

# Economic Burden of Patients with MDD Potentially Eligible for Adjunctive Treatment: A Systematic Literature Review

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Patients potentially eligible for adjunctive treatment incur high direct costs (~\$7,000-\$38,000 PPPY), most of which is attributed to medical costs (~60-85%).



High variability in costs are likely attributable to differences in how cohorts were defined and operationalized.



This study highlights the unmet need for standardized characterization of adjunctive-eligible MDD patients.

## CONCLUSIONS

## RESULTS

- A total of 17 studies met all eligibility criteria
- 11 studies (~65%) consisted of single, non-stratified cohorts; 6 studies (~35%) consisted of cohorts that were further stratified into sub-cohorts
- On average, patients were mostly female (~55-76%), with a mean age of 43 years (38-73 years) (Table 1)

Table 1a. Baseline Characteristics for Non-stratified Cohorts

Author, Year	Amos 2018	Pilon 2020	Cai 2020	Pilon 2019 (1)	Pilon 2019 (2)	Ivanova 2010	Benson 2020	Kubitz 2013	Olchanski 2013	Yan 2020	McIntyre 2014
Study Population Definitions	3+ LOT	3+ LOT	3+ LOT	3+ LOT	3+ LOT	3+ LOT	3+ LOT	3+ LOT	4+ LOT	Adj. AAP	Mixed Features
Patients, N	6411	1582	3317	3224	14170	2312	178	3134	24415	10325	652
Age, Mean (SD)	41 (13)	46 (17)	38 (14)	59 (15)	43 (12)	48 (7)	73 (7)	NR	44 (NR)	48 (16)	38 (13)
Female, N (%)	4117 (64%)	1052 (67%)	2034 (61%)	2064 (64%)	10405 (73%)	1498 (65%)	124 (70%)	2237 (72%)	17965 (74%)	7260 (70%)	432 (66%)
Payer, N (%)											
Commercial	6411 (100%)	1259 (82%)	3218 (97%)	(0%)	(0%)	NR	(0%)	3134 (100%)	20779 (85%)	7949 (77%)	(0%)
Medicare	(0%)	283 (18%)	99 (3%)	3224 (100%)	(0%)	NR	(100%)	(0%)	593 (2%)	1731 (17%)	(0%)
Medicaid	(0%)	(0%)	(0%)	(0%)	(0%)	NR	(0%)	(0%)	687 (3%)	645 (6%)	(0%)
Other	(0%)	(0%)	(0%)	(0%)	(0%)	NR	(0%)	(0%)	2356 (10%)	(0%)	(0%)
Plan, N (%)											
HMO	(0%)	189 (12%)	688 (21%)	(0%)	NR	NR	(0%)	NR	9607 (39%)	NR	(0%)
PPO	4916 (76%)	78 (5%)	1838 (55%)	3224 (100%)	NR	NR	(100%)	NR	7867 (32%)	NR	(0%)
POS	879 (14%)	907 (57%)	333 (10%)	(0%)	NR	NR	(0%)	NR	4736 (19%)	NR	(0%)
Other	(10%)	(26%)	4 (1%)	(0%)	NR	NR	(0%)	NR	2235 (9%)	NR	(0%)

Table 1b. Baseline Characteristics for Stratified Cohorts

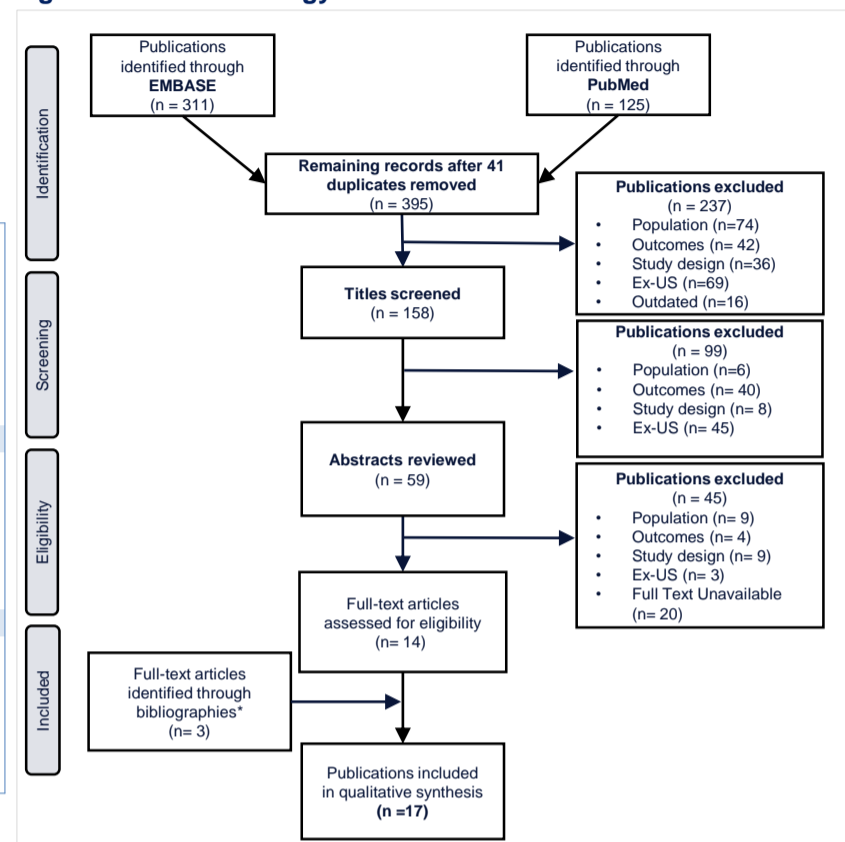
Author, year	Gibson 2010*	Pilon 2019 (3)	Sussman 2019	Olsson 2018†	Shrestha 2020	Seetasth 2018‡
Stratified Sub-cohorts	MGH-AD 3.5-4 MGH-AD 4.5-5 MGH-AD 5.5-6 MGH-AD 6.5+	Mild Moderate Severe	Non-response MDD TRD	Months 1-12 Months 13-24	Commercial Medicare Medicaid	≤1 year of ADT > 1-2 years of ADT > 2 years of ADT
Study Population Definitions	Failed 2 LOT	3+ LOT	2 <sup>nd</sup> LOT 3+ LOT	3+ LOT	3+ LOT	Adj. AAP
Patients, N	22615	455	2153	1455	10734	1112
Age, Mean (SD)	NR	39 (13)	40 (13)	42 (15)	39 (14)	42 (14)
Female, N (%)	16283 (72%)	296 (65%)	1364 (63%)	945 (65%)	6820 (64%)	874 (77%)
Payer, N (%)						
Commercial	22615 (100%)	NR	NR	NR	NR	NR
Medicare	(0%)	NR	NR	NR	NR	NR
Medicaid	(0%)	NR	NR	1503 (100%)	NR	NR
Other	(0%)	NR	NR	NR	NR	NR
Plan, N (%)						
HMO	4975 (22%)	(0%)	(0%)	NR	421 (28%)	4415 (16%)
PPO	8141 (36%)	364 (80%)	1615 (75%)	1091 (75%)	NR	15998 (58%)
POS	3166 (14%)	50 (11%)	301 (14%)	218 (15%)	NR	135 (8%)
Other	6332 (28%)	41 (9%)	237 (11%)	145 (10%)	NR	947 (8%)

Note. Study Population definitions represents how each study defined the potentially adjunctive eligible populations. Percentages may not add up to 100% due to rounding.

\*MGH, Massachusetts General Hospital clinical staging method for treatment resistance; MGH score > 3.5, patients identified as having TRD.  
†months 1-12 following initiation of 3rd line of therapy and months 13-24 following initiation of 3rd line of therapy; \*AAP initiated in one year or less of first ADT use; AAP initiated in one to two years of first ADT use; AAP initiated more than two years of first ADT use.

Abbreviations: LOT, Line of Therapy; MDD-MF, Major Depressive Disorder-Mixed Features; MDD, Major Depressive Disorder; TRD, Treatment Resistant Depression; Adj. AAP, Adjunctive Atypical Antipsychotic; ADT, Antidepressant Treatment; NR, Not Reported

Figure 1. Search Strategy

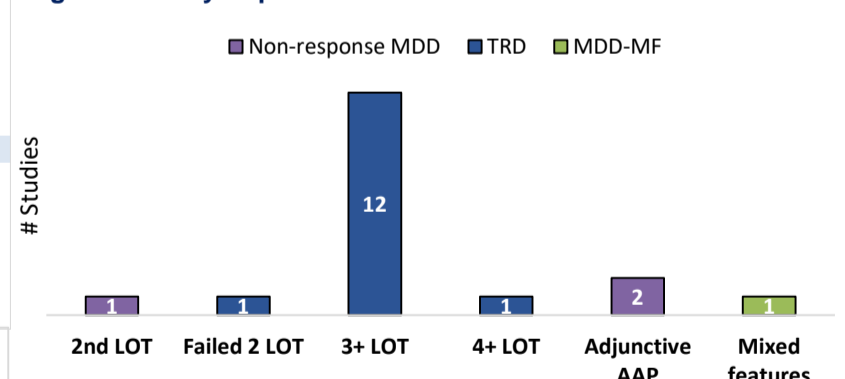


\*Bibliographies of 5 models and 2 reviews were assessed

## Study Population Definitions

- Variable definitions were used to define the potentially adjunctive eligible study populations
- 12 studies (~70%) defined the potentially adjunctive eligible population as initiating a 3<sup>rd</sup> line of therapy, 2 studies (~20%) defined it as being on an adjunctive atypical antipsychotic, others defined it as initiating a 2<sup>nd</sup> line of therapy, having failed a 2<sup>nd</sup> line of therapy or having MDD with mixed features (Figure 2)

Figure 2. Study Population Definitions



Note. Study Population definitions represents how each study defined the potentially adjunctive eligible populations. The number of studies exceed total of 17 since one study included two relevant cohorts.

Abbreviations: LOT, Line of Therapy; TRD, Treatment Resistant Depression; MDD, Major Depressive Disorder; MDD-MF, Major Depressive Disorder with Mixed Features

## All-Cause Direct Costs

- Patients potentially eligible for adjunctive treatment incurred high costs (~\$7,000-\$38,000 PPPY) with medical costs accounting for majority of total all-cause direct costs across all studies (~60-85%)
- Significant variations in all-cause costs were observed (Figure 3)

Figure 3a. All-Cause Direct Costs for Non-stratified Cohorts

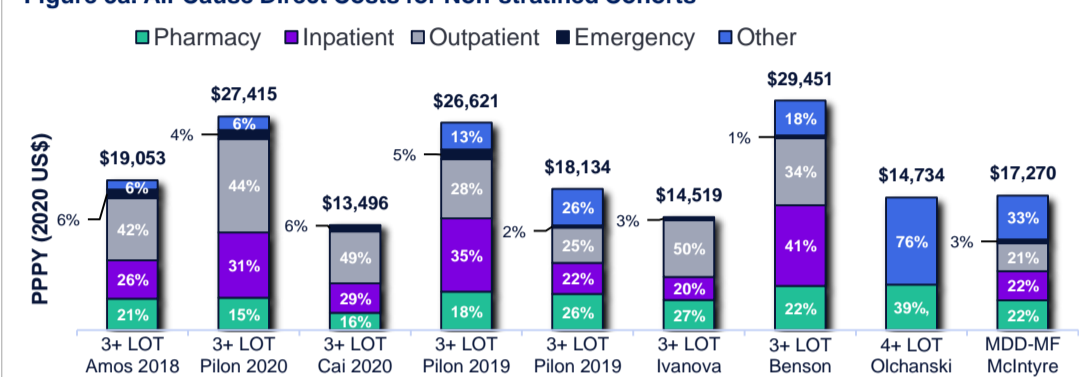
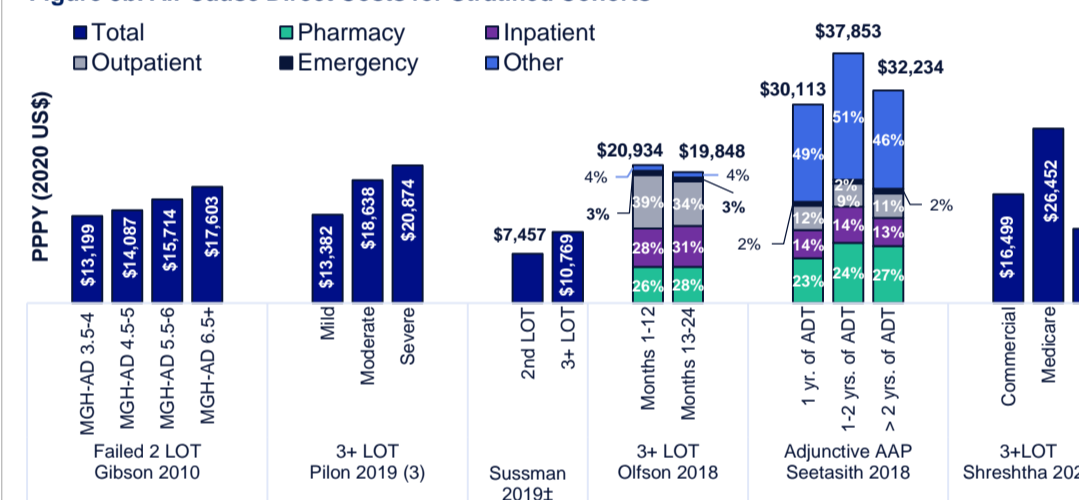


Figure 3b. All-Cause Direct Costs for Stratified Cohorts



Note. Each bar represents percentage breakdown of all cause direct costs within a study cohort. All costs were inflated to 2020 U.S. dollars based on the Consumer Price Index. Some percentages may not sum up to 100% due to rounding and adjustments. Other category includes long-term care, home visit, mental institute visit and/or any visit not previously classified as inpatient, outpatient, Emergency, or pharmacy.

Figure 3b, †Total costs differed from sum of individual categories due to adjustments. ‡Post-TRD annual costs were assessed independently of pre-TRD costs. Figure 4b, \*Depression related costs were reported.

Abbreviations: PPPY, Per-Patient Per-Year; ADT, Antidepressant Therapy; AAP, Atypical Antipsychotics; LOT, Line of Therapy; MDD, Major Depressive Disorder; MGH-AD, Massachusetts General Hospital clinical staging method for treatment resistance; MGH score > 3.5, patients identified as having TRD

## Mental Health Related Direct Costs (MHR)

- Mental health related (MHR) costs generally accounted for ~30% of total direct costs (~\$1,400-\$10,000 PPPY) with medical costs accounting for majority of total MHR direct costs across all studies (~50-90%)
- Significant variations in MHR costs were observed (Figure 4)

Figure 4a. MHR Costs for Non-stratified Cohorts

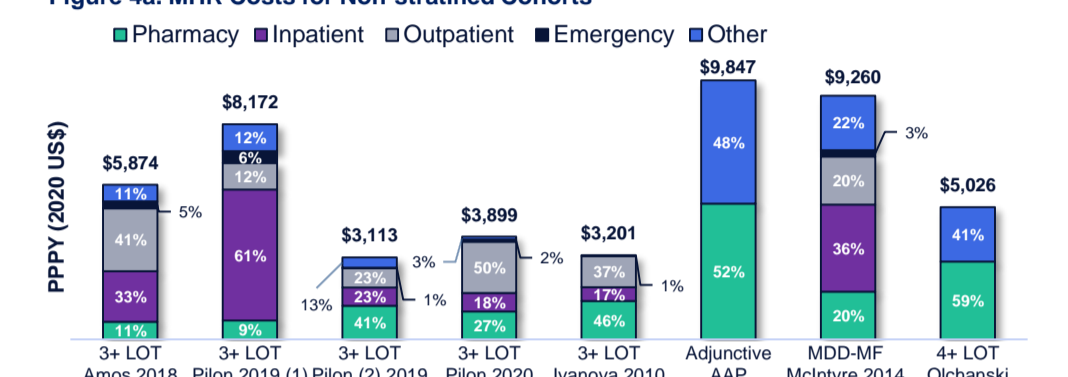
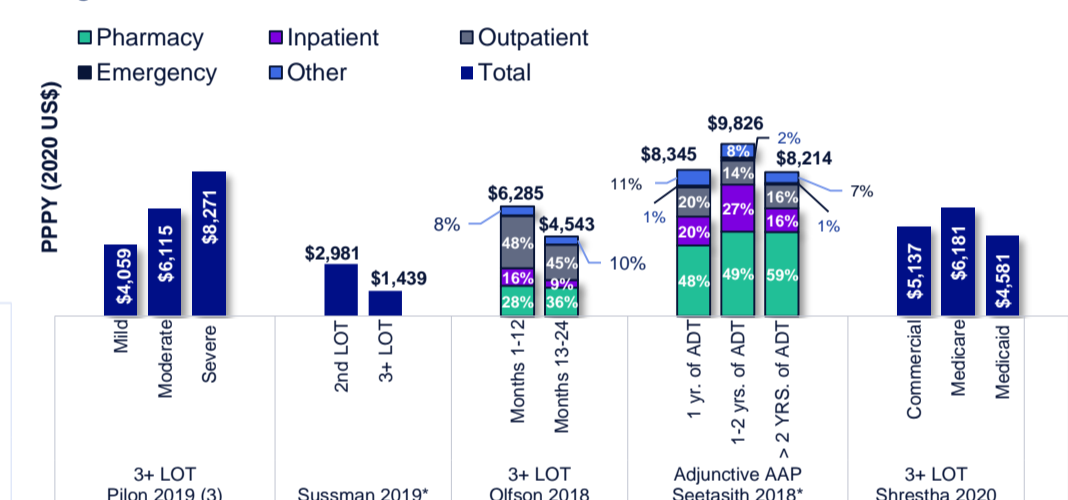


Figure 4b. MHR Costs for Stratified Cohorts



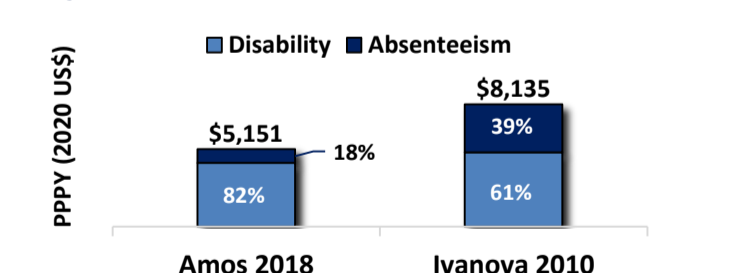
## Indirect Costs

- 2 studies (~12%) reported indirect costs
- While both studies reported similar disability costs (~\$4,234 vs. ~\$4,940), significant variability was observed in absenteeism costs (Table 2, Figure 5)
- On average, indirect costs attributed a smaller percentage to costs compared to direct costs; Amos (~\$5,151 vs. ~\$19,053), Ivanova (~\$8,135 vs. ~\$14,519)

Table 2. Indirect Costs Calculations

	Amos 2018	Ivanova 2010
Disability	Actual employer payments for disability days from disability claims	
Absenteeism	Number of total work loss days and individual employee wage	

Figure 5. Indirect Costs



## Background

- Major Depressive Disorder (MDD) is associated with substantial economic burden, with total costs estimated at \$210.5 billion in 2010<sup>1</sup>
- Of the total burden, 45% were direct costs, 50% were indirect costs, and 5% were suicide-related costs<sup>1</sup>
- Patients with MDD do not always achieve remission and often experience residual symptom burdens<sup>2</sup>
- Based on APA guidelines, adjunctive treatment is an option for patients whose depression is not resolved after initial adequate trial of antidepressant therapy<sup>2</sup>

## Objective

- To summarize the direct and indirect costs of patients with MDD, specifically those potentially eligible for adjunctive treatment

## Information Sources

- Biomedical electronic databases including PubMed and EMBASE were searched for studies from 2010 to 2020; the search was limited to full-text publications in the US, human subjects, and English language only

## Eligibility Criteria

- All titles and abstracts identified from the search strategy were screened for eligibility, and the full-text of studies marked for possible inclusion were reviewed by two authors, independently
- For this review, the potentially adjunctive eligible population was defined as patients with MDD who failed at least one antidepressant treatment

## Risk of Bias Assessment

- Validity of studies were assessed for incomplete outcome data and selective outcome reporting by two reviewers, independently
- Appraisal of individual study quality was based on tailored quality assessment tools developed by methodologists from NHLBI<sup>21</sup>

## INTRODUCTION

## DISCLOSURES

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