

**Online Supplemental Material****Studies included in meta-regression**

Author	Year	Response %	Total	Trial Length(wks)	Comments
Small <sup>19</sup>	1987	40%	38		Treatment-resistant schizophrenia and non-treatment-resistant schizophrenia - 55% response
Kane <sup>4</sup>	1988	30%	134	6	
Mattes <sup>20</sup>	1989	57%	14	Up to 104	Based on 8 did substantially better on clozapine
Davidson <sup>21</sup>	1993	50%	28	5	
Kuoppasalmi <sup>22</sup>	1993	67%	103	26	Based on statement "More than 2/3 improved"
Breier <sup>23</sup>	1993	60%	30	26	
Littrel <sup>24</sup>	1994	48%	42	12	
Lieberman <sup>25</sup>	1994	50%	66	52	Treatment-resistant schizophrenia+ additional 18 patients not tolerant of other antipsychotics
Szymanski <sup>26</sup>	1994	30%	10		
Honer <sup>27</sup>	1995	31%	61	32	
Grace <sup>28</sup>	1996	50%	31	52	
Hoff <sup>29</sup>	1996	14%	30	12	
Wilson <sup>30</sup>	1996	73%	100	48	All improved within 1 week but followed weekly X 18 weeks the every 3 months for 18 months

Aymard <sup>31</sup>	1997	100%	7		4-38 months follow-up
Conley <sup>32</sup>	1997	68%	50		Mean follow up 75 weeks All responders responded within 8 weeks
Aitchison <sup>33</sup>	1997	85%	26		
Rosenheck <sup>34</sup>	1996	57%	205	52	Hospital days reduced from 168.1 to 143.8
Blieden <sup>35</sup>	1998	52%	33	26	
Luchins <sup>36</sup>	1998	75%	28		Cost study, hospital days reduced from 23.5 to 7.6
Sajatovic <sup>37</sup>	1998	30%	97	60	
Buckman <sup>38</sup>	1999	47%	518	60	Cost Study
Percudani <sup>39</sup>	1999	80%	15	52	Cost Study
Rosenheck <sup>40</sup>	1999	39%	122	26	Response at 26 weeks
Simpson <sup>41</sup>	1999	19%	48		48 completed 16 weeks, 36 went on to 2 <sup>nd</sup> and 3 <sup>rd</sup> 16week trials at other doses
Dettling <sup>42</sup>	2000	81%	26	10	
Sajatovic <sup>43</sup>	2000	58%	522	60	
Wahlbeck <sup>44</sup>	2000	50%	10	10	50% dropout
Kane <sup>45</sup>	2001	57%	37	29	
Narendran <sup>46</sup>	2003	67%	9	6	
Honer <sup>47</sup>	2006	26%	34	8	Already clozapine poor responders
Semiz <sup>48</sup>	2007	56%	97	16	
<b>Pooled Total</b>		<b>51%</b>	<b>2571</b>		

\*calculate SD from p<0.001

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### Studies excluded from meta-regression

Author	Year	Response %	Total	Trial Length(wks)	Comments
Kahn <sup>49</sup>	1993	47%	19	5	8 responders 11 non-responders all improved
Jonsson <sup>50</sup>	1995	70%	21	78	15 patients showed "substantial response"
Kronig <sup>51</sup>	1995	40.5%	45	6	"responders" more likely to have serum concentration >350ng/ml
VanderZwaag <sup>52</sup>	1996	*	28	12	39% (18) low; 61% (23) med; 60% (15) high concentration groups responded
Lindenmayer <sup>53</sup>	1998	*	35	12	No overall response metric
Semyak <sup>54</sup>	2001	*	1415	36	Response rate not defined Unclear if treatment-resistant schizophrenia population
Umbricht <sup>55</sup>	2002	59%	37	29	Secondary analysis of patients in Kane trial <sup>45</sup>
Saccchetti <sup>56</sup>	2009	*	74	18	Significant response noted on PANSS but no response rate for treatment-resistant schizophrenia (n=65)

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### Inpatient hospital days with clozapine use<sup>+</sup>

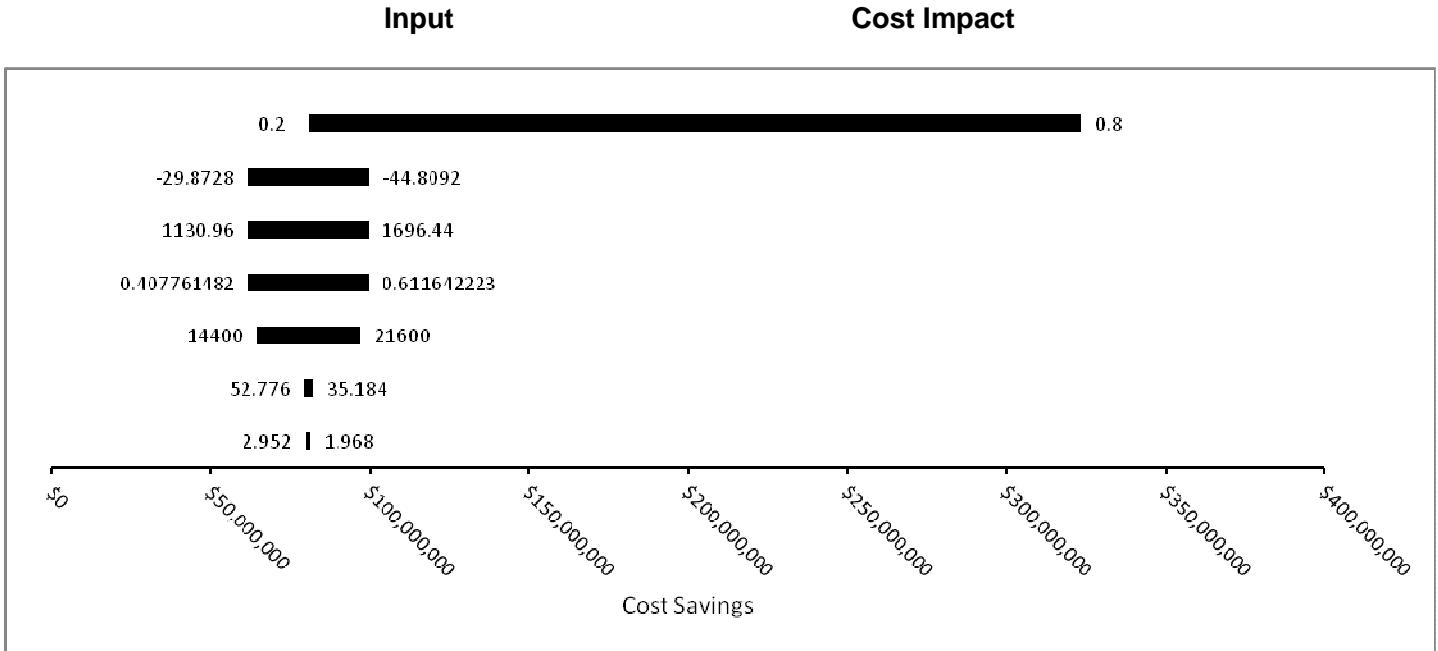
Author	Year	Clozapine (N)	Clozapine Inpatient Days (SD)	Comparator (N)	Comparator Inpatient Days (SD)
Aitchison <sup>33*</sup>	1997	26	6.5 ± 6.5	26	39.5 ± 39.5
Ghaemi <sup>68</sup>	1998	20	4.6 ± 11.3	20	47.7 ± 20
Rosenheck <sup>34*</sup>	1996	205	143.8 ± 143.8	218	168.1 ± 168.1
Luchins <sup>36</sup>	1998	28	7.6 ± 14.9	28	23.5 ± 49.6
Buckman <sup>38*</sup>	1999	243	70.8 ± 70.8	243	152.9 ± 152.9
Percudani <sup>39*</sup>	1999	12	58.8 ± 58.8	12	107.8 ± 58.8
Atkinson <sup>69</sup>	2007	23	74.1 ± 137.3	23	119.8 ± 143.5

<sup>+</sup> SD assumed to equal the mean inpatient days if not otherwise specified

\*calculate SD from p<0.001



**Figure 2: Contribution of inputs to variation in clozapine cost of care.\***



\*Other variables (rates of adverse drug reactions (ADRs), suicide, clozapine discontinuation, costs of ADRs, and laboratory monitoring) each had a smaller impact than the cost of clozapine.