Psychological Issues that Cancer Patients Face:
Moving Forward

Barbara L. Andersen, Ph.D.
Focus of the Discussion

- Physical functioning
- Symptoms (fatigue, sleep, cognitive functioning)
- Health behaviors
- Sexuality
- Compliance/adherence
- Stress
- Anxiety and Depressive symptoms and disorders
Agenda

- Rationale and description
- Psychological treatments
- Moving forward
Why Stress, Depression, and Anxiety?

• Common
• There are known, obvious risk factors
• Impact other emotions, behaviors, biology, and disease endpoints
• Deadly

• They are defined with diagnostic criteria.
• There are validated measures.
• There are currently available, empirically supported psychological and cancer specific interventions.
Biobehavioral Model of Cancer Stress and Disease Outcomes

Cancer Diagnosis & Treatment
- Stress
  - Reduced Quality of Life

Stress
- Depression
- Pain
- Fatigue
- Sleep Prob.

Compliance

Disease: Metastatic

Immunity

Disease: Local

Health Behaviors

CNS Innervation

Neuroendocrine

Inflammatory Cytokines

Disease Course
Co-morbid Psychopathology

- 15-20% with a current depressive disorder (base rate = 6%)
- 11% with a current anxiety disorder (GAD, PTSD, Panic) (= base rate)

- 50% Chronic (recurrent) condition
- 50% with Depression + Anxiety
- Undetected, untreated, and thus, a worsened trajectory
- If detected, under treated
## Depression, Anxiety Comorbidity in Cancer Patients

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Point Prevalence</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Depression</td>
<td>12.7%</td>
<td>1.4-8.0%</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>2.8%</td>
<td>0.5-2.6%</td>
</tr>
<tr>
<td>Sub syndromal</td>
<td>10.8%</td>
<td>1.5-5.9%</td>
</tr>
<tr>
<td>Generalized Anxiety Disorder</td>
<td>3.5%</td>
<td>0.2-7.6%</td>
</tr>
<tr>
<td>PTSD</td>
<td>4%</td>
<td>0.3-2.7%</td>
</tr>
<tr>
<td>Panic Disorder</td>
<td>2.5%</td>
<td>0.3-6.6%</td>
</tr>
<tr>
<td>Adjust. Disorder</td>
<td>14.3%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>
Psychological/behavioral difficulties: Who is at risk? Those with...

History of Depression or Anx. Disorders, =/- sub.use.

And those:

- Male
- Aged
- Alone (actually or functionally)
- Unemployed / low SES
- Receiving the most toxic therapies
- Recurrence/Progressive disease
Example: Cancer Survival:
Gender (male), marital status (alone)
Depression risk: Cancer Therapies

• Taxanes improved breast cancer outcomes when used as adjuvant treatment.

• Clinical trials showed neurotoxicity, pain, and peripheral neuropathy.

Thornton et al., Cancer, 2008
Significant Depressive Symptoms for the Taxane Group

Early trajectory

Late Trajectory

Depressive Symptoms

No Taxane | Taxane

Chemotherapy | Months
Group Differences in Depression (18-22%) 12 and 18 months

- 12-month: CES-D > 10 (% of patients)
- 18-month: CES-D > 10 (% of patients)

* Indicates significance.
<table>
<thead>
<tr>
<th>Type of analysis</th>
<th>No. of studies (%)</th>
<th>Combined effect size</th>
<th>$P$ value</th>
<th>$P$ value for heterogeneity</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall analysis$^a$</td>
<td>50 (100)</td>
<td>1.29 (1.16-1.44)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.50 1.00 1.50 2.00 2.50 3.00 3.50</td>
</tr>
<tr>
<td>Sample size $\geq$3,000</td>
<td>27 (54)</td>
<td>1.10 (1.10-1.14)</td>
<td>&lt; 0.001</td>
<td>0.53</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Sample size $\geq$30,000</td>
<td>16 (32)</td>
<td>1.09 (1.05-1.14)</td>
<td>&lt; 0.001</td>
<td>0.49</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Follow-up $\geq$5 years</td>
<td>34 (68)</td>
<td>1.64 (1.33-2.02)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Follow-up $\geq$10 years$^a$</td>
<td>19 (38)</td>
<td>2.33 (1.63-3.33)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Study quality score $\geq$3</td>
<td>30 (60)</td>
<td>1.19 (1.07-1.33)</td>
<td>0.002</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Fully controlled covariates</td>
<td>20 (40)</td>
<td>1.15 (0.95-1.40)</td>
<td>0.16</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Life-stress exposure</td>
<td>19 (38)</td>
<td>1.09 (1.05-1.13)</td>
<td>&lt; 0.001</td>
<td>0.39</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Stress-prone personality or poor coping style</td>
<td>17 (34)</td>
<td>2.25 (1.54-3.30)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Poor social support$^a$</td>
<td>3 (6)</td>
<td>1.33 (0.70-2.53)</td>
<td>0.39</td>
<td>0.027</td>
<td>0.50 1.00 1.50 2.00 2.50 3.00 3.50</td>
</tr>
<tr>
<td>Unfavorable emotional responses</td>
<td>11 (22)</td>
<td>1.27 (1.07-1.51)</td>
<td>0.008</td>
<td>0.097</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Depression</td>
<td>8 (16)</td>
<td>1.34 (1.11-1.61)</td>
<td>0.002</td>
<td>0.35</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Other emotional distress or poor QOL</td>
<td>3 (6)</td>
<td>1.56 (1.15-2.12)</td>
<td>0.004</td>
<td>0.66</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Any cancer</td>
<td>34 (66)</td>
<td>1.29 (1.11-1.52)</td>
<td>0.001</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>3 (6)</td>
<td>1.07 (0.91-1.27)</td>
<td>0.42</td>
<td>0.38</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>5 (10)</td>
<td>1.12 (0.94-1.34)</td>
<td>0.20</td>
<td>&lt; 0.001</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Stomach cancer</td>
<td>2 (4)</td>
<td>1.09 (0.93-1.27)</td>
<td>0.28</td>
<td>0.64</td>
<td>$\cdot$</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>4 (8)</td>
<td>1.20 (0.90-1.60)</td>
<td>0.22</td>
<td>0.44</td>
<td>$\cdot$</td>
</tr>
</tbody>
</table>
# Depression and suicide

**Who is at risk? Those with...**

<table>
<thead>
<tr>
<th>Cancer</th>
<th>(e.g., 27.7 vs. 16.7/100,000 in 54-59 yr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since diagnosis</td>
<td>(&lt; 5 yrs., 2.38 vs. 1.43-1.58)</td>
</tr>
</tbody>
</table>

And those:

- **Male** (2.09 vs. 1.48 SMR)
- **Aged** [44.6 (50), 57.4 (60), 76.2 (70), etc.]
- **Alone** (37.1 vs 31.5)
- **Distant/Progressive disease** (65.3 vs. 25.1 - 36.1)
- **Disease sites** [Lung, 5.74, stomach (4.68), oral (3.66)]
Significantly Lower NK cell Lysis with Higher Stress (Stg. II/III Breast, N=116) (JNCI, 1998)
Psychosocial well-being and Survival lung cancer

(Kaasa, 1989)
Social Functioning and Survival
Stomach Cancer

(Park et al., 2008)
Physical QoL and Survival
Gynecologic Cancer

(Von Geunigan et al., 2012)
“Lack of energy” and Survival Gynecologic Cancer

(Von Geunigan et al., 2012)
### Table 2. Demographic Characteristics of the Sample

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.7 yr (mean) (range, 39.9–87.2 yr)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>35</td>
<td>87.5%</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>18</td>
<td>45%</td>
</tr>
<tr>
<td>Unmarried</td>
<td>22</td>
<td>55%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>25</td>
<td>62.5%</td>
</tr>
<tr>
<td>Black</td>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Education†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school graduate</td>
<td>26</td>
<td>72.2%</td>
</tr>
<tr>
<td>Partial college</td>
<td>4</td>
<td>11.1%</td>
</tr>
<tr>
<td>College graduate</td>
<td>3</td>
<td>8.3%</td>
</tr>
<tr>
<td>Postgraduate</td>
<td>3</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

* Data missing from one subject.
† Data missing from four subjects.
Interventions
A bit of history...
Bernard H. Fox (1978)

Premorbid Psychological Factors as Related to Cancer Incidence

Bernard H. Fox

Accepted for publication: November 1, 1977
1992 Summary of outcomes from psychological trials (N=19)

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Mood/Emotional Adjustment</th>
<th>Social and Behavioral</th>
<th>Medical or Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Modest improvements in emotional distress; More adaptive coping strategies.</td>
<td>Modest gains in social adjustments.</td>
<td>Immune enhancement and improved survival (Fawzy et al., 1990; 1993).</td>
</tr>
<tr>
<td>Moderate</td>
<td>Significant reductions in emotional distress.</td>
<td>Modest gains in social adjustment.</td>
<td>Symptom (fatigue, anorexia) reduction (Forester, Kornfeld, &amp; Fleiss, 1985).</td>
</tr>
<tr>
<td>High</td>
<td>Significant reductions in emotional distress.</td>
<td>Improvements in global evaluations of quality of life (e.g. life satisfaction).</td>
<td>Symptom improvements (e.g. reductions in pain) and improved survival (Spiegel et al., 1989).</td>
</tr>
</tbody>
</table>

(JCCP, 1992)
Effective Components of Psychological Interventions

- Stress reduction, typically relaxation training
- Information about the disease and treatment
- Behavioral and cognitive coping strategies, e.g., problem solving, assertive communication
- Social support
- Focused interventions for disease-specific problems (e.g., sun protection for melanoma survivors; sexuality for gynecologic survivors)

(JCCP, 1992)
## Efficacy of Psychological Interventions
### Meta-Analyses (N=300+)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>k</th>
<th>Anxiety (95% CI)</th>
<th>Depression (95% CI)</th>
<th>QoL (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unspecified group intervention/varied</td>
<td>7</td>
<td>0.40-0.56</td>
<td>0.47-1.01</td>
<td>0.65-0.90</td>
</tr>
<tr>
<td>CBT</td>
<td>4</td>
<td>0.35-1.67</td>
<td>0.87-1.21</td>
<td>---</td>
</tr>
<tr>
<td>MBSR</td>
<td>3</td>
<td>0.73-0.75</td>
<td>0.58-0.90</td>
<td>---</td>
</tr>
<tr>
<td>Psychoeducation</td>
<td>3</td>
<td>1.59-1.99</td>
<td>0.94</td>
<td>0.91</td>
</tr>
<tr>
<td>Relaxation</td>
<td>2</td>
<td>0.21-0.45</td>
<td>0.30-0.54</td>
<td>---</td>
</tr>
</tbody>
</table>
Reduction in Depression with Intervention

![Graph showing reduction in depression with intervention over 12 months. The graph compares intervention and assessment groups, indicating a decrease in CES-D scores over time.]
Reduction in Inflammation Marker
T Helper : Suppressor Ratio
Intervention lowers inflammation: mediated by reduction in depressive symptoms

A = -0.40**
B = 0.42***
C' = -0.20

Study Arm
Depressive Symptoms (8 months)
White Blood Cell Count (12 months)

(PM, 2009)
45% Reduced Risk of Breast Cancer Recurrence for patients who received a psychological intervention.
60% Reduced Risk of Breast Cancer Death following Recurrence
The future?

A Watershed
Moving Forward, #1 - 4

#1. Screen and implement what exists now.

#2. Expand dissemination/implementation of what exists now.

#3. Stimulate and reinforce innovations in intervention research.

#4. Embrace the “whole” cancer patient.
Screening, Assessment, and Care of Anxiety and Depressive Symptoms in Adults With Cancer: An American Society of Clinical Oncology Guideline Adaptation

Barbara L. Andersen, Robert J. DeRubeis, Barry S. Berman, Jessie Gruman, Victoria L. Champion, Mary Jane Massie, Jimmie C. Holland, Ann H. Partridge, Kate Bak, Mark R. Somerfield, and Julia H. Rowland

ABSTRACT

Purpose
A Pan-Canadian Practice Guideline on Screening, Assessment, and Care of Psychosocial Distress (Depression, Anxiety) in Adults With Cancer was identified for adaptation.

Methods
American Society of Clinical Oncology (ASCO) has a policy and set of procedures for adapting clinical practice guidelines developed by other organizations. The guideline was reviewed for developmental rigor and content applicability.

Results
On the basis of content review of the pan-Canadian guideline, the ASCO panel agreed that, in general, the recommendations were clear, thorough, based on the most relevant scientific evidence, and presented options that will be acceptable to patients. However, for some topics addressed in the pan-Canadian guideline, the ASCO panel formulated a set of adapted recommendations based on local context and practice beliefs of the ad hoc panel members. It is recommended that all patients with cancer be evaluated for symptoms of depression and anxiety at periodic times across the trajectory of care. Assessment should be performed using validated, published measures and procedures. Depending on levels of symptoms and supplementary information, differing treatment pathways are recommended. Failure to identify and treat anxiety and depression increases the risk for poor quality of life and potential disease-related morbidity and mortality. This guideline adaptation is part of a larger survivorship guideline series.

Conclusion
Although clinicians may not be able to prevent some of the chronic or late medical effects of cancer, they have a vital role in mitigating the negative emotional and behavioral sequelae. Recognizing and treating effectively those who manifest symptoms of anxiety or depression will reduce the human cost of cancer.
Stepped care for psychosocial care

- Individual Treatment +/- Pharma
- None needed
- Group Treatment Health Beh. Change
- Patient Education
Moderate Symptomatology
(Score 8-14)

Identify pertinent history / risk factors
• History: Prior depressive disorder, with/without prior treatment
• History: Familial history of depression, with/without prior treatment
• History: Persons with other psychiatric disorders (e.g., GAD), including substance abuse
• Recurrent, advanced, or progressive disease
• Presence of chronic illness(es) in addition to cancer
• Singleton (single not married, widowed, divorced) vs. partnered
• Unemployed or lower socioeconomic status
• Female gender

Patient reports a score of 0 or 1
No Further Screening

None/Mild Symptomatology
(Score 2-7)

• No or minimal symptoms of depression
• Effective coping skills and access to social support
• Few, if any, risk factors

Patient reports a score of 2 or 3 on either item
Complete 7 remaining PHQ-9 items

Moderate to Severe Symptomatology
(Score 15-19)

• Has most depressive symptoms or symptoms which do not remit following Pathway 2 treatment(s)
• Symptoms interfere moderately to markedly with functioning
• Risk factors usually present
• Referral to psychology and/or psychiatry for diagnosis and treatment

Screen at pre diagnosis, other times, and as is relevant

2 item PHQ-9:
1) Little interest or pleasure in doing things (anhedonia)
2) Feeling down, depressed, or helpless (depressed mood)

Patient reports a score of 0 or 1
No Further Screening

None/Mild Symptomatology
(Score 2-7)

• No or minimal symptoms of depression
• Effective coping skills and access to social support
• Few, if any, risk factors

Patient reports a score of 2 or 3 on either item
Complete 7 remaining PHQ-9 items

Moderate Symptomatology
(Score 8-14)

• Subthreshold depressive symptoms
• Functional impairment from mild to moderate
• May have risk factors
• Seek consultation (psychology or psychiatry) for determination of diagnosis

Moderate to Severe Symptomatology
(Score 15-19)

• Has most depressive symptoms or symptoms which do not remit following Pathway 2 treatment(s)
• Symptoms interfere moderately to markedly with functioning
• Risk factors usually present
• Referral to psychology and/or psychiatry for diagnosis and treatment
**Care Map – Depressive Symptoms in Adults with Cancer**

<table>
<thead>
<tr>
<th>Symptomatology</th>
<th>Care Pathway</th>
<th>Intervention Options (low intensity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/Mild</td>
<td>Pathway 1</td>
<td>Offer referral to supportive care services</td>
</tr>
<tr>
<td>Psychosocial (group)</td>
<td>Pathway 2</td>
<td>Self guided or assisted (or computerized) cognitive behavior therapy (CBT); including behavioral activation, problem solving, and relapse prevention</td>
</tr>
<tr>
<td>Pharmacologic, as appropriate</td>
<td></td>
<td>CBT for depression (group)</td>
</tr>
<tr>
<td>Structured physical activity program</td>
<td></td>
<td>Psychosocial interventions (group)</td>
</tr>
<tr>
<td>Psychological (individual)</td>
<td>Pathway 3</td>
<td>Psychological (individual): Cognitive Behavior Therapy, Interpersonal Therapy</td>
</tr>
<tr>
<td>Pharmacologic</td>
<td></td>
<td>Pharmacologic, as appropriate</td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td>Combined</td>
</tr>
</tbody>
</table>

**Psychological (individual)**
- Delivered by licensed mental health professionals using relevant treatment manuals that include some or all of the following content: cognitive change, behavioral activation, biobehavioral strategies, education, and relaxation strategies. Relapse prevention additions are also important.
- Monitor for efficacy.
- Behavioral couples’ therapy can be considered for people with a regular partner and where the relationship may contribute to the development or maintenance of depression.
- After treatment/relapse prevention, consider referral for pharmacotherapy should depressive symptoms not remit or worsen.

**Psychosocial (group)**
- Structured, professionally led, using relevant treatment manuals which include some or all of the following content: stress reduction, positive coping (seeking information, problem solving, assertive communication), enhancing social support from friends/family, coping with symptoms (e.g., fatigue, sexual dysfunction) and bodily changes, health behavior change (diet, activity level, tobacco use), and strategies to maintain change.
- At post treatment, consider referral for individual treatment should depressive symptoms not remit or worsen.

**Pharmacological**
- Anti-depressants, with choice informed by side effect profiles, interactions with current medications and cancer therapies, response, patient age, and preference.
- Monitor regularly for adherence, side effects, and adverse events.
- In most cases, medication needs to be continued after remission of symptoms to reduce the risk of relapse.

**Supportive Care Services for All Patients, As Available and Appropriate**
- Provide education and information (verbal plus any relevant materials) for the patient and family about:
  - Normalcy of stress in the context of cancer
  - Specific stress reduction strategies (e.g., progressive muscle relaxation)
  - Sources of informational support/resources (patient library, reliable internet sites)
  - Availability of supportive care services (e.g., professionally led groups, informational lectures, etc.) for the patient and family at the institution or in the community
  - Availability of financial support (e.g., accommodations, transportation, health/drug benefits)
  - Information about signs and symptoms of depression and avenues for care
  - Information on sleep hygiene and self-management of fatigue
  - Information on other intervention resources for physical activity, nutrition, or relevant others

**Follow-up and ongoing reassessment**
- Monitor for efficacy.
- At post treatment, consider referral for individual treatment should depressive symptoms not remit or worsen.

**Moderate Symptomatology**
- Care Pathway 2
- Psychological (group) or Psychosocial

**Moderate Severe to Severe Symptomatology**
- Care Pathway 3
- Psychological (individual) and/or Psychiatric

**None/Mild Symptomatology**
- Supportive Care and Prevention

**Care Pathway**
- Provide education and information (verbal plus any relevant materials) for the patient and family about:
  - Normalcy of stress in the context of cancer
  - Specific stress reduction strategies (e.g., progressive muscle relaxation)
  - Sources of informational support/resources (patient library, reliable internet sites)
  - Availability of supportive care services (e.g., professionally led groups, informational lectures, etc.) for the patient and family at the institution or in the community
  - Availability of financial support (e.g., accommodations, transportation, health/drug benefits)
  - Information about signs and symptoms of depression and avenues for care
  - Information on sleep hygiene and self-management of fatigue
  - Information on other intervention resources for physical activity, nutrition, or relevant others
#1. Screen and implement what exists now.

#2. Expand dissemination/implementation of what exists now.

#3. Stimulate and reinforce innovations in intervention research.

#4. Embrace the “whole” cancer patient.
NCI Dissemination/Implementation Grant Awards, 2003-2012

(TBM, Neta et al., 2015)
Trainees (N=108)
Usage: Implementation & Sustainment

% of all Patients

Months

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

2 4 6 8 10 12
#1. Screen and implement what exists now

#2. Expand dissemination/implementation of what exists now.

#3 Stimulate and reinforce innovations in intervention research.

- Optimize interventions (NOT “How low can you go”)
- Expand outcomes
  - e.g., health, costs
- Shift some interventions to eHealth
Moving Forward, #4

#1. Screen and implement what exists now.

#2. Expand dissemination/implementation of what exists now.

#3. Stimulate and reinforce innovations in intervention research.

#4. Embrace the “whole” cancer patient.
The Number of Psychosocial Intervention RCTs by 2015

- Adult Cancer Survivors: 307
- Mixed Groups (C+m): 13
- African American Cancer Survivors: 8
- Hispanic Cancer Survivors: 3
- Mixed Minorities (H+AA): 2
- Pacific Islander Cancer Survivors: 1
- Asian American Cancer Survivors: 0
Needs for the Future: Patients

- Overweight/Obese: 44.3%
- Non-Caucasian: 60.0%
- Alone: 70.0%
- Uninsured: 15.4%
- Diabetes: 9.6%
- Substance Use Disorders: 9.3%
- Poverty: 68.8%
- >65 years: 68.8%

The Cancer Patient
Thank you
Acknowledgments

- American Cancer Society & Longaberger
  PBR-89, RSGPB-03-248-01-PBP

- National Cancer Institute
  R01 CA92704, K05 CA098133, 2K05 CA098133, R25E CA163197

- US Army Breast Cancer Program
  DAMD 17-94-J-4165, DAMD 17-96-16294

- National Institute of Mental Health
  R01 MH51487