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Weighing the Evidence for Pediatric Antipsychotic Use

To the Editor: In the February Taking Issue commentary, Dr. Zima (1) warned that the results of our study about evidence-based prescription of second-generation antipsychotics to children (2) should be interpreted cautiously and perhaps are premature, given that clinical studies are ongoing. Furthermore, she suggested that clinicians and researchers keep the "blindfold" off when they attempt to find the balance between evaluating evidence and using it in clinical decision making.

We agree that the blindfold should be kept off, but let's not stand like a statue, either. It is important to learn how second-generation antipsychotics are used among children and to understand more about the risks and benefits of these drug products. The study was initiated in 2006, when none of the second-generation antipsychotics were approved by the Food and Drug Administration (FDA) for any indication in the pediatric population. However, the number of children taking these medications was already increasing significantly in 2006. Thus we believe that the study was not premature. Because more and more children were receiving these products, it was important

that we begin to understand the utilization of second-generation antipsychotics in the pediatric population.

We recognize that there is a temporal nature of shifting evidence and that these results will change as more evidence is generated. Four second-generation antipsychotics are now approved by the FDA for specific indications in pediatric populations. However, even with the growing body of evidence, information is still limited. Other published studies have highlighted the increased use, safety issues, and unknown long-term effects of using these drugs to treat children (3,4). There have been calls for systematic monitoring protocols to address some of the questions surrounding their use in the pediatric population (5).

As Dr. Zima states, there are limitations to our study. Specifically, we did not have access to patients' medical records and could not determine the clinical decision making used to prescribe these products. Thus our linkage of the diagnosis to a prescription claim was limited. To mitigate this limitation, we used a broad two-year time frame around the index second-generation antipsychotic prescription to document diagnoses. This long time frame may have increased the likelihood of detecting any potential evidence-based diagnoses. However, without access to patients' medical charts, we cannot account for diagnoses not documented in the payment records. In addition, we agree with Dr. Zima that determining evidence-based use is not an exact science. But even when prescriptions based on "weak" evidence are excluded, 43% of use was not evidence based. This finding demonstrates the need for further research, perhaps by evaluating medical charts or conducting provider interviews, to better understand clinical decision making and the risks and benefits of using these drugs to treat children.

Should we prescribe first and ask questions later? Problems may occur when prescribing gets in front of the evidence. Clinicians need data to support their decision making about us-

ing second-generation antipsychotics for appropriate conditions in the pediatric population. Use of these medications to treat children should be based on evidence as well as clinical judgment. We owe it to the children we treat. So let's keep the blindfold off and keep asking questions and searching for answers.

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To Screen or Not to Screen for Hepatitis C Infection?

To the Editor: The report by Kakisi and colleagues (1) in the September 2009 issue on the high prevalence of hepatitis C virus (HCV) infection among patients with psychiatric disorders is in line with other reports of increased rates of HCV infection in patient populations with psychiatric disorders (three to ten times the rates in the general population) (1,2). Kakisi and colleagues concluded that routine screening for HCV should be implemented for patients with psychiatric disorders. I contend that the evidence for such recommendation is

equivocal at best and needs to be examined closely and evaluated cautiously (3).

Recommendations of the Centers for Disease Control and Prevention support screening for HCV infection among patients who have psychiatric disorders with a history of intravenous drug use. Routine HCV screening has been implemented for patients at Department of Veterans Affairs hospitals (prevalence around 6%) and for incarcerated individuals (prevalence as high as 20%).

However, the U.S. Preventive Services Task Force (USPSTF), a non-federal group of health experts that makes recommendations about preventive health care, found insufficient evidence to recommend for or against routine screening for HCV infection among high-risk asymptomatic adults (4). The USPSTF made its recommendation because it found no studies proving that screening for HCV infection leads to better long-term clinical outcomes—specifically, to fewer cases of HCV-related chronic disease and fewer deaths that are attributable to actions taken as a result of screening (for example, counseling and treatment) (4).

An argument can be made that adult patients with psychiatric disorders should be screened for HCV because they are a unique population by virtue of their psychiatric symptomatology and because of the increased morbidity and mortality associated with the combination of HCV infection and psychiatric disorders (2,3). Nonetheless, my study of outcomes of HCV screening for patients with psychiatric disorders showed that only a minority of those who screened positive for HCV infection were considered for treatment and an even smaller minority actually received HCV antiviral treatment (2). Freudenreich and colleagues (5) reported that after two years of HCV screening of patients enrolled in a clozapine clinic, none who screened positive were referred for evaluation or received HCV antiviral treatments.

Where does this body of conflicting evidence leave us? HCV is a viral liver infection associated with increased

morbidity and mortality in psychiatric populations. HCV treatments, however, have not been proven to reduce morbidity or mortality. This calls for an individualized approach to screening for HCV in psychiatric populations. Questions that may help target screening include these: What are the risk factors (for example, intravenous drug use or other high-risk practices)? Is a patient in a high-risk group or symptomatic (that is, elevated liver transaminases, fatigue, or cognitive issues)? Will the patient benefit from screening in terms of counseling to modify behavior or reduce and eliminate alcohol intake? Evidence that new HCV antiviral medications improve treatment and reduce morbidity and mortality from HCV infection will make a stronger case for routine HCV screening for patients with psychiatric disorders.

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In Reply: We welcome Dr. Rifai's comments on our study of the prevalence of viral infections, including hepatitis C, in a psychiatric hospital in Greece. We favor the idea of screen-

ing for HCV infection among hospitalized psychiatric patients primarily because we found a high prevalence of this infection in our study hospital, as other studies have found worldwide, and for other reasons that we discuss below.

Proper consideration of underlying mental or psychiatric disease, including substance abuse, is warranted before treatment for chronic HCV infection is initiated. Current HCV therapies with pegylated interferon alpha and ribavirin can cause adverse neuropsychiatric events (depression, suicidal ideation, irritability, and mania) and other troubling symptoms (fatigue, sleep disorders, and appetite disorders).

The American Association for the Study of Liver Diseases has recommended screening for groups with a high prevalence of HCV infection and has stated that antiviral treatment for chronic hepatitis C, coupled with counseling and psychiatric pretreatment, is a valid option for psychiatric patients (1). Recent trials demonstrated sustained virologic response with pegylated interferon alpha and ribavirin for a substantial proportion (>50%) of "difficult-to-treat" psychiatric patients when a multidisciplinary team was employed (2,3).

Many factors, apart from psychiatric ones, determine the eligibility of an HCV-positive patient for antiviral treatment (2). Some of the HCV genotypes do not readily respond to treatment, and physicians await more potent therapies in the near future. For some patients, the decision to treat, which balances presumed effectiveness against potential adverse events, can be deferred until better therapies become clinically available (1).

Apart from antiviral treatment, several approaches can improve the course of chronic hepatitis C disease once it is diagnosed. Vaccination against hepatitis A and B is one approach, because superinfection with these viruses can accelerate liver disease or even lead to fulminant liver failure. Avoidance of alcohol and hepatotoxic drugs is also paramount.

Use of benzodiazepines, for example, can exacerbate hepatic encephalopathy among patients with cirrhosis. The dosage of several medications must be adjusted for patients with hepatic insufficiency. Monitoring for the development of cirrhosis or its complications can also be of value.

The value of infection control for HCV in psychiatric hospitals arises from the fact that the mode of HCV transmission is cryptogenic in approximately 50% of cases. Sharing a common residence presents the risk of using the same objects for personal hygiene, including razors and toothbrushes, and HCV can be transmitted by such practices. Inflicted injuries can also be of concern in this regard.

Beyond issues of eligibility of psychiatric patients for antiviral treatment, potential effectiveness of such treatment, and prevention of virus transmission, we believe that identifying patients with HCV infection in a psychiatric hospital can help improve their overall medical and psychiatric management. We agree, however, with Dr. Rifai that the issue of screening for hepatitis C in this setting is multifaceted and merits further investigation.

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Cervical Cancer Screening of Women With Schizophrenia in Taiwan

To the Editor: Numerous studies have demonstrated that regular Pap smear testing has significantly reduced cervical cancer incidence and mortality over the past 30 years. However, the rate of testing is still low. In particular, research has shown that women with mental illness are less likely than the general population to have Pap smears, because they are not aware of the importance of such screening or because treatment facilities are not easily accessible. However, almost all such studies have focused on patients with depression, anxiety, or intellectual disabilities (1–3), and very few have explored the rate of Pap smear testing among patients with schizophrenia (4). In addition, data are lacking from Asian populations. Therefore, this study aimed to examine the screening rate among patients with and without schizophrenia in Taiwan.

Data were from the Longitudinal Health Insurance Database (LHID). All female patients who visited ambulatory care centers in 2003 and received a principal diagnosis of schizophrenia (any ICD-9-CM 295 code other than 295.7, schizoaffective disorder) were eligible for the study (N=1,690). Because the diagnostic validity of administrative data is often questioned, only patients who had at least two consensus schizophrenia diagnoses three months apart in 2003 were included (N=1,504). We excluded patients under 30 years of age (N=273) because the National Health Insurance (NHI) program provides an annual free cervical cancer screen only for women aged 30 and older. We also excluded patients over age 69 (N=54) and patients given a diagnosis of cervical cancer between 1996 and 2006 (N=2). The final sample included 1,175 female patients with schizophrenia. We then randomly selected 9,400 persons (eight for every patient in the study group) who were matched in age (30–39, 40–49, 50–59, and 60–69 years) from other patients in the 2003 LHID Registry of Benefi-

ciaries. Conditional logistic regression analysis, which was conditioned on age, was conducted to evaluate the association between a diagnosis of schizophrenia and the likelihood of receiving at least one Pap smear test during the three-year period (2004–2006).

Of the total sample of 10,575 patients, 5,552 (52.5%) received a Pap test during the three-year period—403 of the patients with schizophrenia (34.3%) and 5,149 of the patients in the comparison group (54.8%). Conditional logistic regression analysis showed that patients with schizophrenia were significantly less likely than those in the comparison group to receive a Pap smear test (odds ratio=.35, 95% confidence interval=.30–.40, $p<.001$), after adjustment for age, monthly income, number of ambulatory care visits, and level of urbanization and geographic location of the community in which the patient resided.

Our study found that even with the NHI program, which provides free annual screening for cervical cancer, women with schizophrenia were significantly less likely than women without schizophrenia to receive Pap smear tests. These findings suggest a need for more active intervention and comprehensive strategies to increase screening rates among women with schizophrenia.

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The authors report no competing interests.

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Use of Hospital Emergency Services by Youths in Out-of-Home Care

To the Editor: Youths placed in out-of-home settings often receive mental health services from several sectors of care, but the extent to which they use hospital emergency services is uncertain (1). Better information on the use of emergency services in this population merits attention because such services are costly and disruptive to families.

We used Medicaid Analytic Extract (MAX) claims from North Carolina to examine the use of hospital emergency departments among a statewide population of youths under age 22 who received out-of-home care in congregate residential treatment and family-type residential treatment (often referred to as therapeutic foster care) during calendar year 2003 (N=2,937). MAX claims contain the age, race or ethnicity, gender, Medicaid eligibility category, and a primary ICD-9-CM diagnosis. If the youth had more than one out-of-home stay with different primary diagnoses, we selected the most frequent diagnosis. We used North Carolina claims because these data are of high quality and because youths with a psychiatric diagnosis were not enrolled in capitated managed care, as

they are in some states (2). The data did not permit us to examine whether emergency visits occurred before, during, or after out-of-home stays. With SAS software version 9.1, we used chi square tests to examine whether the demographic and diagnostic characteristics of youths who used emergency services (N=1,616) differed from those who did not (N=1,321). We adhered to confidentiality requirements in a data use agreement with the Centers for Medicare and Medicaid Services.

Fifty-five percent of youths (N=1,616) in out-of-home care received emergency services during the year (mean±SD=2.0±2.7 visits). Forty-nine percent (N=1,453) visited the emergency department for a physical health problem, and 19% (N=558) visited the emergency department for a mental health problem.

Twenty-six percent of girls (N=218) received emergency services for a mental health problem, compared with 16% of boys (N=340) ($p<.001$). Thirty-one percent (N=107) of youths diagnosed as having major depression or affective disorders while in out-of-home care visited the emergency department for a mental health problem, compared with 18% (N=250) of those diagnosed as having conduct disorder or emotional disturbances ($p<.001$). Of youths who visited the emergency department for a mental health problem, the proportion who were enrolled in Medicaid because of low income was smaller than the proportions enrolled because of foster care or disability (14%, 22%, and 25%, respectively; $p<.001$). [A table with data on demographic and clinical characteristics of the total sample and by type of emergency visit is included in an online supplement to this letter at ps.psychiatryonline.org.]

We report these preliminary findings to stimulate research on the use of emergency services among youths in out-of-home care and to suggest that systems of care designed for this population should account for the

role of emergency departments. Visits for physical problems may have been common, in part, because youths with emotional and behavioral problems have an increased risk of injuries (3). Although no diagnostic or demographic characteristics were associated with having an emergency visit for a physical health problem, emergency mental health visits were more common among girls, youths with major depression or affective disorders, and youths who were disabled or in foster care. Further research is needed to examine why these groups may be more likely to use emergency departments and how the use of emergency departments is related to the availability of other services (4).

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