The Unmet Needs of Schizophrenia Treatment: A Clinician-Researcher’s Viewpoint

Michael Davidson, MD
Do you need a focus group to find out the unmet needs? Whose needs, whose expectations, whose disappointments? Are the views of researchers and clinicians the same?

• Sources of information
  – RCT and pragmatic trials vs. the intelligence of the crowds
• Interpretation of published data vs. interpretation of personal observation
  – Does the researcher carry her distaste for the placebo effect into the clinical practice?
• Experience
  – Whose experience is biased and in what direction?
What do we have, major tranquilizers for symptoms or disease-centered drugs?

• The initial description based on observations was consistent with a non-specific tranquilizing effect

• Subsequently, we were seduced into the Koch-like approach (pathogenesis-disease-treatment)

• Contributed to the disease-centered drug approach:
  • mirage of DA hypothesis
  • advent of the DSM
  • the physician’s quest for prestige* and the public’s comfort
  • regulatory mandates
  • commercial considerations.

*“The new drugs could wipe out the symptoms of psychotic patients just as internists can use insulin for the elimination of the symptoms of diabetes.” President of the US Society of Biological Psychiatry Himwich, 1955, p. 421

How do major tranquilizers become anti-psychotics?
Is the pendulum swinging again from specific drugs for schizophrenic psychosis to broader indications?

- AD/PD psychosis
- bipolar disorder
- unipolar depression
- mental retardation
- insomnia
- generalized anxiety, PTSD, OCD
- ADHD

Should indication be restricted or broadened, based on disease or on symptoms, or left to the physician’s discretion?
The Wish List
What do we expect treatment to do?

- Prevent the disease or at least change its course
- Suppress psychosis in all treated individuals and do it fast
- Once suppressed, prevent worsening or exacerbation in all treatment-adherent individuals
- Suppress aberrant behavior intended violence, poor judgment and insight, risky life style
- Improve core negative symptoms motivation, mood, and affect
The Wish List (2)

What do we expect treatment to do?

• Improve cognitive, social, and vocational functioning
• Be well-tolerated and easy to administer
• Keep everybody happy: patients, families, nurses, hospital administration, payees, the legal system
• Be cost-effective
• Accomplish it all through an easy-to-understand, biologically-plausible mechanism
The Reality

Schizophrenia patients gainfully employed
data based on linking the national psychiatric registry with payments into
the social security system

Single admission

<table>
<thead>
<tr>
<th>Days of hospitalization</th>
<th>Men=2,609</th>
<th></th>
<th>Women=1,826</th>
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<tbody>
<tr>
<td></td>
<td>Earning over $1000</td>
<td>Earning Under $1000</td>
<td>earning over $1000</td>
</tr>
<tr>
<td>934 days 14&lt;</td>
<td>12%</td>
<td>23%</td>
<td>6%</td>
</tr>
<tr>
<td>784 15-30</td>
<td>10%</td>
<td>18%</td>
<td>4%</td>
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<tr>
<td>1,430 31-91</td>
<td>10%</td>
<td>16%</td>
<td>4%</td>
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<tr>
<td>1,287 days 92&lt;</td>
<td>6%</td>
<td>13%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Multiple admissions

| Men=12,405 |
|-----------------|-----------------|
| earning over $1000 | Earning under $1000 |
| 4%               | 10%               |
The Reality (2)

• In severely ill patients, antipsychotics ameliorate delusions, hallucinations, and poor thought process for intermittent periods only, in many but not all patients.

• Antipsychotics suppress agitation and often induce sedation (tranquilize) in a dose-dependent manner in most of the patients.

• In mildly to moderately ill patients, and in asymptomatic patients, antipsychotics only decrease risk for worsening or exacerbation.
What do physician do when needs are not met?

- Increase doses of antipsychotics
- Change antipsychotics
- Combine antipsychotics
- Add another psychotropic:
  - Anticonvulsants
  - Benzodiazepine
  - Antidepressants
  - Lithium
- ECT, TMS, abracadabra

Is it useful? Is it right? What should they do?

Is the gap between the wish list and reality the unmet need? And is the gap bridgeable?
Are these unmet needs of schizophrenia?

• Is only the disease responsible for the aberrant behavior?
  — what about personality, cultural thresholds, family structure, socio-economic circumstances, or shortcomings of the mental health system?

• Is only the disease responsible for the poor social and vocational functioning?
  — what about education and employment opportunities?

• Is mild cognitive impairment specific to schizophrenia?
Cognitive impairment is not specific to schizophrenia but a part of mental illness in general

Effect size

Diagnostic group

- Mental retardation (n=223)
- Organic personality disorder (n=135)
- Schizophrenia (n=169)
- Antisocial personality disorder (n=222)
- Schizotypal personality disorder (n=78)
- Histrionic personality disorder (n=141)
- Narcissistic personality disorder (n=3938)
- Dependent personality disorder (n=3642)
- Drug abuse (n=29)
- Affective disorder (n=97)
- Dysthymia (n=244)
- Somatoform disorder (n=95)
- Obsessive compulsive disorder (n=73)
- Anxiety disorder (n=693)
- Adjustment disorder (n=417)
- Obsessive compulsive personality disorder (n=96)

Weiser et al., 2004
Is the failure to treat core negative symptoms an unmet need of schizophrenia treatment, or a more general failure?

• A random stratified sample of 5000 individuals aged 25-34 was tested on the negative symptoms items of the psychiatric epidemiology research interview (PERI) as present or absent

• 16% of the normal population scored present on at least one negative symptom item

• Negative symptoms were more prevalent in individuals with:
  – poor social functioning(39%)
  – unemployed(26%)
  – unmarried(23%)
  – cannabis users(21%)

• Should negative symptoms be a treatment target only in schizophrenia?
In normal individuals oxytocin increase trust, (Kosfeld, Heinrichs et al. 2005), empathy (Hurlemann, Patin et al. 2010)
Are we trying to build the new man with the help of a pill?

Do we need more than one pill for the new man?
Unmet needs in summary

• For the short run:
  Safe, well tolerated, very long-term depot antipsychotics which suppress psychotic symptoms in all patients for extended period of time

• For the long run:
  Putative interventions (drugs?) which benefit aspects of cognitive functioning, social interactions, motivation-apathy

• Until the pathophysiology of mental disease is better understood, should the issue of drugs for diseases vs. drugs for symptoms be reconsidered (specificity vs. pseudo-specificity, DSM-5 R, Rdoc)?
What Are The Unmet Needs of Schizophrenia Treatment?
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