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Clin Gastroenterol Hepatol 2018 Aug 20

## Transplanting HCV-Infected Livers into Uninfected Recipients: Is It Cost-Effective?

*Yes, particularly in those with higher model for end-stage liver disease scores, but also in those with lower scores and poor quality of life.*

Emerging evidence shows that direct-acting antiviral agents (DAAs) are effective in eradicating hepatitis C virus (HCV) infection post–liver transplantation. This has made it feasible to consider transplantation of HCV-infected donor livers into uninfected recipients followed by subsequent treatment with a DAA regimen. However, the high cost of DAAs needs to be considered.

To assess the cost-effectiveness of this treatment approach, researchers used a validated mathematical model to compare the clinical and economic outcomes in two hypothetical scenarios. In the first scenario, HCV-negative patients were willing to accept only HCV-negative livers; in the second, they were willing to take either an HCV-positive or HCV-negative liver. Those receiving HCV-positive livers underwent preemptive DAA therapy for 12 weeks starting at or shortly after transplantation.

Accepting any liver was cost-effective (i.e., incremental cost-effectiveness ratio [ICER] <\$100,000 per quality-adjusted life year [QALY]) for patients with a model for end-stage liver disease (MELD) score  $\geq 22$  (ICER range, US\$56,100–US\$91,700 per added QALY) and in patients with low MELD scores but poor quality of life (ICER range, US\$57,000–US\$66,000 per added QALY). For patients with a MELD score of 28 (the median score of patients undergoing transplantation in the United States), the ICER was US\$62,600 per added QALY.



COMMENT: Offering an HCV-positive liver to an HCV-negative recipient and providing preemptive DAA therapy is definitely cost-effective for patients with MELD scores  $\geq 22$  and in others when other factors are considered. Continuing decreases in the cost of HCV therapies will only further justify this approach from a cost-effectiveness standpoint. Some transplant centers already offer this as an option to their patients with the highest MELD scores.

Note to readers: At the time we reviewed this paper, its publisher noted that it was not in final form and that subsequent changes might be made.

CITATION(S): Bethea ED et al. Cost-effectiveness of transplanting HCV-infected livers into uninfected recipients with preemptive antiviral therapy. Clin Gastroenterol Hepatol 2018 Aug 20; [e-pub].  
(<https://doi.org/10.1016/j.cgh.2018.08.042>)

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Gastroenterology 2018 Sep 6

## Budesonide Is an Effective Therapy for Lymphocytic Colitis

*Randomized, controlled trial data show greater response with short-term budesonide compared with placebo or mesalamine.*

Well-controlled data on the effectiveness of budesonide for lymphocytic colitis are sparse. In the current industry-funded, multicenter European trial, investigators sought to demonstrate the superiority of budesonide or mesalamine — a therapy commonly used to treat this condition — over placebo.

Fifty-seven patients were randomized to receive 9 mg budesonide, 3 g mesalamine, or placebo once daily for 8 weeks. The primary endpoint was clinical remission, defined as  $\leq 21$  loose stools in the last 7 days of treatment.

In the intention-to-treat analysis, a higher percentage of the budesonide group met the primary endpoint compared with the placebo group (79% vs. 42%). There was no difference between the mesalamine (63%) and placebo groups ( $P=0.09$ ). Histologic healing was also greater for budesonide versus placebo (68% vs. 21%); again, mesalamine (26%) was similar to placebo. The number of adverse events was higher in the mesalamine group.

COMMENT: This study demonstrates that patients with lymphocytic colitis not only meet clinically relevant endpoints more often using budesonide compared with mesalamine or placebo, but also have a higher likelihood of histologic healing without any added risk for adverse events.

These results are not directly translatable to the U.S., as drug delivery was done via sachets, which are not available here. However, other pharmacokinetic studies suggest comparable efficacy with alternate formulations of both budesonide and mesalamine. Clinicians should feel more comfortable using budesonide as first-line therapy for treating lymphocytic colitis.

CITATION(S): Miehke S et al. Efficacy and safety of budesonide, vs mesalazine or placebo, as induction therapy for lymphocytic colitis. Gastroenterology 2018 Sep 6; [e-pub].  
 (<https://www.ncbi.nlm.nih.gov/m/pubmed/30195447>)

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Lancet 2018 Aug 31

## Novel Antidepressant Appears Rapidly Effective for Postpartum Depression

*In placebo-controlled trials, intravenous brexanolone produced greater reductions in depressive symptoms within 60 hours; this response persisted for 30 days.*

Several studies suggest that functional alterations in the GABA<sub>A</sub> receptor and its allosteric modulator, allopregnanolone, are linked to postpartum depression. In two manufacturer-supported studies, researchers testing the efficacy of brexanolone (an allopregnanolone analogue) administered intravenously over 60 hours in a hospital setting to 246 women with postpartum depression (Hamilton Rating Scale for Depression [HAM-D], >20; onset during the third trimester or within the first 6 months postpartum). In the first trial, brexanolone doses of 60 µg/kg/hour and 90 µg/kg/hour were compared with placebo; in the second trial, the 90-µg/kg/hour dose was evaluated relative to placebo.

At the end of the 60-hour infusion in both studies, HAM-D scores differed significantly from placebo for either brexanolone dose (differences, -5.2 [60-µg] and -2.5 to -3.7 [90-µg]); this effect was sustained at 30 days. At 60 hours, significantly higher proportions of participants achieved remission (HAM-D ≤7) with brexanolone than with placebo (51% vs. 16% [60-µg] and 61% vs. 38% [90-µg]). In addition, likelihood of Clinical Global Impression–Improvement response was greater (84% vs. 56% [60-µg] and 80% vs. 56% [90-µg]). In a combined analysis of both studies plus a third previous study, 94% of patients who responded to the 90-µg dose maintained a response at 30 days. Efficacy was similar regardless of whether other antidepressants were used. The most common side effects were headache, dizziness, and somnolence. Two patients experienced serious side effects (e.g., syncope), all of which resolved with cessation of infusion.

COMMENT: These studies document the antidepressant effects of a novel, rapid-onset agent that yielded larger reductions in HAM-D scores than those traditionally achieved with standard medications for postpartum depression. The need for IV administration may limit brexanolone's availability — nonetheless, its rapid, sustained effects are likely to benefit not just new mothers but also their children as a result of improved maternal caretaking.

CITATION(S): Meltzer-Brody S et al. Brexanolone injection in post-partum depression: Two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet 2018 Aug 31; [e-pub].  
 ([https://doi.org/10.1016/S0140-6736\(18\)31551-4](https://doi.org/10.1016/S0140-6736(18)31551-4))

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## Infant Walkers Still a Common Cause of Injuries

By Amy Orciari Herman, Edited by Susan Sadoughi, MD, and André Sofair, MD, MPH

Infant-walker injuries declined significantly after safety standards were put in place in 2010, but they still sent thousands of U.S. infants to emergency departments in 2014, according to a study in *Pediatrics*.

Using data from the National Electronic Injury Surveillance System, researchers estimated that over 230,000 children younger than 15 months were treated in U.S. EDs for infant-walker injuries between 1990 and 2014. Roughly 90% of injuries involved the head or neck, and 75% occurred when infants fell down stairs in a walker. Although the rate of injuries declined markedly over the study period, some 2000 infants were injured in 2014.

The researchers say their findings support the American Academy of Pediatrics' call to ban infant walkers in the U.S.

**LINK(S):** [Pediatrics article](#) (Free); [Pediatrics early-release page](#) (if above link doesn't work yet) (Free)

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### **What Do Pharmacists Know About Potential Pet Poisons?**

An increasing number of veterinary clients are choosing to fill pet prescriptions through human pharmacies; however, veterinary pharmacology is not a required component of pharmacology training programs in the U.S. A recent article in *Pharmacy Practice* evaluated the baseline knowledge of licensed pharmacists with regard to common pet toxins.

Pharmacists were given a list of 25 substances and asked to evaluate the potential toxicity of each for either a cat or dog. **Fifteen true toxins and 10 nontoxins** were included in the list:

Toxins	Nontoxins
Acetaminophen	Acorn squash
Allium (onions, garlic, chives)	African violets
Artificial sweeteners (xylitol)	Bananas
Caffeine	Famotidine
Chocolate	Green beans
DEET (insect repellent)	Leather
English Ivy	Paper
Ethanol	Pony tail palms
Grapes	Pumpkin
Loratadine	Tomatoes
Macadamia nuts	
Moth balls	
Nicotine	
Sago palm	
Tea tree oil	

Respondents were able to classify 15 of 25 items (60%) correctly as toxic or nontoxic; only 50% of pharmaceutical substances were classified appropriately.

<https://www.americinveterinarian.com/news/what-do-pharmacists-know-about-potential-pet-poisons>

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### **Cigna-Express Scripts Merger Not for Low-cost Drugs**

The Cigna-Express Scripts merger Monday cleared one more hurdle to combining the health insurer and pharmacy benefit manager (PBM). But industry insiders say the bid likely won't improve the high-prescription drug costs facing employers and employees.

Only a quarter of employers say they're optimistic that mergers between health plans and PBMs will have a positive impact on cost, quality, and consumer experience. The majority of employers (56%) are skeptical that they will see improvement from consolidation, and another 18% believe these mergers will lead to higher costs. Cigna's deal for Express Scripts came on the heels of CVS Health's \$68 billion deal to buy insurer Aetna. The recent mergers represent a rapidly changing market.

<https://www.benefitnews.com/news/employers-caution-cigna-express-scripts-merger-not-a-prescription-for-low-cost-drugs?feed=00000152-18a5-d58e-ad5a-99fd665c0000>

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JAMA Pediatr 2018 Sep 4

### **Practice Guideline for Mild Traumatic Brain Injury in Children**

*A CDC expert panel offers evidence-based recommendations for diagnosis, prognosis, and management of mTBI.*

Sponsoring Organization: U.S. Centers for Disease Control and Prevention

Target Audience: Pediatric primary care and emergency care providers

Background and Objective: Mild traumatic brain injury (mTBI) is defined as an acute brain injury resulting from head trauma with disorientation, loss of consciousness, amnesia, or neurological symptoms and a Glasgow Coma Scale score of 13 to 15. A CDC expert working group has now developed the first evidence-based clinical guideline for diagnosis and treatment of pediatric mTBI.

#### Key Recommendations

#### Diagnosis

- Do not routinely obtain head computed tomography (CT), brain MRI, single photon emission CT, or skull radiographs.
- Identify risk factors for serious injury (age <2 years, vomiting, loss of consciousness, severe trauma, amnesia, severe headache, suspected skull fracture, etc.), which may indicate need for urgent CT.
- Use a validated symptom rating scale and neurocognitive testing in evaluation; however, do not use the Standardized Assessment of Concussion alone to diagnose mTBI in children aged 6 to 18 years.
- Do not test for possible biomarkers of mTBI, as none are currently validated.

Prognosis

- Counsel patients and families that symptoms commonly abate within 3 months (in 70%–80%), although each child's recovery will differ.
- Assess premorbid conditions that could delay recovery, such as previous mTBI, neurocognitive disorders, and family stress.
- Consider other risk factors for prolonged symptoms, such as older age, Hispanic ethnicity, lower socioeconomic status, and more-severe presentation. Headaches may persist longer in girls.

Management

- Educate parents to restrict physical and cognitive activity for the first post-trauma days and then allow gradual return to activity.
- Participate in determining a return-to-school plan together with a school-based team.
- Do not treat headaches with opioids or hypertonic saline.
- Address sleep disturbances by counseling on sleep hygiene and, if necessary, refer patients to a sleep disorder specialist.

COMMENT: This guideline includes additional references and recommendations. The authors acknowledge that current recommendations will likely evolve as more robust evidence is developed.

CITATION(S): Lumba-Brown A et al. Centers for Disease Control and Prevention guideline on the diagnosis and management of mild traumatic brain injury among children. JAMA Pediatr 2018 Sep 4; [e-pub].  
 (<https://doi.org/10.1001/jamapediatrics.2018.2853>)

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**Secret Profit-making System Drug Middlemen Use to Make Millions**

As an Iowa pharmacist compared a newspaper article with his own records, he saw that for a bottle of generic antipsychotic prescription, CVS had billed Wapello County \$198.22. But his pharmacy was reimbursed just \$5.73. His question was why was CVS charging almost \$200 for a bottle of medication that it told the pharmacy was worth less than \$6? And what was the company doing with the other \$192.49?

The pharmacist had stumbled across what's known as spread pricing, where companies like CVS mark up—sometimes dramatically—the difference between the amount they reimburse pharmacies for a drug and the amount they charge their clients. It's where pharmacy benefit managers (PBMs) like CVS make a part of their profit. But he didn't think the spread could be thousands of percent.

In an analysis of pharmacy and middleman markups in Medicaid plans around the country, Bloomberg found big spreads on dozens of drugs, and evidence that the spreads are growing. For many widely used generic drugs, state insurance plans are collectively paying millions of dollars in fees to private companies.

<https://www.bloomberg.com/graphics/2018-drug-spread-pricing/>

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