THE PANDEMIC ONE YEAR IN

Silver linings and big reveals

PROVIDERS
Fewer patients, less revenue, more struggle

PAYERS
Bracing for the double peak

Also

Drugs in the Pipeline
Present and future COVID-19 vaccines

Oncology
Consequences of deferred screening and care

Formulary Development
Pricing of COVID-19 vaccines
FOR PATIENTS WITH RELAPSING FORMS OF MS

PLAYING WITH FEWER RELAPSES

• The efficacy of VUMERITY® (diroximel fumarate) is based upon bioavailability studies in patients with relapsing forms of multiple sclerosis (MS) including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Important Safety Information

CONTRAINDICATIONS

VUMERITY is contraindicated in patients
• With known hypersensitivity to diroximel fumarate, dimethyl fumarate, or to any of the excipients of VUMERITY. Reactions may include anaphylaxis and angioedema
• Taking dimethyl fumarate

WARNINGS AND PRECAUTIONS

Anaphylaxis and Angioedema
• VUMERITY can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms in patients taking dimethyl fumarate (which has the same active metabolite as VUMERITY) have included difficulty breathing, urticaria, and swelling of the throat and tongue. Patients should be instructed to discontinue VUMERITY and seek immediate medical care should they experience signs and symptoms of anaphylaxis or angioedema

Progressive Multifocal Leukoencephalopathy
• Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with dimethyl fumarate (which has the same active metabolite as VUMERITY). PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. A fatal case of PML occurred in a patient who received dimethyl fumarate for 4 years while enrolled in a clinical trial
• PML has occurred in patients taking dimethyl fumarate in the postmarketing setting in the presence of lymphopenia (<0.9 x 10^9/L). While the role of lymphopenia in these cases is uncertain, the PML cases have occurred predominantly in patients with lymphocyte counts <0.8 x 10^9/L persisting for more than 6 months
• At the first sign or symptom suggestive of PML, withhold VUMERITY and perform an appropriate diagnostic evaluation. 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 orientation leading to confusion and personality changes

• Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms. Monitoring with MRI for signs consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present

Herpes Zoster and Other Serious Opportunistic Infections
• Serious cases of herpes zoster have occurred in patients treated with dimethyl fumarate (which has the same active metabolite as VUMERITY), including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster meningoencephalitis, and herpes zoster meningomyelitis. These events may occur at any time during treatment. Monitor patients on VUMERITY for signs and symptoms of herpes zoster. If herpes zoster occurs, appropriate treatment for herpes zoster should be administered
• Other serious opportunistic infections have occurred with dimethyl fumarate, including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. These infections have been reported in patients with reduced absolute lymphocyte counts (ALC) as well as in patients with normal ALC. These infections have affected the brain, meninges, spinal cord, gastrointestinal tract, lungs, skin, eye, and ear. Patients with symptoms and signs consistent with any of these infections should undergo prompt diagnostic evaluation and receive appropriate treatment
• Consider withholding VUMERITY treatment in patients with herpes zoster or other serious infections until the infection has resolved

Lymphopenia
• VUMERITY may decrease lymphocyte counts. In the MS placebo-controlled trials with dimethyl fumarate (which has the same active metabolite as VUMERITY), mean lymphocyte counts decreased by approximately 30% during the first year of treatment with dimethyl fumarate and then remained stable. Four weeks after stopping dimethyl fumarate, mean lymphocyte counts increased but did not return to baseline. The incidence of lymphopenia was similar in patients treated with dimethyl fumarate or placebo. There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.8 x 10^9/L or ≤0.5 x 10^9/L in controlled trials, although one patient in an extension study developed PML in the setting of prolonged lymphopenia (lymphocyte counts predominantly <0.5 x 10^9/L for 3.5 years)
• In controlled and uncontrolled clinical trials with dimethyl fumarate, 2% of patients experienced lymphocyte counts <0.5 x 10^9/L for at least six months, and in this group the majority of lymphocyte counts remained <0.5 x 10^9/L with continued therapy. Neither VUMERITY nor dimethyl fumarate have been studied in patients with preexisting low lymphocyte counts.
VUMERITY® (diroximel fumarate) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome (CIS) meeting criteria for MS and patients with clinically definite MS who are at high risk of progression. VUMERITY® is approved for the treatment of patients with RRMS to delay the onset of secondary progressive disease, in adults.

VUMERITY® is contraindicated in patients with liver failure, liver transplant, or death in some patients.

While the role of lymphopenia in these cases is uncertain, dimethyl fumarate has resolved upon treatment discontinuation. Some cases required hospitalization. None of the reported cases resulted in liver failure, liver transplant, or death. However, the combination of new serum aminotransferase elevations with increased levels of bilirubin caused by drug-induced hepatocellular injury is an important predictor of serious liver injury that may lead to acute liver failure, liver transplant, or death in some patients.

VUMERITY® is not recommended in patients with moderate or severe renal impairment.

Please see following pages for Brief Summary of full Prescribing Information.

Study Designs

- **Study 1:** A 2-year, randomized, double-blind, placebo-controlled study in 1234 patients with RRMS. Secondary endpoint: ARR.
- **Study 2:** A 2-year, multicenter, randomized, double-blind, placebo-controlled study in 1417 patients with RRMS. Primary endpoint: ARR.

ADVERSE REACTIONS

- The most common adverse reactions (incidence ≥10% and ≥2% more than placebo) for dimethyl fumarate (which has the same active metabolite as VUMERITY) were flushing, abdominal pain, diarrhea, and nausea.
- Gastrointestinal adverse reactions: Dimethyl fumarate caused GI events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). The incidence of GI events was higher early in the course of treatment (primarily in month 1) and usually decreased over time in patients treated with dimethyl fumarate compared with placebo. Four percent (4%) of patients treated with dimethyl fumarate and less than 1% of placebo patients discontinued due to gastrointestinal events. The incidence of serious GI events was 1% in patients treated with dimethyl fumarate.
- Hepatic transaminases: An increased incidence of elevations of hepatic transaminases in patients treated with dimethyl fumarate was seen primarily during the first six months of treatment and most patients with elevations had levels <3 times the upper limit of normal (ULN) during controlled trials. There were no elevations in transaminases ≥3 times the ULN with concomitant elevations in total bilirubin ≥2 times the ULN. Discontinuations due to elevated hepatic transaminases were <1% and were similar in patients treated with dimethyl fumarate or placebo.
- Eosinophilia adverse reactions: A transient increase in mean eosinophil counts was seen during the first 2 months of therapy.

USE IN SPECIFIC POPULATIONS

Renal Impairment

- No dosage adjustment is necessary in patients with mild renal impairment. Because of an increase in the exposure of a major metabolite, use of VUMERITY® is not recommended in patients with moderate or severe renal impairment.

2. DOSAGE AND ADMINISTRATION

2.1 Blood Tests Prior to Initiation of VUMERITY

Obtain the following prior to treatment with VUMERITY:

- A complete blood cell count (CBC), including lymphocyte count [see Warnings and Precautions (5.4)]
- Serum aminotransferase, alkaline phosphatase, and total bilirubin levels [see Warnings and Precautions (5.5)]

2.2 Dosing Information

The starting dosage for VUMERITY is 231 mg twice a day orally. After 7 days, the dosage should be increased to the maintenance dosage of 462 mg (administered as two 231 mg capsules) twice a day orally. Temporary dosage reductions to 231 mg twice a day may be considered for individuals who do not tolerate the maintenance dosage. Within 4 weeks, the recommended dosage of 462 mg twice a day should be reached. Discontinuation of VUMERITY should be considered for patients unable to tolerate return to the maintenance dosage. Administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to VUMERITY dosing may reduce the incidence or severity of flushing [see Clinical Pharmacology (12.3)].

2.3 Administration Instructions

Swallow VUMERITY capsules whole and intact. Do not crush or chew, or sprinkle the capsule contents on food.

If taken with food, avoid a high-fat, high-calorie meal/snack; the meal/snack should contain no more than 700 calories and no more than 30 g fat [see Warnings and Precautions (5.6) and Clinical Pharmacology (12.3)].

Avoid co-administration of VUMERITY with alcohol [see Clinical Pharmacology (12.3)].

2.4 Blood Tests to Assess Safety After Initiation of VUMERITY

Obtain a complete blood cell count (CBC), including lymphocyte count, 6 months after initiation of VUMERITY and then every 6 to 12 months thereafter, as clinically indicated [see Warnings and Precautions (5.4)].

Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels during treatment with VUMERITY, as clinically indicated [see Warnings and Precautions (5.5)].

2.5 Patients With Renal Impairment

No dosing adjustment is recommended in patients with mild renal impairment.

VUMERITY is not recommended in patients with moderate or severe renal impairment [see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)].

3. DOSAGE FORMS AND STRENGTHS

VUMERITY is available as hard, delayed-release capsules containing 231 mg of diroximel fumarate. The capsules have a white cap and a white body, printed with “DRF 231 mg” in black ink on the body.

4. CONTRAINDICATIONS

VUMERITY is contraindicated in patients

- With known hypersensitivity to diroximel fumarate, dimethyl fumarate, or to any of the excipients of VUMERITY. Reactions may include anaphylaxis and angioedema [see Warnings and Precautions (5.1)]
- Taking dimethyl fumarate [see Drug Interactions (7.1)].

5. WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis and Angioedema

VUMERITY can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms in patients taking dimethyl fumarate (which has the same active metabolite as VUMERITY) have included difficulty breathing, urticaria, and swelling of the throat and tongue. Patients should be instructed to discontinue VUMERITY and seek immediate medical care should they experience signs and symptoms of anaphylaxis or angioedema.

5.2 Progressive Multifocal Leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with dimethyl fumarate (which has the same active metabolite as VUMERITY). PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. A fatal case of PML occurred in a patient who received dimethyl fumarate for 4 years while enrolled in a clinical trial. During the clinical trial, the patient experienced prolonged lymphopenia (lymphocyte counts predominantly <0.5 × 10^9/L for 3.5 years) while taking VUMERITY. Mean lymphocyte counts increased but did not return to baseline. The patient had no other identified systemic medical conditions resulting in compromised immune system function and had not previously been treated with natalizumab, which has a known association with PML. The patient was also not taking any immunosuppressive or immunomodulatory medications concomitantly.

PML has also occurred in patients taking dimethyl fumarate in the postmarketing setting in the presence of lymphopenia (<0.9 × 10^9/L). While the role of lymphopenia in these cases is uncertain, the PML cases have occurred predominantly in patients with lymphocyte counts <0.8 × 10^9/L persisting for more than 6 months.

At the first sign or symptom suggestive of PML, withhold VUMERITY and perform an appropriate diagnostic evaluation. 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 personality [see Warnings and Precautions (5.6) and Clinical Pharmacology (12.4)].

Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms. Cases of PML diagnosed based on MRI findings and the detection of JCV DNA in the cerebrospinal fluid in the absence of clinical signs or symptoms specific to PML, have been reported in patients treated with other MS medications associated with PML. These patients subsequently became positive for JCV by PCR. Therefore, monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Lower PML-related mortality and morbidity have been reported following discontinuation of another MS medication associated with PML in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis. It is not known whether these differences are due to early detection and discontinuation of MS treatment or due to differences in disease in these patients.

5.3 Herpes Zoster and Other Serious Opportunistic Infections

Serious cases of herpes zoster have occurred in patients treated with dimethyl fumarate (which has the same active metabolite as VUMERITY) including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster meningoencephalitis, and herpes zoster meningomyelitis. These events may occur at any time during treatment. Monitor patients on VUMERITY for signs and symptoms of herpes zoster. If herpes zoster occurs, appropriate treatment for herpes zoster should be administered.

Other serious opportunistic infections have occurred with dimethyl fumarate, including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. These infections have been reported in patients with reduced absolute lymphocyte counts (ALC) as well as in patients with normal ALC. These infections have affected the brain, meninges, spinal cord, gastrointestinal tract, lungs, skin, eye, and ear. Patients with symptoms and signs consistent with any of these infections should undergo prompt diagnostic evaluation and receive appropriate treatment.

Consider withholding VUMERITY treatment in patients with herpes zoster or other serious infections until the infection has resolved [see Adverse Reactions (6.2)].

5.4 Lymphopenia

VUMERITY may decrease lymphocyte counts. In the MS placebo-controlled trials with dimethyl fumarate (which has the same active metabolite as VUMERITY), mean lymphocyte counts decreased by approximately 30% during the first year of treatment with dimethyl fumarate and then remained stable. Four weeks after stopping dimethyl fumarate, mean lymphocyte counts increased but did not return to baseline. Six percent (6%) of dimethyl fumarate patients and <1% of placebo patients experienced lymphocyte counts <0.5 × 10^9/L (lower limit of normal 0.91 × 10^9/L). The incidence of infections (60% vs 58%) and serious infections (2% vs 2%) was similar in patients treated with dimethyl fumarate or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.8 × 10^9/L or ≤0.5 × 10^9/L in controlled trials, although one
patient in an extension study developed PML in the setting of prolonged lymphopenia (lymphocyte counts predominantly <0.5 × 10^9/L for 3.5 years) [see Warnings and Precautions (5.2)].

In controlled and uncontrolled clinical trials with dimethyl fumarate, 2% of patients experienced lymphocyte counts <0.5 × 10^9/L for at least six months, and in this group the majority of lymphocyte counts remained <0.5 × 10^9/L with continued therapy. Neither VUMERITY® (dimethyl fumarate) nor dimethyl fumarate have been studied in patients with preexisting low lymphocyte counts.

Obtain a complete blood count (CBC), including lymphocyte count, before initiating treatment with VUMERITY, 6 months after starting treatment, and then every 6 to 12 months thereafter, and as clinically indicated. Consider patients with lymphocyte counts less than 0.5 × 10^9/L persisting for more than six months. Given the potential for delayed recovery of lymphocyte counts, continue to obtain lymphocyte counts until their recovery if VUMERITY is discontinued or interrupted because of lymphopenia. Consider withholding treatment from patients with serious infection until resolution. Decisions about whether or not to restart VUMERITY should be individualized based on clinical circumstances.

5.5 Liver Injury

Clinically significant cases of liver injury have been reported in patients treated with dimethyl fumarate (which has the same active metabolite as VUMERITY) in the postmarketing setting. The onset has ranged from several days to several months after initiation of treatment with dimethyl fumarate. Signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal and elevation of total bilirubin to greater than 2-fold the upper limit of normal have been observed. These abnormalities resolved upon treatment discontinuation. Some cases required hospitalization. None of the reported cases resulted in liver failure, liver transplant, or death. However, the combination of new serum aminotransferase elevations with increased levels of bilirubin caused by drug-induced hepatocellular injury is an important predictor of serious liver injury that may lead to acute liver failure, liver transplant, or death in some patients.

Elevations of hepatic transaminases (most no greater than 3 times the upper limit of normal) were observed during controlled trials with dimethyl fumarate [see Adverse Reactions (6.1)]. Obtain serum aminotransferase, alkaline phosphatase (ALP), and total bilirubin levels prior to treatment with VUMERITY and during treatment, as clinically indicated. Discontinue VUMERITY if clinically significant liver injury induced by VUMERITY is suspected.

5.6 Flushing

VUMERITY may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). In clinical trials of dimethyl fumarate (which has the same active metabolite as VUMERITY), 40% of dimethyl fumarate-treated patients experienced flushing. Flushing symptoms generally began soon after initiating dimethyl fumarate and usually improved or resolved over time. In the majority of patients who experienced flushing, it was mild or moderate in severity. Three percent (3%) of patients discontinued dimethyl fumarate for flushing and <1% had serious flushing symptoms that were not life-threatening but led to hospitalization.

Administration of VUMERITY with food may reduce the incidence of flushing [see Dosage and Administration (2.3)]. Studies with dimethyl fumarate show that administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to dosing may reduce the incidence or severity of flushing [see Clinical Pharmacology (12.3)].

6. ADVERSE REACTIONS

The following important adverse reactions are described elsewhere in labeling:

- Anaphylaxis and Angioedema [see Warnings and Precautions (5.1)]
- Progressive Multifocal Leuкоencephalopathy [see Warnings and Precautions Section (5.2)]
- Herpes Zoster and Other Serious Opportunistic Infections [see Warnings and Precautions (5.3)]
- Lymphopenia [see Warnings and Precautions (5.4)]
- Liver Injury [see Warnings and Precautions (5.5)]
- Flushing [see Warnings and Precautions (5.6)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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 adverse reactions presented in Table 1 below are based on safety information from 769 patients treated with dimethyl fumarate 240 mg twice a day and 771 placebo-treated patients. The most common adverse reactions (incidence ≥10% and ≥2% more than placebo) for dimethyl fumarate were flushing, abdominal pain, diarrhea, and nausea.

Table 1: Adverse Reactions in Study 1 and 2 Reported for Dimethyl Fumarate at ≥2% Higher Incidence than Placebo

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Dimethyl Fumarate 240 mg Twice Daily</th>
<th>Placebo (N=771)%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>40</td>
<td>6</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Nausea</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Pruritus</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Rash</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Albumin urine present</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Erythema</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>2</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Gastrointestinal

Dimethyl fumarate caused GI events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). The incidence of GI events was higher early in the course of treatment (primarily in month 1) and usually decreased over time in patients treated with dimethyl fumarate compared with placebo. Four percent (4%) of patients treated with dimethyl fumarate and less than 1% of placebo patients discontinued treatment due to gastrointestinal events. The incidence of serious GI events was 1% in patients treated with dimethyl fumarate.

Hepatic Transaminases

An increased incidence of elevations of hepatic transaminases in patients treated with dimethyl fumarate was seen primarily during the first six months of therapy. In controlled trials with dimethyl fumarate, 40% of patients experienced elevated transaminase levels. The incidence of serious hepatic transaminase elevations with dimethyl fumarate was <1% and was similar in patients treated with placebo.

Eosinophilia

A transient increase in mean eosinophil counts was seen during the first 2 months of therapy.

Adverse Reactions in Clinical Studies with VUMERITY

In clinical studies assessing safety in patients with RRMS, approximately 700 patients were treated with VUMERITY and approximately 490 patients received more than 1 year of treatment with VUMERITY. The adverse reaction profile of VUMERITY was consistent with the experience in the placebo-controlled clinical trials with dimethyl fumarate.

6.2 Postmarketing Experience

The following adverse reaction has been identified during post approval
use of dimethyl fumarate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Liver function abnormalities (elevations in transaminases ≥3 times ULN) have been reported following dimethyl fumarate administration in postmarketing experience [see Warnings and Precautions (5.5)].

Herpes zoster infection and other serious opportunistic infections have been reported with dimethyl fumarate administration in postmarketing experience [See Warnings and Precautions (5.5)].

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of VUMERITY® (dimethyl fumarate) or dimethyl fumarate (which has the same active metabolite as VUMERITY®) in pregnant women. In animal studies, administration of diroximel fumarate during pregnancy or throughout pregnancy and lactation resulted in adverse effects on embryofetal and offspring development (increased incidences of skeletal abnormalities, increased mortality, decreased body weights, neurobehavioral impairment) at clinically relevant drug exposures [see Data].

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data

Oral administration of diroximel fumarate (0, 40, 100, or 400 mg/kg/day) to pregnant rats throughout organogenesis resulted in a decrease in fetal body weight and an increase in fetal skeletal variations at the highest dose tested, which was associated with maternal toxicity. Plasma exposures (AUC) for MMF and HES (the major circulating drug) at the no-effect dose (100 mg/kg/day) for adverse effects on embryofetal development were approximately 2 times those in humans at the recommended human dose (RHD) of 924 mg/day.

Oral administration of diroximel fumarate (0, 50, 150, or 350 mg/kg/day) to pregnant rabbits throughout organogenesis resulted in an increase in fetal skeletal malformations at the mid and high doses and reduced fetal body weight and increases in embryofetal death and fetal skeletal variations at the highest dose tested. The high dose was associated with maternal toxicity. Plasma exposures (AUC) for MMF and HES at the no-effect dose (50 mg/kg/day) for adverse effects on embryofetal development were similar to (MMF) or less than (HES) those in humans at the RHD.

Oral administration of diroximel fumarate (0, 40, 100, or 400 mg/kg/day) to rats throughout gestation and lactation resulted in reduced fetal body weight and increases in embryofetal death and fetal skeletal variations at the highest dose tested. The high dose was associated with maternal toxicity. Plasma exposures (AUC) for MMF and HES at the no-effect dose (100 mg/kg/day) for adverse effects on embryofetal development were approximately 3 times (MMF) or less than (HES) those in humans at the RHD.

8.2 Lactation

Risk Summary

There are no data on the presence of diroximel fumarate or metabolites (MMF, HES) in human milk. The effects on the breastfeeding infant and on milk production are unknown.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for VUMERITY and any potential adverse effects on the breastfed infant from the drug or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of dimethyl fumarate and VUMERITY did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients.

8.6 Renal Impairment

No dosage adjustment is necessary in patients with mild renal impairment. Because of an increase in the exposure of a major metabolite [2-hydroxyethyl succinimide (HES)], use of VUMERITY is not recommended in patients with moderate or severe renal impairment [see Clinical Pharmacology (12.3)].
Chairman’s Letter

A year of living pandemically

As we were putting this issue of Managed Healthcare Executive to bed, the country passed what many headlines called a grim milestone. The death toll in the U.S. from the COVID-19 pandemic surpassed 500,000. As the Associated Press reported, the number of American lives taken by the viral infection is now more than the populations of the cities of Miami or Kansas City, Missouri. It is more than the number of Americans killed in World War II, the Korean War and the Vietnam War combined.

Numbers can never tell the full story, but they can punctuate. Here we are, a year into the pandemic. Half a million dead. Full stop.

But this pandemic has eddied with crosscurrents — the good and the bad, the up and the down — perhaps especially in U.S. healthcare. As we discuss in this issue, some providers in some parts of the country have been overwhelmed with COVID-19 cases and care. Others, though, have seen empty beds and appointment calendars as the country pulled back from routine healthcare. Provision of that care became more expensive because of personal protective equipment and spacing requirements. Meanwhile, payers cruised through the first part of the year as the claims fell precipitously. But as 2020 went on, healthcare utilization increased. Some saw a “double peak”: expenditures related to COVID-19 and people coming back to the healthcare system for services that they had put off.

COVID-19 has been a solvent, revealing some of the shortcomings of U.S. healthcare. Disparities that follow the contours of race have been laid bare. Underinvestment in public health may be the chicken that came home to roost.

Here we are, a year into the pandemic. Half a million dead. Full stop.

Perhaps the worst is behind us, and the amazing capabilities of U.S. healthcare can show us the way forward.

Mike Hennessy Sr.
Chairman and Founder of MJH Life Sciences®
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Meet the speakers:

Susan Beaton  
VP, Health Plan Strategy, Wellframe

Doug Berkson  
VP, Customer Engagement, Wellframe

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OPINION

Coming together during a pandemic

Collaboration between health plans and providers leads to better quality, an improved experience and lower costs.

An efficient healthcare system depends on strong relationships between health plans and providers. Much of what makes healthcare seamless for consumers happens behind the scenes as health plans, doctors and hospitals work together to improve access, quality and cost of care. Not since the introduction of the ACA has anything redefined these relationships as much as the COVID-19 pandemic.

Many health plans, including my employer, Independence Blue Cross in Philadelphia, have long prepared for — and then responded to — public health emergencies such as the SARS and Ebola viruses. However, as the cases soared during the first weeks of March, it was clear that the COVID-19 pandemic and the spread and danger of this new virus were unprecedented.

Health plans that already excelled at working side by side with their provider networks were in the best position to recognize and respond to the unforeseen challenges.

Before COVID-19 hospitalizations surged, many health plans anticipated making quick policy changes to give providers some relief. The changes included waiving cost sharing for testing and treatment, easing guidelines for patient transfers to make room for more patients with COVID-19, and lifting prior-authorization requirements for acute inpatient admissions from the emergency department. At Independence, we developed a dedicated website and “COVID-19 primary care playbook,” which were updated once or twice a week. This information helped our population health specialists better support primary care doctors in a constantly changing environment.

When personal protective equipment was hard to get, some health plans jumped in to help. Independence purchased and dispensed nearly 500,000 masks to healthcare workers who care for patients in underserved areas in the Philadelphia area and 45,000 to Medicare Advantage members. Through its foundation, Independence supported several local nonprofits focused on helping underserved communities get access to COVID-19 testing. One such organization, the Black Doctors COVID-19 Consortium, has tested more than 20,000 individuals in Philadelphia and is now administering the vaccine.

Independence also helped convene a consortium of regional health providers to share best practices and assess the capacity of our health institutions during the pandemic’s peak.

Notably, the pandemic caused an exponential growth in telemedicine. Concerned that individuals might forgo necessary medical and preventive care for fear of contracting the virus, health plans such as Independence promoted the ease and convenience of telemedicine. In Independence’s Beat COVID-19 public awareness campaign, telemedicine was front and center.

Consumers and doctors now rely on these digital tools as never before. In 2019, telemedicine made up a tiny proportion — 0.12% — of professional claims among our commercial members. Last year, it made up 16% of those claims. It’s safe to say that telemedicine is here to stay as a reliable complement to in-person care.

It will be important for health plans to continue working closely with providers. At Independence, we will continue to evolve our value-based and alternative payments models, which focus on quality, experience and cost of care over quantity of care. This emphasis became even more important during the pandemic as many healthcare providers struggled financially under a system still disproportionately focused on care volume. The paradox of healthcare providers worried about going out of business when they were needed most reinforces the need for value-based payment, which is less vulnerable to volume shifts such as those the pandemic caused. At Independence, we will continue to build upon our value-based programs and primary care capitation payments.

We’ve learned a lot, but this pandemic is far from over. Millions of people need to be vaccinated. This next challenge will require equal determination and collaboration. Fortunately, this past year has taught us that health plans and providers are more than ready and willing to work together to make that happen.

Rodrigo Cerdá, M.D., M.P.H., is vice president of clinical care transformation at Independence Blue Cross in Philadelphia and a member of the Managed Healthcare Executive editorial advisory board.
Biden administration moves to stop Medicaid work requirements

The Trump administration didn’t get very far with healthcare reform; the ACA was neither repealed nor replaced. But former CMS Administrator Seema Verma made a run at revamping Medicaid by using Section 1115 waivers to add working requirements. Now the Biden administration is taking steps to stop the requirements before they get started.

During the Trump administration, 19 states were at some stage of imposing Medicaid work requirements (eight waivers approved, seven pending, and four tied up in court). Mid-February, the new administration sent out letters to two work requirement states, Arkansas and New Hampshire, saying that CMS now has “serious concerns” about testing policies that might lead to loss of healthcare coverage amid the pandemic. Verma made some eleventh hour changes to the waivers that will make it more difficult to undo them, but the Biden administration is working to dismantle those rules.

Changing Medicaid funding so states would receive block grants to run their programs was another change the Trump administration wanted to see. Tennessee has an 1115 waiver that would mean such funding for the state Medicaid’s program and, among other things, a closed formulary. But that waiver is now also in doubt.

Entresto snags broader indication, maybe $5 billion in sales

Entresto (sacubitril and valsartan) may be on its way to becoming a blockbuster drug five times over.

Last month the FDA expanded the indication for Novartis’ heavily marketed heart failure medication beyond people with reduced ejection fraction to include those with healthier hearts with “preserved” ejection fraction.

Novartis executives had indicated earlier that the new indication could mean Entresto will reach $5 billion in annual sales. In the press release touting the approval last month, Novartis said Entresto “may now be appropriate” for about 5 million of the 6 million Americans with chronic heart failure. The company arrived at that figure by adding up the 3 million Americans who have reduced ejection fraction and two-thirds of the 3 million with preserved ejection fraction.

Ejection fraction refers to the percentage of blood that is pumped out of the left ventricle with each heartbeat. Guidelines and studies vary about where they draw the boundary between reduced and preserved ejection fraction, but 40% or lower is often used to define reduced ejection fraction. Research findings, including the study on which this indication expansion was based, suggest that ejection fraction is not so binary and that there may be some people in a middle range (between 40% and 57%) of ejection fraction for whom some medications, such as Entresto, are effective. Entresto faces competition from other classes of drugs, notably the sodium glucose co-transporter 2 inhibitors, in the market for heart failure with reduced ejection fraction.

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MJHLifeSciences.com/news-network
Taming U.S. healthcare spending is a huge, daunting task that has met with little success. But some Yale professors are proposing to take a bite-sized approach as a way to change that.

The “1% Steps for Health Care Reform” project launched by Zach Cooper, Ph.D., and Fiona Scott Morton, Ph.D., promises to offer up “a menu of tangible steps that policymakers can take to lower healthcare costs in the U.S.”

To that end, the project’s website currently has 16 policy briefs posted. Each carries an estimate of the percentage by which proposals in the briefs could reduce healthcare spending. For example, Cooper and Morton estimate that the changes they propose in their policy brief on out-of-network billing by hospital-based physicians could save $60 billion annually, or 5% of commercial healthcare spending.

Aetna got out of the ACA marketplace business in 2018. Now CVS Health, which completed its acquisition of the insurance company in late 2018, is hopping back in and will brand the policies as a “CVS Health-Aetna” product for the first time, Karen S. Lynch, the company’s new president and CEO, said during an earnings call last month.

“As the ACA has evolved, there is evidence of market stabilization and remedies to earlier structural issues,” Lynch said during the Feb. 16 call. “It is now time for us to participate in these markets.”

Lynch said CVS Health would start selling coverage that would start in January 2022, but she shared no details about how many markets the company might sell CVS Health-Aetna coverage in or which ones. She noted that the ACA marketplace market was a big one of 10 to 15 million people.

After a Supreme Court ruling favoring insurers, CVS Health was among those that received a hefty ACA risk corridor payment. The company booked a $307 million risk corridor payment in 2020. The ACA marketplace plans may also benefit from President Joe Biden’s proposal to increase the subsidies that lower premium costs for Americans who buy ACA marketplace coverage.

CVS Health is a huge ($286.7 billion revenues last year), publicly traded company, but like many of its competitors, it has seen the proportion of its government business (Medicare Advantage, Medicaid) grow relative to its commercial business. For example, the number of people in its insured commercial plans decreased from 3,591,000 in 2019 to 3,258,000 in 2020, a difference of 333,000, or 9.3%, according to year-end results posted at the time of the earnings call. Meanwhile, the number of people in its Medicare Advantage plans increased from 2,321,000 in 2019 to 2,705,000 in 2020, an increase of 384,000, or 16.5%.

In celebration of Black History Month last month, Managed Healthcare Executive® featured Sheldon Fields, Ph.D., RN, the associate dean for equity inclusion and a research professor at the College of Nursing at Penn State University, in our “Tuning In to the C-Suite” podcast. Associate Editor Briana Contreras spoke with Fields about equity issues in health care and efforts on behalf of patients and nurses of color.

“Tuning In to the C-Suite” features healthcare professionals, leaders and executives talking about the most important healthcare issues today. The podcast is also home to our “Meet the Board” and “MHE Talks: Improving Patient Access” series. You can catch a new episode of “Tuning In to the C-Suite” every Wednesday on iHeart Radio, Apple Podcasts and Spotify or on the MHE website. Listen in, learn a lot.
Multiple sclerosis (MS) is a chronic disease that involves demyelination of plaque throughout the white and gray matter of the central nervous system. The early stages of MS are usually marked by a relapsing-remitting course of neurological deficits, which progress toward continuous, permanent dysfunction and disability. Of those with a diagnosis of MS, 74% are women. Multiple sclerosis also takes a toll on quality of life because patients often experience an inability to participate in activities of daily living, cognitive impairment and depression. Approximately 62% of those with MS also have comorbidities, the most common including anxiety, hypertension, migraine, smoking or history of smoking, and obesity, according to results from a 2019 study.

In addition to having a clinical impact on disability and comorbidities, MS has been shown to affect patients’ ability to maintain their professional lives, with approximately 50% of patients losing their jobs five years after receiving a diagnosis. Unemployment related to MS is higher than that of any other reason for disability, and loss in productivity contributes to up to 44% of MS-related costs in the United States and Europe. Additionally, employees with MS, when compared with healthy employees, work a higher number of unpaid hours and experience more interpersonal and performance challenges, such as verbal criticism, harassment, declining relationships and poor performance reviews.

The cost burden of MS is also significant. Following congestive heart failure, MS is the second most costly chronic condition, with total all-cause, per-patient direct and indirect healthcare costs reaching up to $54,244 per year. For those who have a severe disability associated with MS, costs can exceed $100,000 per year. The high cost of MS care is also one factor that can lead patients to join Medicare before the age of 65 or decrease their financial assets to become eligible for Medicaid for healthcare coverage.

The clinical and economic burden of disease among patient with MS, although substantial across the broad spectrum of patients, may disproportionately affect patients of color. Black and Hispanic Americans particularly have been found to experience heightened challenges with an MS, with differences ranging from prevalence and disease course to treatment access and outcomes. This article explores common disparities and how they influence the burden of MS in racial and ethnic minority populations.

### Differences in Prevalence and Disease Course

The prevalence of MS in the United States varies by race and ethnicity. A retrospective, observational cohort study reviewed more than 1 million patients in a Northern California healthcare system to quantify MS prevalence. Of these patients, 3,286 had MS. Results demonstrated that among the cohort, the age-adjusted period prevalence of MS was highest among non-Hispanic Black patients, with 521.3 people per 100,000. White patients had the second-highest age-adjusted period prevalence (384.6 per 100,000), Hispanic patients had the third highest (183.7 per 100,000), and Asian patients had the lowest (63.9 per 100,000). Regarding gender differences, Black women had the highest age-adjusted period prevalence of all groups (677.0 per 100,000). In addition to experiencing a higher prevalence of MS, Black individuals often receive a diagnosis at a younger age than do White individuals. They can experience a disproportionately greater number and
severity of MS manifestations, such as relapses; poor recovery; visual impairments; and challenges with walking, balance and coordination. Their disease typically progresses rapidly, with earlier onset and, ultimately, greater level of disability. According to results from a retrospective review of 1,300 patients with MS, Black patients (n=40) presented with a higher expended disability status scale (EDSS) score at time of diagnosis than did White patients (n=31 [mean, 2.9±0.2 vs. 1.8±0.2; difference between means, 1.1±0.3; P=0.0002]). By the 4-to-6-year follow-up, the EDSS score for Black patients (n=60) grew to nearly double that of White patients (n=45 [mean, 5.7±1.5 vs. 2.9±0.3; difference between means, 2.8±1.7; P=0.0008]). With each 1-unit increase of the EDSS score, there was a 1.3 times greater likelihood that the patient was Black rather than White. Black patients also used unilateral assistance devices more often than White patients (hazard ratio [HR], 2.2; 95% confidence interval [CI], 1.5-3.5), as well as the use of wheelchairs (HR, 2.5; 95% CI, 1.3-4.5). Although receiving early successful treatment may help delay the advancement of MS-related disability, the more aggressive progression of MS experienced by Black patients does not appear to be related to a delayed diagnosis of MS or treatment.

Although MS prevalence is lower for Hispanic patients than Black and White patients, Hispanic patients tend to be younger at the time of diagnosis, particularly if they were born in the United States. Results from a retrospective study showed that the percentage of Hispanic patients with relapsing-remitting MS (vs other disease subtypes) was much higher than that of Black or White patients. Both Hispanic and Black patients had a shorter mean disease duration than White patients. The Patient-Derived Multiple Sclerosis Severity Score (P-MSSS), adjusted for age and gender, was significantly higher for Hispanic patients (3.9±2.6) and Black patients (4.5±3.0) than it was for White patients (3.4±2.6; P<0.0001 for each comparison). Race remained a significant predictor for P-MSSS when also adjusting for insurance coverage.

Treatment Disparities
Disparities exist across the healthcare system regarding the treatment of MS among racial and ethnic minority populations. Notably, racial and ethnic minority subpopulations are consistently underrepresented in clinical trials, which makes it difficult to ascertain variations in the efficacy of treatment. According to results from a 2014 PubMed review of nearly 60,000 articles on MS, Black and Hispanic patients are represented in less than 1% of published literature.

Black, Latino and White patients do not receive the

“'We have to remedy the inequities in our care. Certainly, you want the cutting-edge MS care to be available to everybody with MS. We want to have studies that help us to understand why MS may differ based on race/ethnicity so that we can take the best possible care of every individual with MS.”

Patricia K. Coyle, M.D.
Stony Brook University Neurosciences Institute
Stony Brook, New York

To view the interview with Dr. Coyle and other videos, visit managedhealthcareexecutive.com/population-health-perspectives.
same services for MS, according to results from a 2010 retrospective study funded by the National MS Society. The study reviewed data from the registry of the North American Research Committee on Multiple Sclerosis (NARCOMS) Project on Black patients with MS (n = 1313), Latino patients with MS (n = 715) and White patients with MS (n = 26,967). Latino patients were less likely to use rehabilitative, supportive and alternative therapies compared with Black patients and White patients; 33.8% of Latino patients never received occupational therapy versus 21.1% of Black patients and 24.1% of White patients. In fact, more Latino patients had never had a home health aide (40%) compared with Black (28%) or White (30%) patients. Black patients were much less likely to receive an evaluation and treatment at an MS clinic than White and Latino patients (36.8% vs 49.2% and 47.0%, respectively). In addition, more Black patients (56.1%) had never received care from a neurologist specializing in MS than Latino patients (47.2%). Seeing a neurologist is associated with an increased likelihood of a patient using a disease-modifying treatment (DMT).17

Access Challenges
The barriers to MS care experienced by racial and ethnic populations can be attributed to a wide variety of factors, such as low health literacy, limited education, low income and a lack of insurance coverage. Results from the NARCOMS study demonstrated that 29.3% of Black patients earned less than $15,000 annually versus 19.5% of Latino patients and 14.3% of White patients. An income between $50,000 and $75,000 annually was earned by 16.0% of Black patients versus 23.2% of Latino patients and 27.7% of White patients. Regarding insurance coverage, fewer Black patients with MS had private insurance coverage than Latino and White patients (57.6% vs 65.8% and 72.3%, respectively). Medicaid covered 10.8% of Black patients versus 7.4% of Latino patients versus 3.7% of White patients. A retrospective claims analysis conducted in 2012 among patients with MS covered by commercial insurance (n = 18,269) and Medicaid insurance (n = 1715) revealed noteworthy healthcare discrepancies between the 2 groups. Overall, per-patient annual costs for MS care were similar; however, the Medicaid group had up to 5 times higher inpatient and emergency department (ED)-related costs and a higher number of visits. During 2012, 21.5% of Medicaid patients and 6.7% of commercial patients visited the ED one or more times, and 6.9% of Medicaid patients and 1.6% of commercial patients had one or more inpatient admissions.19

The Medicaid group exhibited higher rates of MS-related complications than did the commercial group, such as gait abnormalities (17.3% vs 10.4%); burning, numbness or tingling (21.9% vs 17.9%); dizziness/vertigo (14.6% vs 9.2%); and urinary incontinence (16.0% vs 5.8%; P < .001 for all). The Medicaid group also had a higher rate with nearly all comorbidities, such as hypertension (35.7% vs 30.2%), diabetes (16.6% vs 9.6%) and asthma (15.9% vs 6.0%; P < .001 for all).19

Results from the analysis showed that the Medicaid group experienced lower pharmacy-related costs, which could be attributed to DMT use: 32.5% of Medicaid patients used DMTs versus 52.1% of commercial patients.19 The authors noted that insufficient care coordination and patient education regarding correct use of DMTs could contribute to the higher rate of hospitalizations and MS-related complications experienced by the Medicaid group.19 In addition to experiencing a lack of care coordination and patient education regarding DMTs, racial and ethnic minority groups may encounter coverage barriers in accessing the DMTs they need for optimal outcomes. Coverage criteria vary by insurance provider; therefore, patients receiving drug coverage from different providers may experience different levels of access and coverage for DMTs.20 High copays and lack of coverage for certain therapies limit treatment options for most patients.21

In a consensus paper updated in 2019, the MS Coalition stated that giving patients access to all FDA-approved DMTs was imperative for optimal management of MS. A broad range of therapy options is important for adults with early and active disease, the latter being more likely to be experienced by Black or Hispanic patients. In addition, because Black patients may experience lower efficacy with certain DMTs, therapy options should not be restricted for this population.14

Conclusions
Multiple sclerosis can profoundly affect the lives of those who receive the diagnosis, and racial and ethnic minorities appear to experience unique challenges
regarding disease characteristics and access to care. Among these groups, the disease course may be more active\textsuperscript{18} and the MS manifestations more severe.\textsuperscript{21} For Black patients, certain DMTs may be less effective.\textsuperscript{22} Because they sometimes experience barriers to care related to health literacy, income or health insurance coverage,\textsuperscript{22} these groups may benefit from increased management across the care continuum that ensures access to patient education, financial and other support resources, and treatment tailored to their unique disease course.

**REFERENCES**


Now that we’re about a year into the COVID-19 pandemic, many healthcare experts are looking at how the industry responded and categorizing what areas were positive and which parts need improvement.

In the plus column, for example, is the unprecedented speed of decision-making and execution of those decisions. Practices transitioned to virtual platforms in a matter of weeks, sometimes days. COVID-19 vaccines were developed in a matter of months.

But healthcare’s ledger is hardly all positive. It is clear that the long-neglected and underfunded public health infrastructure was ill-prepared at best. Public health is always joined to politics, but in 2020 they were hopelessly tangled, with dire consequences, as reflected in the disproportionate number of Americans who died from healthcare has successfully pivoted and collaborated. But COVID-19 also has spotlighted flaws in how hospitals are financed and the weakness of the public health infrastructure.

The silver linings and big reveals

Healthcare has successfully pivoted and collaborated. But COVID-19 also has spotlighted flaws in how hospitals are financed and the weakness of the public health infrastructure. by Keith Loria
COVID-19 relative to the number of deaths from the virus in other countries. Moreover, the accolades for vaccine testing and development in 2020 have been followed by criticism of — and confusion about — distribution of the vaccines this year.

The silver linings
Still, many healthcare leaders speak with pride about how their organizations — and the sector, in general — responded to the pandemic. Alexa B. Kimball, M.D., M.P.H., CEO and president of the Harvard Medical Faculty Physicians at Beth Israel Deaconess Medical Center in Boston, notes that a year into the COVID-19 pandemic, the industry has seen incredible innovation, true collaboration for the good of all patients, improved communication, and sharing of resources among hospitals and caregivers.

“For healthcare, the silver linings of the pandemic have included the expansion and rapid deployment of telehealth, the discovery that even large academic institutions could pivot in a nimble fashion and the incredible innovation necessitated by the pandemic,” she says. “In an age when healthcare is sometimes criticized as a business with a cold bottom line, collaboration took the place of competition.”

Hospitals within systems anchored to academic medical centers were able to share expertise, expedite patient transfers, and redistribute personal protective equipment and ventilators to other facilities where they were in short supply, Kimball says. Physicians and staff members across a healthcare network collaborated and communicated in ways that will benefit them for years to come, she says. “Community hospitals that are part of larger networks benefited from the availability of specialists and supportive infrastructure, and those of us who are part of those large networks learned of the incredible talent of care providers within our networks,” Kimball says.

Ben Kornitzer, M.D., chief medical and quality officer for Agilon Health, a Long Beach, California, company that advises physician practices, says that the pandemic accelerated the transition to value-based care and created incentives for physicians to care for vulnerable individuals who weren’t able to be seen in person.

“We saw an increased ability to meet the patient where they are — telehealth, remote monitoring, home visits, medical care in parking lots and so on,” he says. “One of our PCPs even did a televisit with a patient on a construction crane hundreds of feet in the air.”

No one wants to be so insensitive as to talk about winners amid a pandemic, yet there’s no question that some groups and organizations have prospered in the year since the first cases were discovered in the U.S. Michael Abrams, M.A., co-founder and managing partner of Numerof & Associates, a healthcare consulting firm headquartered in St. Louis, notes that the pandemic has left many insurers in a strong financial position. “So many elective procedures and routine visits have been deferred during the pandemic that medical claims for most insurers during the second and third quarters of 2020 were dramatically lower than originally anticipated, creating a windfall profit for most payers,” he says. Flush with cash, companies such as Anthem, many of the Blues plans and others have announced rebates to plan members now as opposed to waiting until August 2021, when the medical-loss ratio requirements of the ACA would require them to do so anyway, Abrams says.

Abrams also sees telehealth providers coming out of the pandemic as winners. Before the pandemic, healthcare systems had generally little interest in telehealth, partly because of low reimbursement and regulatory obstacles. “But with the onset of COVID-19, hospitals facing the choice of telehealth visits or nothing quickly ramped up,” he says. “Telemedicine giants have seized the moment, responding to exploding demand for their services. CMS and other big payers have helped in a big way by increasing the number of telehealth services eligible for enhanced government payments and, at least during the pandemic, paying for telehealth visits at the same rate as in-office visits.”

Adnan Iqbal, M.S., MBA, CEO of Luma Health, says Americans can
view COVID-19 as an impetus for improved healthcare in the future. The pandemic has caused illness and death and economic hardship, Iqbal says, but it also has been transformative. "The pandemic has very quickly forced healthcare to deliver better patient care — including increased digital options and virtual care, which offer added convenience. The status quo has absolutely been kicked to the curb," he says.

The pandemic one year in

"Hospital economics do not serve their true public function, and that was laid bare during the pandemic."

— BEN KORNITZER, M.D., CHIEF MEDICAL AND QUALITY OFFICER FOR AGILON HEALTH

The reveals
According to data compiled by Bloomberg News, more than three dozen hospitals have entered bankruptcy this year. Meanwhile, the American Hospital Association is projecting hospital and health system losses of more than $323 billion through 2020. Kaufman Hall has projected that more than half of all hospitals will report negative margins from the fourth quarter of 2020.

"Those medical centers and systems that rely on patients from outside of their network's geographic area clearly experienced large declines in patient volume during the pandemic," Kimball says. "Patients weren't getting on planes to go to cancer centers or specialty hospitals providing elective, none emergent surgery."

During the initial spike in infections between March and April 2020, the healthcare industry lost 1.5 million jobs. More than half a million jobs remained lost six months later, with losses spread across the major healthcare sectors of hospitals (22.7%), ambulatory care settings (39.6%) and long-term care facilities (37.7%). The pandemic has been especially hard on small medical practices, Kimball says.

"The necessary investments in PPE (personal protective equipment), the need for physically distanced compatible waiting rooms and the overall decrease in routine care all have played a role in the economic burden to these practices," she says. The fact that hospitals that treated many patients with COVID-19 often struggled financially is an indictment of how hospitals are funded, Kornitzer says. Many healthcare experts believe the industry needs to re-envision what hospitals do, how they do it, and how their services are reimbursed.

"Hospital economics do not serve their true public function, and that was laid bare during the pandemic," Kornitzer says. "Hospitals have increasingly relied on high-margin specialty service lines and elective procedures to cross-subsidize critical services that often lose money, such as general medical admissions."

Kornitzer also says the pandemic has shined a negative but needed light on the care that older Americans receive. "The warehousing and unacceptably high mortality of our older patients in long-term and nursing facilities must be reevaluated at every level," Kornitzer says. He sees a shortage of personalized and primary care in addition to the need to focus on holistic medicine and palliative care.

Abrams believes the pandemic put a spotlight on the failure of the industry — and political leaders — to pivot from a transactional model of treatment that only reacts when individuals are sick, to a population health model that addresses the management of chronic conditions across time and through multiple service delivery modalities. He says more emphasis needs to be placed on the importance of social determinants of health and population health.

"The disproportionate impact of COVID-19 on disadvantaged populations and those with chronic conditions highlighted the costs that come with the choices made to date," he says. "Disadvantaged populations and many essential workers have had a disproportionate share of infections and deaths. And these subpopulations make it that much harder to bring COVID-19 under control. Had a population health approach been the organizing principle across the industry, we would all have been better prepared to weather this onslaught.

The pandemic also made clear how reliant the U.S. is on other countries, especially China, for critical active pharmaceutical ingredients, drugs such as penicillin and statins, and products such as personal protective equipment, Abrams notes. "While no industry could have accommodated the explosion in demand for things such as PPE driven by COVID-19 without shortages, the fact that our supply chains extended across continents and were hostage to the political agendas of other countries was a miscalculation that imposed a price on all of us," Abrams says.

Finally, Abrams sees a big lesson to be learned in the hidden vulnerability of the fee-for-service payment model. "For years, the industry has resisted payment models that made prudent use of resources and actual delivery of desired outcomes a factor in reimbursement, labeling them as 'too risky,'" he says. "But as hospitals
Although TV footage has shown hospitals overflowing with patients since the COVID-19 pandemic hit the U.S. last March, the coffers of many hospitals and other healthcare providers are far from overflowing. In fact, they are running dry because millions of Americans didn’t get medical care last year and are continuing to put it off this year.

“Folks actively avoided going to the emergency department,” says Aaron Wesolowski, vice president of policy research, analytics and strategy for the American Hospital Association (AHA).

Utilization of in-patient and out-patient care also decreased. As a result, hospitals and healthcare systems lost at least $323 billion in 2020, according to a recent AHA report. At the start of 2021, the number of people going to the hospital remained low, leading to reduced hospital revenue. “The decrease in patient volume ‘that drove revenue losses in a lot of cases [in 2020] is still present,’ Wesolowski says.

It’s not just hospitals that have been affected. Providers of all kinds — primary care physicians, specialists, dentists, clinics — have experienced sharp declines in patient volume. Because they have many days of cash on hand and access to capital, healthcare systems anchored by large hospitals should be able to weather the months of low revenue. But for many medical practices,

Federal assistance programs and telehealth have helped, but they haven’t made up for the shortfall from lack of services. by SUSAN LADIKA

THE PANDEMIC ONE YEAR IN

Providers struggle with loss of revenue

Hospital losses

From March 2020, when cases started to spike in the U.S., through June, hospitals and health systems lost an estimated $202.6 billion, according to the AHA. Utilization bounced back some during the second half of the year. Still, the association estimated that hospitals would lose at least $120.5 billion more from July to December. In addition to dealing with revenue losses from declines in utilization, hospitals had to purchase more personal protective equipment and other supplies.

A survey of 275 hospitals by Strata Decision Technologies found that emergency department visits dropped by 50% initially in March and were down by 25% in September as compared with data from 2019.

Inpatient volumes in September were approaching 2019 levels, but inpatient surgeries and procedures were down 18.6% overall, Strata’s survey showed. Outpatient volumes initially dropped by 56%, but by September they had been down just 1.5% compared with the previous year, according to the survey results. “Recovery is not evenly distributed, as some areas have come back strongly, while other

The lack of elective procedures “is the core financial challenge they are trying to recover from.” — ROGER B. WEEMS, VICE PRESIDENT OF ADVISORY SERVICES AT PREMIER

Keith Loria, a frequent contributor to Managed Healthcare Executive®, is a freelance writer in the Washington, D.C., area.
Despite the telehealth increase, almost 70% of physicians were still providing fewer total visits (in-person + telehealth) at the time of the survey than pre-pandemic.

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Average total visits fell from 101 to 72 per week

Source: American Medical Association

Despite the telehealth increase, almost 70% of physicians were still providing fewer total visits (in-person + telehealth) at the time of the survey than pre-pandemic.
Despite large profits in 2020, health insurers see volatility ahead

Companies could be hit with a double peak of claims for COVID-19 patients and care that people put off because of the pandemic.

by JOSEPH BURNS

For health insurers, making actuarial calculations is like driving a car while using only the rearview mirror. This analogy was never truer than it was early last year, when actuaries read about the first reported cases of COVID-19 and feared a looming tsunami of the dreaded IBNR — incurred but not reported — claims.

Since then, actuaries have learned that any planning they did in 2019 likely had little value as COVID-19 infections spread nationwide, employers laid off workers, and governors shut down schools and businesses. Although some costs rose due to increased spending for the care of insured members who contracted the SARS-CoV-2 virus, the shutdown of other healthcare services eased the financial pain for many insurers.

“The pandemic and resulting...
“By all accounts, the publicly traded health insurers did very well last year.”

— SARA R. COLLINS, PH.D., VICE PRESIDENT FOR HEALTHCARE COVERAGE AND ACCESS AT THE COMMONWEALTH FUND

The pandemic one year in

Economic crisis have upended any expectations about what health spending, utilization and the subsequent financial performance of insurers might have looked like this year,” according to a report in December 2020 from Kaiser Family Foundation researchers.

Many for-profit insurers reported record profits in the second quarter and for the full year of 2020 because their members did not visit the hospital or see their physicians at usual levels. Some of those sky-high profits were tempered in subsequent quarters when pent-up demand for care caused insurers’ costs to rise. The financial ups and downs of a pandemic-afflicted year became apparent early in 2021 when three major health insurers reported on their financial performance for 2020’s fourth quarter and the full calendar year.

On Jan. 20, the nation’s largest insurer, UnitedHealth Group, reported its full-year 2020 profit of $15.4 billion, including $2.2 billion in profits for the fourth quarter, $3.2 billion in the third quarter and $6.6 billion in the second quarter.

The insurer said profits were substantially higher than normal due to the unprecedented delay in elective and nonemergency procedures, the Star Tribune in Minneapolis reported.

On Feb. 3, Humana reported a loss of $458 million in 2020’s fourth quarter, a considerable drop from the $593 million in profit the company reported for the fourth quarter of 2019. The insurer attributed the loss to a big jump in hospital admissions for patients with COVID-19 in nearly all of its markets.

Although spending for non-COVID-19 care fell below normal levels by approximately 15%, Humana said that drop did not offset the rise in costs for testing and treating members with COVID-19. For 2020, however, Humana reported a profit of $4.6 billion, a 40% increase over the company’s 2019 profits of $3.5 billion.

The day after Humana reported its financial results, Cigna reported $4.1 billion in profit for the fourth quarter of 2020, a big jump over the $977 million in 2019’s fourth quarter. For the full year, Cigna earned $8.5 billion in profits, a 66% increase from the company’s profits of $5.1 billion for 2019.

“By all accounts, the publicly traded health insurers did very well last year,” said economist Sara R. Collins, Ph.D., vice president for healthcare coverage and access at The Commonwealth Fund. “By that I mean they were quite profitable.”

**MLR trends**

Among insurers, the all-important medical-loss ratio (MLR) fell. Most health plan companies had higher costs due to payment for members’ COVID-19 treatments, but they also had lower costs because so many Americans delayed elective and other nonemergency care. “In general, they had lower claims from less utilization, and that was in all coverage segments: the individual market, the group market, Medicare Advantage (MA) and Medicaid managed care,” Collins explains.

The Kaiser Family Foundation’s analysis was similar. Using data from the National Association of Insurance Commissioners compiled by Mark Farrah Associates, researchers found that average profit levels at the end of September in the four main insurance markets — individual, group, MA and Medicaid managed care — were high and that MLR levels were low or flat compared with levels in the third quarter of previous years. “These findings suggest that many insurers have remained profitable even as both COVID-19-related and non-COVID-19 care increased in the third quarter of 2020,” the researchers wrote.

Another view of the health insurance market comes from Fitch Ratings, which analyzes companies’ credit worthiness. While stating that 2020 was a turbulent year for insurers, Fitch reported that these companies had strong operating performance in 2020, and Fitch expects that level of performance to continue in 2021. Fitch report added, however, that this year could see “elevated volatility” among insurers and from one quarter to the next.

Although MLRs declined in the second quarter of 2020 as health-care utilization fell, Fitch does not expect MLR levels to go down again this year. “Fitch currently has stable outlooks on nearly all of its ratings in the U.S. health insurance sector,” the company stated in its 2021 outlook report.

**Insurers helping out**

This situation is common among large, publicly traded, for-profit insurers. “You can’t really generalize for the entire health insurance market, because every market is unique,” says Margaret A. Murray, CEO of the Association for Community Affiliated Plans (ACAP) and a member of the Managed Healthcare Executive editorial advisory board. ACAP represents 78 nonprofit health insurers serving more than 20 million low-income
members with complex healthcare needs. Those 20 million members represent more than a third of all Americans in Medicaid managed care plans, according to ACAP.

In August, ACAP reported that its member health plans contributed more than $17.5 million to support physicians, hospitals and community health centers (CHCs) that needed financial assistance during the pandemic. With those funds, the providers and CHCs paid for personal protective equipment, donated to food banks and food delivery services such as Meals on Wheels, and provided shelter for homeless members who had COVID-19 but were not hospitalized, ACAP reported.

Some of ACAP’s insurers have insured members in long-term care settings and others who need care at home. “We provide support for these members so they can stay at home or in nursing homes or other settings,” Murray notes. Some of those plans have had high hospitalization rates, and many of their members died of COVID-19, she says.

“Our plans actually lost a lot of members to COVID-19, and, as a result, they really took a hit financially,” Murray says. “But, at the same time, our plans make a lot of capitated payments to their physicians and sometimes to hospitals, and those payments allowed providers to maintain full operations throughout the year.”

ACAP members reported that the capitated payments to network physicians and hospitals have supported providers throughout the pandemic when revenue from fee-for-service payment withered due to lack of utilization. In addition, keeping physicians and hospitals solvent during a pandemic is in all health plans’ interests because it helps plans retain providers, which helps them to hold on to their insured members, as well.

Ceci Connolly, president and CEO of the Alliance of Community Health Plans (ACHP), agreed that one of the lessons learned from the pandemic was the value of capitated payment. ACHP has 24 nonprofit health plans serving 22 million insured members. ACHP’s member plans include powerhouses such as Geisinger Health Plan, Harvard Pilgrim Health Care and Kaiser Permanente.

Early last year, the CEOs of ACHP’s member plans feared the pandemic would last beyond a year and worked with their actuaries to prepare budgets over two years. “That’s a smart way for us to think about the challenges they would face in their operations and prepare to have the financial resources to cover the costs that could come up during an unprecedented level of uncertainty,” Connolly says.

“Uncertainty is challenging for actuaries because they’re supposed to forecast risk accurately over a certain time and then ensure that they have the dollars to care for all of the people in their membership,” she adds. “Over the years, they’ve [become] good at that because they understand the population and what are … the standard number of heart attacks and babies born and that kind of thing. But the pandemic provided an unexpected level of risk that no one could have predicted.”

More claims to come
Notwithstanding the COVID-19 vaccines, many health insurance experts are concerned about the cost of care related to COVID-19 infections and a potential surge that could create a double peak in costs and claims for services that Americans have put off. Using data from a PwC report on medical cost trends, CNBC reported that if most of the care that health plan members deferred in 2020 is delivered this year, medical costs could rise 10% above pre-pandemic levels. That would result in the highest rate of medical-cost inflation since 2007, CNBC stated.

Large employers also are bracing for huge bills from deferred care, CNBC reported, citing the results of a survey from the American Benefits Council. “Large self-insured employers worry that delayed treatment this year will result not only in a higher number of medical claims in 2021 but also higher overall costs for more acute care,” CNBC said.

The pandemic has scrambled predictions. If, as Connolly suggested, actuaries dislike uncertainty, they will loathe this assessment from PwC’s analysts: COVID-19 has created so much uncertainty that it’s difficult to say precisely whether medical-cost trends will be significantly lower or higher this year.

Joseph Burns is an independent journalist in Brewster, Massachusetts, who covers healthcare.
The COVID-19 vaccine race was a sprint.

Now for the hurdles

Will emerging variants make the leading vaccines less protective? by JAIME ROSENBERG

As the COVID-19 pandemic in the U.S. surpasses the one-year mark, the numbers are sobering: more than 27 million Americans infected; a death toll of over half a million.

Despite uncertainty about the pandemic’s future, appreciation of the scale and speed of healthcare innovation is warranted. Vaccines to protect against the SARS-CoV-2 virus were developed and deployed in less than a year. The FDA issued emergency use authorizations for two COVID-19 RNA vaccines at the end of 2020: the Pfizer-BioNTech vaccine and the Moderna vaccine. New drugs, such as the monoclonal antibody bamlanivimab, have joined steroids in improving treatment for patients.

But in January and most of February the pace of the distribution of the vaccines wasn’t as remarkable as that of the vaccine and treatment research. Many states had not received the number of doses they were promised. Pfizer said millions of doses of its vaccine were in storage, a situation that may change after the company and the FDA agreed the vaccine could be stored at normal freezer temperatures. As of Feb. 28, the CDC’s COVID-19 vaccine tracker showed 75.2 million doses had been administered, and Bloomberg’s tracker showed 78% of the doses supplied to the states had been administered.

President Joe Biden has vowed to speed up the rollout, bolstering the distribution plan with a $20 billion national vaccination program. He also announced the purchase of another 200 million doses of vaccines from Moderna and Pfizer-BioNTech and an increase in the number of doses being shipped to the states.

Back in the pack

Meanwhile, the emergency use authorization for Johnson & Johnson’s vaccine means there will be three vaccines available in the U.S. The company submitted its request for an emergency use authorization (EUA) in early February, and the go-ahead from the FDA came on Feb. 27. The EUA was based on phase 3 results that showed the J&J Johnson is 66% effective at preventing moderate to severe cases of COVID-19 compared with the 95% protection against symptomatic COVID-19 seen in late-stage trials of the Pfizer-BioNTech and Moderna vaccines. But the J & J vaccine has the advantage of being a one-dose vaccine that could mean more coverage. Novavax, a relatively small biotech company in Gaithersburg, Maryland, is a David among the Goliaths in the race to deploy a COVID-19 vaccine. Novavax reported positive phase 3 trial results at the end of January. The company will most likely seek approval in the U.K. before the U.S.

The Oxford-AstraZeneca vaccine has had a bumpy ride. The UK’s equivalent of the FDA approved emergency use for the vaccine in late December based on results that showed 62% efficacy from two doses but, oddly, higher efficacy among the study volunteers who received a low dose followed by a standard one. In early February, preliminary data showed that it was effective in reducing transmission after just one dose, a result that led to consideration of whether a vaccine strategy emphasizing single doses might make sense. A few days later, however, other data showed that the vaccine was only 22% effective against the South African variant, or B.1.351, of SARS-CoV-2. As a result, South African officials halted its use in that country.

GlaxoSmithKline’s website states that it is one of the largest vaccine companies in the world, with a portfolio of more than 30 vaccines that generated about $9 billion in revenues last year. But GlaxoSmithKline is well off the pace when it comes to COVID-19 vaccines. A vaccine it was developing with Sanofi had to be redesigned when it failed to trigger immunity in older people.
In February, it announced that it was building on an existing relationship with CureVac, a German biopharmaceutical company, to develop a “multivalent approach (to COVID-19 vaccines) to address multiple emerging variants in one vaccine.”

**Here come the variants**

The desire for good news and progress against the pandemic may have led to a premature sigh of relief when the Pfizer-BioNTech and Moderna became available in the U.S. The emergence of variants in January and February may be another setback in the yearlong effort to stem COVID-19 infections, illness and death. Three notable variants have been detected in the U.S.:

- **The U.K. variant B.1.1.7**, which in Britain is referred to as the Kent variant (Kent is a county east of London), spreads more easily and quickly than other variants and may be more deadly than the original strain, although that is still an open question. Some experts think the U.K. strain, which was first reported in the U.S. in December 2020, will become the dominant one circulating in the U.S. this spring.

- **The South Africa variant**, designated B.1.351, shares some of the same mutations as B.1.1.7 but appears more difficult to protect against. It was reported in the U.S. at the end of January.

- **The Brazil variant**, which has the scientific label of P.1, has 17 unique mutations and was reported in the U.S. in late January.

Naturally, there’s some worry that these new variants will evade the protective effect of the current crop of vaccines — and the vaccine-lit end of the COVID-19 tunnel will darken. But variance doesn’t necessarily mean immunological evasion; some preliminary data suggest that the current crop of vaccines and vaccine candidates will do just fine against the U.K. strain. There is more concern about the South African variant — and not just with respect to the AstraZeneca-Oxford vaccine. A study of Novavax’s vaccine among 4,400 people in South Africa showed that the vaccine was just 49% effective against the South Africa variant.

A Moderna study of a small group of people who received two doses of its vaccine showed antibody levels that would likely fend off the variants, especially the U.K. one. Moderna has also developed a version of its vaccine that is tailored to produce an immune response to South African variant. A phase 1 trial was of that vaccine is scheduled to start this month.

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The price tags on the COVID-19 vaccines

Governments are the only buyers so far, and the amounts they are paying varies. by DEBORAH ABRAMS KAPLAN AND PETER WEHRWEIN

At the start of the COVID-19 pandemic last year, physicians were unsure which medications would effectively treat the disease and there was no vaccine. The race to find both novel and repurposed therapeutics and develop vaccines has been a multinational effort, although heavily funded by U.S. government dollars. Several therapies have now been granted emergency use authorization by the FDA. About 60 million doses of the Pfizer-BioNTech and Moderna vaccines have been administered, and the pace of vaccination is increasing to about 1.4 million doses a day. The Johnson & Johnson vaccine will be available this month, so the pace of vaccination may pick up even further.

But who is paying for these treatments and vaccines — and at what price?

So far, governments around the world have been the only purchasers of the COVID-19 vaccines, so the price has been set by government contracts. But different countries are paying different prices. South Africa, for example, reportedly paid $2.25 per dose for the Oxford-AstraZeneca vaccine in January, more than twice the price of $2.15 per dose paid by the European Union (EU), according to a report in BMJ. The South African government has announced that it is holding back on administering that vaccine because it may be less effective against the country’s namesake variant.

The EU is also paying less for the Pfizer-BioNTech vaccine than the U.S., $14.70 per dose versus $19.50, according to figures reported in BMJ. On the other hand, the U.S. is paying less for the Moderna vaccine (about $15) than the EU (about $18), according to the BMJ piece. The contribution governments have made toward vaccine research is the explanation for the price differences. Moderna is charging the U.S. less for its vaccine because the U.S. government funded research that led to the vaccine’s development. Similarly, the EU supported research that led to the development of the Pfizer-BioNTech vaccine, thus the lower price for that vaccine for the EU.

Post-pandemic pricing?

There’s no question that the Pfizer-BioNTech and Moderna vaccines have altered the course of the pandemic and, notwithstanding all the early problems with distribution, the vaccines have seeded some hope that herd immunity can be reached and transmission, slowed down if not stopped altogether. But as time goes on, those two vaccines may be seen as pricey frontrunners. The Oxford-AstraZeneca and J & J are likely to present a trade-off: less efficacy but a much lower price. The phase 3 clinical trial results for the single-dose J&J vaccine showed that it is 66% effective at preventing moderate to severe cases of COVID-19 compared with the 95% effectiveness of the Pfizer-BioNTech and Moderna vaccines. But J&J is expected to price its single-dose vaccine at about $10 per dose, which would make it roughly a quarter of the price of the Pfizer-BioNTech vaccine, presuming that it stays a single-dose vaccine and the price stays the same.

But the long game of the companies that have thrown themselves into getting COVID-19 vaccines on the market may be quite different from the one they are playing now. It is entirely possible that COVID-19 vaccination will become as routine as flu vaccination. There might be some downward pressure on prices as payers other than governments get involved. On the other hand, during an earnings call in early February, Pfizer CFO Frank D’Amelio described Pfizer’s $19.50-per-dose price as “pandemic
pricing” and “that’s not a normal price like we typically get for a vaccine, $150, $175 per dose.”

D’Amelio said just a bit later during the call, “Now let’s go beyond a pandemic-pricing environment, the environment we’re currently in. Obviously, we’re going to get more on price. And clearly, to your point, the more volume we put through our factories, the lower unit cost will become. So clearly, there’s a significant opportunity for those margins to improve once we get beyond the pandemic environment that we’re in.”

Like Pfizer, Moderna has indicated that it may raise its prices after the pandemic ends, anticipating that COVID-19 will be endemic. The Moderna CEO said during a conference call last year that the pandemic pricing would be “well below value.”

**U.S. government investment**

But should the vaccine developers profit off their efforts? During a House Committee on Energy and Commerce hearing last summer, manufacturers were asked whether they would sell the vaccine at cost. Moderna and Merck (which announced in January that it was dropping out of the COVID-19 vaccine development race) said they would not sell their vaccines at cost. J&J said it wouldn’t make a profit from the vaccine during the pandemic. AstraZeneca said its U.S. deal would not make a profit.

The first vaccine pricing announcement came in July, when the U.S. government contracted with Pfizer and BioNTech to purchase enough vaccines for 50 million Americans. It’s no coincidence that the price of $19.50 per dose was similar to the pricing of the flu shots. Pfizer has said the research and development costs of its vaccine approach $1 billion, and the company declined to take direct government funding.

But other companies have accepted huge government checks. AstraZeneca received up to $1.2 billion upfront, in exchange for at least 300 million doses. J&J is also receiving government money from the federal government’s Biomedical Advanced Research and Development Authority (BARDA). Early in the pandemic, BARDA agreed to provide $456 million toward the company’s research and development effort. In August, the federal government agreed to pay J&J $1 billion for 100 million doses of its vaccine, thus the $10-a-dose price. As of mid-July, Boston-based Moderna had received $955 million in U.S. funding. The company said in August that it would charge between $32 and $37 per dose for its vaccine, although company officials also said the price would be adjusted depending on the amount ordered. That may explain the price of $15 per dose price charged to the U.S. for its order of 100 million doses. Still, the company has been criticized for its pricing, partly because it has received so much government research support.

The Lown Institute in Boston gave Moderna one of its Shkreli Awards in January: The awards are for the “worst examples of profiteering and dysfunction in health care.”

Deborah Ann Kaplan write about medical and practice management topics.

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**6 ways of arriving at a price**

Last year, the Institute for Clinical and Economic Review (ICER), a drug pricing group in Boston, organized the ways that COVID-19 vaccines and therapeutics might be priced into six categories. Some are only theoretical. Here is the list:

**Unrestricted pricing.** Let companies determine pricing and receive patent rights. This is the way list prices for drugs are determined now, although what drugmakers actually charge is complicated by discounts, rebates, and various government programs and rules.

**Cost-recovery pricing.** The government, private payers or both determine a ceiling price based on development and production costs. The price is supposed to allow the drugmaker to recoup their costs but no more. The drugmaker retains patent rights.

**Value-based pricing.** The government, private payers or both set a ceiling price that is determined by sort of cost-effectiveness research done ICER. The company retains the patent rights.

**Monetary prizes.** The government would offer a substantial monetary prize to incentivize discovery. The first successful vaccine developer is awarded the entire prize. The government keeps the patent and contracts out manufacturing, offering the vaccine.

**Compulsory licensing.** A successful developer receives royalties, but the government allows other manufacturers to use, sell or import the therapeutics without needing permission. The government can mandate the right to license the product to the government.

**Advanced market commitments and subscription models.** Funders subsidize research and development by committing to a future purchase price and order amount, if successful. The developer can change prices for other purchasers who do not participate.
Remote patient monitoring, once the province of early adopters and healthcare’s gadget geeks, has become mainstream during the COVID-19 pandemic. Hospitals are using remote monitoring to reduce spending on personal protective equipment and free up beds for patients with COVID-19. Many clinicians appreciate that this technology allows them to keep tabs on patients in continuous real time instead of periodically at checkups. There are also pluses for patients.

“There are many aspects of patient care delivery and monitoring that can now be successfully accomplished outside of the traditional healthcare setting,” says Donna Morrow, vice president of clinical operations at Noteworth, a digital health company headquartered in Hoboken, New Jersey. “This is providing peace of mind to the patient and reducing exposure.”

Eric Rock, founder and CEO of Vivify Health, says the immediate future of remote patient monitoring will rest on its scalability and the level of information it provides.

“Instead of asking the exact same biometric measurement questions of someone every day, [remote patient monitoring] will engage the patient with more meaningful content that is tailored and adaptive to patients’ responses,” he says. “The tool will have its own rules and logic built in and will ask a sequence of questions much [as] a nurse would. Intelligent content has been shown to facilitate patient engagement, which positively [affects] outcomes.”

**FDA regulations help**

That may all be true, but there’s also the grittier reality that the future of remote patient monitoring, as with so much else in healthcare, depends on federal government regulation and reimbursement, especially Medicare reimbursement. Part of the reason for the crescendo of remote patient monitoring is an FDA decision in March 2020 to relax its regulation and a subsequent guidance in October that expanded upon the policy.

“In the context of the COVID-19 public health emergency,” the FDA guidance states, “the leveraging of current noninvasive patient monitoring technology will help eliminate unnecessary patient contact and ease the burden on hospitals, other healthcare facilities and healthcare professionals [who] are experiencing increased demand due to the COVID-19 pandemic as it relates to diagnosis and treatment of patients with COVID-19 and ensuring other patients who require monitoring for conditions unrelated to COVID-19 can be monitored outside of healthcare facilities.”

Philip Golz, vice president, commercial, at Spire Health, which sells remote patient monitoring technology for chronic respiratory disease, says changes in the 2021 Medicare physician fee schedule finalized by CMS at the beginning of December 2020 also will bolster remote monitoring.

“In particular, [it is helped by the requirement] that the technology used for [remote patient monitoring] is capable of transmitting data automatically and at least 16 days per month,” he says. “The new changes aim to ensure the technologies provide meaningful data and are patient-friendly.”

**Clinicians see the benefits**

Remote patient monitoring is part and parcel of the COVID-19-inspired shift to telehealth. Anish Sebastian, CEO and co-founder of Babyscripts, a virtual maternity
Pandemic opens minds, loosens providers’ purse strings for remote patient monitoring

“As with everything health related, data privacy and security are also going to be concerns.”
—ANISH SEBASTIAN, CEO AND CO-FOUNDER OF BABYScriPS

Care company in Washington, D.C., says that before the pandemic, telehealth was an option that set a practice apart from the competition. Now it’s standard-issue healthcare. “Because of COVID-19, providers really had no choice but to let go of their concerns about telehealth and implement virtual solutions for their patients,” he says. “Before, (remote patient monitoring) was being tested out and piloted primarily with low-risk patients, but COVID-19 drove providers to offer it for all risk profiles, sometimes supplemented with in-person visits.”

Now that clinicians have seen the benefits of remote patient monitoring, they are much more comfortable weaving it into their practices, he says. “It’s especially important for health systems that are feeling the financial strain of the pandemic to offer these enhancements to patients, and we’re seeing new reimbursement codes and payer reimbursement mechanisms that are making it easier for practices to use (the technology),” Sebastian says.

Prior to the public health emergency, Medicare coverage of remote patient monitoring services was limited to patients with one or more chronic conditions. However, as patients were being encouraged to stay at home, the need for remote monitoring to treat patients with acute, time-limited conditions (such as COVID-19) became all the more critical. Confirmed in the 2021 Final Rule, CMS clarifies that providers may furnish RPM to collect/analyze physiological data from patients with acute and chronic conditions.

It’s also attractive to patients who worry about possible exposure to the virus during an in-person visit. “With the availability of remote patient monitoring, [Noteworth] is allowing providers to keep patients out of the hospital and physician office settings,” Morrow says. “This is especially important for the at-risk population. And with the changes enacted by CMS to open the patient population that could utilize remote patient monitoring, this expanded to the acute conditions as well. This opened up greater engagement and accountability for the patient and the care team.”

Robin Hill, chief clinical officer of Vivify Health, notes that leveraging remote patient monitoring quickly has enabled clinicians to keep an eye on their patients without going into the home. “Because of the social isolation, using our solution to provide that human touch virtually helped support our patients holistically,” she says. “Our solution has also helped decompress some pressure on health systems that were at capacity with the influx of [patients with] COVID-19 by being able to remotely screen and/or monitor patients and/or employees [for the virus].”

Tomas C. Walker, vice president of clinical affairs at Dexcom, a San Diego-based maker of continuous glucose monitoring systems, says changing standards of care in the current COVID-19 environment led to rapid development in monitoring technologies.

“One of the clinicians we work with told us that the hospital staff and administrators grasped the value and the potential of remote monitoring and care and that they will never go back,” Walker says. “I think we can safely state that the genie is out of the bottle on this one. Remote care and telehealth have been given a huge opportunity with COVID-19, and we are seeing the benefits of a lot of previously unnoticed work.”

Well-suited for diabetes care

Although remote patient monitoring isn’t confined to any particular demographic, it may be especially valuable when it comes to caring for elderly people. About 1 in 4 seniors lives alone. Even before the pandemic, access to in-person care was far from a sure bet. Social distancing requirements because of COVID-19 make in-person care even more difficult, so remote patient monitoring is extremely important in this group.

Walker says that remote patient monitoring is a hot topic right now, with data from continuous glucose monitoring playing a central role. His company has integrated data from Bluetooth-connected insulin pens into its reports. “Clinicians who may be used to looking at insulin pump printouts where you can see insulin dosing and meal boluses now get that same feature (virtually) with continuous glucose monitoring.”
Remote monitoring is bringing together data produced by insulin pumps, glucose meters, smart pens and other devices that people who have diabetes depend on, says Diana Isaacs, Pharm.D., continuous glucose monitoring program coordinator for the Cleveland Clinic Diabetes Center. "There are now more sophisticated mobile apps that can connect with these devices and automatically upload data to a portal so data can be viewed in nearly real time," she says. "Also, many of the systems can be set up to flag for things (such as) hyperglycemia and hypoglycemia. There are also smart scales and blood pressure cuffs. Many apps can integrate with Apple’s Health app to view other things, too, (such as) heart rate, (daily number of) steps and sleep quality."

Maternal health has seen a big jump in remote patient monitoring, with companies such as Babyscripts taking the lead. "Pregnant moms are more anxious than the typical population (about risking) exposure to COVID-19 by coming into the office," Sebastian observes. "They’re also the perfect age for using technology in their healthcare, making them an ideal demographic for remote monitoring."

Still, partly because remote patient monitoring is relatively new to the healthcare field, there are problems that need to be sorted out, not the least of which is payment. "The reimbursement through insurance companies is inconsistent," Isaacs says. "Fortunately, the coverage is improving, but not all plans reimburse yet, and copays can vary."

Isaacs also noted that the number of remote monitor systems has proliferated. "We don’t yet have the perfect system that can work with all devices and directly send data to the electronic medical record," she says.

Sebastian says incorporating remote monitoring — and the data it produces — into the workflow of clinicians is a concern: "If workflow is not simple, intuitive and well-integrated, [remote patient monitoring] is going to fail."

"One of the clinicians told us that the hospital staff and administrators grasped the value and the potential of remote monitoring and care."

— Tomas C. Walker, Vice President of Clinical Affairs at Dexcom

Some of the biggest worries about remote monitoring have been privacy and security. They haven’t gone away, even if the pandemic has shifted attention away from them. "As with everything health related, data privacy and security are also going to be concerns," Sebastian says. "Even with the COVID-19 surge, providers are still wary of handling sensitive information through technology because of the potential for security breaches."

Golz notes that remote patient monitoring is still considered new by many. He sees more innovation in the offering. "We believe that, as it evolves, [remote patient monitoring] will become more robust as the monitoring technology improves, the evidence supporting its use develops and the ability to share data across systems increases," he says.

"Changes [such as] those described in the 2021 physician fee schedule continue to drive the industry toward offering technology that is easy for patients to use and provides clinical value."

Sebastian thinks there will be remote patient monitoring in every person’s home in the next 10 to 15 years, maybe sooner. "Insurers are starting to see the benefits and are finding mechanisms for reimbursement outside the normal CPT and billing codes," he says. "With financial barriers removed by the payer, providers are going to make [remote patient monitoring] a standard enhancement to the delivery of care."

Physician shortages have made asynchronous methods of care delivery an imperative. For patients who are facing barriers of access — social or geographic — a remote connection to the provider is even more important for continuity of care. "That’s why Walker sees remote patient monitoring as a robust part of future healthcare for both inpatient and outpatient care."

"Now that (clinicians) have had the opportunity to engage in this, we are seeing the full potential of remote monitoring and distant care," says Walker. Just as remote learning became an option in education, remote care has become an option in healthcare, says Walker. "Patients and clinicians have been thinking about this for a long time, and now that they are engaged in this practice, it is not going away."

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Cancer experts and clinicians fear a subtler, slow-motion effect of the pandemic: more cancer-related illness and death for years to come as a consequence of people not being screened and treatment being delayed.

Some of those missed screenings and diagnostic tests may have been unnecessary, even harmful. American healthcare — including cancer care — has plenty of low-value care. And it’s too soon for evidence of increased illness and death (and expense) from deferred screenings and care to emerge. However, there is enough experience with the pandemic for researchers to start combing through data that show how much cancer screening and treatment decreased in 2020.

A study published in November 2020 in JCO Clinical Cancer Informatics is a prime example. A research team led by Debra Patt, M.D., Ph.D., MBA, FASCO, had access to data that included about 6.2 million Medicare fee-for-service claims. They sifted through the data to identify billing patterns for cancer screening services, evaluation and management, biopsies, certain cancer-related surgeries (mastectomy, colectomy, prostatectomy) and chemotherapy. They examined data from the first five months of the pandemic, March through July, and compared the claims with the same months in 2019.

Predictably, the sharpest drop-off in every cancer-related service, as reflected in claims, was in April. Patt and her co-investigators found an 85% decrease in mammography claims in April 2020 compared with April 2019. By July, the difference had decreased to 9%. Other services also bounced back a bit, but not all of them, and their results show that many categories of cancer care stayed well below 2019 levels from March through July. For example, claims for administration of chemotherapy drugs were approximately one-third lower in July 2020 than in July 2019. Overall, the study results paint a picture of a widespread, pandemic-related retreat from normal cancer screening and treatment.

Variations in care

Still, many cancer centers and oncologists responded to the pandemic by finding ways to maintain their level of service, especially when it came to treatment. At Virginia Commonwealth University (VCU) Massey Cancer Center in Richmond, cancer care was deemed an essential service. “We knew we needed to do everything possible to continue providing care,” says Khalid Matin, M.D., FACP, associate medical director of the Cancer Service Line at VCU Massey Cancer Center and interim chair of the Division of Hematology, Oncology and Palliative Care. “But, (as with) all other healthcare providers, we had to make a lot of decisions early in the pandemic about how to best provide care that kept patients and staff as safe as possible,” Matin adds.

VCU Health delayed elective procedures in March, April and May. “While this did not include cancer care, it did include some preventive screenings such as colonoscopies and routine mammograms,” Matin says. “The services reopened as we gained experience providing care during the pandemic and established appropriate safety protocols.” VCU Massey Cancer Center continued clinical trials in which patients were in active treatment. The opening of new clinical trials and nontreatment trials paused, says Matin, but enrollment resumed in the spring “when we became more comfortable with safety procedures.”
As a physician-led insurer, ISMIE understands the stress and pressure administrators and frontline healthcare professionals have felt over this past year. It hasn’t been easy, but we’re with you every step of the way. ISMIE is committed to helping our policyholders keep patients safe while reducing their risk.

To find out more about how ISMIE protects medical practices, download our “Managing Risk, Maximizing Safety” whitepaper at ismie.com/risk.
Consequence of delays
Direct evidence of the consequences of reduced screenings and deferred care may not be apparent for some time, but there are projections and a track record of research to use for comparison.

The National Cancer Institute (NCI) predicts there will be as many as 10,000 additional deaths during the next 10 years related to the delayed diagnosis of breast and colorectal cancers. “Although we do not have data to show a direct correlation to screening delays, we experienced an influx of (patients with newly diagnosed breast cancer) in the summer after providers began offering mammography services,” says Kandace McGuire, M.D., chief, section of breast surgery, at VCU’s Massey Cancer Center.

There is plentiful research showing that delays in cancer care can lead to additional illness and a greater likelihood of death. For example, evidence shows an association between a longer time-to-treatment period — the interval between diagnosis and the start of treatment — and mortality risk. Research published in December in JAMA Network Open added to the evidence. Using pre-pandemic data for patients with breast, prostate, non-small cell lung and colon cancers, the researchers found the effect of treatment delay especially pronounced for patients with colon cancer. In a review study published in BMJ in November that combined data from 34 studies with 1.3 million patients, researchers found that that each four-week delay in surgical treatment for seven different cancers resulted in a higher mortality risk.

“The negative impact to the overall well-being of (patients with cancer) is immeasurable.”

“The more aggressive or fast-growing the cancer, the more dangerous the delays. Variability can occur among cancers that occur at the same site. “Slow-growing breast cancers may not change much within a year, but fast-growing breast cancers could have a more advanced stage and more limited prognosis with a year’s delay in diagnosis,” Patt notes.

The University of Michigan researchers developed the OncCovid model to weigh the risks and benefits of delayed treatment in a systematic way. They also folded in the risk of COVID-19 infection in healthcare settings. Their results, published in JAMA Oncology in December, showed the web-based tool may be useful in making judgments regarding cancer care delays based on the patient’s cancer and COVID-19 risk.

The NCI COVID-19 in Cancer Patients Study (NCCAPS) investigates how COVID-19 and cancer interact. Researchers are collecting blood samples, medical information and medical images from 2,000 people with cancer who also have COVID-19. They will be followed for up to two years. Researchers at Baylor College of Medicine in Houston are recruiting patients for NCCAPS. “I think this study is incredibly important to obtain data on these two major current causes of mortality,” says Claire Hoppenot, M.D., assistant professor of gynecologic oncology at Baylor’s Dan L. Duncan Comprehensive Cancer Center. Some study results have shown that patients with cancer are more likely to have poor COVID-19 outcomes. The cancer center at Baylor is prioritizing vaccination of patients with cancer who are receiving treatment, Hoppenot says.

Nonmedical support
The pandemic has affected cancer care beyond medical treatments. Cancer centers and clinicians now work to situate patients in a supportive web of nonmedical services — a web that has been frayed by the pandemic. Although canceling in-person support groups and restricting visitors helps reduce the spread of COVID-19, these measures can also have serious negative impacts for patients with cancer, says Elizabeth Koelker, M.H.A., FACHE, a director of The BDO Center for Healthcare Excellence & Innovation, a healthcare consultancy in Beavercreek, Ohio. It is well documented and understood that the best practice in cancer care delivery is a treatment approach that addresses the mind, body and spirit of patients with cancer. Support groups address the loneliness and isolation associated with a cancer diagnosis, and exercise rehabilitation programs have scientifically proven positive effects on long-term survival. Although many efforts to
resume screening and standardized treatment such as chemotherapy, radiation, and surgery have occurred, other treatments remain indefinitely suspended. “The negative impact to the overall well-being of (patients with cancer) is immeasurable,” Koelker says.

Although many healthcare systems are starting to loosen their visitor policies, cancer programs are mostly sticking to the no-visitor policy. “This can be a profound source of stress to patients who find comfort and strength in the presence of a trusted loved one during treatment,” Koelker says. “While it’s too soon to measure, many providers anticipate an overall decrease in (adherence) from patients missing their treatment appointments because their support person can’t be present.”

Some centers allow an exception to the no-visitor policy by permitting one visitor for initial consults, which tend to be overwhelming and full of crucial information. Overall, integrative services such as massage therapy, acupuncture, art and music therapy, and even exercise rehabilitation remain suspended at most comprehensive cancer programs, according to Koelker.

“As institutions move forward, they need to understand the importance of caring for the mind and spirit,” Koelker says. “Providers must enable patients to seek support in a virtual environment, such as virtual support groups, which can help patients feel more connected.”

What can be done
Providers needn’t stand idly by as people delay cancer care, Patt notes. She suggests three steps that providers can take:

- Inform the public that it’s safe to get cancer screening and medical care more broadly. They should announce when they have implemented CDC protocols that make services safe to deliver care.
- Stress the importance of cancer screening for reducing cancer-related morbidity and mortality.
- Lower or remove barriers, such as lack of transportation, to getting care.

Baylor College of Medicine is devising individualized cancer treatments for patients with early-stage cancers, such as early low-grade endometrial cancer or atypical hyperplasia, which can be treated effectively with hormonal therapy if surgery is delayed, Hoppenot says.

In hospitals where operating rooms aren’t in use, patients who can’t be moved to another hospital but have known metastatic ovarian cancer are being treated with chemotherapy, with a plan for surgery when operating rooms open again. “This is not an uncommon treatment plan for patients, even outside of COVID-19,” Hoppenot says. “Where we have to prioritize, algorithms include surgical risk algorithms (potential need for inpatient or ICU care), potential for cure of the cancer with surgery and symptom control, as well as those with alternative (hormonal or chemotherapy) options until they can have a surgery date.”

Approximately 40% of VCU Massey Cancer Center’s appointments are now virtual. Staff are working to keep patients out of medical facilities whenever possible but still allows visits for treatments, laboratory tests, scans and other things that can only be done in person, McGuire says.

VCU Massey Cancer Center also has implemented a robust testing system; all patients are tested for COVID-19 prior to treatment. Patients scheduled for surgery are tested 48 hours prior to their operation. If the patient tests positive, the procedure is delayed when possible. In rare cases where surgery cannot be rescheduled, special operating rooms are assigned for patients who tested positive for COVID-19.

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