DIAGNOSING AND TREATING MENTAL DISORDERS IN PEOPLE OF COLOR

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Otsuka

Discussion of off-label or investigational use: 

yes
In diagnosis
In treatment
In access to care

Greater than for other ethnic groups

Increasing

- US racial and ethnic minorities are less likely to receive even routine medical procedures, and they experience a lower quality of health services

Supplemental Surgeon General’s report on mental health of minorities, 2 2001
- No substantial difference in prevalence
- Significant illness burden
- Lack of access
Past Year Mental Health Treatment, by Race/Ethnicity

- AI/AN: 13.2%
- Asian: 4.5%
- Black: 8.7%
- Hispanic: 6.8%
- White: 16.0%
- More than 1 race: 18.8%
Unintentional injuries, mainly motor vehicle crashes, were the fifth leading cause of death for the total population, but they were the leading cause of death for minorities aged 1 to 44 years.

The death rate for HIV/AIDS was 4.5 for the total population but 39.9 for African American men aged 25 to 44 years.

Homicide remains the number one cause of death for young African American males.

Substance abuse and mental disorders associated with increased risk for all the above.
Suicide rates by ethnicity and age group—United States, 1996–98
Suicide

- Suicide was the third leading cause of death for Black Americans between the ages of 15 and 24.
- Young males (ages 20-24) had the highest rate of suicide in the black population, 18.18 per 100,000.
- Black Americans have a lifetime prevalence rate of attempted suicide of 4.1%, similar to the general population rate of 4.6%.
DEPRESSION AFFECTS GENERAL MEDICAL CONDITIONS

- Association with Myocardial Infarction: Depressed individuals are far more likely to die from an MI.
- 40% of those with Diabetes Mellitus
- Common in obesity
- Risk Factor in Breast and Other Cancers
- Stroke and depression
BARRIERS

Black Mental Health Stats

African American Beliefs About Depression
63% Depression is personal weakness
31% Depression is a health problem
56% Depression is a normal part of aging

Hopelessness (12 percent)
Lack knowledge of treatment/problem (17 percent)
Fear (17 percent)
Lack money/Insurance (29 percent)
Refusal of Help (31 percent)
Embarrassment/Shame (38 percent)
Denial (40 percent)

Barriers Hindering AA Depression Treatment
Persistent disparities

- OVER DIAGNOSIS OF SCHIZOPHRENIA
- Bipolar Disorder
- PTSD
- UNDERDIAGNOSIS OR UNDER RECOGNITION OF DEPRESSION
Schizophrenia More Common in African Americans?
OVERDIAGNOSIS OF SCHIZOPHRENIA

THE PROTEST PSYCHOSIS

HOW SCHIZOPHRENIA BECAME A BLACK DISEASE

JONATHAN M. METZL

"The most important book on schizophrenia in years."
—SHARON E., Harvard Medical School
## Diagnosis of Psychiatric Patients in Emergency Room Settings

<table>
<thead>
<tr>
<th>% In Maryland ER</th>
<th>Schizophrenia</th>
<th>Bipolar disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>40.9</td>
<td>35.2</td>
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<tr>
<td>Black</td>
<td>58.9</td>
<td>18.9</td>
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</table>

<table>
<thead>
<tr>
<th>% In California ER</th>
<th>Schizophrenia</th>
<th>Bipolar disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>45.3</td>
<td>13.4</td>
</tr>
<tr>
<td>Black</td>
<td>47.9</td>
<td>5.6</td>
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</tbody>
</table>
Relationship between stress and unhealthy behavior

Blacks

Whites


Race and unhealthy behaviors: chronic stress, the HPA axis, and physical and mental health disparities over the life course.
Vicious Cycle

- Self treatment with drugs
- Drug related violence
- Increased risk of traumatic experiences
- Increased risk of mental problems
HAPPINESS AND A HAPPY ATTITUDE IS A CHOICE IF YOU ARE INFORMED!!!!

You can have the opportunity to see if your problems might benefit from additional support. We are offering MENTAL HEALTH SCREENING for interested individuals. Private, confidential, no embarrassing questions, and information about support.

Facilitated by: William B. Lawson, M.D., Ph.D., DFAPA
Professor and Chairman
Howard University Department of Psychiatry and Behavioral Sciences
AND THE PSYCHIATRY MEDICAL STUDENT INTEREST GROUP
WhatsMyM3 is a validated, three-minute tool that screens for symptoms of depression, bipolar disorder, PTSD, and anxiety, and can be used to monitor changes in symptom severity over time. A screen for alcohol is now part of the test. The tool is also available for iPhone and Android smartphones.

It differs from other mental health screening tools, such as the PHQ-9 and the MDQ, in that these are all unidimensional — they only measure one domain of symptoms, like depression or bipolar disorder. The M3 is multidimensional, measuring four areas of symptoms in one quick tool.

Furthermore, when compared to results from the standardized interview tool, the Mini International Neuropsychiatric Interview (link is external) (the MINI measures for 15 different mental illness diagnoses), WhatsMyM3 provides a total mental health score that is 83 percent sensitive in finding true positives and 76 percent specific in finding true negatives. In addition to the total score, there are four subscores, one each for depression, bipolar, PTSD, and anxiety.
DIFFERENTIAL TREATMENT

- Receive more prn medication
- Receive higher doses of psychotropic medication
- Receive more different medications
- Receive more injections of medication
- More likely to receive depot medication
- Less likely to receive antidepressants
- Less likely to receive psychotherapy
- More likely to be prematurely terminated from psychotherapy

(Chung et al. 1995; Flaherty & Meagher 1980; Lawson 1986; Price et al. 1985; Segal et al. 1996; Strakowski et al. 1993)
African American and other ethnic minorities

- Lower adherence rate  Diala 2000, Mark et al, 2004
- Different attitudes to medication?
- More side effects?
- Less efficacy?
The “Race” Drug

- VA trial - no benefit for the two congestive heart failure medications
- Post analysis of data - benefit for African Americans
- Trial in African Americans - effective
- FDA approves for African Americans
- NitroMed markets BiDi

- BlackNews.com - Wrong Debate On "Race Drug"
- ... BlackPR.com Press Release
- Wrong Debate on "Race Drug"
  By Earl Ofari Hutchinson, BlackNews.com Columnist
  Months before ...

- RaceSci: History of Race in Science: In Media
- New Drug Combo Intensifies Race-Based Medicine Debate
- SUSAN J. LANDERS AMNews, 12/06/2004 Washington --
  When it comes to health care access, outcomes and even treatment issues, it is clear that ...

- NPR: Race-Specific Drug Comes in at High Cost
HUMAN GENOME PROJECT

- TEASE OUT THE HUMAN GENOME
- IDENTIFY ALL GENES
- DETERMINE THEIR FUNCTION
Inter-ethnic differences (+):
- Caucasians: 5%–10% are PMs
- **Asians**: 1%–6% are PMs

At least 9 mutant forms of the enzyme:
- 33%–50% of **Asian** and African EMs are SMs (less active)

Polymorphism (+)

Edeki 1996; Richelson 1997; Sjoqvist et al. 1997
Bertilsson et al. 1992; Sjoqvist et al. 1997
MISMATCH MEDICATION AND PHARMACOKINETICS

Finding
Lower doses of antipsychotics in Asians and Latinos Lin, 1999
Lower doses of antidepressants in Asians and Latinos Lin, 1999
Higher plasma levels African Americans, Asians, some Latinos Lin 1999

Genotypical Differences
Shift to the Right for African Americans and Asians for CYP2D6
Fewer Rapid or Poor Metabolizers
More Slow Metabolizers (Bradford, 2000; Mendoza et al, 1999)

Receive more prn medication
Receive higher doses of psychotropic medication
Receive more different medications
Receive more injections of medication
More likely to receive depot medication
Less likely to receive antidepressants
(Chung et al. 1995; Flaherty & Meagher 1980; Primm and Lawson 2010; Price et al.1985; Segal et al. 1996; Strakowski et al.1993)
Clinical Findings Tricyclic Antidepressants
- Lower doses of antidepressants in Asians and Latinos Lin, 1999
- More side effects in African Americans Ziegler, Biggs 1977
- Higher plasma levels African Americans, Asians, some Latinos Lin, 1999

Genotypical Differences
- Shift to the Right for African Americans and Asians for CYP2D6 for antidepressants
- Fewer Rapid Metabolizers
- Fewer Poor Metabolizers
- More Slow Metabolizers (Bradford, 2000; Mendoza et al, 1999)
SSRI’S AND SNRI’S

- Generally less affected by the P450 system especially CYP2D6
- Better side effect profiles
- Less toxicity
- Less likely to be associated with induction of mania
- Most approved for treatment of PTSD, Panic, and OCD
Head to head comparisons SSRI’s and other agents
Sequential treatment in a naturalistic setting
40% African Americans
Serotonin 2A receptor predictive of response
17% Ethnic minority

Clinicians had claimed AA not as responsive to SSRI’S
AA not as responsive to citalopram in STAR* D
Polymorphism of serotonin 2A related to treatment response is not as common in African Americans

FIRST GENERATION ANTIPSYCHOTICS

- OFTEN USED
- PARENTAL FORMS
- DEPOT
- CHEAP
- Higher plasma levels
- Faster treatment response
- But:
- Limited or no antidepressant response
- More movement disordered side effects
Schizophrenia 60 y.o. and Older

Tardive Dyskinesia

Percentage

African American
Caucasian
ATYPICAL ANTIPSYCHOTICS

- Improved efficacy
- Negative symptoms
- Cognition
- Antidepressant effects
- Less extrapyramidal side effects
- Lower risk for tardive dyskinesia
AA vs. whites on Medicaid less likely to receive olanzapine or risperidone Olpolka et al 2003, 2004

AA less likely to receive new agents despite controlling for clinic, SE, health system Herbeck et al 2004

AA in US Schizophrenia Care and Assessment Program less likely to receive new agents Mark et al 2003

AA less likely to receive new agents in outpatient study of two states Kreyenbuhl et al, 2003

AA less likely to receive newer agents in national outpatient database Daumit et al, 2003
Visceral Adiposity: The Critical Adipose Depot

- Subcutaneous Fat
- Abdominal Muscle Layer
- Intra-abdominal Fat
ATYPICALS ARE NOT ALL ALIKE

- **EFFICACIOUS**
  - **CLOZAPINE**
    - Most efficacious, treats tardive dyskinesia
    - Side Effects: Agranulocytosis, seizures, hypersalivation, weight gain
  - **ZYPREXA (OLANZAPINE)**
    - Efficacious but causes weight gain
- **PARTIAL AGONIST**
  - **ABILIFY (Aripiprazole)**
- Long acting
  - **Risperdal Consta** (risperidone depot)
  - **Zyprexa relprev (olanzapine depot)**
  - **Invega**

- **MOST EPS (DOSE RELATED), PROLACTIN**
  - **Risperidone (Risperdal)**
- **APPROVED FOR DEPRESSION**
  - **Seroquel (quetiapine)**
- **LESS WEIGHT GAIN**
  - **Geodon (ziprasidone)**
  - **Abilify (Aripiprazole)**
  - **Invega (paliperidone)**
  - **Fanapt (iloperidone)**
  - **Saphris (asenapine)**
  - **Latuda (lurasidone)**
ZIPRASIDONE IN BLACK PATIENTS WITH SCHIZOPHRENIA: ANALYSIS OF FOUR SHORT-TERM, DOUBLE-BLIND STUDIES

William B. Lawson, MD, PhD, Barry K. Herman, MD, MMM, Antony Loebel, MD, Irina Lazariciu, MSc, and Mansoor Malik, MD

CNS Spectr. 2009;14(9):478-486
Ziprasidone in Black Patients

Objective: To better understand the efficacy and tolerability of atypical antipsychotics among racial groups, we reviewed data from four short-term (4–6 weeks), fixed-dose, placebo-controlled trials of ziprasidone for black, white, and overall populations of patients with schizophrenia.

Methods: Efficacy of ziprasidone in the black, white, and overall schizophrenic populations was compared to placebo using standard efficacy measures (Positive and Negative Syndrome Scale [PANSS] total, PANSS negative, Brief Psychiatric Rating Scale [BPRS], Clinical Global Impression-Severity [CGI-S], CGI-Improvement [CGI-I]).
Ziprasidone in Black Patients

**FIGURE 1.** Improvement in BPRS: ziprasidone versus placebo

*P<.01; 1 P<.0001 compared to placebo.

BPRS=Brief Psychiatric Rating Scale; LS=least squares; LDCF=last observation carried forward.


**FIGURE 2.** Improvement in PANSS total: ziprasidone versus placebo

*P<.005 compared to placebo.

PANSS=Positive and Negative Syndrome Scale; LS=least squares; LDCF=last observation carried forward.

Black patients receiving ziprasidone demonstrated statistically significant improvements from baseline in PANSS total, PANSS negative, and BPRS, and improvements in CGI-S and CGI-I (n=99–149) compared with placebo (n=41–66); improvements were comparable to those observed in the overall population (n=451–639) and the white population (n=310–430). Interaction effect (treatment by race) was not significant for any efficacy variables. Ziprasidone was well-tolerated among black patients (n=175). Adjusted mean (least squares mean) overall weight gain in black patients receiving ziprasidone (n=124) was 1.8 kg. There were no increases in total cholesterol, triglycerides, or random glucose in the black population.
Manic Syndrome Score

*p < 0.05.
Divalproex > placebo.
Lithium in African Americans

- Greater RBC/plasma ratio
- Consequence either of stress or middle passage
- More side effects at standard plasma levels
- Effective at low plasma levels?
- Poorer compliance?

GeneSight® is a clinically focused technology developed by Assurex Health that measures and analyzes important genomic variants affecting the metabolism and response to behavioral health medications in individual patients. These laboratory-developed genomic tests serve as a clinical treatment support tool for your practice, providing you with objective genetic-based patient information in advance of making a medication decision for your patient. Knowing a patient’s genetic profile and having it available in a clear and easy to interpret report can help you understand which medications the patient could metabolize properly and help inform treatment choices unique to each patient.
Finding the right medicine to treat depression is largely trial and error. But now with the swab of a Qtip, a Mason-based company is helping doctors nationwide choose medicine that are genetically proven to work best on each patient.

Assurex Health is a personalized medicine company built around gene profiling technology licensed from the Mayo Clinic and Cincinnati Children’s Hospital Medical Center. Its chief product, GeneSight Psychotropic, is a test that analyzes how a person’s genes might affect the way their body responds to medicine commonly prescribed to treat depression, posttraumatic stress disorder (PTSD), anxiety, bipolar disease, schizophrenia or other behavioral health conditions.

The results of the cotton swab DNA test tell doctors what medicines appear to not interfere with their patients genetic profile, the medicines with the potential to interfere with it and those that are incompatible with a patient’s genetic makeup. While there’s no guarantee the medicine will always work, the test is clinically proven to double the chances that it will.
Little data available for clinical trials of recently approved drugs

Estimated to average substantially less than 5% in pivotal trials supporting drug safety and efficacy

< 1% of studies in biological psychiatry when ethnicity is identified
Many federal agencies require some degree of participation of ethnic minorities as subjects.

Pharmaceutical companies claim they recognize the value of ethnically diverse clinical trial populations.

Many research intensive academic medical centers are in inner city localizations with large minority populations yet they claim that they cannot find or recruit African American subjects.
POTENTIAL PARTICIPANTS' ATTITUDES

- Awareness of Tuskegee Syphilis Study associated with lack of participation
- Deep distrust of research and investigators
- Social distance and lack of social network with investigators
- Concerns about exploitation
Question:
Do you think it is a good idea to try to identify genes that may increase or decrease a person’s risk for bipolar disorder? (Circle one)

1. Very bad idea
2. Bad idea
3. Neutral
4. Good idea
5. Very good idea
Figure 4 Favor Gene Identification

Caucasian

If One Supports Gene Identification

African American

Graphs by Ethnicity

\textit{chi}^2(4\text{-df}) = 60 \ P < 0.0001
Comprehensive literature search to identify all published health research studies that report consent rates by race or ethnicity. 20 health research studies that reported consent rates by race or ethnicity. These 20 studies reported the enrollment decisions of over 70,000 individuals for a broad range of research, from interviews to drug treatment to surgical trials.

- African-Americans had a nonsignificantly lower overall consent rate than non-Hispanic whites (82.2% versus 83.5%; odds ratio [OR] ¼ 0.92; 95% confidence interval [CI] 0.84–1.02).
- Hispanics had a nonsignificantly higher overall consent rate than non-Hispanic whites (86.1% versus 83.5%; OR ¼ 1.37; 95% CI 0.94–1.98).
- In ten clinical intervention studies, African-Americans’ overall consent rate was nonsignificantly higher than that of non-Hispanic whites (45.3% versus 41.8%; OR ¼ 1.06; 95% CI 0.78–1.45). For these same ten studies,
  - Hispanics had a statistically significant higher overall consent rate than non-Hispanic whites (55.9% versus 41.8%; OR ¼ 1.33; 95% CI 1.08–1.65)
  - For the seven surgery trials, which report all minority groups together, minorities as a group had a nonsignificantly higher overall consent rate than non-Hispanic whites (65.8% versus 47.8%; OR ¼ 1.26; 95% CI 0.89–1.77).

Conclusion

- Very small differences in the willingness of minorities, most of whom were African-Americans and Hispanics in the US, to participate in health research compared to non-Hispanic whites.
More research is needed in mental disorders outside of the mental health system especially for ethnic minorities

More research is needed in “personalized medicine”

Advances in pharmcogenetics should be translated to the practice setting
Between 1999 and 2006, professionals from racial-ethnic minority groups increased from 17.6% to 21.4% in psychiatry, from 8.2% to 12.9% in social work, and from 6.6% to 7.8% in psychology.

Reporting race-ethnicity in clinical trials has improved from 54% in 2001 to 89% in 75 studies of similar disorders published by 2010, although few ethnic-specific analyses are being conducted.