THE WHO World Mental Health Survey Initiative
IFPE Congress, Vienna Austria

Presenters include Ronald Kessler, Josep Maria Haro, Yueqin Huang, J. (Hans) Ormel, Kate Scott, Michael Schoenbaum, and Jordi Alonso

April 18, 2009
The WHO World Mental Health Survey Initiative

- A coordinated series of community psychiatric epidemiological studies carried out in countries throughout the world, many of them never having previous information about the prevalence, treatment, or societal burden of mental disorders.
- Implementation is facilitated by access to a WMH Data Collection Coordination Centre that provides key infrastructure support and consultation from experts in survey research.
Key elements of the WHO World Mental Health Survey Initiative

- Common survey sample, interviewer training, and field quality control procedures
- A common validated diagnostic instrument, the WHO CIDI
- A number of important CIDI enhancements
- Consistent translation, back-translation, and harmonization procedures
- Cross-national clinical reappraisal validation studies
- Centralized data cleaning, coding, and analysis
- Cross-national collaboration in report preparation
- Cambridge University Press WHO book series
The WMH study design

- Nationally or regionally representative household surveys
- Adults 18 and older
- Subsamples of spouses of target respondents
- Standardized interviewer training and monitoring
- Standardized face-to-face interviews
The WMH study design (cont.)

- Sample of at least 5000 interviews per country
- Both CAPI and PAPI versions
- Shared training, quality control, and data processing protocols
CID1 Enhancements

- Assessment of sub-threshold diagnoses
- Expanded assessment of symptom severity using standardized versions of widely-used clinical severity scales (e.g., HAM-D, YBOCS)
- Expanded assessment of disorder-specific role impairment using the SDS
- Expanded assessment of overall role impairment using the WHO-DAS and HPQ
- Parallel analyses of role impairments caused by marker chronic physical disorders
WHO World Mental Health (WMH) Survey Consortium

- 28 countries
- All regions of the world
- National household samples of at least 5,000 people
- A total of over 200,000 interviews
WMH sample characteristics by WHO region

<table>
<thead>
<tr>
<th>Country</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nigeria</td>
<td>6752</td>
</tr>
<tr>
<td>South Africa</td>
<td>4351</td>
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</table>
### WMH sample characteristics by WHO region

#### Regional office for the Americas

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Brazil</td>
<td>5014</td>
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<td>Colombia</td>
<td>4426</td>
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<td>Mexico</td>
<td>5782</td>
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<td>Peru</td>
<td>3912</td>
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<tr>
<td>United States</td>
<td>9282</td>
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## WMH sample characteristics by WHO region

Regional office for South-East Asia

<table>
<thead>
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<tbody>
<tr>
<td>India</td>
<td>2992</td>
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<tr>
<td>Nepal</td>
<td>3500</td>
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## WMH sample characteristics by WHO region

### Regional office for Europe

<table>
<thead>
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<tr>
<td>Belgium</td>
<td>2419</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>5318</td>
</tr>
<tr>
<td>France</td>
<td>2894</td>
</tr>
<tr>
<td>Germany</td>
<td>3555</td>
</tr>
<tr>
<td>Italy</td>
<td>4712</td>
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### WMH sample characteristics by WHO region

**Regional office for Europe (cont.)**

<table>
<thead>
<tr>
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<th>Sample Size</th>
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<tbody>
<tr>
<td>Israel</td>
<td>4859</td>
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<tr>
<td>Netherlands</td>
<td>2372</td>
</tr>
<tr>
<td>N. Ireland</td>
<td>3097</td>
</tr>
<tr>
<td>Portugal</td>
<td>4500</td>
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<td>Romania</td>
<td>2357</td>
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## WMH sample characteristics by WHO region

### Regional office for Europe (cont.)

<table>
<thead>
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<tbody>
<tr>
<td>Spain 1</td>
<td>5473</td>
</tr>
<tr>
<td>Spain 2</td>
<td>6000</td>
</tr>
<tr>
<td>Turkey</td>
<td>5235</td>
</tr>
<tr>
<td>Ukraine</td>
<td>4725</td>
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</table>
Regional office for Eastern Mediterranean

<table>
<thead>
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<th>Sample Size</th>
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</thead>
<tbody>
<tr>
<td>Iraq</td>
<td>4332</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>5000</td>
</tr>
<tr>
<td>Lebanon</td>
<td>2857</td>
</tr>
<tr>
<td>Country</td>
<td>Sample Size</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Australia</td>
<td>9000</td>
</tr>
<tr>
<td>China 1</td>
<td>12,335</td>
</tr>
<tr>
<td>China 2</td>
<td>7500</td>
</tr>
<tr>
<td>Japan</td>
<td>3417</td>
</tr>
<tr>
<td>New Zealand</td>
<td>12,992</td>
</tr>
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</table>
A complete list of WMH collaborators, contact information, publications, and appendix materials for the presentations in this session can be found at:

www.hcp.med.harvard.edu/wmh
Prevalence estimates of DSM-IV disorders in the WHO world mental health (WMH) surveys

On behalf of WMH investigators
Yueqin Huang, MD, MPH, PhD
Institute of Mental Health,
Peking University, Beijing, China

April 18, 2009
Objective

To present an overview of data on lifetime and 12-month prevalence and age-of-onset (AOO) of DSM-IV disorders in the WHO World Mental Health (WMH) Surveys.
Method

- Data come from community surveys in the first 17 WMH countries. Combined sample includes more than 70,000 respondents.

- Disorders were assessed with the WHO Composite International Diagnostic Interview (CIDI 3.0).
Result

- Lifetime DSM-IV disorders are common in all countries studied.
Twelve-month (12-mo) prevalence of any WMH-CIDI/DSM-IV disorder

Prevalence

United States
Ukraine
Colombia
New Zealand
France
Lebanon
South Africa
Netherlands
Mexico
Belgium
Germany
Israel
Spain
Italy
Japan
PR China
Nigeria
Twelve-month (12-mo) prevalence of WMH-CIDI/DSM-IV anxiety disorders
Twelve-month (12-mo) prevalence of WMH-CIDI/DSM-IV mood disorders
 Twelve-month (12-mo) prevalence of WMH-CIDI/DSM-IV disruptive behavior disorders

Disruptive Behavior Disorders

United States
Ukraine
Colombia
PR China
Lebanon
France
Netherlands
South Africa
Belgium
Mexico
Germany
Spain
Italy
Japan
Nigeria

Prevalence
Twelve-month (12-mo) prevalence of WMH-CIDI/DSM-IV substance disorders

- Ukraine
- South Africa
- United States
- New Zealand
- Colombia
- Mexico
- Netherlands
- Belgium
- PR China
- Israel
- France
- Lebanon
- Japan
- Germany
- Nigeria
- Spain
- Italy

Prevalence
Results

- AOO curves show anxiety and disruptive behavior disorder to have the earliest onsets, followed by substance and mood disorders.

- The median lifetime AOO of any disorder is in early adolescence in most countries with anxiety and disruptive behavior disorders most often temporally primary in comorbid clusters.
Standardized age-of-onset distributions of DSM-IV/CIDI anxiety disorders in the WMH surveys
Standardized age-of-onset distributions of DSM-IV/CIDI mood disorders in the WMH surveys

Cumulative lifetime probability of disorders

Age at onset

Colombia
NCS-R
Mexico
Ukraine
PR China
Japan
Israel
Lebanon
Nigeria
Belgium
France
Germany
Italy
Netherlands
Spain
New Zealand
S. Africa
All
Standardized age-of-onset distributions of DSM-IV/CIDI disruptive behavior disorders in the WMH surveys
Results

- Lifetime comorbidity is consistently found to be a strong predictor of 12-month prevalence and severity among lifetime cases.

- The majority of 12-month cases are classified as mild or moderate.

- However, severe mental disorders are associated with serious role impairment.
The proportion of 12-month CIDI/DSM-IV mental disorders classified as severe in the WMH countries

Percent classified as serious

- Israel
- Belgium
- Netherlands
- Mexico
- South Africa
- New Zealand
- United States
- Colombia
- Ukraine
- Lebanon
- Germany
- Spain
- France
- Italy
- China
- Japan
- Nigeria
Mean days out of role among respondents with 12-month severe mental disorder.
Why do prevalence estimates vary so greatly across countries?

Methodological variation

- Willingness to report mental illness to an interviewer
- Adequacy of the DSM system to characterize psychopathology in the country
- Sensitivity of the CIDI and the local translation to operationalize the DSM criteria in the country
- Symptom threshold differences across countries
Why do prevalence estimates vary so greatly across countries?

Methodological research is currently underway to evaluate all these possibilities:

- Clinical reappraisal interviews in new WMH surveys.
- Debriefing interviews with WMH respondents.
- Calibration studies with MI estimates of clinical diagnoses.
Why do prevalence estimates vary so greatly across countries?

Substantive variation

- Differential exposure to stressful experiences
- Differential vulnerabilities
- Genetic differences
Why do prevalence estimates vary so greatly across countries?

Substantive research in progress

- Molecular genetics collaboration
- Focused comparative studies of traumatic stress (e.g., South Africa and Northern Ireland)
Conclusion

- The WMH surveys show that throughout the world mental disorders are commonly occurring, seriously impairing, often comorbid, and typically having first onsets in childhood or adolescence.

- These results raise the question whether early interventions with mild cases might be able to reduce the persistence or severity of these disorders over time.
Results of the WMH-CIDI Clinical Reappraisal Study

On behalf of WMH investigators
Josep Maria Haro, MD, MPH, PhD
Saint John of God Research Foundation
Barcelona, Spain

April 18, 2009
Why do a clinical reappraisal?

- Community epidemiological surveys find high prevalence estimates. Are these estimates accurate? Or are they due to a high rate of false negatives?
Why do a clinical reappraisal?

- Previous clinical reappraisal studies of the DIS and earlier versions of the CIDI have been mixed in their results. K has been as low as .20 for some disorders in some studies, but considerably better in other studies.
Why do a clinical reappraisal?

- At the same time, concerns can be raised about the accuracy of clinical diagnoses in community surveys. Booth (1998), for example, found that consistency of CIDI diagnoses with SCID diagnoses improved from $K = .53$ to $K = .67$ when the SCID diagnoses were improved using LEAD standard criteria.
Why do a clinical reappraisal?

- As another indication that clinical diagnoses are not always completely accurate in community surveys, Eaton and colleagues found in the Baltimore ECA follow-up study that respondents with baseline DIS diagnoses that were not confirmed by clinical interviews nonetheless had significantly elevated risk of subsequent adverse outcomes indicative of psychopathology (e.g., hospitalization for mental disorders, work disability for mental disorders).
Objectives of this presentation

- To present the results of the WMH clinical reappraisal studies.
- To describe the results of an innovative approach to *calibration* rather than *validation*.
- Do discuss ongoing WMH methodological studies aimed at improving CIDI diagnostic assessments.
Blinded clinical reappraisal interviews were carried out with a probability subsample of WMH survey respondents in a number of participating countries.

CIDI cases were over-sampled to increase statistical power.

The clinical reappraisal data were weighted to adjust for the over-sampling of CIDI cases so as to generate unbiased estimates of concordance.

DSM-IV criteria were used.

The SCID was used as the gold standard interview.
Study design (cont.)

- Experienced clinical interviewers were trained in the SCID and were required to have good concordance with ratings in a set of standardized taped interviews before participating.

- SCID sections were rotated to prevent differential effects due to respondent burden.

- Clinical interviews were taped and reviewed by supervisors.

- Biweekly rater meetings with supervisors were used to review difficult cases and to prevent drift.

- Interviews were carried out both face-to-face and by telephone.
<table>
<thead>
<tr>
<th>Study Group</th>
<th>Sample Size (n)</th>
<th>Duration</th>
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<tbody>
<tr>
<td>US Adolescents</td>
<td>347</td>
<td>Lifetime</td>
</tr>
<tr>
<td>US Adults</td>
<td>325</td>
<td>Lifetime</td>
</tr>
<tr>
<td>ESEMeD Adults</td>
<td>143</td>
<td>Twelve-month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(France, Italy, Spain)</td>
</tr>
</tbody>
</table>
The CIDI is conservative for some disorders in estimating lifetime prevalence.

The CIDI is generally unbiased, in comparison, in estimating 12-month prevalence.
## Individual-level concordance

### I. Any Anxiety Disorder

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>K</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCS-A</td>
<td>.88</td>
<td>.63</td>
<td>.89</td>
<td>.88</td>
<td>.71</td>
<td>.96</td>
</tr>
<tr>
<td>NCS-R</td>
<td>.73</td>
<td>.48</td>
<td>.54</td>
<td>.91</td>
<td>.75</td>
<td>.80</td>
</tr>
<tr>
<td>ESEMeD</td>
<td>.88</td>
<td>.42</td>
<td>.84</td>
<td>.93</td>
<td>.31</td>
<td>.99</td>
</tr>
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</table>
## Individual-level concordance (cont.)

### II. Any Mood Disorder

<table>
<thead>
<tr>
<th>Test</th>
<th>AUC</th>
<th>K</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCS-A</td>
<td>.89</td>
<td>.80</td>
<td>.81</td>
<td>.97</td>
<td>.88</td>
<td>.94</td>
</tr>
<tr>
<td>NCS-R</td>
<td>.75</td>
<td>.54</td>
<td>.55</td>
<td>.94</td>
<td>.74</td>
<td>.87</td>
</tr>
<tr>
<td>ESEMeD</td>
<td>.83</td>
<td>.56</td>
<td>.69</td>
<td>.97</td>
<td>.50</td>
<td>.99</td>
</tr>
</tbody>
</table>
### III. Any Substance Disorder

<table>
<thead>
<tr>
<th></th>
<th>AUC</th>
<th>K</th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCS-A</td>
<td>.94</td>
<td>.88</td>
<td>.89</td>
<td>.99</td>
<td>.90</td>
<td>.99</td>
</tr>
<tr>
<td>NCS-R</td>
<td>.88</td>
<td>.77</td>
<td>.79</td>
<td>.97</td>
<td>.82</td>
<td>.97</td>
</tr>
</tbody>
</table>
We also examined CIDI-SCID concordance for diagnoses of individual anxiety, mood, and substance disorders.

Estimates of K and AUC were for the most part relatively comparable to those for overall disorder classes.

For example, in the NCS-R, where AUC was .88 for any anxiety disorder, AUC was in the range .79-.90 for panic disorder, specific phobia, social phobia, and PTSD.
In a validation study, we study individual-level concordance of diagnoses.

Each CIDI respondent in a validation study is assigned a dichotomous classification of either yes or no on the diagnosis.
In a calibration study, we generate individual-level predicted probabilities of clinical diagnoses based on CIDI data (including item-level data).

Each calibration study respondent is assigned a predicted probability of clinical diagnosis in the range 0.00-1.00.
Validation studies are useful in assessing accuracy of clinical decisions.

Individual-level classification accuracy is less important than aggregate accuracy, though, in epidemiological studies.

Dichotomous diagnoses throw away information that can be important in epidemiological analysis (e.g., the distinction between respondents with 51% and 91% probabilities of clinical diagnosis).
How do we implement calibration?

- We use stepwise regression methods of various sorts (e.g., CART, random forests, etc.) to predict clinical diagnoses from CIDI item-level data.

- Significant interactions between CIDI data and socio-demographic data indicate differential concordance that can be built into the calibration.

- Interactions can be examined between CIDI data and socio-demographic data to discover evidence of differential concordance across important segments of the population.
How do we implement calibration? (cont.)

- It is important to cross-validate results to guard against over-fitting.
- Individual-level predicted probabilities of clinical diagnosis are generated from the final prediction equations.
How do we implement calibration? (cont.)

- Data analysis can use the predicted probabilities as the outcomes to calculate prevalence (e.g., the mean of the predicted probability is the prevalence estimate).

- Or the predicted probabilities can be used as weights in logistic regression analysis.

- Or the predicted probabilities can be used for imputation.

- Simulation using the Multiple Imputation (MI) approach can be used to take prediction error into consideration in carrying out substantive analyses.
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Dich</th>
<th>Cont</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panic disorder</td>
<td>.72</td>
<td>.93</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>.67</td>
<td>.84</td>
</tr>
<tr>
<td>MDD</td>
<td>.75</td>
<td>.87</td>
</tr>
<tr>
<td>Drug dependence</td>
<td>.62</td>
<td>.95</td>
</tr>
</tbody>
</table>
Limitations of the WMH clinical reappraisal studies

- An important limitation of this work is that the studies were confined to developed countries.

- We encouraged all countries to carry out clinical reappraisal studies, but competing demands for limited resources led this not to be done.

- We have a separate clinical reappraisal study using the SCAN in Brazil that is being analyzed right now.

- Nepal and Saudi Arabia are planning clinical reappraisal studies next year.
Another limitation is that we did not validate the assessments of externalizing disorders.

In the US, the diagnosis of adult ADHD was validated against the standard research diagnostic interview used in clinical studies of adult ADHD. AUC was .78 for adolescents and .86 for adults.

Given the importance of externalizing disorders, future methodological studies are needed to validate CIDI diagnoses of these disorders.
Another limitation: We did not assess NAP.

Previous research (e.g. Bebbington, Eaton, Kendler) shows fully-structured interviews do a poor job of assessing NAP.

We are engaged in a new survey in Saudi Arabia that is trying to tackle this problem using informant reports.

This approach builds on the work of Silove and Patel in East Timor, but using a more extensive screen.

We’re also experimenting with “network” sampling (sometimes referred to as “multiplicity” sampling) to extend this approach so that we capture information about psychotics who live alone or are homeless.
Improving the CIDI

- Validation and calibration are well and good, but we also need to recognize that the CIDI is far from perfect and to use the results of these studies to improve it.

- To that end, we have carried out methodological studies aimed at pinpointing particularly problematic symptoms and diagnoses for future investigation.

- Qualitative interviews are being carried out in several countries with clinical reappraisal study respondents to help gain insights into these problems as well as into ways to fix them.
We also have the issue of cultural congruence of constructs.

And then there is the issue of the community-level perception of the legitimacy of the task itself rather than of the individual questions: Will people tell strangers about their emotional problems? If not, how can we address this problem? (e.g., A-CASI)
The development of lifetime comorbidity among DSM-IV disorders in the WHO World Mental Health Surveys

On behalf of WMH investigators
J. (Hans) Ormel, PhD
University Medical Center Groningen
The Netherlands

April 18, 2009
Two and three factor models that account for comorbidity

Internalizing

> Females

anxious
misery

.70 - .90

Externalizing

> Men

c.30 -.50

DEP  DYS  GAD  PAN  AGO  SOC  SIM  ALC  DRUG  CD  ANTISOC

Rationale (1) - CFA too restrictive

- The tests of these models have for the most part been based on confirmatory factor analysis (CFA).

- CFA assumes that individual disorders are conditionally independent after controlling for an underlying common vulnerability.

- CFA does not allow for
  - the possibility of other common causes that are related only to a subset of disorders
  - dynamic associations among disorders in predicting first onset or persistence of each other
  - and implicitly combines information about onset and persistence-recurrence
Rationale (2) - Canonical approach: an alternative to CFA

- A less restrictive approach is one that allows for dynamic associations in a canonical framework.
- This approach can distinguish between predictors of first onset and persistence-recurrence,
- Allows individual disorders to have predictive effects on each other.
- We investigate the extent to which these predictive effects can be parsimoniously characterized as due to effects through one or more common pathways (canonical variates).
Conventional and canonical models of temporally primary disorders predicting subsequent onset of other disorders

Independent of residuals

I and E are weighted composites

Effects flow through common pathways
<table>
<thead>
<tr>
<th>Factor</th>
<th>Developed</th>
<th>Developing</th>
</tr>
</thead>
<tbody>
<tr>
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<td>8.0</td>
<td>6.6</td>
</tr>
<tr>
<td>2.</td>
<td>1.8</td>
<td>2.3</td>
</tr>
<tr>
<td>3.</td>
<td>1.2</td>
<td>1.5</td>
</tr>
<tr>
<td>4.</td>
<td>0.9</td>
<td>1.2</td>
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Person-Year Factor Analysis (Promax Rotation): Internalizing

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Developed I</th>
<th>Developed II</th>
<th>Developing I</th>
<th>Developing II</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDE</td>
<td>.85</td>
<td>.04</td>
<td>.86</td>
<td>.03</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>.42</td>
<td>.31</td>
<td>.70</td>
<td>.10</td>
</tr>
<tr>
<td>GAD</td>
<td>.87</td>
<td>.03</td>
<td>.95</td>
<td>.01</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>.80</td>
<td>.06</td>
<td>.71</td>
<td>.09</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>.98</td>
<td>.00</td>
<td>1.0</td>
<td>.00</td>
</tr>
<tr>
<td>Social phobia</td>
<td>.82</td>
<td>.05</td>
<td>.97</td>
<td>.00</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>1.0</td>
<td>.00</td>
<td>1.0</td>
<td>.00</td>
</tr>
<tr>
<td>OCD</td>
<td>.75</td>
<td>.08</td>
<td>1.0</td>
<td>.00</td>
</tr>
<tr>
<td>PTSD</td>
<td>.69</td>
<td>.12</td>
<td>.70</td>
<td>.11</td>
</tr>
<tr>
<td>SAD</td>
<td>.66</td>
<td>.13</td>
<td>.74</td>
<td>.08</td>
</tr>
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</table>
Person-Year Factor Analysis (Promax Rotation): **Externalizing**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Developed</th>
<th></th>
<th>Developed</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>Alcohol use disorder</td>
<td>.02</td>
<td>.93</td>
<td>.00</td>
<td>1.0</td>
</tr>
<tr>
<td>Drug use disorder</td>
<td>.01</td>
<td>.99</td>
<td>.00</td>
<td>1.0</td>
</tr>
<tr>
<td>ODD</td>
<td>.05</td>
<td>.85</td>
<td>.01</td>
<td>.94</td>
</tr>
<tr>
<td>IED (Intermit. Explosive Dx)</td>
<td>.09</td>
<td>.76</td>
<td>.52</td>
<td>.21</td>
</tr>
<tr>
<td>Conduct disorder I</td>
<td>.01</td>
<td>.99</td>
<td>.01</td>
<td>.95</td>
</tr>
<tr>
<td>Conduct disorder II</td>
<td>.01</td>
<td>.97</td>
<td>.02</td>
<td>.89</td>
</tr>
<tr>
<td>Attention-deficit disorder</td>
<td>.22</td>
<td>.54</td>
<td>.22</td>
<td>.50</td>
</tr>
<tr>
<td>Hyperactivity disorder</td>
<td>.12</td>
<td>.70</td>
<td>.18</td>
<td>.56</td>
</tr>
</tbody>
</table>
Fitted canonical model of T1 and T2 observed and latent variables.

Extension of T1 canonical model with T2 latent I and E variables. Very restrictive model as all T1-T2 links flow through I and E.
Summary of results

- Canonical model fits better than the unrestricted model for all 18 outcomes (disorders).

- The model was replicated for four age-of-onset ranges – childhood (ages 4-12), adolescence (ages 13-19), young adulthood (ages 20-29), and middle age (ages 30-44) – to investigate the consistency of residual effects to protect against over-fitting.

- Although the restrictive model fits well, some consistently significant residual effects were found.
First, the associations between T1 and T2 observed and latent internalizing variables
Normed effects (odds-ratios) of the T1 observed scores on the T1 latent scores and of the T2 latent scores on the T2 observed scores in the total sample: *Internalizing*

<table>
<thead>
<tr>
<th>Disorders</th>
<th>Time 1</th>
<th>Time 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depressive episode</td>
<td>2.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>1.6</td>
<td>2.9</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>1.1</td>
<td>2.4</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>0.9</td>
<td>2.7</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>3.9</td>
<td>3.4</td>
</tr>
<tr>
<td>Social phobia</td>
<td>3.5</td>
<td>3.2</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>15.3</td>
<td>2.8</td>
</tr>
<tr>
<td>OCD</td>
<td>5.6</td>
<td>2.9</td>
</tr>
<tr>
<td>PTSD</td>
<td>1.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Separation anxiety disorder</td>
<td>3.3</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Phobias markers of I-vulnerability; T2 outcomes equally influenced by I-vulnerability
Second, the associations between T1 and T2 observed and latent **externalizing** variables
### Normed effects (odds-ratios) of the T1 observed scores on the T1 latent scores and of the T2 latent scores on the T2 observed scores in the total sample: **Externalizing**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Time 1</th>
<th>Time 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use disorder</td>
<td>0.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Drug use disorder</td>
<td>2.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Oppositional defiant disorder</td>
<td>5.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Intermittent explosive disorder</td>
<td>3.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Conduct disorder I</td>
<td>2.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Conduct disorder II</td>
<td>2.8</td>
<td>2.9</td>
</tr>
<tr>
<td>Attention-deficit disorder</td>
<td>3.4</td>
<td>4.1</td>
</tr>
<tr>
<td>Hyperactivity disorder</td>
<td>3.4</td>
<td>4.1</td>
</tr>
</tbody>
</table>

**Opposition & poor control markers of E-vulnerability; T2 outcomes differently influenced by E-vulnerability.**
Third, the associations between T1 and T2 latent I and E variables
Fourth, the residual effects

Only 10 out of the 306 residual effects of T1 lifetime disorders on risk of first onset of disorders at T2 were consistently significant; i.e. had excess association not accounted for by the canonical model.

In other words, these pairs of disorders had less or more association than could flow through the latent I and E variables.
### Normed residual effects (odds-ratios) of disorders known to be closely related

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Outcome</th>
<th>OR</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD1</td>
<td>CD2</td>
<td>4.5-5.2</td>
<td></td>
</tr>
<tr>
<td>CD2</td>
<td>CD1</td>
<td>3.2-4.3</td>
<td></td>
</tr>
<tr>
<td>ALC</td>
<td>DRUG</td>
<td>1.5-6.6</td>
<td>But reverse</td>
</tr>
<tr>
<td>GAD</td>
<td>MDE</td>
<td>1.5-2.5</td>
<td></td>
</tr>
<tr>
<td>MDE</td>
<td>GAD</td>
<td>2.0-6.0</td>
<td>Only early-onset</td>
</tr>
</tbody>
</table>

CD1=overt aggression; CD2=covert aggression
### Normed residual effects (odds-ratios) of disorders NOT known to be closely related

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Outcome</th>
<th>OR</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCD</td>
<td>BPD</td>
<td>1.6-3.7</td>
<td>Only early-onset</td>
</tr>
<tr>
<td>IED</td>
<td>OCD</td>
<td>1.5-4.0</td>
<td>Highly consistent</td>
</tr>
<tr>
<td>IED</td>
<td>MDE</td>
<td>1.5-1.9</td>
<td>Only later-onset</td>
</tr>
<tr>
<td>IED</td>
<td>PD</td>
<td>1.8-2.2</td>
<td></td>
</tr>
<tr>
<td>IED</td>
<td>DRUG</td>
<td>0.2-0.6</td>
<td>Highly consistent</td>
</tr>
</tbody>
</table>

Uncontrolled anger (frustration) risk factor for later I-disorders
The canonical model provides a generally good fit to the onset data.

But there are clear violations of the model for particular associations (10).

These results show clearly that some predictors of first onset of the disorders considered here are actually predictors of the underlying vulnerability to all disorders in the class. They are not unique predictors of individual disorders.

The distinction between predictors unique to particular outcomes and general to an entire class of outcomes could be important for both theoretical and practical reasons.
Mult Regression of T2 Psychopathology on T1 Temperament traits – The TRAILS study

<table>
<thead>
<tr>
<th>Temperament Predictor</th>
<th>Internalizing (residual)</th>
<th>Externalizing (residual)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frustration (anger control)</td>
<td>0.16***</td>
<td>0.18***</td>
<td>0.25***</td>
</tr>
<tr>
<td>Effortful Control (attention)</td>
<td>-0.04</td>
<td>-0.25***</td>
<td>-</td>
</tr>
<tr>
<td>Fearfulness</td>
<td>0.12**</td>
<td>0.02</td>
<td>0.13**</td>
</tr>
</tbody>
</table>

**General and dimension-specific effects**

Ormel et al 2005

Standardized (z-score) variables; outcome = mean across informants; beta’s.
Childhood adversity, early onset mental disorders and adult onset physical conditions

On behalf of WMH investigators
Kate M. Scott, PhD
Wellington School of Medicine and Health Sciences
Otago University, Wellington, New Zealand

April 18, 2009
Research questions

- Do childhood adversities predict the onset of a range of chronic physical health conditions adulthood?

- Do early onset mental disorders predict the onset of a range of chronic physical health conditions in adulthood?

- Are the associations of early onset mental disorders with physical condition onset independent of their shared background of childhood adversities?
Childhood adversities as predictors of adult-onset physical conditions: background

- Research on the fetal origins of obesity and cardiovascular disease.
- Research on effect of early life stress on the developing neuroendocrine and immune systems: chronic dysregulation may influence disease development (allostatic load).
- Substantial epidemiological research on association of childhood adversities with physical outcomes, but usually focal assessment of one adversity/one outcome and seldom includes mental disorders.
Early-onset mental disorders as predictors of adult-onset physical conditions: background

- Mental disorders can be secondary to physical conditions. Also possible (though more controversial) that mental disorders might be a risk factor for physical condition onset.

- Solid evidence for prospective relationship between depression symptoms and subsequent cardiovascular disease and diabetes, but less for other physical conditions.

- No research on relationships between early onset mental disorders and later onset physical conditions.

- If early onset mental disorders are associated with physical condition onset, is this independent of childhood adversity (since it is a risk factor for both)?
Methods

- 10 WMH surveys (n=18,303). AOO for mental disorders and physical conditions: enabled use of prospective analytical approach within survival analysis framework
- Outcome variables: adult onset (21+) condition - self report of doctor’s diagnosis of: asthma; hypertension; heart disease; self report of chronic headache, chronic spinal pain
- Predictors: early onset (<21) depressive or anxiety disorders; childhood (<18) adversities (physical abuse, sexual abuse, parent death, parent divorce, parent mental disorder, parent substance abuse, parent criminal behaviour, family violence, family economic adversity)
- Analysis: Cox proportional hazard models assessing risk of the physical condition onset as a function of predictors, adjusting for sex, age, country (and current mental disorder)
## Effects of childhood adversities and early-onset mental disorders on risk of adult-onset conditions (adj for each other + age, sex, country): hazard ratios

<table>
<thead>
<tr>
<th>Depression or anxiety &lt;21</th>
<th>Asthma</th>
<th>Hypertension</th>
<th>Spinal pain</th>
<th>Heart disease</th>
<th>Arthritis</th>
<th>Headache</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.5*</td>
<td>1.3*</td>
<td>1.6*</td>
<td>1.7*</td>
<td>1.4*</td>
<td>1.6*</td>
<td>1.2</td>
</tr>
<tr>
<td>1 childhood adversity</td>
<td>1.2</td>
<td>1.0</td>
<td>1.1*</td>
<td>1.2</td>
<td>1.0</td>
<td>1.4*</td>
<td>1.1</td>
</tr>
<tr>
<td>2 childhood adversities</td>
<td>1.4*</td>
<td>1.2</td>
<td>1.3*</td>
<td>1.6*</td>
<td>1.3*</td>
<td>1.4*</td>
<td>1.2</td>
</tr>
<tr>
<td>3+ childhood adversities</td>
<td>1.6*</td>
<td>1.2*</td>
<td>1.6*</td>
<td>2.2*</td>
<td>1.4*</td>
<td>1.6*</td>
<td>1.6*</td>
</tr>
</tbody>
</table>
Conclusions

- Childhood adversities (3+) predicted all physical conditions; some conditions were predicted by fewer adversities.

- The strength of specific childhood adversities as predictors varied across conditions; physical abuse related to all conditions.

- Early onset mental disorders predicted all physical conditions except diabetes, and did so independently of childhood adversities.
Next steps

- Expand sample to include all 30 countries.
- More refined analyses are needed of the separate and joint effects of childhood adversities.
- Similar analyses are needed of the separate and joint effects of mental disorders.
- And we need to expand the analysis of mental disorders to include consideration of impulse-control disorders and substance disorders.
Next steps (cont.)

- We need to examine modifiers and mediators of effects which have not yet been explored in depth.
- We need to examine time course: the influence of when in the life course the mental disorder occurs (similarly for physical condition); temporal proximity of predictor and outcome.
- Analyses need to be repeated for respondents in different age groups as a way of indirectly investigating the effects of recall bias.
The treatment gap in the WHO World Mental Health Surveys

On behalf of WMH investigators
Michael Schoenbaum, PhD
National Institute of Mental Health
Bethesda, MD, United States

April 18, 2009
The WMH Services Workgroup

- Josep Maria Haro  Spain
- Laura Andrade  Brazil
- Oye Gureje  Nigeria
- Yueqin Huang  China
- Viviane Kovess  France
- Carmen Lara  Mexico
- Phil Wang  USA
The Assessment of Treatment in the WMH Surveys

- 12-month treatment: Prevalence, sector, intensity, and adequacy

- Lifetime treatment: Prevalence, sector, speed
Twelve-month treatment by severity of DSM-IV mental disorder

- **LOW INCOME**
  - Nigeria

- **LOW-MIDDLE INCOME**
  - China
  - Colombia
  - South Africa
  - Ukraine

- **HIGH-MIDDLE INCOME**
  - Lebanon
  - Mexico

- **HIGH INCOME**
  - Belgium
  - France
  - Israel
  - Germany
  - Italy
  - Japan
  - Netherlands
  - New Zealand
  - Spain
  - USA

- **Countries**

- **% in treatment**

- **Colors**
  - Blue = Serious
  - Red = Moderate
  - Yellow = Mild
Twelve-month treatment by severity of DSM-IV mental disorder

Countries

LOW INCOME
- Nigeria

LOW-MIDDLE INCOME
- China
- Colombia
- South Africa
- Ukraine

HIGH-MIDDLE INCOME
- Lebanon
- Mexico

HIGH INCOME
- Belgium
- France
- Israel
- Germany
- Italy
- Japan
- Netherlands
- New Zealand
- Spain
- USA

% in treatment

Blue=Serious
Red=Moderate
Yellow=Mild
Twelve-month treatment by severity of DSM-IV mental disorder
Twelve-month proportional treatment in the mental health specialty sector

- **LOW INCOME:**
  - Nigeria
- **LOW MIDDLE:**
  - China
  - Colombia
  - South Africa
  - Ukraine
- **HIGH MIDDLE:**
  - Lebanon
  - Mexico
- **HIGH:**
  - Belgium
  - France
  - Germany
  - Israel
  - Italy
  - Japan
  - Netherlands
  - New Zealand
  - Spain
  - USA

Blue = Serious
Red = Moderate
Yellow = Mild
Twelve-month proportional treatment in the mental health specialty sector

Blue=Serious
Red=Moderate
Yellow=Mild
Twelve-month proportional treatment in the mental health specialty sector
Twelve-month proportion of treated cases who received “minimally adequate” treatment

Blue=Serious
Orange=Any Severity
Twelve-month proportion of treated cases who received “minimally adequate” treatment

Blue=Serious
Orange=Any Severity

Countries:
- LOW INCOME: Nigeria
- LOW-MIDDLE: China, Colombia, South Africa, Ukraine
- HIGH MIDDLE: Lebanon, Mexico
- HIGH INCOME: Belgium, France, Germany, Israel, Italy, Japan, Netherlands, New Zealand, Spain, USA

% receiving adequate treatment/any treatment
Some General Trends in the Data

- Proportional treatment is strongly related to percent of GNP spent on healthcare.
- Most treatment is in the general medical sector in the vast majority of countries.
- Generally monotonic relationships exist between severity and probability of treatment.
- Despite these dose-response relationships, only between 11% (China) and 61% (Belgium) of people with a serious disorder receive treatment in a year.
Some General Trends in the Data (cont.)

- A trend exists for severity of disorder to be related to probability of treatment being in the specialty sector.
- But this association is significant in only 7 countries.
- Even in these 7 countries, significant proportions of the cases seen by specialists are mild.
- The proportion of patients with adequate treatment is lower in low-income countries.
- The association between severity of disorder and probability of treatment being at least minimally adequate is significant in only 3 countries – Netherlands, Spain, and USA.
Conclusions

- Disturbingly high levels of unmet need
- Even among people with serious disorders
- Even in developed countries, although much more so in developing
Conclusions: Developing countries

- Low government expenditures reduce access to care
- Out-of-pocket spending is difficult
- South Africa is an exception, where 8.6% GNP is spent on health care and treatment in our data is higher than for other developing countries
Conclusions: Developed countries

- There are noticeably lower treatment rates in Japan and Italy in our data than in other developed countries.

- This could reflect the government expenditures being lowest in these countries of all the developed countries studied.
What is the best way to spend the few mental health resources that nations have?

- Diversion of limited resources to people with low need
- Weak association between specialty treatment and severity could indicate poor prioritization
- The general medical sector provides the most services, but also has the lowest rate of treatment adequacy
- We need to ensure that GM treatment quality is improved, possibly using a collaborative care model
Burden of disease estimates from the WMH Surveys

On behalf of WMH investigators
Jordi Alonso, MD, PhD
Institut Municipal d’Investigacio Medica (IMIM)
Barcelona, Spain

April 18, 2009
Concerns about valuing disability in previous studies

- Expert valuations only
- Simplistic scenarios (health states)
- Comorbidity not taken into account
Objective

- To estimate the relative burden attributable to specific diseases taking into account co-existence of other disorders.
Mental disorders/groups

- **Depression** (MDD)
- **Bipolar** (Bipolar I, II Mania and Hypomania)
- **Panic** (Panic; Agoraphobia)
- **Specific phobia**
- **Social phobia**
- **GAD**
- **PTSD**
- **Alcohol** (Abuse, Dependence)
- **Drugs** (Abuse, Dependence)
Chronic physical conditions/groups

- **Musculoskeletal** (Arthritis)
- **Chronic Pain** (Neck/Back pain; Other somatoform pain)
- **Headache/Migraine**
- **Digestive** (Stomach or intestine ulcer; IBD)
- **Respiratory** (Asthma, Allergies, Any other chronic lung disease)
- **Neurological problems**
- **Cancer**
- **Cardiovascular** (Stroke, Heart attack, Heart disease, HBP)
- **Diabetes**
- **Insomnia**
Other variables

Dependent Variable:
- VAS: Own overall physical and mental health in the last 30 days (*0 worst possible, 100 best possible*)

Adjusting Variables:
- Age, sex, country
VAS distribution

- High percentage (17%) of individuals with 100
- Skewed distribution, few individuals with low scores

OLS can provide biased estimations
Model selection

- Alternatives to OLS models:
  - Two-part models
  - Specifications of quasi-likelihood GLM

- Criterion for the selection of the models:
  - Graphs of means of predicted values in each model vs means of observed values, by deciles of the predicted values
  - Comparison of the means of the predicted values for different groups of interest vs means of the observed values
  - Comparison of the Mean Square Error (MSE) and the Mean Absolute Predict Error (MAPE) for each model
Predicted vs observed by deciles
Estimating the disorder effects

1. **Estimate the model** with individual disorders, number of disorders (starting from 2) and 18 interaction terms with number of comorbid disorders, and adjusted.

2. Save the **predicted values** and **coefficients** from the **final model** for VAS

3. Use the coefficients to estimate the **new predicted value** but now fix **one of the disorders to 0** and change the interaction and the number of disorders terms consistently

4. Calculate the **difference between the original predicted values** and the ones obtained in point 3

   ➢ **INDIVIDUAL EFFECT**: Mean of the differences among the individuals with the disorder
Estimating the disorder effects

**Example:**

Suppose an individual with MDE and 2 other disorders (SP and Cardiovascular)

\[
V_{AS_i} = \beta_0 + \ldots + \beta_j M_{DE_i} + \beta_{j+1} SP_i + \ldots + \beta_k \# Diseases_i + \beta_{k+1} \cdot M_{DE_i} \cdot \# comorb\_i + \beta_{k+2} \cdot SP_i \cdot \# comorb\_i + \ldots = \beta_0 + \ldots + \beta_j \cdot 1 + \beta_{j+1} \cdot 1 + \ldots + \beta_k \cdot 3 - \beta_{k+1} \cdot 1 \cdot 2 + \beta_{k+2} \cdot 1 \cdot 2 + \ldots
\]

\[
V_{AS_{i\_NO\_MDE}} = \beta_0 + \ldots + \beta_j \cdot 0 + \beta_{j+1} \cdot 1 + \ldots + \beta_k \cdot 2 + \beta_{k+1} \cdot 0 + \beta_{k+2} \cdot 1 \cdot 1 + \ldots
\]

- To get the effect of depression:

\[
\text{INDIVIDUAL EFFECT} = \text{MEAN}\left( V_{AS_i} - V_{AS_{i\_NO\_MDE}} \right) \text{ among individuals with MDE}
\]

Standard errors are estimated with the **Jackknife** repeated replication method taking into account stratification and clustering.
Individual effects for each disorder
Individual effects for each disorder, by development status
Ranks of *individual* disorder effects
Estimating societal disorder effects

- Population effects (Societal Effects) can be obtained taking into account the prevalence of each disorder.

\[
\text{SOCIETAL EFFECT} = \text{MEAN} \left( VAS_i - VAS_{i, NO_MDE} \right) \quad \text{among those in the overall sample}
\]

- They can be calculated as the mean of the differences in the overall sample.
Societal effects for each disorder

- Back/neck pain
- Cardiovascular
- Arthritis
- Headache or Migraine
- Depression
- Insomnia
- Diabetes
- Respiratory disease
- Digestive
- Neurological
- Specific Phobia
- Panic Disorder
- Posttraumatic Stress Disorder
- Alcohol Abuse
- Social Phobia
- Generalized Anxiety Disorder
- Bipolar Disorder
- Drug Abuse
- Cancer

Overall
Ranks of societal disorder effects
Ranks of the *individual* vs the *societal* effects
Burden of disease taking comorbidity into account...

- **Rank ordering** of effects of disorders is relatively consistent in developed and developing countries.

- **Heterogeneity** of “individual” effect of disorders is higher than that of “societal” effect.

- A **summary effect** can be estimated for each disorder accounting for comorbidity and observed patterns of disorders.
A complete list of WMH collaborators, contact information, publications, and appendix materials for the presentations in this session can be found at:

www.hcp.med.harvard.edu/wmh