from the hospital?” or whatever other barrier there is.

Health policy research has always been my outlet to both understand what the heck are the underlying mechanisms and to identify stupidity sometimes — and to try, as best as I can, to help inform better policy in the future.

Telehealth is here to stay. What does that mean for in-person care and retail clinics?

It’ll be very interesting to see how this plays out in this kind of landscape. For example, a person becomes ill — a relatively healthy person who has the symptoms of a urinary tract infection or sinusitis — and they’re trying to figure out where to go. We are continuously adding new options of care. Urgent care has always been there. Then the retail clinics came along. Now we have these new forms of telehealth. Even within telehealth we have several options from the synchronous kinds like Amwell and Doctor on Demand, as well as the asynchronous kinds such as Lemonaid.

It’s remarkable the level of choice the average American has. Certainly, with all that competition, it’s going to be more and more difficult to get patients in the door. I certainly think we will see more competition and fewer patients at some of these sites.

But a theme of my work is that when you make care more convenient, more people get care. The other thing I like to emphasize to people is that choice comes with its downsides. The average American doesn’t always know where to go to get care. You have this phenomenon that patients have to self-triage themselves in terms of where to go. We have a problem that we never faced before. The average American didn’t go to nursing school or medical school. How are they supposed to know? We need tools, triage tools, like symptom checkers and other things to help people. I think with every new advance, new problems emerge.”
“One of my great concerns is that during the pandemic it’s been quite consistent that rural patients are less likely to use telemedicine. So that existing disparity I’m very, very fearful is getting worse.”

Why is it important for payers to adopt new alternative payment models or value-driven initiatives? How are these models helping that transition to value-based care?

I think it’s widely recognized in the U.S. healthcare system that many of the issues we face are due to the fee-for-service system and the degree that we can move to alternative payment models so we can improve the population health and address costs. Telemedicine is also a great example where many of the concerns about overuse and increased spending go away if we use some of the new alternative payment models.

But the truth is, we also recognize that the shift has not been easy. There are all sorts of complexities from an administrative and regulatory framework. We know that we need to move in that direction. We just constantly must be iterating and trying new models until we figure out the models that effectively move us away from the fee-for-service system.

Outside your research and work as a hospitalist, what are some of your hobbies or interests?

In the past year or two, the pandemic has really changed me on the exercise front. I used to run, but now it’s become more serious with a group I joined. We’re out there at 5 o’clock in the morning, every morning. It’s really been amazing for me because we’ve all gotten to the point of being a little stir crazy. This group has been critical for my mental well-being. It’s led me to do a lot of things I had never done before, like run a half-marathon. It’s become a huge part of my life, both for my mental and physical well-being.
Beauty may be in the eye of the beholder, but drug price trends are in the way you crunch the numbers.

In a piece posted on the Health Affairs Forefront blog last month, Anna Anderson-Cook, Ph.D., and her colleagues at Arnold Ventures argued that analyses by IQVIA and others that show relatively level or even decreased net drug prices in recent years may be misleading. Arnold Ventures, formerly The Laura and John Arnold Foundation, is a philanthropic organization that supports a variety of criminal justice, education and healthcare projects. In healthcare, it has been one of the main supporters of Civica Rx, a non-profit drug manufacturer, and the Institute for Clinical and Economic Review, a cost-effectiveness research organization in Boston.

One of the interesting points raised by Anderson-Cook and her colleagues is that overall trends “do not apply to the commercial market or to Medicare Part D, where net prices are both significantly higher and growing more rapidly” than they are for other payers. They cite Medicaid as an example of a payer that skews overall results. Medicaid plans have considerably lower net drug costs (costs after rebates and other discounts) than Part D plans because of Medicaid-specific rebates rules that result in larger rebates for Medicaid programs.

The Arnold Ventures researchers also made the case that year-over-year comparisons of net prices for drugs that are already on the market paint an incomplete picture because of the number and expense of new drugs.

Citing a Congressional Budget Office report, Anderson-Cook and her colleagues noted that in 2017 drugs launched after 2015 cost 12 times as much as drugs already on the market in 2015. What’s more, new drugs tend to do well, saleswise, once they are approved and on the market. The Arnold Ventures researchers pointed to a Part D dashboard maintained by CMS that shows that 30 brand-name drugs launched after 2015 were top sellers in Part D by 2019.

So far the cost of these new brand-name drugs has been offset by the shift from brand-name products to generics among the older drugs. The migration to generics has kept increases in net spending per beneficiary in Part D plans on a relatively even keel, meaning it hasn’t surpassed inflation.

The researchers also noted that at 90% the generic dispensing rate may have reached its upper limit. If brand-name drug costs continue to escalate while the generic market stays at 90%, there will be upward pressure on Part D spending, notwithstanding the level-to-moderate spending in the recent past. They cited a 2021 Medicare Trustees Report that projects that the cost of the Part D program will grow by 6.1% annually over the next five years. Biosimilars to the brand-name biologics may have their intended effect, tugging down prices of the biologics, but so far they haven’t had the same effect on prices that generics have had on small-molecule drugs, say the authors.

Without comprehensive reform, Anderson-Cook and her colleagues concluded, the cost of brand-name drugs will “grow aggressively,” straining the Medicare budget and the resources of the program’s beneficiaries.

—Peter Wehrwein
Fixing the coverage gap after incarceration

Healthcare insurance in the U.S. can be spotty, even with expansion of coverage under the Affordable Care Act. One of the remaining problem areas is coverage for people who are leaving prison or jail. In nonfederal cases, state and county governments pay for healthcare during the period people are incarcerated. But once they are released, there is often a gap before they get signed up for coverage by Medicaid or another payer. For people with chronic health conditions, that gap can lead to medical conditions getting out of control and acute episodes that lead to hospitalization or premature death.

The federal Medicaid Reentry Act of 2021 is designed to remedy the situation. Currently, Medicaid programs are explicitly prohibited from covering incarcerated individuals. The proposed law would permit Medicaid to cover people starting 30 days before they are to be released. Advocates and public health officials say that would mean a smoother transition and increase the chances that recently incarcerated people will receive the medical services they need.

But the Reentry Act could have some unintended consequences. Utsha Khatri, M.D., of the Institute for Heath Equity Research at the Icahn School of Medicine at Mount Sinai in New York and Tyler N.A. Winkelman, M.D., M.Sc., of the Health, Homelessness, and Criminal Justice Lab at the Hennepin Healthcare Research Institute in Minneapolis outlined a few of the consequences in an opinion piece published in April in the New England Journal of Medicine. Would prisons and jails put off medical care until the 30-day period before release so the cost would fall on a Medicaid program? Would care be substandard? New quality improvements might need to be developed and supported. And the Reentry Act may have little, if any, effect on coverage in the 12 states that haven’t expanded Medicaid, they noted. There are also practical problems of implementing coverage and working with prison and jail officials.

Many people in jail are awaiting trial, incarcerated because they couldn’t afford bail or were denied it. Khatri and Winkelman said they agree with the National Association of Counties and the National Sheriffs’ Association that the Reentry Act should be amended so the ban on Medicaid coverage for incarcerated people would not extend to people in jail who are awaiting trial. They also noted the Reentry Act wouldn’t deal with the larger issue of the harms done by mass incarceration. In their view, the Reentry Act should be “coupled with broader policies redirecting people away from the harmful carceral system.” In 2021, the Reentry Act was attached to the sweeping Build Back Better legislation that passed in the House but stalled in the Senate. Khatri and Winkelman said Congress may consider the Reentry Act as a separate piece of legislation this year.

—Peter Wehrwein

Listen to our podcasts!

Risk assessments are important to payers and providers — and, ultimately, to patients. In a recent episode of our “Tuning In to the C-Suite” podcast, Editor Briana Contreras spoke with Emad Rizk, M.D., chairman, president, and CEO of Cotiviti, about the topic of risk assessment and about how adopting risk assessment tools that include data about social determinants of health can help reduce bias and improve healthcare.

“Tuning In to the C-Suite” is our main weekly podcast. But we also have a subseries called “MHE Talks: Improving Patient Access.” And we feature the members of our editorial advisory board in the “Meet the Board” subseries (see page 11).

Have a suggestion for a future guest? Please drop Briana Contreras a line at BContreras@mjhlifesciences.com.

To listen to episodes of “Tuning In to the C-Suite,” or either subseries, go to our website, www.managedhealthcareexecutive.com and you will find them under the Media tab. You can also search out our podcasts on Apple, Spotify and iHeart Radio podcasts.

Listen in. Learn a lot.
DEEP DIVE

The Epstein-Barr virus as a cause of multiple sclerosis

Bridget A. Bagert, M.D., M.P.H., director of the Ochsner Multiple Sclerosis Center in New Orleans, discussed recent epidemiologic findings linking infection with the Epstein-Barr virus to multiple sclerosis. Bagert reviewed the accumulation of evidence that supports a causal link, including pathological findings that have identified RNA and proteins from the Epstein-Barr virus in the brains of people with multiple sclerosis.


BEHIND THE SCIENCE

Advances in antiretroviral treatment of AIDS and preexposure prophylaxis for prevention of HIV

Ann Melvin, M.D., M.P.H., of Seattle Children’s Hospital; Jessica Islam Ph.D., M.P.H., of the Moffitt Cancer Center; and Patricia de los Rios, global medical affairs director of ViiV Healthcare, discussed advances in antiretroviral therapy as a treatment for AIDS and preexposure prophylaxis (PrEP) for prevention. Despite the advances, they said access to treatment and PrEP remains an issue, especially on a worldwide basis.


INSIDE THE PRACTICE

Development and use of an open-access data resource to guide immunotherapy for cancer

Yu Shyr, Ph.D., professor and chair of the Department of Biostatistics at Vanderbilt University Medical Center and director of the Vanderbilt Center for Quantitative Sciences, discussed Cancer-Immu, an open-access resource that links onco-immunologic genomic data and immunophenotype with biological insights to help oncologists select the appropriate immune checkpoint blockade. Shyr spoke about the clinical problems posed by immunotherapy and how the developers of Cancer-Immu hope their platform will help solve them.

HEADING UPSTREAM

There’s a long history to recognizing that social factors shape people’s health. But the social determinants of health are getting more attention than ever.

Will that attention turn into action and lasting change?

By TIMOTHY KELLEY

How is this for a medical scenario? Through her stethoscope, a doctor hears a rattle in Mr. Rodriguez’s chest. “Urban-air congestion!” she declares, flinging the window open and aiming a magic spray at the polluted outdoors. “Two spritzes each morning for a week,” she says, handing her patient the bottle, “and you — and the neighborhood — should be fine.” Ms. Jackson has diabetes of the lives-too-far-from-veggies variety; her doctor gives her a wand she can wave to instantly transform her paved yard into a luxuriant garden with tomatoes, basil, beets and Brussels sprouts. Then there’s Mr. Diefenbaker, whose home is on a remote dirt road. His chronic conditions are worsening because he has trouble coming in for office visits — he can’t afford a car, there’s no bus line nearby and the neighbor who gives him rides is undependable. “Stat!” the doctor calls to her assistant, who pecks notes on a digital tablet. “Get a new light-rail transit system going past Mr. Diefenbaker’s house!”

These are fantasies, of course. We don’t live in such a magical healthcare world, but we do enjoy the next best thing: the widespread understanding that the origins of health or illness extend way beyond the proximal effect of a clogged artery, swollen tissue or genetically damaged cancerous cells. In healthcare there is agreement that our health status reflects not just what our
bodies and brains are doing but also how the social determinants of health (SDOH) have affected it. The government gets it. The rather lumpy definition of SDOH by HHS is "the conditions in the environments where people are born, live, learn, work, play, worship and age that affect a wide range of health, functioning and quality-of-life outcomes and risks." But we’ve been hearing about SDOH for some years now, and it’s fair to ask: How much good has understanding and acknowledging the concept actually done?

There’s no doubt that SDOH have become prominent in healthcare policies and discourse. “In the past decade,” says Laura Gottlieb, M.D., M.P.H., a professor of family and community medicine at the University of California, San Francisco, “things have moved from people understanding the impact of social determinants to an acceptance that there’s a role for delivery systems and payers to do something about them to improve equity in health outcomes.”

Margaret Murray, a member of the Managed Healthcare Executive editorial advisory board and CEO of the Association for Community Affiliated Plans (ACAP), a trade association representing 78 nonprofit health plans, says her group was studying SDOH “before it was cool.” SDOH are "baked into the DNA" of its members, health plans that were started by federally qualified community health centers, local governments and children’s hospitals, she says. She points to member-plan initiatives such as a job-support program at CareSource in Ohio and “food as medicine” campaigns aimed at food-insecure areas by CareOregon and Geisinger Health of Pennsylvania. In many cases, Murray says, plans are paying for these efforts themselves. Because such an approach isn’t sustainable in the long run, ACAP has proposed an SDOH rebate add-on, which, as Murray explains, “would be a way of giving plans some extra money to help with the social determinants of their beneficiaries who are enrolled in D-SNPs” — that is, dual-eligible special-needs plans for people entitled to both Medicare and Medicaid.

AN OLD IDEA’S NEW CLOUT
Recognition that circumstance impinges on biology does not belong solely to the 21st century. The ancient Romans noticed that there were higher death rates near marshes and swamps. Rudolf Virchow, a 19th-century German physician, writer and politician, is renowned for his theory of cellular pathology, which helped lay the foundation for modern medicine. But he’s also considered the founder of social medicine, famous for insisting that “medicine is a social science, and politics is nothing else but medicine on a large scale.”

Fast-forward to 20th-century Britain, where Thomas McKeown was named a professor of social medicine at the University of Birmingham in 1945. He studied Western societies’ increases in life expectancy, and in the 1970s he argued that these were due less to medicine’s advances than to economic growth and the improved nutrition it brought. Critics complained that McKeown slighted the role of public health policies such as those aimed at cleaning up drinking water and ending bovine tuberculosis, but the spotlight he’d shone on social factors remained bright.

Then there is Sir Michael Marmot, whose renowned Whitehall studies, which started in the 1960s, tracked a cohort of British civil servants. The Whitehall results defied the expectation that top executives facing the presumably heaviest stress would have the greatest cardiac risk. They showed that heart attacks — along with many other ills — actually increased as one went down the “social gradient.” It’s not clear who coined the term SDOH, but in 1999 the World Health Organization (WHO) published Social Determinants of Health: The Solid Facts, a report (co-edited by Marmot) that listed 10 areas in which social conditions influenced health.

“Poor social and economic circumstances affect health throughout life,” the report stated — that part wasn’t surprising. People who couldn’t afford medical care or healthy food or a safe home were clearly at extra risk. But those British bureaucrats at the bottom of Marmot’s studies weren’t poor; they had stable paychecks and presumably could buy the basics needed for good health maintenance. Yet the document insisted: “Even junior office staff tend to suffer much more disease and earlier death than more senior staff.” Who knew — besides WHO — that health so closely tracked wealth?

Continued on page 19
ProMedica has done ambitious work in Toledo’s UpTown neighborhood, yes? Yes. Seven years ago, in what was once a food desert, we opened a grocery that has served 58,000 customers. We’ve helped approximately 200 homeless individuals connect to services and get housed. We’ve connected 5,000 individuals to jobs and support and provided financial coaching to more than 800 people, increasing their average monthly income by $352 and helping them raise their credit scores by an average 79 points. And among 1,753 participants in our food clinic, we’ve seen a 20% reduction in (emergency department) visits (compared with a 12% decline for similar patients not enrolled in the program), with $6,400 in savings.

Can you prove your success with statistics on health status itself? That’s difficult; health outcomes are the last piece to measure. But across the country we’ve seen some very small pilot programs where we’re able to measure health outcomes. Where we see that most is in our work in maternal health. We’re scaling a program that connects high-risk expectant moms with community health workers, and it has shown improved birth outcomes and decreases in NICU (neonatal intensive care unit) stays.

Isn’t addressing SDOH mostly a matter for Medicaid? That’s one of the myths. Actually, a great many Medicare patients and almost 50% of the commercial patients who come through our doors (have) some type of need. Social and economic factors really span across populations and demographics.

What have you learned from your experience with SDOH? One, that this work is all interconnected and it really takes a village — the integration of payers and providers, community members, nonprofit organizations, even employers. Two, we’ve been able to use teleservices, especially during the pandemic. For example, we’re now providing financial coaching across the country virtually. Three, it’s critical to engage the people we’re serving in the decision-making process. No longer can we in healthcare sit in our office buildings and hospitals and create solutions by ourselves.

Is healthcare still struggling to get a grip on SDOH? Especially in the aging population, we’ve seen an uptick in social isolation, which COVID-19 has exacerbated. That’s an area where we’re still really testing and piloting. From an industry perspective, we’re trying to understand what moves the needle. I’d also cite the need for scalability. Many initiatives in individual markets are working, but we’ve got to figure out, Can you get those to scale? Can you do them across markets?

The use of data is key, isn’t it? Part of our work is focused on ROI (return on investment). That’s our north star at the end of the day — to be able to prove which interventions are effective. So we use data analytics. We partner with the startup tech firm Socially Determined (based in Washington, D.C.), which braids together our intervention data with EMR (electronic medical record) and claims data sets to understand what drives value.

Any lessons in the use of data? We see patients for a very limited time, so we’ve been focused on creating seamless, no-touch workflows integrated into the EMR. As more providers get into this space, those who were going in a different direction come back to this approach from an efficiency and effectiveness perspective.

What’s next? We’re starting to use a proactive approach, not waiting until someone comes into our doctors’ offices or hospitals but targeting individuals and populations that may not be getting care today but have a social determinant need.

Despite everything you’re doing, is the SDOH effort is still just getting off the ground nationally? I’m a little more optimistic than that. Payers are now starting to fund different social and economic supports. We closed 2021 with eight different contracts with payers who are providing food funding and financial coaching. And CMS is offering innovation grants to fund things like this. I think we’re starting to see the momentum shift.
**A MATTER OF JUSTICE**

In the past decade or so, says Damon Francis, M.D., medical director of Homeless Health Center at Alameda Health in California, "healthcare has become aware of the social determinants of health as an explanatory model for why some people are healthy and others aren’t.”

Francis is also chief medical officer for Health Leads, a national nonprofit aimed at addressing health inequities. And although social determinants affect everyone, most conversations about SDOH quickly segue into the related topic of health equity.

For example, take air quality and our hypothetical Mr. Rodriguez. A study published in March 2022 in Environmental Science & Technology Letters showed that although the discriminatory home lending practice of redlining was banned in the U.S. more than 50 years ago, it’s still affecting people’s health. According to an article in The Washington Post, researchers examined air-quality data for 202 cities where redlining had been practiced and found nitrogen dioxide levels markedly higher in neighborhoods that had been tagged in the 1930s as undesirable for mortgage lending. Because zoning officials often used redlining-based grades when deciding where to place highways or industrial plants, minority neighborhoods such as Boyle Heights in Los Angeles ended up being encircled by major freeways with heavy, pollutant-spewing diesel truck traffic. Thus its residents were and still are disproportionately exposed, as the Post reported, to pollutants that can “inflamm[e] human airways, reduce lung function, trigger asthma attacks and … damage the heart and cause strokes.”

Racism is an inescapable part of the SDOH story. And the fatal knee restraint that Derek Chauvin put on George Floyd’s neck in May 2020 challenged complacent acceptance of the impartiality of public institutions when it comes to race. Having already hired its first chief health equity officer in 2019, the American Medical Association adopted a policy in November 2020 recognizing racism as “an urgent public health threat” and calling for best practices to combat it “considering that studies show historically marginalized populations in the U.S. have shorter lifespans, greater physical and mental illness burden, earlier onset and aggressive progression of disease, higher maternal and infant mortality, and less access to healthcare.”

After Floyd’s death, the phrase “abolition medicine” began to appear in the literature, building on recent social criticism that linked this century’s patterns of incarceration and policing to the legacy of slavery. According to an article in the July 2020 edition of The Lancet, abolition medicine “means challenging race-based diagnostic tools and treatment guidelines that reinforce antiquated and scientifically inaccurate notions of biological race.”

In March 2022, Gottlieb and two co-authors urged that abolition be added to the “five A’s” — awareness, adjustment, assistance, alignment and advocacy — suggested by the National Academies of Science, Engineering and Medicine in 2019 as the recipe for remediating SDOH. The addition was warranted, they argued, because even the best-intentioned interventions can fall short and become part of the problem. “Inattention to structural and systemic racism as fundamental causes of individuals’ socioeconomic risks,” they warned in AMA Journal of Ethics, “means that healthcare’s social care practices will prove insufficient for improving health outcomes for marginalized patients.”

Gottlieb explains that the complex structural barriers facing those who would address SDOH in marginalized communities defy easy comprehension. “I personally haven’t been able to really, fully understand why social care is so hard,” she says.

**THE PANDEMIC’S PRICE**

The murder of George Floyd and the Black Lives Matter movement thrust SDOH and health equity issues into the consciousness of U.S. healthcare. But so has the COVID-19 pandemic with its disproportionate impacts on Black Americans. “There are more and more people who have social needs now,” says Therese Wetterman, M.P.H., a former Health Leads director and who is director of network success for Aledade, a health services company that supports private practices.

Wetterman believes the widely noted pandemic-induced increase in wealth disparities in the past two years, both in the U.S. and abroad, is bound to result in adverse in health outcomes. The COVID-19 pandemic has forced a reconsideration of many healthcare issues.

“I work with a lot of primary care practices,” Wetterman says, “and I think the impact of the pandemic on primary care has created significant capacity constraints that make it really difficult for practices to add on addressing social needs as well.” ACAP’s Murray says one thing the industry has learned from the pandemic is that “the states don’t collect good
data on race and ethnicity, which makes it harder to target your work.”

**CMS IS AWARE**

Still, one of the most heartening developments in recent years, Gottlieb says, is the way government at all levels has heard the message about SDOH. She notes that Alex Azar, HHS secretary during much of the Trump administration, saw that SDOH helped shape health inequities and that greater flexibility was needed to pay for services that addressed them. The Biden administration has made health equity a priority. In November 2021, CMS Innovation Center issued a “refresh” white paper that outlined its objectives for the next decade. Acknowledging that the ACA had authorized CMS to test payment and delivery models, it quoted Daniel Tsai, director of the Center for Medicaid and CHIP Services, that henceforth “health equity will be at the forefront of all policy decisions for Medicaid, not an afterthought.” One of the Innovation Center’s declared goals is to “develop new models and modify existing models to address health equity and social determinants of health,” according to the white paper. “CMS is considering various incentives to encourage and sustain participation, such as upfront payments, social risk adjustment, benchmark considerations and payment incentives for reducing disparities or screening for SDOH,” Janet C. Walker, senior counsel at Crowell & Moring LLP’s Health Care Group, and two co-authors wrote recently. Some states — notably Oregon and New York — are doing interesting things with Section 1115 waivers that allow special demonstration projects. Oregon aims ambitiously at eliminating healthcare inequities by 2030 with SDOH services and infrastructure improvements; New York proposes creating new organizations to drive referral networks and facilitate interventions.

Growing use of value-based contracting should theoretically afford providers the flexibility to use funds for initiatives that can reduce healthcare costs even though they’re not medical interventions. The Biden administration recently dropped the direct contracting program and launched the Accountable Care Organization Realizing Equity, Access and Community Health, or ACO REACH. The ACO REACH program adds the element of implementing “initiatives to measure outcomes, utilizing risk-adjusted payments, and creating financial incentives to improve patient experience.”

**A TALE OF TWO COUNTIES**

Social determinants of health (SDOH) have been on the minds of local, county and state governments for years. These two jurisdictions have been conspicuously active in pioneering innovative programs to address SDOH:

**KENT COUNTY, MICHIGAN**

Not every U.S. county was bold enough in 2012 to make a 13½-minute video titled “Framing Social Determinants of Health” challenging itself to do a better job of addressing the wellsprings of health disparities. But this home of Grand Rapids did. “We must measure our success by impact,” declared one community leader on the video, citing the need for improvements in rates of diabetes and high blood pressure among Black and Latino residents. Added the leader, “Shame on us if we’re having this conversation a year from now.”

A decade later, the nation has learned humility about the complex task of addressing SDOH — and so has Kent. Although survey numbers aren’t available for the number of patients with hypertension, the rate of self-reported diabetes did decline among Black adults in the county between 2014 and 2020, from 18.9% to 15.9%. But disparities lived on (the comparable figures for White adults: 8.5% to 7.6%) despite many initiatives, including improvements to local parks and a partnership with the YMCA’s “Veggie Van,” a mobile farmers’ market that provides produce to stores in food-desert areas.

Kent County is still waging the SDOH fight by, for example, putting CDC grant money to work addressing needs identified by the community. A neighborhood group, Seeds of Promise, advised the county to focus on housing and a program was shaped accordingly. Asked what advice she’d offer other counties with high-need populations, Teresa Branson, chief diversity, equity and inclusion officer for the county’s Health Department (and narrator of that video in 2012), says it’s vital to build trust with sometimes skeptical community residents. “Don’t plan anything without the community,” she says. “We’ve been guilty of doing that for years in public health,” Branson adds. “We think we have the answers, and a lot of times we don’t.”

—Timothy Kelley
surably reduce health disparities.”

Increasing use of Z codes — introduced in 2015 as part of changes to the medical billing code system and used for nonmedical conditions such as homelessness or the death or disappearance of a spouse — reflects today’s broader understanding of the health consequences of social ills. For the nearly half million Medicare fee-for-service beneficiaries with Z-code claims in 2017, the top two chronic conditions were hypertension (72%) and depression (53%).

In July 2021, a formal bipartisan Congressional Social Determinants of Health Caucus was formed in the U.S. House of Representatives, chaired by Democratic Rep. Cheri Bustos of Illinois. The relevant issues fall under the domain of many different federal departments and agencies; caucus members hope legislative efforts can be more focused and effective when they’re looked at through an SDOH frame.

**A FRAGMENTED SYSTEM**

Physicians and nurses, of course, are too busy already. They don’t have much time to spend on new SDOH initiatives, even in the role of simply collaborating with the community service organizations that work with payer and provider organizations to meet social needs. That, experts say, is why there’s a need for people specially trained to provide culturally competent care — to screen for SDOH needs and arrange interventions with sensitivity and without patronizing or stigmatizing assumptions. In an era when it’s difficult to find workers in many parts of the economy, this promises to be another SDOH challenge.

But Gottlieb insists that clinicians can’t be let off the hook. “If I’m prescribing a medicine a patient can’t afford and there are cheaper alternatives, that’s just bad medicine,” she says. “Doctors need to know a patient’s insurance status, what’s covered, what’s not. They need to know if a medication must be taken with food and the patient doesn’t have enough food, or if it needs to be refrigerated and the patient doesn’t have a refrigerator. We’re setting patients up for failure when we don’t have social risk data at hand.” Gottlieb knows she is asking a lot, given what she calls “our fragmented, inefficient, very expensive healthcare sector.”

Indeed, the cacophony of different business relationships complicates the questions of how to struc-

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**MARICOPA COUNTY, ARIZONA**

You can say “ACCESS” when you speak of the 40-year-old agency that administers the Arizona’s Medicaid program, but you don’t spell it that way. It’s AHCCCS, or Arizona Health Care Cost Containment System. Medicaid expansion dollars under the ACA have made possible “exciting partnerships” to address social determinants of health, says Blythe FitzHarris, Ph.D., LCSW. She’s the chief clinical officer at Mercy Care, a nonprofit health plan that serves people eligible for AHCCCS benefits.

Although transportation to doctor visits is a Medicaid-covered benefit, the funding also permits the plan to contract with providers to expand services not directly covered, such as meal deliveries to pregnant women or transportation to a support-group meeting. “We work with our cities and counties to ‘braid’ funding,” FitzHarris explains. “We say to them, ‘If you can partner with us and deliver a subsidy, then we can deliver the service supports,’ recognizing that most of these folks who are receiving county assistance also likely qualify for Medicaid.”

When experts say it’s not yet clear what mix of SDOH interventions is ideal, they get no argument from FitzHarris. But she’s happy to share some numbers from Maricopa County, which Phoenix is. They’re not new — they come from a January 2018 report — but they show the kind of things Mercy Care has been doing. For a certain high-need population, healthcare costs were approximately $20,000 per member, per quarter, before a housing subsidy initiative was implemented. The program cut the total cost of care by 24% (per member, per quarter), the cost of behavioral health professional services by 23% and behavioral health facility costs by 46%.

Mercy Care’s SDOH work can get pretty granular, as one summertime experience showed. “In our (emergency department) reports, we had someone who was continually going in,” FitzHarris says. It turned out that “the individual’s air conditioner didn’t work. He had some physical ailments. But we’re in Phoenix — it’s 120 (degrees)! ” Mercy Care worked with local utilities to fix the electrical problem in his home. “And, lo and behold, he stopped going to the emergency (department) so much,” FitzHarris says.

—Timothy Kelley
ture incentives and pay the costs of addressing SDOH. Homeless Health Center’s Francis acknowledges, “Even the same payer and the same provider may have multiple different relationships with each other, some of which are adversarial, some collaborative.”

MAKING THE CASE

In recent years there’s been a spate of studies and papers about making the business case for SDOH, exploring how an organization can prove to itself or its stakeholders that investing in these interventions is worthwhile. Among the most recent is an issue brief published by The Commonwealth Fund in January and written by Wetterman and Lea Tompsett, Aledade’s vice president of network success. Its title is neither brief nor catchy, but it gets the point across: “Capturing Value in Social Health: Lessons in Developing the Business Case for Social Health Integration in Primary Care.”

The authors argue that many SDOH interventions have been just pilot programs and that long-term funding is required to integrate these services into primary care — for example, to pay the salaries of the new community health workers or navigators who start out being a cost center rather than a revenue generator. Wetterman and Tompsett mention a pilot project by the Collaborative to Advance Social Health Integration, which folded in social health interventions into primary care in a range of settings in varying stages of evolution toward value-based payment.

“I think what our paper highlighted was that you can make the business case for addressing social needs in a variety of different payment environments,” says Wetterman. “But it takes strong evaluation structures that are aligned with financial modeling to really show the value. That was new for a lot of the practices we worked with.”

Francis admires the study but would prefer the plural — business cases — because of the central issue of who is making the case — and to whom and about what. Does the payer, for example, reap all of the savings? “Over the past three or four years, the innovation that’s happening in communities around this issue has exploded,” Francis says. “But we’re still very early in understanding which of these things we’re going to be able to replicate across a bunch of different places. We’re far away from the place where the executive can say, ‘I want to buy three of those social determinants interventions, plug-and-play, and they’re going to work for our community.’ I think people want that really desperately. But we’re not there.”

How much good has the SDOH concept done? It has undoubtedly stimulated thinking in healthcare and promising demonstration projects. But Gottlieb has concerns. “I sometimes worry that the enthusiasm around identifying and intervening with social determinants is being pushed without the strength of evidence that would lead to sustainability and effectiveness,” she says.

“The data about where the financial savings are and where you need to direct the social programs — which ones give you the biggest bang for the buck — are kind of all over the place,” she continues. “If I were a Medicaid managed care organization, it’s not totally obvious to me how comprehensive my social needs program would be. Do I target only the sickest of the sick? Or the ‘rising risk’ — people who aren’t yet super sick but seem likely to become so? Or everyone? How big a dose, for which patient and when? On those questions I wouldn’t put my money down yet.”

Francis, too, strikes a cautionary note. “I would advocate clearer thinking about mechanisms that improve public health,” he says, “and less breathless promotion of interventions that are expensive, modestly effective and possibly inequitable in the distribution of their outcomes.” He agrees that Gottlieb’s “How big a dose … trio of questions haven’t yet been answered. But he also says that even when they are, these SDOH interventions won’t make a difference relative to changes in public policy. Citing the example of smoking, he argues that all the smoking-cessation tools in the world — brochures, counseling, nicotine gum — didn’t change things on the level that raising cigarette taxes and banning smoking in restaurants did.

“How do the ways healthcare systems address individual health-related social needs drive societal awareness around what we need to do for SDOH?” Francis asks. “That’s the most interesting question for me.”

Amid studies, pilot programs and widespread excitement, SDOH hasn’t yet reached what was once called “the end of the beginning.” “The difficulty with measuring ROI (return on investment) is that people’s lives are multifactorial,” says Enrique Martinez-Vidal, M.P.P., vice president for quality and operations at ACAP. “They’re complicated.”

That complexity is not stopping his health-plan trade group from unveiling a Center for Social Determinants of Health Innovations in summer 2022. The goal is to share ideas and thus spare member plans the proverbial reinvention of the wheel. For SDOH, however, nothing quite so elegant as the wheel has been invented.

Timothy Kelley is an editor and writer in New York.
For atopic dermatitis treatment, an abundance of options

Across the globe, new drugs — injections, topical and oral — are being developed to help patients with eczema

by ROSANNA SUTHERBY, PHARM.D.

Atopic dermatitis (AD), also known as eczema, is a chronic inflammatory skin condition affecting up to 10% of adults and 20% of children in the United States. It is characterized by persistent severe itching and skin barrier disruptions. The cycle of itching and scratching perpetuates inflammation and damage to the skin, leading to infections and diminished quality of life. Symptoms of AD can disrupt sleep and have negative social and emotional effects.

Until recently, treatment for atopic dermatitis has been limited to topical corticosteroids and calcineurin inhibitors for mild to moderate AD, whereas systemic steroids, immunosuppressants and phototherapy were used for moderate to severe cases. The systemic treatments are effective but come with undesirable side effects.

An overactive immune response under the skin and compromised skin tissue on the surface are the source of AD symptoms. New agents target immune system pathways and cells directly involved in the pathology of the condition.

Janus kinase inhibitors
Researchers have shown that AD may be partially caused by over-activity of Janus kinases (JAKs), a group of inflammatory cytokines. The JAKs include JAK1, JAK2, JAK3 and tyrosine kinase 2. Blocking JAK signaling pathways can dampen the production of cytokines responsible for AD symptoms, and inhibiting select JAKs can help manage specific AD symptoms.

New JAK inhibitors have been used for several autoimmune diseases, and a handful are moving through the pipeline as potential treatments for AD. The JAK inhibitors are an important addition to AD treatment for people who haven’t responded to other treatments. “They’re amazing for these (patients with more severe cases). They have a huge, huge impact on quality of life,” said Peter A. Lio, M.D., at a session on atopic dermatitis at the annual meeting of the Academy of Managed Care Pharmacy in March. Lio is a clinical assistant professor of dermatology and pediatrics at Northwestern University’s Feinberg School of Medicine and founding director of the Chicago Integrative Eczema Center.

Incyte’s Opzelura (ruxolitinib) cream is the first topical JAK inhibitor approved by the FDA as a treatment for AD. Opzelura, which received approval in September 2021, is a JAK1 and JAK2 inhibitor indicated for the short-term treatment of mild to moderate AD in patients age 12 and older.

Earlier this year, the agency approved two oral JAK1 inhibitors that address the need for systemic therapy for moderate to severe AD. Pfizer’s Cibinqo (abrocitinib) promises relief for adults with refractory moderate to severe AD and AbbVie’s Rinvoq (upadacitinib) was approved as a treatment for adults and children age 12 and older with refractory moderate to severe AD.

Olumiant (baricitinib), an oral JAK1 and JAK2 inhibitor marketed by Eli Lilly and Incyte, was the first of its class approved in the European Union and Japan to treat moderate to severe AD in adults. In phase 3 studies, once-daily dosing of Olumiant, combined with topical corticosteroids, significantly improved signs and symptoms of AD compared with placebo and topical corticosteroids. The companies say they are on track to complete an additional phase 3 study later and are awaiting approval from the FDA.

Delgocitinib, a topical JAK inhibitor, inhibits all members of the JAK family. It is approved in Japan as a topical ointment for adults and children age 2 and older. The drug was developed by Japan Tobacco and is distributed under the brand name...
Corectim by Torii Pharmaceutical, a Japanese company.

Danish company Leo Pharma is conducting phase 3 trials investigating the potential use of a delgocitinib cream in adults with moderate to severe chronic hand eczema, a type of atopic dermatitis affecting the fingers and back of the hands.

Further back in the topical JAK inhibitor pipeline is a product being developed by Aclaris Therapeutics. After failing to meet end points with its first investigational topical JAK inhibitor, Aclaris is following up with topical solution ATI-1777. This JAK1 and JAK3 inhibitor showed positive results in a phase 2a trial, and the company has said it will move forward with a larger phase 2b trial for potential use in adults with AD.

**Monoclonal antibodies**
Monoclonal antibodies play a significant role in alleviating AD symptoms through blockade of cytokines critical to AD pathophysiology. The cytokines interleukin (IL)-4, IL-13 and IL-31 are of particular interest. AD’s skin barrier disruptions are driven by inhibition of certain proteins essential for healthy skin barrier function. IL-4 and IL-13 play a significant role in inhibiting those proteins. IL-31 promotes activation of the itch response on nerve cells and eosinophils, a type of disease-fighting white blood cell.

In 2017 the FDA approved Dupixent (dupilumab), an IL-4 receptor antagonist developed by Regeneron and Sanofi, to treat AD in adults. Lio sees Dupixent as a turning point in AD treatment: “It has changed everything and allows us to really offer sustained control for a huge group of people who never had it before, in a really safe way,” he said at the AMCP meeting.

In May 2020 the FDA approved Dupixent for children age 6 and older, and in August 2021 the companies reported meeting all end points in a phase 3 trial evaluating the use of the monoclonal antibody in children as young as 6 months. Adlyxin (tralokinumab), developed by Leo Pharma, is an IL-13 antagonist approved by the FDA in December 2021. Both biologics offer systemic treatment for moderate to severe atopic dermatitis not responding to topical treatments.

In August 2021, the FDA gave Lilly’s IL-13 inhibitor, lebrikizumab, a fast track designation, which means more frequent meetings with the FDA and a rolling review, both of which are intended to shorten the time to an approval decision.

Nemolizumab, an IL-31 inhibitor from Swiss dermatology specialist Galderma, is another drug in late-stage development. By binding to IL-31 receptors, nemolizumab keeps the interleukin from potentiating the itch sensation. In phase 2 studies, there was significant reduction in itching in patients taking nemolizumab compared with those taking placebo.

**Tapinarof**
Tapinarof is a topical first-in-class therapeutic aryl hydrocarbon receptor-modulating agent developed by biopharmaceutical company Dermavant Sciences. It is a nonsteroidal topical option for patients with mild AD. Tapinarof inhibits pathways involved with inflammatory cytokines that mediate AD symptoms. After positive phase 2 trial results, Dermavant started a phase 3 trial evaluating the use of tapinarof cream in patients age 2 and older with AD.

**Difamilast**
New Jersey-based Medimetriks and Japan’s Otsuka Pharmaceuticals are developing difamilast, a topical phosphodiesterase-4 (PDE-4) inhibitor for patients age 15 and older with mild to moderate AD. PDE-4 is involved in the production of proinflammatory cytokines responsible for symptoms of AD and other inflammatory disorders. In two phase 3 trials conducted in Japan, a higher proportion of patients who received difamilast ointment experienced clear to almost-clear skin compared with participants who used placebo.

Otsuka announced in September 2021 that Japanese regulators had approved difamilast, which in Japan is being sold under the brand name Moizerto. Medimetriks is preparing to launch phase 3 trials in the U.S. If difamilast makes it on to the market, it would join Eucrisa (crisaborole) as the second topical PDE-4 inhibitor used for AD treatment. The FDA approved Eucrisa in 2016.

Rosanna Sutherby, Pharm.D., is a medical writer and community pharmacist in High Point, North Carolina.
Humira, the biosimilars are coming, the biosimilars are coming!

Circle 2023 on your calendar — that’s when as many as 11 adalimumab biosimilars are headed for the US market

by TONY HAGEN

In recent years, rheumatologists have become more accepting of biosimilars, and their willingness to use these agents will be critical to the success of biosimilar versions of Humira (adalimumab) coming to the U.S. market in 2023. Clinical data supporting safety and efficacy of these biosimilars will be paramount in prescribing decisions, and Humira biosimilars that also have interchangeability designations will have an advantage in that respect, says Marcus Snow, M.D., chair of the American College of Rheumatology’s Committee on Rheumatologic Care and an assistant professor in the Division of Rheumatology at the University of Nebraska College of Medicine.

Humira is widely used in rheumatology to manage inflammatory and autoimmune conditions such as psoriatic arthritis, Crohn disease, polyarticular juvenile idiopathic arthritis and ankylosing spondylitis.

“The switching of a (patient with well-controlled disease) to a different product is concerning,” Snow says. “The FDA designation of interchangeability provides a lot of comfort for rheumatologists because they can look at the data supporting switching between biosimilars and bio-originators and see that there has not been any drop in efficacy or increase in antibody production. Interchangeability data are going to be very, very helpful, and I think this designation will increase the use of (Humira) biosimilars as they become available,” Snow says.

Interchangeable status is awarded to biosimilars that have not shown any difference in patient outcomes in clinical studies of multiple switches between the biosimilar and its reference product. A biosimilar with interchangeable status can be dispensed in place of an originator brand without the need for physician approval, although states have placed some restrictions on this practice. For example, physicians in many states can insist that the originator brand be used for a particular patient rather than a biosimilar.

Just a few developers of Humira biosimilars have applied for interchangeable status, but even without it, all biosimilars are as safe and efficacious as their reference products, according to the FDA. Snow says it’s difficult to bring a rheumatic disorder under control, so it’s important to have that extra level of trust that a biosimilar won’t lead to a setback.

“I think that’s the biggest concern rheumatologists have,” Snow says.

Differences in Humira biosimilars

Until the need for individual COVID-19 vaccines increased drug-makers’ revenues by tens of billions of dollars, Humira for years was the world’s top-selling drug, generating $20.69 billion in global revenues for AbbVie in 2021 alone.

So far, the FDA has approved seven biosimilars of Humira, and next year as many as 11 of these agents could be available, based on pending applications.

Not all biosimilars of Humira are alike, so physicians and payers will have plenty to think about when choosing between these products for clinical practice or placement on a formulary tier.

These biosimilars vary by concentration, citrate content, needle size, and potential for allergic reactions to latex. Citrate is a buffer that can cause pain upon injection, so citrate-free Humira is preferred by some patients. Similarly, smaller needles can be less painful. Latex is present in some needle coverings and can contaminate needles, affecting patients with allergies.

Boehringer Ingelheim has obtained interchangeable status for...
Next year, the Humira biosimilars cage match begins

As many as 11 biosimilars to Humira may come on the market next year

<table>
<thead>
<tr>
<th>Product</th>
<th>Company</th>
<th>Launch date</th>
<th>Seeking interchangeability</th>
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<tbody>
<tr>
<td>ABP 501*</td>
<td>Amgen</td>
<td>TBD</td>
<td>Yes</td>
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<tr>
<td>Abrilada</td>
<td>Pfizer</td>
<td>Nov. 20, 2023</td>
<td>Yes</td>
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<tr>
<td>Amjevita</td>
<td>Amgen</td>
<td>Jan. 31, 2023</td>
<td>Yes</td>
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<tr>
<td>AVT-02*</td>
<td>Teva</td>
<td>TBD</td>
<td>Yes</td>
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<tr>
<td>CT-P17*</td>
<td>Celltrion</td>
<td>TBD</td>
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<tr>
<td>Cyltezo</td>
<td>Boehringer Ingelheim</td>
<td>July 1, 2023</td>
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<td>Organon</td>
<td>June 30, 2023</td>
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<td>Viatris</td>
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<td>Sandoz</td>
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<td>Idacio†</td>
<td>Fresenius Kabi</td>
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<tr>
<td>Yusimry</td>
<td>Coherus BioSciences</td>
<td>July 1, 2023</td>
<td>No</td>
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*Not approved by the FDA yet. †Approved in Canada.
Sources: Cardinal Health, The Center for Biosimilars

“Interchangeability data are going to be very, very helpful, and I think this designation will increase the use of (Humira) biosimilars as they become available.” —MARCUS SNOW, M.D., UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE

Cyltezo, its biosimilar of Humira, and Alvotech is seeking interchangeable status for its own Humira biosimilar, Simlandi, although Simlandi will be a much higher concentration formulation than Cyltezo (100 milligrams vs. 50 milligrams respectively).

Other biosimilar makers, such as Samsung Bioepis, which is based in South Korea, and Organon of Jersey City, New Jersey, have decided that the interchangeable designation is not essential for marketing success. They also avoid jumping through additional FDA hoops. Samsung Bioepis and Organon will market Hadlima and are seeking approval for a 100-milligram formulation, which is considered to have an advantage because it is high concentration and low volume, making it more convenient to administer.

Amgen has the pole position

The FDA first approved Humira as a treatment for rheumatoid arthritis in 2002. By contending that Humira’s patent protections extend beyond 2023, AbbVie has been able to compel all biosimilar makers so far to settle on licensing terms, rather than come to market as free agents. The most recent to settle was Alvotech, an Icelandic company that faced patent infringement and trade secret allegations over Humira. Alvotech decided to pay royalties to AbbVie rather than wage a legal battle that might have caused it to miss out on next year’s coming-out party for Humira biosimilars. As of now, Alvotech’s Humira biosimilar, AVT02, is set to enter the fray in July 2023.

However, Amgen may be in the best position among the companies jockeying for biosimilar market share. Its Humira biosimilar, Amjevita, is scheduled to hit the market in January 2023, giving it a six-month head start on the others.

Economics of biosimilar pricing

The wave of Humira biosimilars in 2023 could lead to savings for patients and payers and the knock-on effect of improved access due to lower costs. The success of these biosimilar competitors capturing market share from Humira will hinge on pricing, according to Wayne Wine-
garden, Ph.D., a senior fellow in business and economics and director of the Center for Medical Economics and Innovation at Pacific Research Institute who has written extensively about biosimilar markets. Past experience with biosimilars in other therapeutic categories has shown that it takes a large price difference for biosimilars to wrest market share from the originator, he says. “You want to see the biosimilars coming in at 40% to 50% discounts; if they come in at 10% or something very close to the originator’s price, that would certainly temper people’s excitement or interest in switching. You need to grab people’s attention with a discount,” Winegarden says.

Another important factor is formulary placement by payers. Payers are favorably disposed toward biosimilars, but how much so depends on how much more inexpensive the biosimilars are, Winegarden explains. At the same time, the list price isn’t the same as the net price, and manufacturer rebates and other factors influence formularies and which tiers products are placed on. It is possible that AbbVie will counter biosimilar competition by offering rebates for use of Humira or force payers into bundling deals that penalize them with reduced access to other drugs if they prefer biosimilars over Humira.

“This is where we need policy changes, particularly making sure consumers benefit from rebates,” Winegarden says. There has been much criticism of rebates that allow savings for payers while patients continue to pay the same amount out of pocket, or even more if manufacturers raise their list prices.

Biosimilar competition outside the United States has steadily chipped away at Humira’s revenues. But in the U.S., AbbVie has had the adalimumab market to itself. The company has seen revenues from Humira grow continually, largely by increasing the price. From 2019 to 2020, AbbVie increased the price of Humira by 9.6%, and in early 2021 the company increased it another 7.4%. By the beginning of 2021, the average sales price for a full year’s supply was as much as $84,000.

**AbbVie’s countermoves**

Anticipating steep revenue declines next year when biosimilar versions of Humira appear on market, AbbVie is attempting to switch patients with inflammatory disorders to two relatively new products, Skyrizi (risankizumab) and Rinvoq (upadacitinib). Skyrizi has been approved as a treatment for plaque psoriasis and psoriatic arthritis, and Rinvoq, for rheumatoid and psoriatic arthritis, ulcerative colitis and atopic dermatitis. These efforts have worked from a sales perspective. Global revenues for Skyrizi have grown from $355 million in 2019 to $2.9 billion in 2021. Rinvoq had an enormous jump from $47 million in revenues in 2019 to $1.7 billion in 2021.

In an earnings conference call in February, AbbVie CEO Richard Gonzalez explained that the snowballing revenue growth is expected to reach $4.4 billion and $2.7 billion for Skyrizi and Rinvoq in 2022, respectively, and eventually top $15 billion in combined revenue for the two drugs by 2025. AbbVie wants to get Skyrizi and Rinvoq approved for all the indications that currently apply to Humira. But AbbVie is still bracing for “significant erosion” of approximately 45% in Humira revenues from 2022 to 2023, with more declines in 2024 as biosimilars gain traction, according to Gonzalez.

Skyrizi and Rinvoq may be increasing in market share, but they are brand-name drugs that will command high prices by virtue of their newness. Physicians who have determined that their patients will benefit from Humira may bypass Skyrizi and Rinvoq and prescribe Humira or a biosimilar, Winegarden says.

Snow agrees. Humira is an important drug in the rheumatologist’s armamentarium, and although Skyrizi and Rinvoq have their own merits, rheumatologists will continue to use Humira and its biosimilars for managing rheumatic disorders, the Nebraska rheumatologist explains. “In some cases they’re not going to be direct competitors, but in some cases, they will be. They’re different enough that it’s not like they’re a direct replacement.”

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Tony Hagen is a medical, business and environmental editor and writer in Florence, New Jersey.
A conversation with
Jason Gorevic, CEO of Teladoc

Jason Gorevic has been CEO of Teladoc Health since 2009. In a interview with Managed Healthcare Executive ® Managing Editor Peter Wehrwein, Gorevic discussed the company’s deal with Amazon to provide telehealth services through Alexa smart speaker technology, its goal to increase per-participant revenues by providing “whole person virtual care,” and whether Teladoc is a threat to primary care and the brick-and-mortar healthcare system.

This transcript has been edited for clarity and length.

Let’s talk about the recent news that Teladoc has become the telehealth service available through Amazon’s Alexa. Do you see this as being a major line of business for you? Are you contracting with new providers to support that service? How big a deal is this?

We haven’t released any volume projections that we expect through it. What I can say is that I think it’s an indication, given Amazon’s scale, of their confidence in us.

And really, I think there’s only one player who could really handle that kind of scale and deliver the kind of quality and reliability that we do. We don’t feel like we have to make significant investments in order to handle the Amazon volume, and, of course, we always adjust and continue to date our forecasts for volume.

In a recent interview you talked a lot about growth on a per-participant basis. You used a figure of $2.50 per participant, and you referenced increasing that 27-fold, as I recall, to something like $65 per participant. Could you just unpack those numbers a little bit?

Pretty close, $68. When we talk about $68, we think about the prevalence of various conditions that we treat within a population, the population that doesn’t have a primary care relationship who may engage with us and our Primary 360 product on a virtual primary care relationship. And we think about the incidence of bringing things such as mental healthcare as well as episodic acute care to a consumer, and what the total opportunity is based on that prevalence. It really does go from where we are today, which is about $2.50, all the way up to $68, on a sort of population adjusted basis.

So you will be in the market with this bundle of services, and you’ll go (for instance) to UnitedHealthcare or Empire BlueCross BlueShield with this bundle, and you will say to them, “Sign up with us — we’ll provide the service to your members for $68 per member per month”? Not exactly. Our products, like our chronic care programs, are on a per-participant, per-month basis.

We get paid for the consumers who engage with us and are using our connected blood glucose monitor, connected scale, connected blood pressure cuff, and engaging with us.

So, we go to a payer, and we say, “Hey, we’d love to provide a virtual primary care relationship like Primary 360. We think it would be great if you (were to) roll out a virtual-first plan design that incent someone to engage virtually and you’ll pay us a base fee for that, and we have all different structures that we work with health plans on for that.”

And then as we engage the population, we’d love to get access to claims data so that we know who the people with diabetes are in the population so that we can target them, reach out to them, with offers around our diabetes program, maybe our prediabetes program or hypertension program.

We only want to be paid when we engage those people and they’re actually using those services. It’s not exactly a single, all-in-one bundled price that’s on a population basis. It’s variable, depending on engagement.

You have this suite of services
and you’ve referenced tying them all together. But in 2022, where do you see the strongest growth in terms of getting more revenue on a per-participant basis? Mental health continues to be the fastest growing part of our business and has been now for a couple of years.

Having said that, on a per-consumer, per-month basis, when we go to a health plan, we generally find that the chronic care programs are for us the highest revenue, because for the payer it’s the highest value. Everyone knows that those populations tend to drive an outsized portion of the healthcare costs.

What would you say to people who say you’re in the business of pushing out the community provider, the physician down the street? We have waitlists of physicians who want to participate with us. Some of that is because a lot of physicians, as you know and it is well documented, become burned out in the traditional delivery model, in the physical setting, especially after the past two years of being sort of armored with PPE (personal protective equipment).

We also integrate with the physical delivery system because we recognize that there is a limitation to what can be done virtually and, at some point, a large portion of the population needs to be seen in person.

Really, we want to act as a concierge, to help them get the appointment, get registered and get into that physician as quickly as possible.

What about healthcare systems? If I were one of these big healthcare systems, and I counted on having a relationship and referrals through primary care physicians, some of whose practices may be ones I just recently purchased, I would see what you’re doing as being against my interest.

We have a large part of our business that provides technology and services to hospital systems so that they can deliver virtual care to their patient populations. We want them to be able to take advantage of our expertise and our platform. And in many cases, we wrap our physician network around them to take patient requests, after hours, nights, weekends, or to increase their capacity.

Our relationship with Microsoft, which was announced about six months ago, is really an example of where we build our technology into the Microsoft workflow, things such as Microsoft Teams, so that the hospital system can make those capabilities available to their physicians in a way that is really seamless to their workflow, integrates with their scheduling applications and things like that.

We actually find that hospitals appreciate the opportunity to take advantage of a purpose-built solution that is truly for the delivery of virtual care as opposed to sort of a generic video widget or something that is an EMR (electronic medical record) -focused widget that that is an add-on to their EMR, which most physicians don’t like to begin with.

As you know, the public health emergency led to waivers of some telehealth restrictions. Is there any particular rule or regulation or piece of legislation that you see as being instrumental to what you’re trying to do in terms of growing this complete set of services? Let me start by saying the waivers that were put in place are not a requirement for the continued growth and success of our business. Most of those relate to Medicare fee-for-service reimbursement. That’s not really part of our business. So that’s not a requirement.

Where I do hope that we’ll continue to see some — there’s good dialogue — movement in continuing to focus on the opioid crisis and mental health and making sure that we take advantage of virtual care to its fullest capability.

There are some changes to some of the regulations about what you can prescribe remotely. That could be beneficial to helping with expanding capacity and access to care for those suffering from opioid addiction.
Health plans prepare to post prices for consumers

Price-transparency rule allows insurers to cut MLR payments by using incentives to encourage consumers to choose low-cost, high-value providers  

by JOSEPH BURNS

On July 1, Brian Walsh, account executive with the price transparency company Turquoise Health, will be watching closely to see which health insurers publish the rates they pay hospitals, physicians and other healthcare providers.

Having consulted with many of the nation’s small and midsize health insurers, Walsh is confident that most — if not all — of the insurers he’s talked to are preparing to comply with the new federal transparency rule. How many health plans will comply with the Transparency in Coverage final rule will be fascinating enough. But health insurers and observers of the industry will also be keeping an eye on how health insurers use a new financial tool built into the rule that is designed to encourage consumers to choose high-value, low-cost hospitals, physicians and other healthcare providers.

Under the rule, HHS will also allow health insurers to use incentives, such as by waiving or lowering co-payments or deductibles, to encourage their members to shop for services from lower-cost, higher-value providers. When they use such incentives, health plans will be able to give enrollees a part of the savings when their enrollees get services from lower-cost, higher-value consumers, according to CMS. Moreover, they can include the savings they share with enrollees in the numerator of their medical-loss ratios (MLR), along with incurred claims and other expenses related to improving healthcare. In this way, HHS allows insurers to reduce what they would pay in rebates under the MLR rules. Since the MLR rules went into effect under the Affordable Care Act (ACA) in 2014, health insurers have paid millions in rebates to consumers. Industry observers say insurers are likely to welcome the chance to reduce what they pay under the MLR rules while encouraging consumers to choose lower-cost and higher-value hospitals and providers.

One problem: How will health plans define high-value providers?

Choosing value in healthcare is challenging because it’s often in the eye of the beholder, according to A. Mark Fendrick, M.D., director of the University of Michigan Center for Value-Based Insurance Design. The challenge in defining value, says Fendrick, is that quality is linked to what the consumer pays. “Value is the combination of the quality of care you get for the price you pay,” Fendrick explains. “It’s best described as a fraction of value over price.” Some consumers will choose the lowest-cost hospitals, physicians and providers, while others may choose hospitals and providers based on the quality they deliver or a combination of higher quality and lower price, Fendrick says.

As of Jan. 1, HHS has required hospitals to post what they charge.

“Transparency across plans means there will be more competition and maybe less variation in what they pay.”

— A. MARK FENDRICK, M.D., UNIVERSITY OF MICHIGAN CENTER FOR VALUE-BASED INSURANCE DESIGN
for their care and services under the Hospital Price Transparency final rule. But for Fendrick, the Transparency in Coverage rule is more significant because consumers, researchers and other insurers will be able to see what their competitors pay.

“Transparency across plans means there will be more competition and maybe less variation in what they pay,” says Fendrick.

The rule applies to most health insurers that were not grandfathered in under the ACA and to health plans offering nongrandfathered health insurance coverage in the individual and group markets. HHS defines a grandfathered plan as one that someone purchased on or before March 23, 2010, which is when the ACA was signed into law. These plans are not sold on the ACA exchanges; instead, insurers or their agents market them to consumers.

Insurers will need to make public machine-readable files showing what they pay for all covered items and services to in-network providers and the allowed amounts they pay and the billed charges they get from out-of-network providers.

Hospitals will also need to provide a price-comparison tool on the internet that will allow individuals to get an estimate of what they would pay out of pocket for a specific item or service from a named provider or group of providers, for 500 shoppable items and services.

Upon request by consumers, insurers also would be required to make this price-comparison information available, HHS said. Failing to provide this information will result in fines of $100 per day for each violation or for each affected individual.

Joseph Burns is an independent journalist in Brewster, Massachusetts, who covers healthcare and health insurance.
A s consumers embrace wellness apps to help them do everything from reducing stress to improving their sleep, some health insurers are throwing their weight behind the trend, offering members free access to certain apps designed to improve health and well-being. “People are looking for an easy way to get better,” says Anne Hoverson, vice president of digital transformation at Florida Blue, which looks to “curate the right thing at the right time” for its members.

The first health and wellness apps were introduced more than a decade ago and, even today, “most don’t do much,” says Bryce Williams, vice president of MindBody Medicine for Blue Shield of California. “They’re just kind of a transitory experience for most people.”

But some apps can play a vital role in member care, he adds. “We felt the field had matured far enough that it was a really great opportunity that could help our members.”

The California insurer has a special website called Wellvolution that offers tools to help members do such things as manage their diabetes, lose weight and deal with mental health issues. The abundance of wellness apps can create what behavioral economists call overchoice: People freeze up when facing too many options. Blue Shield of California makes sure that all apps on the Wellvolution website have been clinically validated and deemed effective in real-world settings, according to Williams. The company launched Wellvolution in 2008 and started “experimenting” with apps in 2010. Williams says. Now, members who go to the site can discuss health concerns and the insurer will suggest apps and other tools to help them meet their goals.

Health plan members do not pay extra for the programs. They may be connected to apps such as Ginger, which provides online mental health care; WW (previously Weight Watchers) to lose weight; Clickotine to quit smoking; and Virta Health to manage diabetes. In an email to Managed Healthcare Executive®, Blue Shield of California said that all of the payment models in Wellvolution are pay for performance. In the case of Ginger, the health plan says it pays on milestone basis, and the milestones include engagement, sustained engagement and clinical outcomes based on common mental health scoring tools.

Florida Blue launched a new section of its website last year where members can relay their health concerns and be linked to appropriate care. Plan members have no-cost access to meQuilibrium, an app designed to reduce stress and build resiliency using cognitive behavioral therapy at a time when many Americans are struggling because of the mental toll of the COVID-19 pandemic. A Florida Blue member with diabetes might have access to Livongo for Diabetes, which monitors blood glucose readings through a connected device. Members may receive automated “nudges” to help them stay on track or can chat with a care coach or diabetes educator. The Livongo for Diabetes website says it is a $75-per-month benefit paid for by an employer or health plan.

Why now?

As demographics shifted and younger people, who are more inclined to use apps, started to sign up for healthcare coverage, Florida Blue began to increase its app offerings, Hoverson says. Meanwhile, app development, including wellness apps, boomed. The wellness apps also cater to the high value people place on convenience. “There is no appointment, no travel time, no waiting room. An app “is always there for you, always in the palm of your hand,” Williams says. The pandemic has also been a factor, propelling a major shift to virtual care and familiarity with getting healthcare
delivered digitally. The pandemic, says Hoverson, “brought down a lot of barriers.”

That growing demand for virtual care has also fueled a wave of investment in the overall digital health sector, which includes apps. Noom, the weight loss program and app that uses cognitive behavioral techniques, raked in the largest investment in the digital health area in 2021, bringing in $540 million, according to Rock Health, a venture fund that focuses on digital health.

Overall, venture funding for digital health start-ups soared to $29.1 billion last year, a new record, according to Rock Health, and about double the investment funding in 2020. The 2021 money went to 729 deals, with the average deal reaching almost $40 million. Digital health start-ups in the fitness and wellness sector drew $4.3 billion in funding last year, according to Rock.

One issue with health and wellness apps is covering their cost. Some are available to consumers for free, many charge a monthly subscription fee and others are available only to health plan members.

The digital health company Big Health has tackled the issue by working with a pharmacy benefit manager (PBM). Big Health promotes its apps, which use cognitive behavioral techniques, as non-drug alternatives for insomnia and anxiety. The company says its apps — Sleepio for insomnia and Daylight for anxiety — have undergone clinical study, including 13 randomized clinical trials.

“The company works with CVS Caremark, the PBM arm of the pharmacy giant. "By pioneering the ability to bill through the PBM, employers and health plans can easily add Big Health to their formulary and pay for their use via a drug claim, which is the same way they pay for medications," Big Health co-founder and CEO Peter Hames said in an email. A person can access a Big Health app only if their employer has signed them up.

Concerns about apps

Big Health and a few other companies are trying to break away from the pack with claims that their apps have passed clinical trial muster. But in a recent opinion piece in JAMA, David Simon, Ph.D., a research fellow at the Petrie-Flom Center for Health Law Policy, Biotechnology, and Bioethics at Harvard Law School, and his colleagues from Harvard discussed the dearth of regulation of many wellness products, including direct-to-consumer apps that people use to help assess their health. “The FDA tends to focus on the risk a product might pose to consumers, they noted. The agency draws a line between devices that diagnose diseases and conditions or purport to cure, treat or prevent disease and those intended for general use and wellness. “Even though some general wellness products may be ‘devices,’ the FDA will not regulate these products if they only promote a healthy lifestyle or help reduce the risk of certain chronic diseases based on accepted interventions,” the authors wrote.

Simon said in an interview that one of his concerns is whether consumers who use wellness apps are “aware they are not meant to diagnose diseases.” There are also questions about reliability of the information generated by wellness apps and what physicians can or should do with that information.

As for regulation, “the FDA can’t be out there policing tens of thousands of apps that exist” with the agency’s limited resources, said Simon.

Health plans benefit

By offering apps, health plans hope to increase connection and engagement with members.

For Florida Blue members, apps can serve to manage chronic conditions more effectively, Hoverson says. “The better they do, the healthier they are,” which can reduce emergency room visits and hospital admissions while lowering costs for the insurer.

Williams of Blue Shield of California agrees. He says offering the apps “improves the lives of those we serve. By improving health, all the rest (on the business side) is going to take care of itself.”

Susan Ladika is an independent journalist in Tampa, Florida, who writes about business and healthcare.
HIV preexposure prophylaxis (PrEP) has a critical role in ending the HIV epidemic in the United States. This article will explore the current state of HIV PrEP uptake in this country and describe measures that can help to both increase awareness of HIV PrEP and improve adherence to this important prevention strategy.

High-risk behaviors related to, and populations affected by, HIV infection
In the United States, an estimated 1.2 million people aged 13 years or older were living with HIV in 2019; an estimated 13.3% of these patients, however, had not received a diagnosis.1 Behaviors that increase the risk of acquiring HIV infection include sexual activity with an infected person and injection of illicit drugs.2-4 Individuals who inject illicit drugs and have an HIV-positive injecting partner or share injection equipment are at highest risk of HIV acquisition.2

Although HIV infection can occur in persons of any age, gender, race, ethnicity or sexual orientation, HIV disproportionately affects gay and bisexual men and other men who have sex with men (MSM) in the United States.7 Members of racial and ethnic minority communities are also highly affected. In the United States, 42.1% of new HIV infections occurred in Black populations in 2019, a rate that was more than eight times higher than that reported among White populations (5%).3 Individuals with Hispanic/Latino ethnicity comprised 21.7% of newly infected people.3

HIV PrEP
Clinical guidelines
HIV PrEP involves taking medication to prevent HIV infection. Clinical practice guidelines issued in 2021 by the Centers for Disease Control and Prevention (CDC) recommend informing all sexually active adults and adolescents about HIV PrEP, screening all sexually active patients for an HIV PrEP indication and screening all adult patients for use of injectable illicit drugs. The guidelines also recommend that clinicians discuss HIV PrEP with sexually active patients and prescribe it to those who are at risk of HIV infection or who request a prescription. Similarly, clinicians should prescribe HIV PrEP to patients who inject illicit drugs and are at risk for acquiring HIV or who request it.2

Oral PrEP
Two drug combinations are recommended by the CDC for oral HIV PrEP.2 In 2012, Truvada, a combination pill composed of emtricitabine and tenofovir disoproxil fumarate (F/TDF), became the first FDA-approved HIV PrEP agent.5 Daily F/TDF is indicated for adult and adolescent men and women weighing at least 35 kilograms; its use is recommended for those who report either illicit drug injection or sexual practices that place them at risk of acquiring HIV infection.2 Another oral pill, Descovy, gained FDA approval for HIV PrEP in 2019.7 This combination of emtricitabine and tenofovir alafenamide (F/TAF) is indicated for daily oral use in transgender women and in sexually active men or adolescents weighing at least 35 kilograms; it is also recommended for those who report sexual practices that place them at risk of acquiring HIV.2 Another oral pill, Descovy, gained FDA approval for HIV PrEP in 2019.7 This combination of emtricitabine and tenofovir alafenamide (F/TAF) is indicated for daily oral use in transgender women and in sexually active men or adolescents weighing at least 35 kilograms; it is also recommended for those who report sexual practices that place them at risk of acquiring HIV.2-7 The effectiveness of F/TAF has not been studied in individuals at risk of HIV infection from receptive vaginal sex, so it is not recommended in this population.2-7

Long-acting, injectable PrEP
In December 2021, the FDA approved the first injectable option for HIV PrEP, Apretude (a monthly injection of long-acting tenofovir alafenamide and rilpivirine). This combination has been shown to be as effective as daily oral PrEP in preventing HIV infection.2-7 Such options can be especially useful for individuals who have difficulty adhering to oral PrEP regimens, as missed doses can reduce the effectiveness of oral PrEP.

Opportunities for identifying and addressing barriers to HIV PrEP
HIV PrEP can be an effective tool in the fight against the HIV epidemic, but it is important to consider the challenges that may prevent individuals from accessing and adhering to this prevention strategy.2-5 By identifying and addressing these barriers, we can work towards ensuring that all individuals at risk of HIV infection have the opportunity to benefit from this critical prevention strategy.
(cabotegravir; CAB) is a long-acting, injectable drug indicated for adults and adolescents who weigh at least 35 kilograms; its use is recommended in those who report sexual practices that place them at risk of acquiring HIV. The CDC recommends that CAB be given, as indicated, every two months by injection into the gluteal muscle with an optional oral four-week lead-in. Intramuscular (IM) CAB therapy may be appropriate for patients who have significant renal disease, difficulty in adhering to oral HIV PrEP or a preference for receiving injections every two months versus using oral PrEP. For patients taking oral HIV PrEP, laboratory tests recommended before or during PrEP use include estimated creatine clearance, hepatitis B-virus serology and lipid panel testing; however, these tests are not required for patients taking CAB for HIV PrEP. Unlike oral HIV PrEP medications, CAB can be taken by patients with severe renal impairment or end-stage renal disease.  

**IM CAB: Clinical studies**

IM CAB was evaluated in clinical studies that involved a wide range of participants, including cisgender women (HPTN 084; NCT03164564) and cisgender MSM and transgender women who have sex with men (HPTN 083; NCT02720094).  

HPTN 083 was a phase 2b/3, international, multicenter, double-blind, randomized controlled trial (RCT) that examined the safety and efficacy of IM CAB injection administered every eight weeks versus daily oral F/TDF given to adult cisgender MSM and transgender women who have sex with men. Incidence of HIV infection was lower in the CAB arm (n = 2,282) than in the F/TDF arm (n = 2,284; 0.41 vs. 1.22 per 100 person-years, respectively), and the risk of infection was 66% lower in the CAB arm than in the F/TDF arm (hazard ratio, or HR, 0.34; 95% confidence interval, or CI, 0.18-0.62; p-value < .001). The safety population included 4,562 patients (CAB arm, 2,280 patients; F/TDF arm, 2,202 patients). In this population, 92.5% reported side effects of grade two or higher, 32.7% reported side effects of grade three or higher and 5.3% reported serious side effects, with similar frequencies of events noted across the two groups. Among patients who received active CAB injections, 2.4% of patients (50 of 2,117 patients) discontinued injections because of injection-related side effects.  

HPTN 084 was an RCT that evaluated IM CAB versus oral F/TDF given in three phases to 3,224 sexually active cisgender women. Among the 1,614 women in the CAB arm, the incidence of HIV infection was lower (0.2 per 100 person-years; 95% CI, 0.06-0.52) than that recorded among the 1,610 women in the F/TDF arm (1.86 per 100 person-years; 95% CI, 1.3-2.57). Overall, women in the CAB group had an 89% lower risk of HIV infection than did women in the F/TDF group (HR, 0.11; 95% CI, 0.01-0.31; p-value = .00027). Any site reaction was experienced by 32% of patients in the CAB arm and 9% of patients in the F/TDF arm; reactions of grade two or higher were noted among 7% and 1% of patients, respectively.
and there were no discontinuations due to injection-site reactions in either study arm.11

Importance of adherence
Adherence to oral HIV PrEP is critical to prevent HIV acquisition.2 For patients who may struggle to achieve high adherence to oral HIV PrEP, IM CAB provides an alternate option. Rather than taking a daily pill, patients need to receive only one injection of CAB every two months. The results of clinical trials have shown that IM CAB provides 66% to 89% higher efficacy than does oral F/TDF.2,11,12

Managed care considerations
In 2019, substantial evidence that PrEP could reduce risk of HIV acquisition via sexual activity or illicit drug injection led to a U.S. Preventive Services Task Force (USPSTF) A rating for the recommendation that it be offered to persons at high risk of HIV infection.4 The USPSTF guidelines are currently being updated, and injectable CAB was not yet approved by the FDA when the 2019 version was released. According to the provisions of the Affordable Care Act (ACA) part 47, this A rating requires most insurers to cover PrEP with no cost-sharing.10 No-cost coverage must include not only medication but also counseling (including for adherence, risk reduction and mental health counseling) and the laboratory testing and office visits necessary for initiation or continuation of PrEP use.13

Per ACA part 47, plans and issuers are allowed to employ reasonable medical management techniques regarding HIV PrEP coverage, which may include no-cost coverage of generic PrEP but imposition of cost-sharing on the equivalent branded version. If a patient’s healthcare provider deems use of the covered drug to be medically inappropriate, plans and issuers must provide a mechanism to waive cost-sharing for a more appropriate medication.13 For individuals who lack prescription drug coverage, the U.S. Department of Health and Human Services has made F/TDF and F/TAF available free of charge through the Ready, Set, PrEP program.2

PrEP uptake: Current status, barriers and opportunities
As of 2018, of nearly 1.2 million people in the United States who had indications for HIV PrEP therapy, only approximately 220,00 individuals received a prescription.2 The reasons for this relatively low uptake of HIV PrEP are multifactorial. A review of literature published from 2016 to 2019 identified the following key barriers: low awareness of HIV PrEP among providers and patients, especially those individuals at risk for or living with HIV; low perception of personal HIV risk; social stigma associated with PrEP use; provider bias (whether implicit racial/ethnic prejudice or bias against LGBTQ+ patients); patient distrust of the healthcare system; lack of access to medical care or financial assistance; and provider and patient concerns about side effects and medication interactions.11

One method for increasing uptake of HIV PrEP is to facilitate discussion of PrEP between healthcare providers and patients.2 This includes taking sexual histories of patients, which can help identify patients who are at risk for HIV infection and who may benefit from HIV PrEP. This method also includes providing information about PrEP so patients can respond openly to

To view the interview with Douglas Krakower, M.D., and other videos, visit https://www.managedhealthcareexecutive.com/view/addressing-disparities-and-increasing-access-to-hiv-prep

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Beth Israel Deaconess Medical Center, The Fenway Institute
Boston Medical School
Boston, Massachusetts

Managed Healthcare Executive
risk assessment questions and discuss PrEP with others who may benefit from its use.2

To promote adherence, providers should establish trust and bidirectional communication with their patients who start HIV PrEP. Providers should stress the need for adherence, educate patients on potential medication side effects, help create dosing schedules, identify and address barriers to adherence, and monitor HIV PrEP adherence in a nonjudgmental manner. A multidisciplinary approach can also help. The 2021 CDC PrEP guidelines emphasize that a care team of healthcare professionals (e.g., physicians, nurses, pharmacists) working together can improve a patient’s HIV PrEP medication adherence.2

Conclusions
PrEP has a critical role to play in ending the HIV epidemic in the United States. Efforts should be focused on preventing infection via expanded awareness of, and access and adherence to, HIV PrEP for everyone at risk of sexual or injection-acquired infection. The 2021 FDA approval of an injectable option for HIV PrEP provides clinicians and patients with an effective therapeutic choice that does not require remembering to take a pill every day. In addition, to promote widespread HIV PrEP use, it is crucial to address barriers that contribute to lack of patient access or withdrawal from PrEP care.2

REFERENCES
There’s a cancer problem in the U.S., say many experts, and dazzling new treatments and brilliant scientific advances are not going to solve it. The problem is cancer’s disproportionate effect on Black people in the United States, who have the highest death rate and shortest survival periods of any racial or ethnic group in the country. For many of the most common cancers (lung, breast, colon, prostate), the incidence rate among Black people is lower than the rate among white non-Hispanic people, yet the death rate among Black people is higher. Most of these disparities are nothing new and have long been recognized. What has changed is the thinking (and research) into their causes. For many years, the tip of the cancer research spear was directed at genetic and biological explanations. Researchers and policymakers as well as oncologists are now focusing on societal factors and structural racism as the root cause of much of the disparity.

Research and discussion about the high cancer rates among Black Americans used to be dominated by genetics and the search for biological differences. Now attention has shifted to the social determinants of health. by KEITH LORIA

The problem is cancer’s disproportionate effect on Black people in the United States, who have the highest death rate and shortest survival periods of any racial or ethnic group in the country. For many of the most common cancers (lung, breast, colon, prostate), the incidence rate among Black people is lower than the rate among white non-Hispanic people, yet the death rate among Black people is higher.

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Anita Johnson, M.D., FACS, chief of surgery and leader of the Women’s Cancer Center at Cancer Treatment Centers of America in Atlanta, says the challenges to accessing cancer care for minorities are multifactorial. Many can be traced to the social determinants of health (SDOH) that can put access to quality care, insurance, oncologists and clinical trial enrollment out of reach.

“Other challenges, such as access to healthy food options and environmental circumstances that expose individuals to carcinogens, also play a role,” continues Johnson, who also mentions the cultural barriers created by the lack of minorities in the health care professions. For example, recent research has shown that only 3% of oncologists in the U.S. are African American.

Christina Chapman, M.D., an assistant professor of radiation oncology at the University of Michigan Medical School, says the vast majority of the cancer-related issues that minority populations face are due to past or ongoing rules, norms, or laws that maintain societal inequity.

“Downstream problems like a lack of access to high-quality screening and treatment, or to clinical trials, are heavily rooted in societal inequity,” she says. “In the long term, social reform is needed to address inequity in income, wealth and health insurance access. In the short to medium term, health systems and cancer care providers need to recognize how inequity affects their patient populations and use existing resources that do help ensure that everyone has access to current therapies instead of solely focusing on new innovations that will not be accessible to many in the population.”

Social determinants … of cancer
Most cancers are caused by a complicated web of factors. The causal pathway gets even more complex with outcomes such as the five-year survival rate and death because of the many issues that influence access and the use of health care. All this complexity comes under the heading of SDOH, which loom large in the current understanding of the causes of cancer disparities.

“For example,” says Johnson, “regardless of education level, Black women in the U.S. are known to have a higher rate of unemployment than White women. Being gainfully employed frequently provides individuals with benefits like health insurance and paid time off. These are important contributing factors to accessing care, which can lead to earlier diagnoses of cancer and subsequently better outcomes, as well as the ability to seek and maintain cancer treatment.”
The incidence of breast cancer among White and Black women is similar, but Black women are 40% more likely to die from the disease. Higher rates of obesity and other health problems may be a factor (they may have upstream SDOH causes). Black women are also more likely to be diagnosed with aggressive types of the disease, such as triple-negative breast cancer and inflammatory breast cancer.

However, much of the mortality disparity can be ascribed to the cancer being diagnosed at a later, less treatable stage.

“Unfortunately, from experience — and now an increasing amount of empirical research — we know that the challenges are numerous and complex,” says David Arons, J.D., CEO of the National Brain Tumor Society. “To name just a few challenges, (we have) cost, geography (distance to primary and specialty care because of a paucity of providers in rural underserved areas), cultural competence and unconscious bias, language barriers, mistrust and technological divides.”

For many types of cancer, SDOH heavily influence prevention, early detection and mitigation of disease, adds Arons. For example, he says, easy access to physical exercise including bikeable and walkable places near one’s home and access to nutritious food are associated with reduced chances of childhood obesity, which has been linked to the development of a number of cancers later in life.

Arons lists some other risk factors for cancer that are rooted in SDOH. Lack of education, combined with the marketing efforts of tobacco companies, leads to higher rates of smoking, which is a major risk factor for lung and other cancers. Living in neighborhoods with high levels of air or water pollution puts people at risk.

Interestingly, Arons says the SDOH that shape the contours of risk and mortality for many cancers in the U.S. do not appear to affect brain cancer rates. In fact, incidence rates are actually higher in highly educated White populations.

Niraj Mehta, M.D., a radiation oncologist at GenesisCare, an Australian cancer care company that has expanded to the U.S., says that the biggest challenges for people living in poorer neighborhoods is access to care and removing the impediments to getting that care. These include lack of transportation and childcare and limited or no time off for their treatments.

“Such patients often present at a later stage of diagnosis and are often afflicted with comorbidities such as poor nutrition and obesity,” he says. “Meaningful education needs to go well beyond typical ‘awareness’ efforts. Many for-profit private equity organizations and hospitals likely have minimal impact in these communities. Bottom-line organizations typically do not explore these communities in depth to understand their needs on cancer and health in general.”

In Mehta’s opinion, one of the first steps to redressing disadvantageous SDOH is funding outreach efforts by...
local physicians who have the cultural and sociodemographic sensitivities needed to work with patients in those poor neighborhoods.

**Disparity in clinical trials**

One area of disparity that has received a good deal of attention lately is enrollment in clinical trials. African Americans make up approximately 13% of the U.S. population, yet less than 2% to 3% of patients enrolled in cancer clinical trials are Black. Breastcancer.org, a nonprofit website for information about breast cancer, reported that between 2% and 9% of the participants in the trials that led to FDA approvals of four new breast cancer treatments in 2020 were Black. The proportion of Latino Americans was similarly small.

“This is one specific example, but it reflects the trend that we see of inadequate representation of minorities in clinical trials,” says Johnson of Cancer Treatment Centers of America in Atlanta.

In May 2021, *JCO Oncology Practice*, an American Society of Clinical Oncology journal, published a special package of 16 articles and editorials about cancer disparities. A number of them focused on the low enrollment of Black patients with cancer in clinical trials. A study of clinical trials that led to FDA approval of an oral cancer drug showed that just 889 of 35,933 (2.47%) patients in the trials were Black.

Vonetta M. Williams, M.D., Ph.D., a radiation oncologist at Memorial Sloan Kettering Cancer Center in New York, New York, says those numbers are very concerning because research has shown an association between clinical trial enrollment and improved outcomes. Williams says it is misguided to point to the attitudes of Black Americans as the reason for the low enrollment. “Many studies have cited mistrust (on the part of) Black Americans as a significant factor despite evidence showing that when offered enrollment, Black Americans consent to trial enrollment at similar rates to (those of) other groups,” she notes.

Ideas about how to increase enrollment of Black Americans in cancer clinical trials have proliferated. Williams says among the most promising are assessing trials’ inclusion and exclusion criteria to determine whether they are unnecessarily restrictive for certain populations. For example, many trials have cutoff points for the glomerular filtration rate, a measure of kidney function, that has led to the exclusion of Black Americans. Transportation and housing can also loom large as obstacles for some potential volunteers, notes Williams.

Lack of Medicaid coverage of the costs associated with participating in a trial has been another barrier for many Black patients. But at the beginning of 2022, the Clinical Treatment Act went into effect. It requires Medicaid to cover the routine costs of clinical trial participation for Medicaid enrollees with a life-threatening condition, including cancer.

Johnson says communication and connection between providers and minorities can help combat distrust of the health care system and improve health literacy.

Arons notes that the National Brain Tumor Society continues to argue for a policy that would include all National Cancer Institute-designated cancer centers as essential community providers in all marketplace health plans sold on the ACA exchanges. Lower-income individuals can sometimes end up in health plans with slimmed-down provider networks that exclude the cancer centers, he says.

**Black and White differences in cancer death rates**

For some common cancers, the death rate among Black patients is more than two times higher than it is among White patients.

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Male Black (per 100,000)</th>
<th>Male White (per 100,000)</th>
<th>Rate ratio</th>
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<tr>
<td>Stomach</td>
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<td>3.0</td>
<td>2.51</td>
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<td>Prostate</td>
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<tr>
<td>Myeloma</td>
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<td>1.96</td>
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<tr>
<td>Larynx</td>
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<table>
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<th>Cancer</th>
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<tr>
<td>Uterine cervix</td>
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<tr>
<td>Breast</td>
<td>28.0</td>
<td>19.9</td>
<td>1.41</td>
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</tbody>
</table>

Races are exclusive of Hispanic ethnicity. Rates are per 100,000 and age-adjusted to the 2000 U.S. standard population. The rate ratio is the unrounded rate among Black patients divided by the unrounded rate among White patients.

Source: Source: Cancer Facts & Figures for African Americans/Black People 2022-2024
Why LTACHs Are Often the Right Choice for Critically Ill Patients

By Sean R. Muldoon, MD, MPH, FCCP CMO and Audra Early, SVP Strategy and Network Development, Kindred Hospitals

Establishing the appropriate care delivery path for patients after a stay in the ICU or med-surg unit is essential to improving outcomes, reducing readmissions, and managing total costs of care. Because of their clinical capabilities, long-term acute care hospitals (LTACHs) are often ideal treatment and recovery settings for medically complex patients and therefore valuable partners in healthcare networks.

Benefits to Payers Through a Specialized Patient Focus
Recent trends show that patients are being admitted to short-term acute care hospitals with increasingly complicated conditions, thereby amplifying the need for post-acute care partners who can help these patients fully recover.

Licensed as acute care hospitals, LTACHs are often the most appropriate next level of care for medically complex patients who need to see a physician every day. Physicians at LTACHs lead interdisciplinary teams made up of nurses, therapists, and other clinicians who provide coordinated, patient-specific care. Additionally, these teams provide onsite 24/7 respiratory coverage for critical pulmonary patients, including those needing ventilator weaning.

Despite increasing medical complexities, a recent ATI Advisory study reported that LTACH patients are almost half as likely to readmit to the hospital as SNF residents are. Additionally, MedPAR claims analysis suggest that, for medically complex patients, LTACH’s per-patient-day costs are generally lower than those of a short-term acute hospital.

LTACHs, therefore, are important partners within the healthcare ecosystem that provide efficient and effective care for this niche patient population.

Comprehensive Rehabilitation for Lasting Recovery
Rehabilitation services at an LTACH are integrated with specialized acute care to help patients with medically complex conditions achieve the fastest and most complete recovery possible.

Early rehabilitation in an acute-care setting, made possible through the expertise of LTACH PTs, OTs, and SLPs, can have a considerable impact on care efficiency. One study found that improving access of ventilator patients to early mobilization may reduce their length of stay by up to 4.5 days and shorten their time on ventilation by 2.5 days.

As such, partnership with LTACHs can help certain patients fully recover more quickly and can positively impact length of stays and efficient care.

How Kindred Hospitals Can Help
Kindred Hospitals specialize in the treatment of patients who require intensive care and rehabilitation in an acute hospital setting. The clinical capabilities at Kindred Hospitals allow them to improve patient outcomes and their focus on transparency, patient access and collaboration make them valuable partners.

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REFERENCES
2. Kindred Hospitals calculations using data from CMS MEDPAR, 2019

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Hepatitis C is making a comeback

Rates dipped in the 1990s, but the opioid crisis and contaminated needles have caused an increase in new acute cases.

by SUSAN KREIMER

In the United States, hepatitis C seemed like one those diseases that might be hailed as a success story. Transfusions with unscreened blood products were a major source of infections before a test for the virus that causes the disease started being used in the 1990s. Afterward, infections from transfusions in the United States stopped occurring. Then in the mid-2010s, new medications, such as Sovaldi (sofosbuvir) and Harvoni (ledipasvir and sofosbuvir), that acted directly on the virus, became available. Although their price was a major issue, they were remarkably effective at curing the infection and were a huge improvement over an arduous regimen that many patients had difficulty sticking with.

But as it turned out, it was too soon to celebrate. Hepatitis C virus (HCV) has staged a comeback, largely because of the opioid epidemic and transmission through contaminated needles. The number of acute cases of hepatitis C in the U.S. has more than doubled since 2012, according to the CDC, jumping from 24,700 cases to 57,500 acute cases in 2019. The public health agency says that in 2019, there were 14,242 deaths in the U.S. that listed hepatitis C as the cause of death.

"Chronic HCV infection kills more Americans than HIV and all other reportable infectious diseases except COVID-19," says David Thomas, M.D., a professor at the Johns Hopkins University School of Medicine who cares for patients with chronic HCV.

Health officials have responded with efforts to make screening for hepatitis C routine. Meanwhile, the prices of the direct-acting antiviral medications have fallen. Even so, states are experimenting with ways to pay for the drugs that lessen the cost burden and may make the medications more readily available.

HCV often asymptomatic

The hepatitis C virus (HCV) is most commonly transmitted through contaminated blood. Transmission may occur through unscreened transfusions and blood products, contaminated injections during medical procedures, or injection drug use. Infection from transfusions and unsafe medical procedures is a problem that haunts healthcare systems in the developing world but not those in richer countries that have taken steps to screen their blood supplies and make medical procedures safer. Sexual transmission is a possibility, but much less likely.

Unlike some pathogens, "this virus doesn't really come from contact, like when you shake someone's hand," says Steven Flamm, M.D., a professor of gastroenterology and hepatology and medical director of liver transplantation at Northwestern University Feinberg School of Medicine in Chicago. "It doesn't come from sharing forks. It doesn't come from doorknobs."

Symptoms of acute infection may include jaundice (yellowing of the skin and eyes), dark urine, extreme fatigue, nausea, vomiting and abdominal pain. But in many cases acutely infected individuals have no symptoms.

Over time, HCV infection can lead to fibrosis, which is scarring of the liver. Two or three decades after infection, approximately one-third of people with HCV develop cirrhosis, a late-stage liver disease in which healthy tissue is replaced with scar tissue, resulting in irreversible damage, Flamm says. "Until recent years, hepatitis C was the No. 1 reason for liver transplantation, not only in the United States but in the Western world," he adds.

Routine testing

Many states are striving to address HCV through screening and improved access to effective treatment, according to Philip A. Chan, M.D., M.S., an infectious diseases specialist at the Rhode Island Department of Health and associate professor at Brown University. "Routine testing for HCV is key to identifying chronic hepatitis C for treatment and also for preventing onward transmission," says Chan.

Routine testing in people with risk factors is important, says Chan, because people with chronic

Continued on page 44
Appropriate use of PrEP has been proven to significantly reduce the risk of getting HIV; however, only about 1 in 5 persons with an indication for PrEP is receiving it. Numerous factors contribute to both access and adherence to PrEP medications. Addressing educational needs, coverage policies, and therapeutic innovations may increase access to and uptake of PrEP to prevent HIV infection.

Throughout this Population Health Perspectives video series, our expert faculty will discuss the following:

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- Adherence support and patient education programs

**Patient Access:**
- Disparities and inequities in access
- Utilization management strategies and challenges

**Future Opportunities:**
- New and novel dosage forms
- Potential challenges and logistical concerns for PrEP therapies

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hepatitis C usually don’t have any symptoms that would prompt a clinician to order a test. A crucial step in preventing liver damage and death from HCV is acknowledging that it’s a silent killer, says Neil Gupta, M.D., M.P.H., chief of the epidemiology and surveillance branch in the division of viral hepatitis at the CDC.

The CDC’s new screening guidelines may be helping more people receive an earlier diagnosis. In April 2020 the agency issued an update recommending that all people 18 years or older be tested at least once and that women undergo screening during each pregnancy.

The CDC noted, however, that people with ongoing risk factors should be tested more often.

Until that announcement, testing was recommended only for baby boomers. Three-fourths of U.S. adults with hepatitis C are baby boomers, according to the National Institutes of Health. Many of them were infected several decades ago, mainly from blood transfusions, and may not know they’re at high risk for the virus.

Along with baby boomers, adults ages 18 to 36 also have high rates of infection, largely because of the sharing of needles for drug use.

Injection drug use

“The epidemics of opioids and heroin use have really fueled the rise in hepatitis C that we are seeing right now,” says Dawd S. Siraj, M.D., M.P.H., a professor in the division of infectious diseases at the University of Wisconsin School of Medicine and Public Health in Madison. Hepatitis C is a disease that affects the marginalized and stigmatized segments of the United States, he notes, including people who are unhoused. Homelessness is a big risk factor in addition to opioid and heroin use.

Educating communities about injection drug use and accessibility of needle exchange programs is helping to flatten the curve of HCV infection. These organized programs enable drug users to replace used needles with sterile ones, says Larry Lutwick, M.D., a retired Mayo Clinic professor who is the moderator of ProMED (Program for Monitoring Emerging Diseases), an online surveillance initiative for infectious diseases throughout the world. "Based on data, this does not lead to increased injection drug use and does decrease the acquisition of HCV and HIV," Lutwick says.

True game changers

Although there is no HCV vaccine, the direct-acting antivirals have transformed treatment, so it is easier and more effective.

Until 2014, treatment involved injection of interferon, which was only somewhat effective and resulted in significant side effects. The direct-acting antivirals were pills, not injections, and cured HCV approximately 95% of the time while dramatically decreasing toxicity, says Joseph K. Lim, M.D., a professor and director of the viral hepatitis program at Yale School of Medicine.

For most patients, treatment consists of one to three pills daily for two to three months, Lim says. Afterward, patients still need to be monitored for liver cancer even if they are cured of the infection.

The catch with the direct-acting antiviral medicines has been their price. Lack of access to the curative medications is still an issue in many parts of the world, according to the World Health Organization (WHO).

But Thomas says that “in the United States, the cost of HCV treatments can no longer be an impediment. Prices have dropped considerably, and a complete cure of HCV costs less than a one-year supply of some other widely accepted medications.” But, he adds, “the number of actual prescriptions now is lower than it should be, given that there remain 2 million persons living with a potentially fatal, transmissible and curable infectious disease.”

Louisiana and other states have negotiated “Net/fix” subscription plans for paying for the antivirals whereby they pay a set price for an unlimited number of prescriptions. “That type of strategy caps spending for the state and removes the incentive to make treatment hard to get as a way of saving money,” Thomas says.

Susan Kreimer is an independent journalist in New York.

Hepatitis C acute infections are increasing in the U.S.

According to CDC estimates, the number of acute infections more than doubled from 24,700 to 57,500 in 2019

Source: CDC 2019 Viral Hepatitis Surveillance Report

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