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Impact Of Major Depressive Disorder On Patients, Caregivers, Payers & Employers

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Objectives

- Explore the burden of major depressive disorder (MDD) on the patient, caregiver, payer, and employer.
- Discuss the negative impact of residual symptoms.
- Understand the importance of remission in optimizing overall functioning and quality of life.

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Did You Know?

- Per a 2001 report, patients with MDD were approximately 20 times more likely to commit suicide than the general public.[1]
- Having 1 employee with depression was reported to cost an employer between an estimated $20,000 and $35,000 in direct and indirect costs over 2 years (2004–2007 data).[2]
- In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study (a randomized, controlled treatment trial in outpatients with MDD [N = 4041]), patients who were treatment responders without remission were about twice as likely as those in remission to suffer a relapse during the first year following successful treatment.[3,4]

1. Osby U et al. *Arch Gen Psychiatry*. 2001:58:844-850
2. Ivanova JI et al. *Curr Med Res Opin*. 2010;26:2475-2484
3. Rush AJ et al. *Am J Psychiatry*. 2006;163:905-1917
4. Thase ME. *J Clin Psychiatry*. 2009;70(suppl 6):4-9

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Prevalence Of MDD

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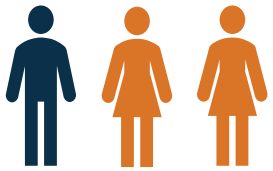
Prevalence Of Depression

US depression rate by adult age group[2]

	18-25	26-49	50+
Depression Rate	13.1	7.7	4.7



Nearly twice as common in women than in men[1,3]

- Of the adults reporting MDD, 63.8% reported severe impairment, representing 4.5% of adults in the US[2]

8 years

The projected median time between MDD onset and first contact with a care provider[4]

1. Brody et al 2018 *NCHS Data Brief* No 303
2. https://www.nimh.nih.gov/health/statistics/major-depression.shtml
3. Bogren et al 2018 *Eur Arch Psychiatry Clin Neurosci* 268: 179-189
4. Wang et al 2005 *Arch Gen Psychiatry* 62: 603-613

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Impact Of MDD On Patients, Caregivers, And Offspring

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Impact Of MDD On Patients And Others

- The impact of MDD on patients includes the comorbidity of MDD and other illnesses,[1] the negative impact on the patient's quality of life (QoL),[2] and the increased risk of suicide.[3]
- The impact of MDD on caregivers includes the negative impact on the caregiver's QoL,[4] concerns about the future,5 and interpersonal difficulties with the patient.[5]
- The impact of MDD on a patient's children include an increased risk of mental and physical illnesses[6,7] and higher healthcare expenditures in the children.[8]

1. Goodwin G et al Dial Clin Neurosci 2006; 8:259-265
2. IsHak WW et al. *Qual Life Res*. 2013;22:585-596;
3. Sokero TP et al. *Br J Psychiatry*. 2005;186:314-318;
4. Zendjidjian X et al. *J Affect Dis*. 2012;136:660-665;
5. Martire LM et al. *Psychiatry Res*. 2009;168:67-77;
6. Pilowsky DJ et al. *J Acad Child Adolesc Psychiatry*. 2006;45:452-460;
7. Weissman MM et al. *Am J Psychiatry*. 2006;163:1001-1008;
8. Olfson M et al. *Med Care*. 2003;41:716-721.

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Burden Of Disease To The Individual

In a 2012 review of the societal costs of MDD to the individual:

- Physical:
  - From meta-analyses of longitudinal studies (mostly from the US), MDD was a consistent predictor of the subsequent first onset of a variety of chronic physical disorders (ie, coronary artery disease, stroke, diabetes, heart attacks, and certain types of cancer).
- Financial:
  - Personal earnings and household incomes of people with MDD were found to be substantially lower than those of people without depression (though it was unclear whether depression was primarily a cause, a consequence, or both).
- Education:
  - Several studies showed that MDD was associated with an approximate 60% elevated risk of failure to complete secondary school than otherwise comparable youth in high-income countries.

1. Kessler RC. *Psychiatr Clin North Am*. 2012;35(1):1-14

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Impact On Patient QoL

- Early studies noted that greater MDD symptom severity was associated with poorer QoL.[1,2]
- A 2013 US-based, cross-sectional study was conducted with 319 consecutive outpatients seeking treatment for DSM-IV–diagnosed MDD at an urban hospital-based outpatient clinic from 2005 to 2008. The report found that:
  - MDD may negatively impact different aspects of an individual's life, leading to substantial impairment in QoL.[3]
- Further, individuals with MDD scored >2 standard deviations (SDs) below community norm means on the Quality of Life, Enjoyment, and Satisfaction Questionnaire–Short Form (Q-LES-Q; 39.8% [SD 16.9] vs 78.3% [SD 11.3])[3]:
  - Increasing levels of depressive symptom severity were associated with poorer QoL, functioning, and work productivity outcomes
  - Areas of greatest impairment included work, sexual drive, mood, economic status, and overall sense of wellbeing.
- Remission from MDD was associated with significant ($p < 0.05$) improvement in QoL, as measured by the Short Form-12 Health Survey (SF-12).[4]

1. Trivedi MH et al. *J Clin Psychiatry*. 2006;67:185-195
2. Daly EJ et al. *Ann Clin Psychiatry*. 2010;22:43-55
3. IsHak WW et al. *Qual Life Res*. 2013;22:585-596
4. Rubio JM et al. *J Clin Psychiatry*. 2013;74:e445-e450

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Impact On Patient QoL: Disability

- In a systematic review of epidemiology data, depressive disorders were:[1]
  - A leading cause of disability-adjusted life years (DALYs) in 2010
  - The second-leading cause of years lived with a disability in 2010.
- Unipolar major depression is predicted to be the second-leading worldwide cause of DALYs in 2020 (after ischemic heart disease), compared with being the fourth-leading cause in 1990.[2]

1. Ferrari AJ. *PLOS Medicine*. 2013;10:e1001547. doi:10.1371/journal.pmed.1001547
2. Murray CJ and Lopez AD. *Science*. 1996;274:740-743

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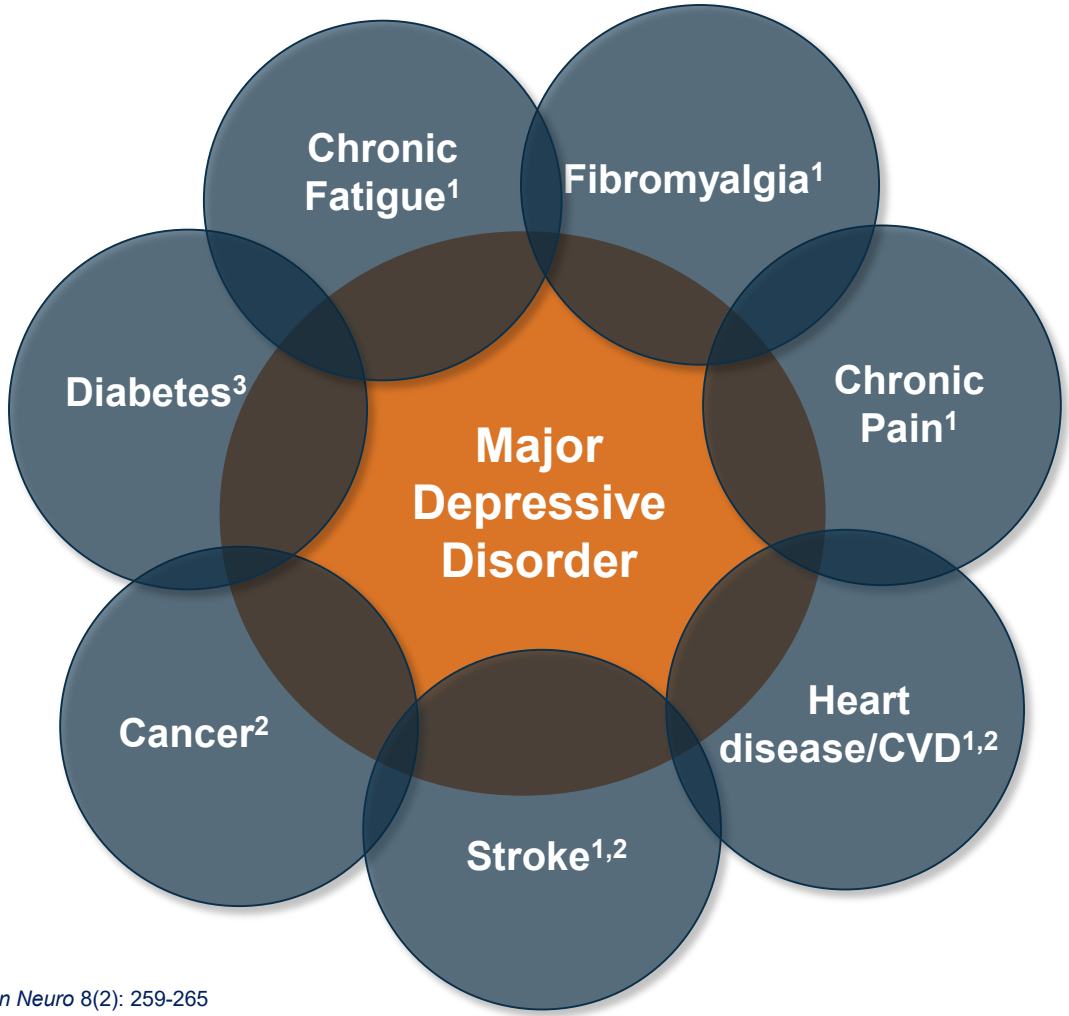
Association Between Depression And Other Medical Illnesses



1. Goodwin G et al. 2006. *Dial Clin Neuro* 8(2): 259-265
2. Kang HJ et al 2015. *Chonnam Med J* 51: 8-18
3. Mezuk B et al 2008. *Diabetes Care* 31: 2383-2390

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Depression As A Risk Factor For Heart Disease:
A Scientific Statement From The American Heart Association

- A 2014 report based on a systematic literature review of depression and adverse medical outcomes after acute coronary syndrome (ACS) noted:
  - 53 Studies and 4 meta-analyses met inclusion criteria.
- The majority of relevant studies (21/32) suggested that depression was a risk factor for all-cause mortality after ACS.
- The majority of relevant studies (8/12) suggested that depression was a risk factor for cardiac mortality after ACS.
- The American Heart Association panel of authors suggested that depression should be elevated to the status of a risk factor for poor prognosis in patients with ACS.

1. Lichtman JH et al. *Circulation*. 2014;129. Epub ahead of print.

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Suicide Risk In MDD

- In a Finnish study of 269 patients diagnosed with MDD:
  - Significant differences between those attempting suicide and those not attempting suicide were seen in terms of:
    - Severity of index episode of depression ($p = 0.02$)
    - Amount of suicidal ideation and anxiety ($p = 0.008$ and 0.026, respectively)
    - Prevalence of suicide attempts during the index episode ($p = 0.003$)
    - Time to full remission ($p = 0.002$)
    - Total time in depression ($p = 0.002$).

1. Sokero TP et al. *Br J Psychiatry*. 2005;186:314-318.

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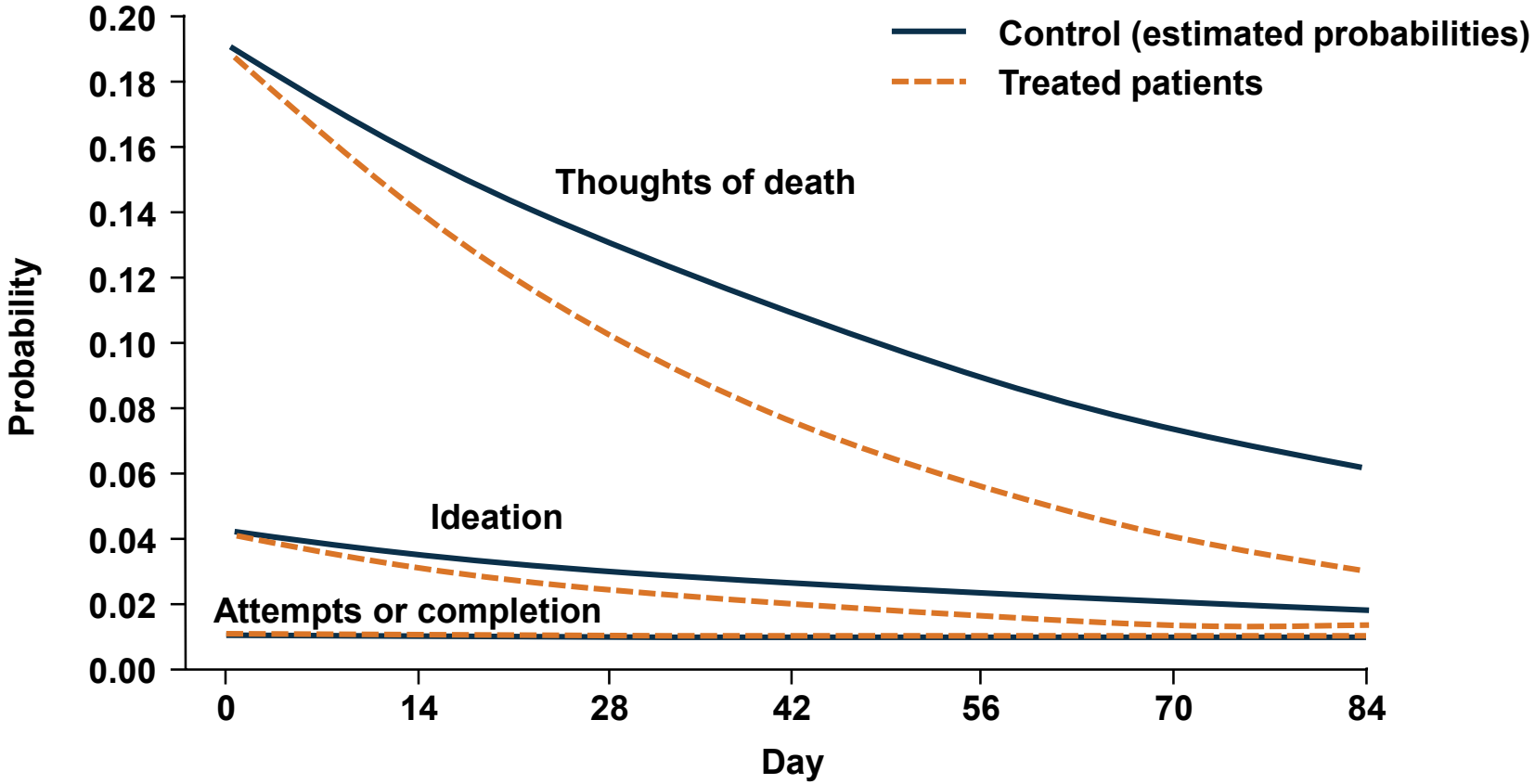
Suicidal Thoughts, Ideations, And Attempts In MDD



Note: Data from this 2012 publication are derived from 31 randomized controlled trials of fluoxetine and venlafaxine in patients with MDD (amounting to a total of 53260 person-week observations).

1. Gibbons RD et al. *Arch Gen Psychiatry*. 2012;69(6):580-587.

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Suicide Attempts In MDD: Depression-Related Characteristics

Characteristic	No suicide attempt (n = 182)	Suicide attempt (n = 16)	P-value
Severity of depression at baseline, n (%)			0.02
Mild	11 (6)	-	
Moderate	99 (54)	4 (25)	
Severe	72 (40)	12 (75)	
Mean (SD) time to full remission, months	4.0 (4.7)	8.1 (7.5)	0.002
Mean (SD) total time in depression, months	4.4 (4.7)	8.6 (7.1)	0.002

- Data from a 2005 report on the Finnish Vantaa Depression Study showed that, of the 41 discrete suicide attempts that occurred in 16 patients over 18 months, 25 occurred during a major depressive episode, 12 during partial remission, and 4 during full remission.
- The risk of a suicide attempt was almost 8-fold higher during a major depressive episode compared with a period of full remission (relative risk 7.54).

SD, standard deviation.

1. Sokero TP et al. *Br J Psychiatry*. 2005;186:314-318.

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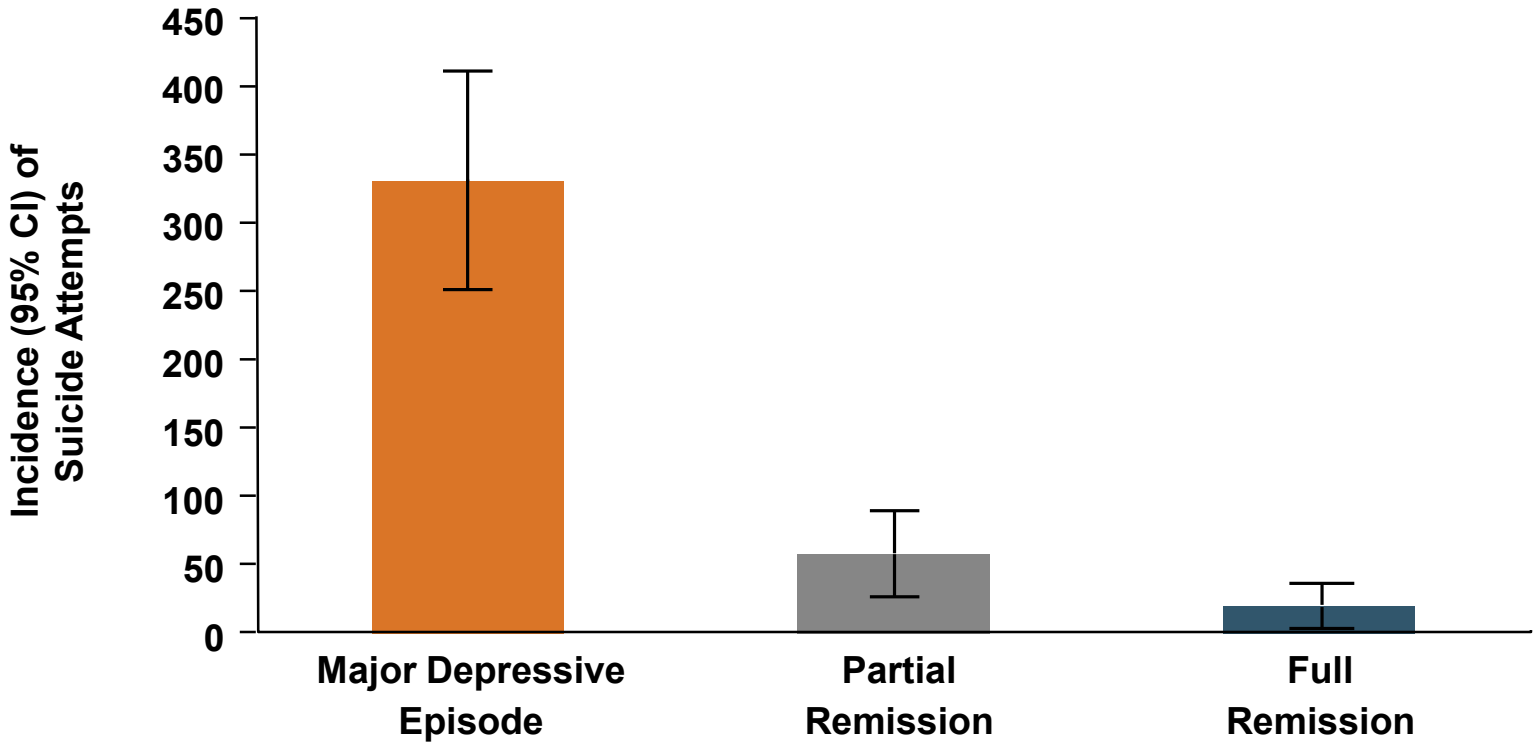
Incidence Of Suicide Attempts In MDD



Note: Data indicate the incidence rate per 1000 patient-years based on Poisson distribution

Over 5 years follow-up in this Finnish study, the risk of suicide attempts was nearly 21-fold greater during a major depressive episode compared with full remission (N = 332 vs 16 per 1000 patient-years).

1. Holma KM et al. *Am J Psychiatry*. 2010;167:801-808.

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Factors Related To Suicide Attempts In MDD

186 Individuals in Thailand with MDD who had attempted suicide were assessed between October 2006 and May 2009 and compared to 4 times as many case-controls:

- Factors related to suicide attempts:
  - Stressful life events
  - Alcohol use
  - Intermittent/poor psychiatric medication adherence
  - Up to 2 previous suicide attempts
  - Prescribed antipsychotics.
- Factors inversely related to suicide attempts:
  - Increasing years of MDD treatment
  - Being prescribed an antidepressant (particularly norepinephrine and/or a serotonin reuptake inhibitor).

1. Ruengorn C et al. *Int J Gen Med*. 2012;5:323-330.

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Impact Of Being A Caregiver

- A 2004 US report estimated that more than 44 million Americans were caregivers of people with a wide range of disabilities, including mental health issues[1,2]:
  - Most caregivers said they experienced few adverse issues but those who provided the most hours and the most intense care experienced the most strain.
- The well-being of caregivers was noted as a public health concern due to the associated psychological and physical problems[1,3]:
  - Specific psychological problems included depression and anxiety[1]
  - Specific physical problems included decreased immunity, greater cardiovascular reactivity, slow wound healing, and increased risk for serious illness.[3]
  - Risk of mortality was also increased in caregivers who experienced caregiver strain[4]:
    - Mortality risks were 63% higher than among noncaregiving controls.

1. Phillips AC et al. *Br J Clin Psychology*. 2009;48:335-346
2. National Alliance for Caregiving/AARP. *Caregiving in the U.S.* 2004. Washington DC
3. Schulz R et al. *JAMA*. 1999;282:2215-2219
4. Perkins M et al. *Psych Sci Soc Sci*. 2013;68:504-512

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MDD During And After Pregnancy

- There appears to be an increased risk of depression during pregnancy compared with subsequent years[1]:
  - In a long-term UK-based study of 151 mothers from an inner-city location who were followed from pregnancy for 16 years, 90% of women who were depressed during pregnancy became depressed in the future.
- Pregnant women with psychiatric disorders rarely seek mental health treatment[2]:
  - Data from a US National Survey of > 14,500 women (conducted between 2001–2002) found that 26% of nonpregnant women had sought treatment for a mood disorder in the past 12 months, compared with 14% of pregnant women.
- The risk of MDD may be increased during the postpartum period
  - One study found a significantly higher prevalence of MDD in postpartum women than in nonpregnant women.

1. Pawlby S et al. *J Affect Dis*. 2009;113:236-243
2. Vesga-Lopez O et al. *Arch Gen Psychiatry*. 2008;65:805-815

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Increased Risk Of Illness In Children Of Depressed Parents

- It has been reported that children of depressed parents are approximately:
  - 6 Times more likely than those without depressed parents to have MDD or dysthymia[1]
  - 5 Times more likely to have depression by age 16[2]
  - 4 Times more likely to have anxiety[1]
  - 3 Times more likely to have a mood or anxiety disorder[3]
  - 3 Times more likely to be diagnosed with substance dependence[3]
  - 6 Times more likely to have cardiovascular disease[3]
  - 2 Times more likely to have neuromuscular disease.[3]

Remission of parental depression has been associated with a reduction in child diagnosis and symptoms[4]

1. Pilowsky DJ et al. J Acad Child Adolesc Psychiatry; 2006;45:452-460
2. Pawlby S et al. *J Affect Disorders*. 2009;236-243
3. Weissman MM et al. *Am J Psychiatry*. 2006;163:1001-1008
4. Weissman MM et al. *JAMA*. 2006; 295(12):1389-98

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Healthcare Expenditures In Children Of Depressed Parents

Mean total annual child health expenditure*
$282 vs $214
(p = 0.0006)

Mean total annual child mental health expenditure*
$513 vs $338
(p = 0.0006)

*For children of parents with depression compared with children of parents without depression in the US
Study used data from a 1997 Medical Expenditure Panel Survey; values then inflated to 2001 US dollars.

1. Olfson M et al. *Med Care*. 2003;41:716-721

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Impact Of MDD On Payers And Employers

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US-Based HEDIS Antidepressant Medication Management Measures

- Eligible member population:
  - ≥ 18 Years of age and diagnosed with major depression, newly treated with antidepressant medication, and remained on antidepressant medication treatment.
- Effective acute-phase treatment:
  - The percentage of members who remained on an antidepressant medication for at least 84 days (12 weeks).
- Effective continuation-phase treatment:
  - The percentage of members who remained on an antidepressant medication for at least 180 days (6 months).

1. National Committee for Quality Assurance. *The State of Health Care Quality*. Oct 2014

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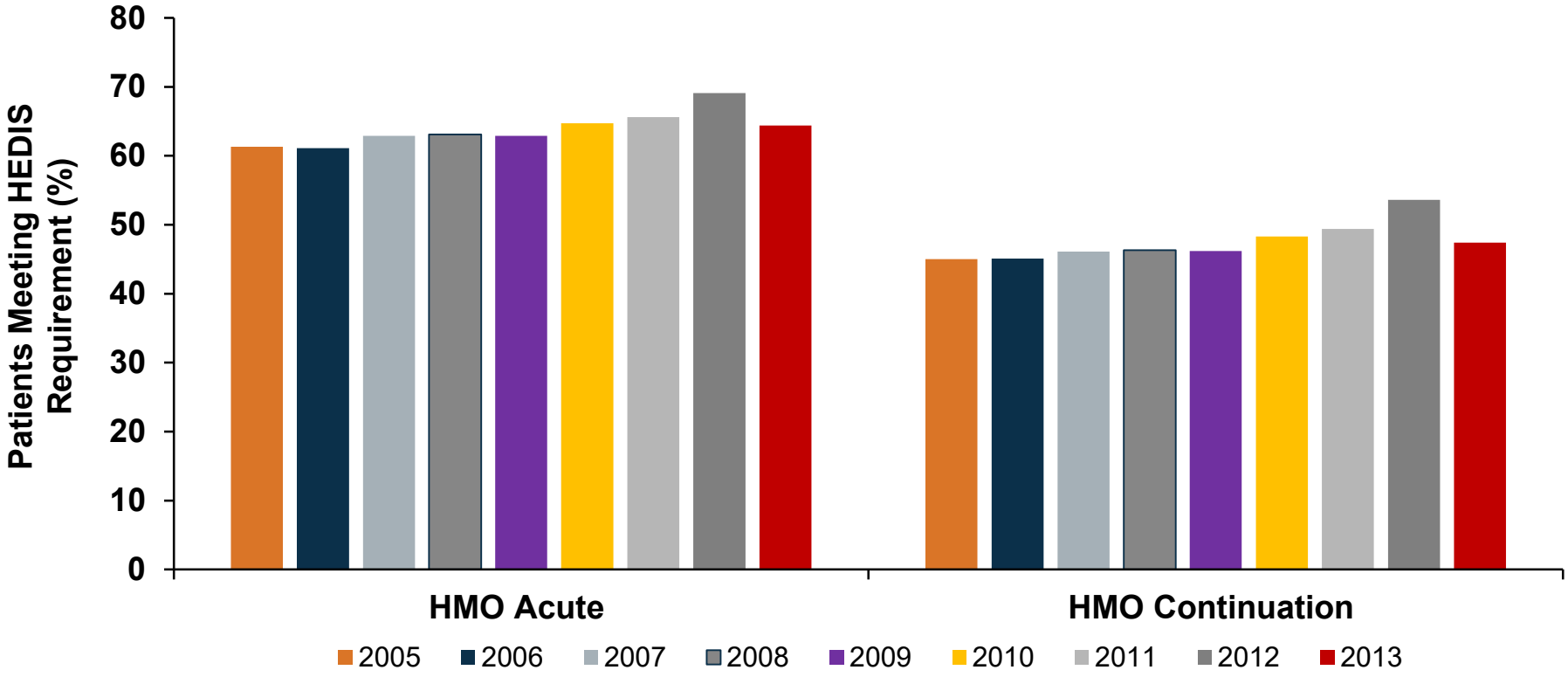
Impact On Payers: Commercial Plan Performance On HEDIS (HMO Values)



Follow-up rates for the HEDIS antidepressant measures have improved minimally over time

These data are for HMO Commercial plans.

1. National Committee for Quality Assurance. *The State of Health Care Quality*. Oct 2014

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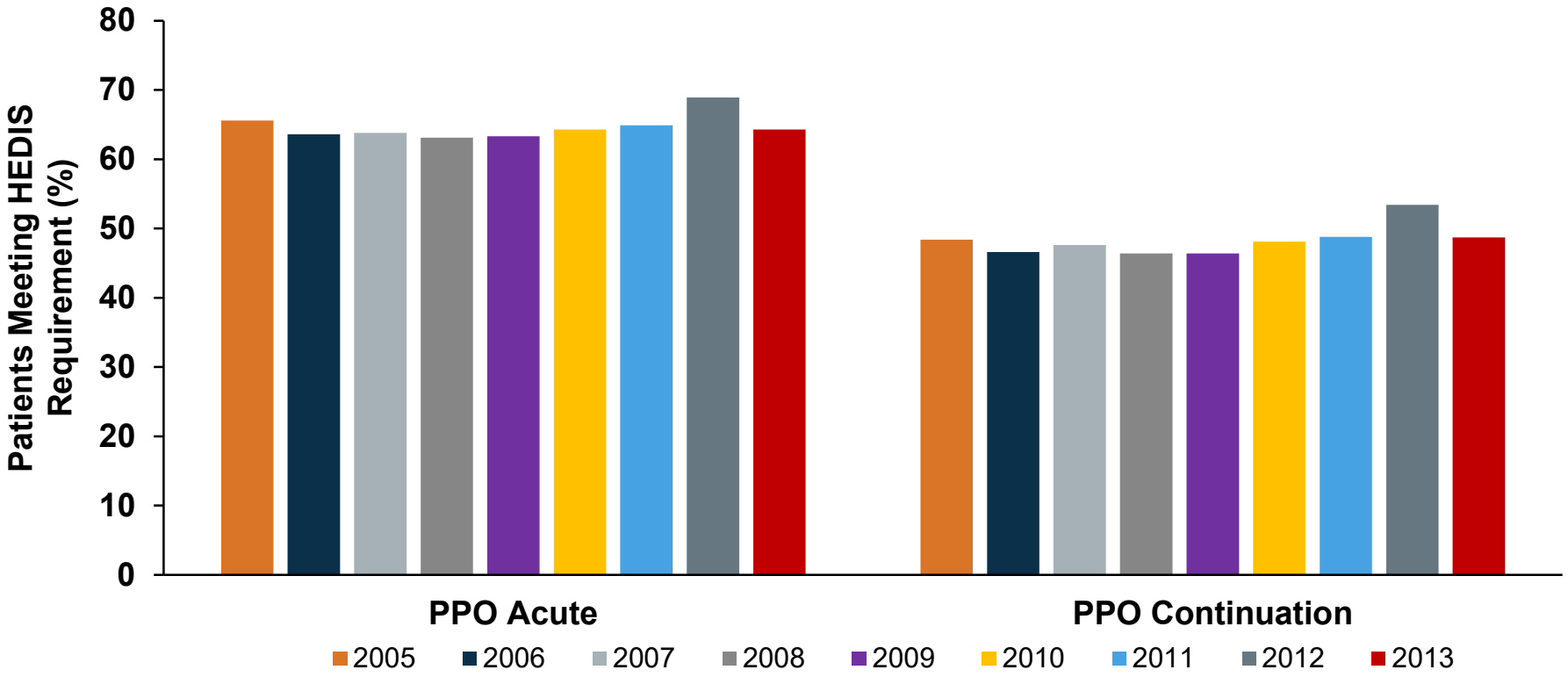
Impact On Payers: Commercial Plan Performance On HEDIS (PPO Values)



Follow-up rates for the HEDIS antidepressant measures have improved minimally over time

These data are for PPO Commercial plans.

1. National Committee for Quality Assurance. *The State of Health Care Quality*. Oct 2014

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Impact Of MDD On Employers

- Depression adversely affects functioning, but a 2004 study was one of the first to report on the magnitude of its impact on work productivity in the US[1]:
  - Depression contributed to reduced functioning, decreased work productivity, and absenteeism.
- Productivity at work is an important business-related metric, and depression-specific costs to corporate America are being quantified.[1]
- National payers have developed programs aimed at improving depression outcomes[2]:
  - One program for severely affected members showed that participants gained 7.7 work days per month and reduced costs associated with emergency room use, inpatient length of stay, outpatient visits, and behavioral health inpatient stays.

1. Rost K et al. *Med Care*. 2004;42:1202-1210
2. Golinkoff M. *J Manag Care Pharm*. 2007;13(suppl S-a):S23-S27

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Impact Of MDD On Employers: Absenteeism And Presenteeism

- Evidence about the total cost of health, absence, short-term disability, and productivity losses was synthesized for 10 health conditions in a 2004 US study.
- Cost estimates from a large medical/absence database were combined with findings from several published productivity surveys.
- Ranges of condition prevalence and associated absenteeism and presenteeism losses were used to estimate condition-related costs and were monetized utilizing the year 2001 average hourly wages and benefits for all US companies.
- Based on average annual impairment and prevalence estimates:

1 Employee with depression/sadness/ mental illness costs an employer:

$4700/year for absenteeism

$250/year for presenteeism*

*On-the-job productivity losses.

1. Goetzel RZ et al. *J Occup Environ Med*. 2004;46:398-412

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Impact Of MDD On Employers:

Employees With Depression Who Are Likely To Be Treatment Resistant

Direct 2-year costs:

Likely treatment resistant: $22,784
MDD controls: $11,733

Indirect 2-year costs:

Likely treatment resistant: $12,765
MDD controls: $6885

Costs are in 2007 US dollars. Direct 2-year costs are “all-cause direct costs.”

1. Ivanova JI et al. *Curr Med Res Opin*. 2010;26:2475-2484

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Cost Of Lost Productive Work Time (LPT) Among US Workers With Depression

- N = 219 workers with MDD.
- LPT among those with depression was compared to expected LPT in subjects without depression projected to the US workforce.
- Of the 219 patients with depression (including MDD, partial remission, dysthymia), 77% reported some LPT during the 2-week recall period, the majority of which time was lost at work:
- MDD accounted for 48.5% of LPT among those with depression, with the majority of the cost explained by reduced performance at work
- LPT was higher for patients with MDD (mean of 8.4 hours/week), followed by those with partial remission (5.3 hours/week), and dysthymia (3.3 hours/week).

1. Stewart WF et al. *JAMA*. 2003;289:3135-3144

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Reasons For Lost Productive Time (LPT) Between Workers With And Without Depression

Type of LPT	MDD population: mean (SE) LPT (hours / worker / week)	Expected mean LPT in absence of depression
Absenteeism	1.2 (0.4)	0.4
Presenteeism	7.2 (1.3)	1.1
Total LPT	8.4 (1.3)	1.5
Pain/weakness/fatigue	10.0 (1.2)	5.1
Gastrointestinal complaints	10.7 (1.5)	2.0
Panic/anxiety	9.3 (1.7)	4.1
Faintness/dizziness	8.9 (2.4)	4.5
Autonomic instability	9.5 (1.9)	6.5
Ears ringing/head or nose fullness	8.1 (1.2)	2.8
Sensory or nerve impairment	10.0 (1.4)	3.2
None	5.8 (3.7)	0.8

SE, standard error.

1. Stewart WF et al. *JAMA*. 2003;289:3135-3144

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Unemployment And Disability

- In a nationally representative US survey, over 4000 US workforce respondents (English speaking, ≥ 18 years of age) were classified by clinical severity of depression (from “severe” to “not depressed”).
- For those 539 employees reported as having depression, prevalence rates of unemployment or disability increased significantly with MDD severity, as did the monthly salary-equivalent of lost performance.

MDD Severity	Unemployment/ disability (%)	(Estimated) Monthly cost of reduced work and performance ($)
Mild	16	44
Moderate	23	188
Severe	31	199

1. Birnbaum HG et al. *Depress Anxiety*. 2010;27:78-89

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Cost Of MDD: Stable VS Nonstable Disease

- Stable MDD has lower costs than less-stable disease*:
  - Per a 2009 analysis of claims data (from 1999–2004) for US privately insured employees with MDD, annual per-patient adjusted costs (2005 values) were:
    - Stable patients: $6215
    - Intermediately stable: $7317
    - Nonstable: $9948.
  - Total cost differences between stable, intermediately stable, and nonstable patients were statistically significant ($p < 0.001$).

*Stable patients maintained treatment during the initial period (first 12 weeks) without switching or adding treatment during the subsequent period (Week 13–26), or they discontinued treatment during the initial period without restarting another treatment in the subsequent period (ie, they do not require further treatment). Nonstable patients either switched or added on treatments during the subsequent period and did not achieve stability of symptom management.

1. Birnbaum HG et al. *Pharmacoeconomics*. 2009;27:507-517

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Total Societal Costs (2000)

Type of cost	Dollars (in billions)	Percentage of Total	Cost/Case (in dollars)
Total costs*	83.08	100.0	8118
Direct cost†	26.09	31.4	3309
Inpatient	8.88	10.7	1127
Outpatient	6.80	8.2	863
Pharmaceutical	10.40	12.5	1319
Suicide-related costs‡	5.45	6.6	302
Workplace costs§	51.54	62.0	4507
Absenteeism	36.25	43.6	3169
Presenteeism	15.30	18.4	1337

*Total costs = direct, suicide-related, and workplace costs.

†Direct treatment costs were estimated based on published utilization data for individuals recorded as receiving any medical treatment for depression in 2000.

‡Suicide-related costs were estimated using a human capital framework based on the total number of suicides by age and gender cohort in 2000, as reported by the Centers for Disease Control.

§Workplace costs were estimated as the wage-based value of both absenteeism (ie, days missed from work due to depression) and presenteeism (ie, reduced productivity while at work due to depression).

Note: Cost/case may not equal total cost divided by population estimates due to rounding.

1. Greenberg PE et al. *J Clin Psychiatry*. 2003;64(12):1465-1475

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Residual Symptoms And Remission In MDD

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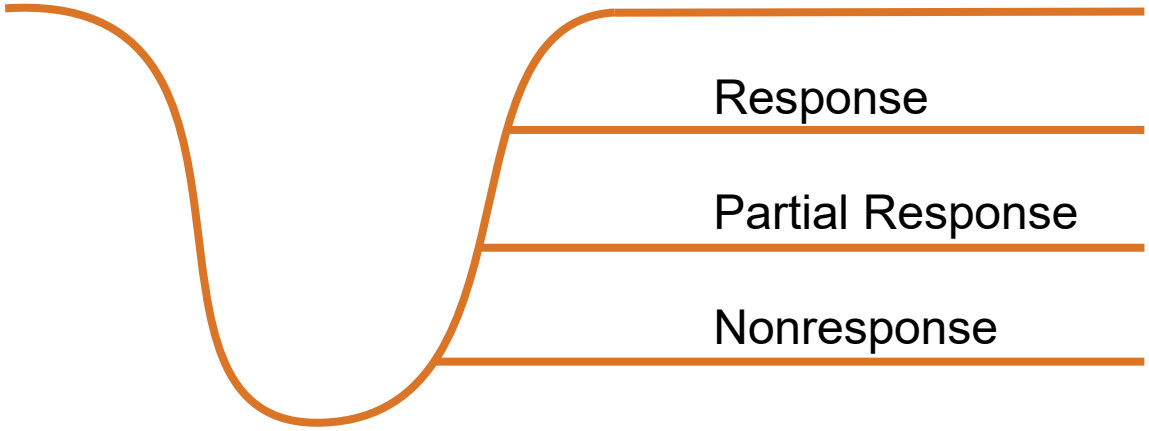
Remission Is The Goal



% Reduction in Score

Remission	MADRS: total score ≤ 8[1]
Response	MADRS: ≥ 50%[1]
Partial Response	HAM-D: 50%[2]
Nonresponse	HAM-D: < 50%[2]

Remission has also been defined as attainment of a virtually asymptomatic status (17-item Hamilton Depression Rating Scale [HDRS] score ≤ 7).[3]

1. Weisler R et al. *CNS Spectrums*. 2009;14(6):299-313
2. Mauskopf JA et al. *J Depress Anxiety*. 2009;26:83-97
3. Zimmerman M et al. *J Clin Psychiatry*. 2012;73:790-795

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Common Unresolved Or Residual MDD Symptoms

- Types, and frequencies, of residual symptoms[1]:

- Guilt (28.1%)
- General somatic symptoms (27.1%)
- Depressed mood (27.1%)
- Psychic retardation (13.8%)
- Agitation (13.3%)
- Motor retardation (5.9%)
- Suicidal ideation (2.5%)

Other residual/unresolved MDD symptoms that have been reported included: core mood symptoms,[2] anxiety,[2,3] irritability and/or inner tension,[3] somatic symptoms (including pain),[2,4] sexual dysfunction,[3] and impairment of work and/or activities.[3]

1. Iovieno N et al. *J Depress Anxiety*. 2011;28:137-144
2. Romera I et al. *BMC Psychiatry*. 2013;13:51
3. Trivedi MH et al. *J Clin Psychiatry*. 2008;69(2):246-258
4. Trivedi MH. *J Clin Psychiatry*. 2004:6(Suppl 1)12-16

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Residual Symptoms After Remission: STAR*D Proportion Of Remitters With At Least Mild or Moderate Levels Of Residual Symptoms (n = 943)

	At least mild symptoms* (% of patients)	At least moderate symptoms† (% of patients)
Weight increase	71.3	21.7
Mid-nocturnal insomnia	54.9	40.5
Increased appetite	50.6	9.5
Sleep-onset insomnia	29.5	9.7
Sad mood	27.1	0.4
Hypersomnia	24.0	2.4
Energy	22.5	1.7
Concentration/decision making	20.9	0.9
Weight decrease	16.7	4.5
Early morning insomnia	16.6	6.8
Restless	15.2	0.9
Decreased appetite	12.2	0.6
Involvement	9.4	1.8
Outlook self	6.8	0.4
Slowed down	5.8	0.3
Suicidal ideation	1.3	0.3

*Defined as any 16-item Quick Inventory of Depressive Symptomatology, Self-Report ($QIDS\text{-}SR_{16}$) item ≥ 1; †Defined as any $QIDS\text{-}SR_{16}$ item ≥ 2.
QIDS-SR, Quick Inventory of Depressive Symptomatology; STAR*D, Sequenced Treatment Alternatives to Relieve Depression.

1. Nierenberg AA et al. *Psychol Med*. 2010;40(1):41-50

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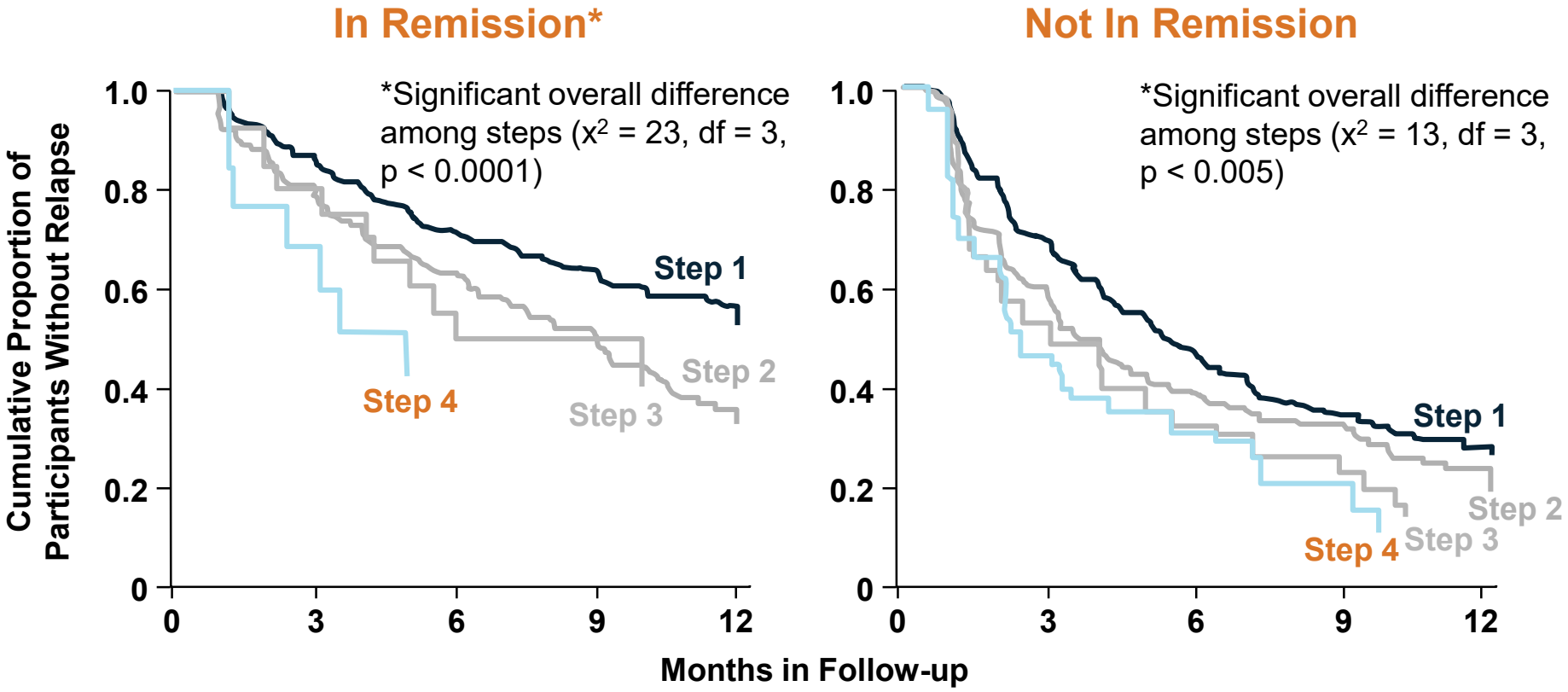
Comparison Of STAR*D Participants

Relapse During Follow-up Phase by Number of Acute Treatment Steps for STAR*D Participants Who Entered the Follow-up Phase:



*Remission defined as Quick Inventory of Depressive Symptomatology-Self-Report ($QIDS\text{-}SR_{16}$) ≤5.

1. Rush AJ et al. *Am J Psychiatry*. 2006;163:905-1917

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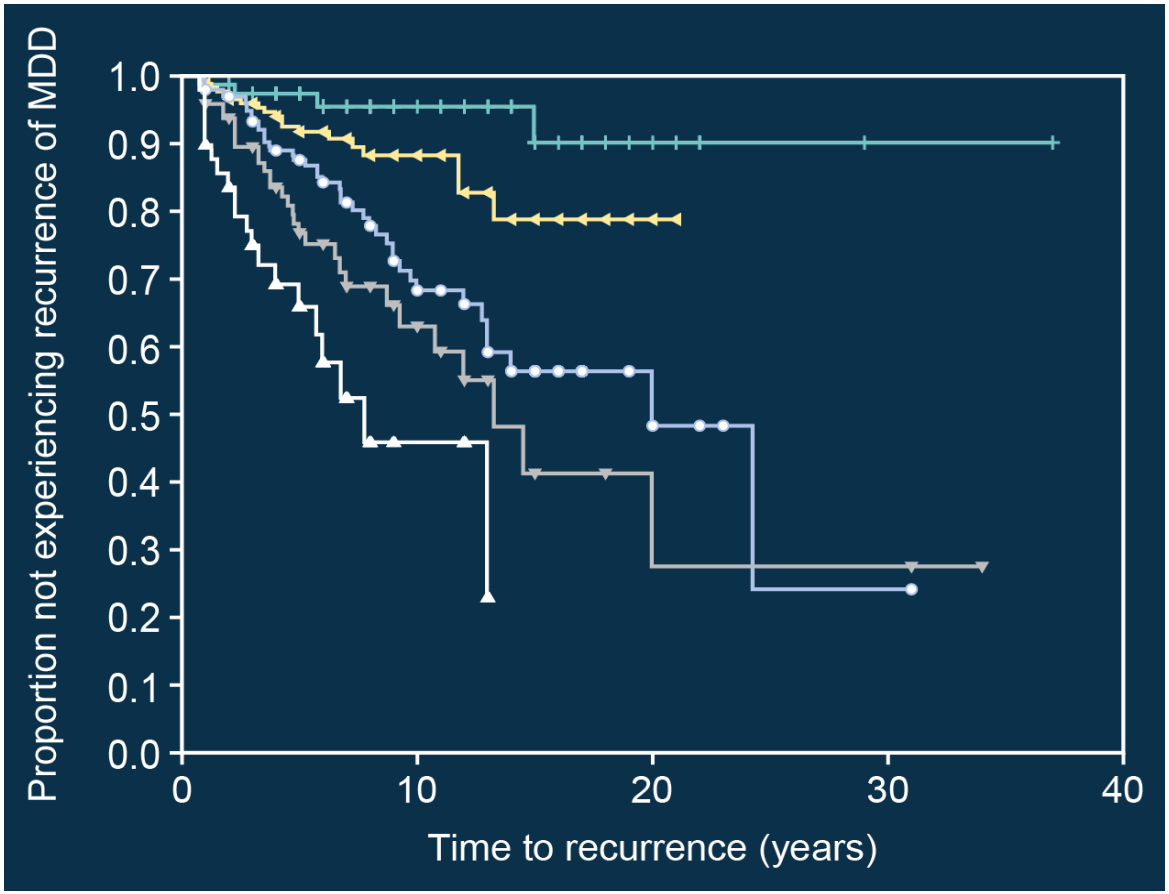
Predictors Of Recurrence In MDD



No. of Predictors of Recurrence:

0 + (n = 78)

1 ◀ (n = 175)

2 ○ (n = 197)

3 ▼ (n = 97)

≥ 4 △ (n = 49)

Survival curve of time to recurrence of a major depressive episode (MDE) in a cohort from The Netherlands Mental Health Survey and Incidence Study (NEMESIS) divided into respondents with 0 (+), 1 (◀), 2 ( ) 3 (▼), or ≥ 4 ( ) predictors.

Predictors were: age < 30 years; ongoing difficulties present; traumatic youth experiences present; severe last depressive episode; or recurrent MDD.

1. Hardeveld F et al. *Psychol Med*. 2013;43:39-48

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Symptoms Predictive Of Poor Outcome

- Anxiety[1]:
  - Patients with anxious depression (defined as a baseline Hamilton Depression Rating Scale-21 anxiety/somatization factor score ≥7) were less likely to remit (49% vs 62%) and took longer to remit (44 vs 30 days) vs nonanxious depression.
- Anxious distress[2]:
  - New DSM-5 specifier for Depressive Disorders
  - Associated with higher suicide risk, longer duration of illness, and greater likelihood of treatment nonresponse.
- Subthreshold anxiety[3]:
  - Patients with MDD and subthreshold anxiety (defined as anxiety disorder not otherwise specified) had a longer latency of antidepressive response and a lower decrease in symptoms severity vs MDD and any anxiety disorder.

DSM, Diagnostic and Statistical Manual; MDD, major depressive disorder; NOS, not otherwise specified.

1. Wiethoff K et al. *J Clin Psychiatry*. 2010;71:1047-1054;
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC: American Psychiatric Association; 2013
3. Altamura et al. *Int J Neuropsychopharm*. 2004;7:481-487

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Reported Predictors Of Poor Response To Treatment

- Medical cormorbidity[1]:
  - Hypercholesterolemia
  - Greater body weight
  - Hypofolatemia
  - MRI white matter hyperintensities.
- Depressive symptoms[1]:
  - Hopelessness
  - Cognitive impairment (executive dysfunction)
  - Somatic symptoms
  - Psychomotor retardation.

In addition, lack of an early treatment response has been reported to be predictive of a poor treatment response.[2]

1. Papakostas GI et al. *Dialogues Clin Neurosci*. 2008;10:439-451
2. Henkel V et al. *J Affect Disord*. 2009;115:439-449

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Residual Symptoms

- From a meta-analysis of randomized, double-blind, placebo-controlled trials published between 1980 and mid-2007, pooled results noted that about approximately half of patients receiving antidepressants experienced a ≥ 50% reduction in symptoms.[1]
- Among patients with MDD treated in one of two academically affiliated, depression-specialty clinics, only 50% achieved full remission.[2]
- Compared with patients who achieved full remission, those with residual symptoms had[1]:
  - A greater risk of relapse and recurrence
  - More chronic depressive episodes
  - Shorter duration between episodes
  - Continued impairment in work and relationships.

1. Papakostas GI. J *Clin Psychiatry*. 2009;70 (suppl 6):16-25
2. Papakostas GI et al. *Dialogues Clin Neurosci*. 2008;10:439-451

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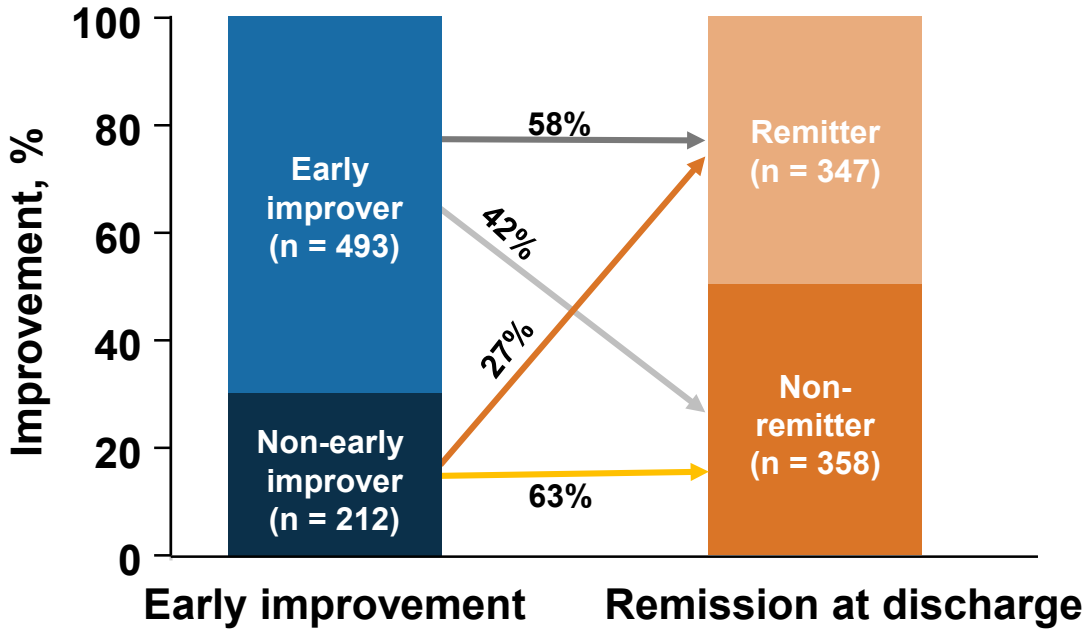
Early Improvement And Remission



- Results from 2 publications (a German study of 795 patients with major depression[1] and a systematic review of 41 trials in MDD [N = 6562][2]) found that earlier onset of response before 2 weeks of treatment was common and highly predictive of better later outcomes.
- Based on results from these and other studies, Möller et al recommended that, if no improvement was observed after 2 weeks, then treatment should be adjusted or changed immediately.[3]

1. Henkel V et al. *J Affect Disord*. 2009;115:439-449
2. Szegedi A et al. J Clin Psychiatry. 2009;70:344-353
3. Möller HJ et al. *Medicographia*. 32;2010:139-145

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Identifying The Inadequately Treated Patient

- A meta-analysis of 41 clinical trials (N = 6562) revealed that a treatment response or remission was unlikely if there was no improvement within the first 2 weeks of treatment.[1]
- Assessment tools to evaluate changes in symptom states during the first 4 weeks of treatment may also predict treatment response at 12 weeks[2]:
  - A US post-hoc analysis of 996 patients treated for MDD; data were collected from October 1992 to November 1994.
  - Dividing the HAM-D-17 into symptom clusters (mood, sleep/psychic anxiety, appetite, and somatic anxiety/weight) and evaluating change scores at 4 weeks correctly assigned up to 70% of patients as late responders or nonresponders at 12 weeks.

1. Szegedi A et al. *J Clin Psychiatry*. 2009;70:344-353
2. Trivedi MH et al. *J Clin Psychiatry*. 2005;66(8):1064-1070

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Summary

- Major depressive disorder can have a pervasive impact on patients, caregivers, payers, and employers.
- Major depressive disorder has been linked to:
  - Chronic physical disorders
  - Increase risk of suicide
  - Reductions in quality of life
  - Adverse effects on employment and work productivity
- In 2010, major depressive disorder was noted as a leading cause of disability-adjusted life years
- Residual symptoms after remission are common and may negatively impact patient functioning and outcome.

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