

# ECONOMIC BURDEN OF BIPOLAR DISORDER TYPE I (BD-I) IN THE US: A SYSTEMATIC REVIEW OF THE LITERATURE

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## BACKGROUND

- Bipolar disorder (BD) is one of the leading causes of disability secondary to mental/behavior disorders worldwide, especially because of its early age of onset, elevated relapse rates and high rate of comorbid conditions.
- Bipolar Disorder type I (BD-I) is a chronic and severe mental illness characterized by at least one manic episode with the possibility of other major depressive or hypomanic episodes.

## OBJECTIVES

The goals of this systematic (SR) review of the literature were to evaluate the following aspects of BD in the United States (US):

- financial costs (direct and indirect) imposed by the disease
- impact of specific pharmacological treatments on costs
- impact of BD on employability and work performance (presenteeism and absenteeism)
- impact of BD on Health-Related Quality of Life (HRQOL) in comparison to controls
- evolution of HRQOL during the course-of-illness (including changes secondary to specific pharmacological treatments)

## METHODS

- A comprehensive search was performed in Medline and EMBASE (2006 to 2016) for studies addressing the aspects described above.
- Inclusion criteria:
  - studies enrolled US patients
  - data were collected or papers published after year 2000 so the results could more closely mirror current standards of care
  - patients should be euthymic, in a manic or mixed episode, or recovering after a manic or mixed episode
- Exclusion criteria:
  - studies focused on patients enrolled after a depressive episode

## Figure 1. Search Strategies

**Cost of illness**

SR in MEDLINE: ("Bipolar Disorder"[Mesh] OR (bipolar AND disorder)) AND "Costs and Cost Analysis"[Mesh] AND systematic[sb]. For studies published after the most updated SR (Complement): ("Bipolar Disorder"[Mesh] OR (bipolar AND disorder)) AND "Costs and Cost Analysis"[Mesh]

SR in EMBASE: ('bipolar disorder'/exp OR 'bipolar disorder') and (('cost of illness'/exp OR 'cost of illness')

**Impact of BD over employability and work productivity**

SR in MEDLINE: ("Bipolar Disorder"[Mesh] OR (bipolar AND disorder)) AND (employment OR unemployment OR absenteeism OR presenteeism OR workplace OR productivity OR work functioning OR work disability OR sick leave) AND systematic[sb]. Complement: ("Bipolar Disorder"[Mesh] OR (bipolar AND disorder)) AND (employment OR unemployment OR absenteeism OR presenteeism OR workplace OR productivity OR work functioning OR work disability OR sick leave)

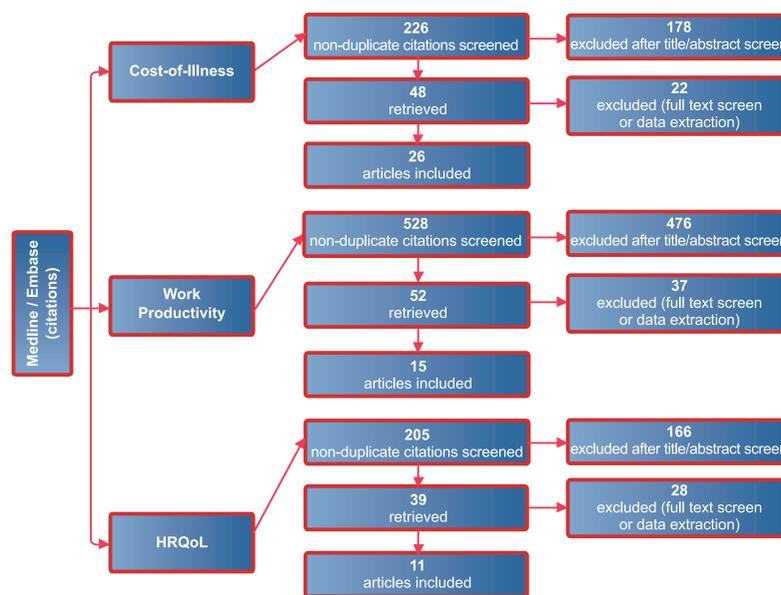
SR in EMBASE: ('bipolar disorder'/exp OR 'bipolar disorder') and ('employment'/exp OR 'employment' OR 'unemployment'/exp OR 'unemployment' OR 'absenteeism'/exp OR 'absenteeism' OR 'presenteeism'/exp OR 'presenteeism' OR 'workplace'/exp OR 'workplace' OR 'productivity'/exp OR 'productivity' OR 'work functioning'/exp OR 'work functioning' OR 'work disability'/exp OR 'work disability' OR 'work functioning' OR 'sick leave'/exp OR 'sick leave')

**Health-Related Quality-of-Life**

SR in MEDLINE: ("Bipolar Disorder"[Mesh] OR (bipolar AND disorder)) AND (quality of life OR "Quality of Life"[Mesh] OR sf-36 OR sf-12 OR eq-5d) AND systematic[sb]. Complement: ("Bipolar Disorder"[Mesh] OR (bipolar AND disorder)) AND (prospective OR naturalistic OR longitudinal) AND (quality of life OR "Quality of Life"[Mesh] OR sf-36 OR sf-12 OR eq-5d)

SR in EMBASE: (('bipolar disorder'/exp OR 'bipolar disorder') and ('quality of life'/exp OR 'quality of life'))

## Figure 2. Prisma Flow Diagram



## RESULTS

### Cost-of-illness

- 26 studies were included <sup>1-26</sup>
- Main reasons for exclusion: lack of US patients, lack of specific data on BD, older data (collected before year 2000), study design and analysis only for patients with BD specific features (e.g.: depression).
- Annual societal costs per patient with BD varied from \$1,904 to \$33,090, with productivity losses making up to 20%-94% of costs.
- Overall direct healthcare costs ranged from \$8,000-\$14,000 per patient purchasing parity power.
- Total annual health care costs were higher for patients with BD than for those without the disease (\$12,764 vs \$3,140 per patients per year).
- Improved adherence to medication was related to lower medical costs in BD (1-point increment in MPR reduced \$123-\$439 in mental health expenditures per patients with manic/mixed symptoms receiving antipsychotics per year).

## RESULTS

### Employability & Work Productivity

- 15 studies were included <sup>4,9,16,27-38</sup>
- Main reasons for exclusion: lack of US patients, lack of specific data on BD, older data (collected before year 2000), studies not addressing the impact of BD over employment or work functioning (e.g.: predictors of employment) and studies addressing only the impact of specific patient characteristics over employment or productivity (e.g.: cognition, comorbid diabetes, comorbid personality disorders).
- 40% to 60% of patients with BD were employed, with higher employment rates during early phases of disease compared to later stages.
- Mean annual absence costs per patient (sick leave, short/long-term disability, and workers' compensation) were significantly higher for employers of patients with BD when compared with those without the disease (\$1,995 vs \$885).
- See the main results for studies in this category listed below.

### MAIN RESULTS OF STUDIES EVALUATING EMPLOYABILITY AND WORK PRODUCTIVITY IN PATIENTS WITH BD

#### Absenteeism and presenteeism

- Employees with BD had 18.9 days of work absence per year vs. 7.4 days for those without BD. Gardner 2006 <sup>9</sup>.
- Employees with BD were less likely to be present at work. Absence rates over 1 year resulted in significant productivity losses. Kleinman 2005 <sup>16</sup>.
- BD related absenteeism was 27.7 days and BD related presenteeism was 35.3 days. Kessler 2006 <sup>33</sup>.
- Patients with BD not working/studying: 47.2%. Missed days at work: 8.36 (average) Shippee 2011 <sup>37</sup>.
- Proportion of employed / unemployed patients
- In one study 60% of patients with BD-I were employed at baseline, but only 31% remained so at 52 weeks. Chengappa 2005 <sup>28</sup>.
- An observational study showed that 46.6% of patients with BD-I were employed at baseline and termination while 30.4% were unemployed. Gilbert 2010 <sup>30</sup>.
- In another study, the proportions of patients with BD employed were: 66% (baseline), 64% (6 months), 63% (12 months) and 62% (24 months). Simon 2008 <sup>38</sup>.
- For patients with BD hospitalized early in the illness: 54% worked/studied full-time at 6 months and 21% part-time. Dickerson 2010 <sup>29</sup>.
- Employment status for patients with BD: full-time (25%), part-time (16%), unemployed (41%), retired (17%), student (1%) Hirschfeld 2003 <sup>32</sup>.

- The mean performance as worker, homemaker or student (Strauss and Carpenter 5-point scale) for young adults living with BD was 2.4 (at 2 years); 2.5 (at 4.5 years) and 2.6 (at 7-8 years). Goldberg 2005 <sup>31</sup>.
- BD has "complex, varied and intermittent effects" on work functioning, so it is necessary to develop appropriate measures of occupational functioning among these patients. Michalak 2007 <sup>36</sup>.

- Costs
- A cost analysis study comparing before and after BD treatment showed reductions in direct medical costs after starting treatment, specially for the cohort receiving atypical AP only. Brook 2007 <sup>27</sup>.
- Accurate and timely recognition of BD was associated with lower costs due to work loss. Birnbaum 2003 <sup>4</sup>.

- Health-Related Quality-of-Life
- 11 studies were included <sup>39-49</sup>
- Main reasons for exclusion: lack of US patients, lack of specific data on BD, older data (collected before year 2000), studies not addressing measures of QoL or utility by validated tools (e.g.: SF-36, SF-12, EQ-5D, Q-LES-Q-SF), studies addressing specific BD populations (e.g.: patients with comorbidities).
- HRQOL is impaired in patients with BD compared with healthy individuals and with patients diagnosed with other chronic psychiatric and medical conditions.
- BD pharmacological and non-pharmacological treatments have a positive effect on HRQOL.
- See the main results for studies in this category listed below.

- MAIN RESULTS OF STUDIES EVALUATING HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH BD
- Physical Component Scores (PCS) worsened with age while Mental Component Scores (MCS) tended to improve in older patients with BD. Fenn 2005 <sup>40</sup>.
- Youths with BD and their caregivers had lower HRQOL compared to youths with asthma, obesity, atopic dermatitis, and chronic depression. Freeman 2009 <sup>41</sup>.
- Short and long sleep duration were associated with poorer function and QoL compared to normal sleepers. Gruber 2009 <sup>42</sup>.
- Illicit drug use adversely affected mental HRQOL while increased number of medical comorbidities negatively affected physical HRQOL. Kilbourne 2009 <sup>44</sup>.
- Patients with BD receiving adjunctive olanzapine had greater improvement in HRQOL compared to the placebo group. Namjoshi 2004 <sup>46</sup>.
- No statistically significant differences were found in HRQOL for patients with BD treated with olanzapine or divalproex Revicki 2003 <sup>47</sup>.
- Depressive symptoms significantly related to impaired HRQOL. Higher scores were achieved by patients in euthymia. Zhang 2006 <sup>49</sup>.
- Treatment with lithium or quetiapine was associated with significant improvements in HRQOL, regardless of the drug used. Deckersbach 2016 <sup>39</sup>.
- BD carries a substantial burden in HRQOL especially in the mental domains. Significant improvements in HRQOL were seen with asenapine vs olanzapine and placebo in patients with mixed episodes. Michalak 2014 <sup>45</sup>.
- There is a double burden of aging and disease in patients with BD. Weisenbach 2014 <sup>48</sup>.

\*These studies comprise the same populations but report different analysis.

## CONCLUSIONS

- When compared with other populations, patients with BD imposed higher medical costs for payers.
- However, treatment adherence was associated with reduced health expenditures.
- Both employability and work productivity were negatively affected by the disease, as was HRQoL.

## LIMITATIONS

- Regarding cost of illness analysis, impact on employment and work productivity and quality of life assessments, there is scarce data specific for patients with BD-I (most studies include patients with BD as a group).
- Quality-of-life impact resulting from treatment has been addressed mainly in short-duration studies (up to 12 weeks of follow-up). There is also need for long-term studies addressing the evolution of HRQOL in BD patients.

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