

## Appendix E. Risk of Bias

**Table E.1. Risk of bias for RCTs (Cochrane ROB tool) for included studies**

Author, Year	Sequence Generation	Allocation Concealment	Blinding of Participants, Personnel	Blinding of Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall RoB
Bertella, 2017 <sup>3</sup>	Low ROB	Low ROB	High ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB
Bhatt, 2013 <sup>4</sup>	Low ROB	Low ROB	High ROB	Unclear	Low ROB	Low ROB	High ROB	High ROB
Borel, 2011 <sup>6</sup>	Low ROB	Low ROB	High ROB	Low ROB	Low ROB	Unclear	High ROB	High ROB
Bourke, 2006 <sup>7</sup>	Low ROB	Unclear	High ROB	High ROB	Low ROB	Unclear	Low ROB	High ROB
Casanova, 2000 <sup>10</sup>	Low ROB	Unclear	High ROB	Low ROB	Unclear	Unclear	Unclear	High ROB
Cheung, 2010 <sup>12</sup>	Low ROB	Low ROB	High ROB	Unclear	High ROB	Low ROB	Low ROB	High ROB
Chiang, 2003 <sup>13</sup>	Low ROB	Unclear	High ROB	Unclear	Low ROB	Unclear	Low ROB	Moderate ROB
Clini, 2002 <sup>16</sup>	Unclear	Low ROB	High ROB	Low ROB	High ROB	Low ROB	High ROB	High ROB
De Backer, 2011 <sup>19</sup>	Unclear	Unclear	Unclear	Unclear	Low ROB	Unclear	Low ROB	Moderate ROB
Dreher, 2010 <sup>21</sup>	Unclear	Unclear	High ROB	High ROB	Low ROB	Unclear	High ROB	High ROB
Duiverman, 2008, 2011 <sup>22, 23</sup>	Low ROB	Unclear	High ROB	Unclear	Low ROB	Low ROB	Low ROB	Moderate ROB
Duiverman, 2017 <sup>24</sup>	Unclear	Unclear	High ROB	High ROB	High ROB	Low ROB	High ROB	High ROB
Funk, 2010 <sup>27</sup>	Low ROB	Unclear	High ROB	High ROB	Low ROB	Low ROB	Low ROB	Moderate ROB
Garrod, 2000 <sup>30</sup>	Unclear	Low ROB	High ROB	Unclear	Low ROB	Unclear	Unclear	High ROB
Gay, 1996 <sup>31</sup>	Unclear	Unclear	High ROB	High ROB	Low ROB	Unclear	Unclear	High ROB
Hazenberg, 2014 <sup>33</sup>	Low ROB	Unclear	High ROB	High ROB	Low ROB	Low ROB	Low ROB	Moderate ROB
Howard, 2016 <sup>36</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB	High ROB	Moderate ROB
Köhnlein, 2014 <sup>37</sup>	Low ROB	Low ROB	High ROB	Low ROB	Low ROB	Low ROB	High ROB	High ROB
Marquez-Martin, 2014 <sup>38</sup>	Low ROB	Unclear	High ROB	Unclear	Low ROB	Unclear	Low ROB	Moderate ROB
Masa, 2015 <sup>40, 41</sup>	Low ROB	Unclear	High ROB	Unclear	Low ROB	Unclear	Low ROB	Moderate ROB
Masa, 2016 <sup>42</sup>	Unclear	Unclear	High ROB	Unclear	Low ROB	High ROB	Low ROB	High ROB
McEvoy, 2009 <sup>43</sup>	Low ROB	Low ROB	High ROB	Unclear	Low ROB	Low ROB	Low ROB	Moderate ROB
Murphy, 2012 <sup>45</sup>	Unclear	Low ROB	High ROB	Unclear	Low ROB	Low ROB	Low ROB	Moderate ROB
Murphy, 2017 <sup>46</sup>	Low ROB	Low ROB	High ROB	Low ROB	Low ROB	Low ROB	High ROB	High ROB
Oscroft, 2010 <sup>49</sup>	Low ROB	Unclear	High ROB	Unclear	Low ROB	Low ROB	Low ROB	Moderate ROB
Oscroft, 2014 <sup>50</sup>	Low ROB	Low ROB	High ROB	High ROB	Low ROB	Unclear	High ROB	High ROB
Piper, 2008 <sup>55</sup>	Low ROB	Low ROB	Unclear	Unclear	Low ROB	Low ROB	Low ROB	Low ROB
Sin, 2007 <sup>62</sup>	Low ROB	Unclear	Low ROB	Low ROB	Unclear	Unclear	Unclear	Moderate ROB
Struik, 2014 <sup>64</sup>	Low ROB	Unclear	High ROB	Unclear	Low ROB	Low ROB	High ROB	Moderate ROB
Zhou, 2017 <sup>70</sup>	Low ROB	Low ROB	High ROB	Low ROB	Low ROB	Unclear	High ROB	High ROB

ROB: Risk of Bias

**Table E.2. Risk of bias for observational studies (Newcastle-Ottawa Quality Assessment Scale) for included studies**

Author, Year	Representativeness of the Study Population	Ascertainment of Exposure	Assessment of Outcome	Adequate of Followup	Conflict of Interest	Overall RoB
Aboussouan, 1997 <sup>1</sup>	Low ROB	Low ROB	Unclear	Low ROB	Unclear	Moderate ROB
Benhamou, 1997 <sup>2</sup>	High ROB	Low ROB	Low ROB	Low ROB	Unclear	High ROB
Blankenburg, 2017 <sup>5</sup>	Low ROB	Low ROB	Low ROB	High ROB	Low ROB	Moderate ROB
Budweiser, 2007 <sup>8</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB
Buyse, 2003 <sup>9</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Unclear	Moderate ROB
Castillejo, 2014 <sup>11</sup>	High ROB	Low ROB	Low ROB	Low ROB	Unclear	High ROB
Clini, 1996 <sup>14</sup>	High ROB	Low ROB	Low ROB	Low ROB	Unclear	High ROB
Clini, 1998 <sup>15</sup>	High ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB
Coco, 2006 <sup>17</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Unclear	Low ROB
Crespo, 2009 <sup>18</sup>	High ROB	High ROB	High ROB	Low ROB	Unclear	High ROB
Doménech-Clar, 2003 <sup>20</sup>	Low ROB	Low ROB	Low ROB	High ROB	Unclear	High ROB
Durao, 2018 <sup>25</sup>	Low ROB	Low ROB	Low ROB	Unclear	Low ROB	Low ROB
Farrero, 2005 <sup>26</sup>	Low ROB	Low ROB	Unclear	Low ROB	Unclear	Moderate ROB
Gad, 2014 <sup>28</sup>	Low ROB	Low ROB	High ROB	Low ROB	Low ROB	Moderate ROB
Galli, 2014 <sup>29</sup>	Low ROB	Low ROB	Low ROB	Low ROB	High ROB	Low ROB
Gonzalez-Bermejo, 2013 <sup>32</sup>	High ROB	High ROB	High ROB	Low ROB	Unclear	High ROB
Heinemann, 2011 <sup>34</sup>	Low ROB	Low ROB	High ROB	Low ROB	Unclear	High ROB
Hitzl, 2009 <sup>35</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB
Masa, 2000 <sup>39</sup>	High ROB	Low ROB	Low ROB	Low ROB	Low ROB	Moderate ROB
Munoz, 2005 <sup>44</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Unclear	Moderate ROB
Nauffal, 2002 <sup>47</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Unclear	Moderate ROB
Oscroft, 2010 <sup>48</sup>	High ROB	Low ROB	Low ROB	Low ROB	Unclear	Moderate ROB
Paone, 2014 <sup>51</sup>	Low ROB	Low ROB	Low ROB	High ROB	Low ROB	Low ROB
Perez de Llano, 2005 <sup>52</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Unclear	Low ROB
Pinto, 1995 <sup>53</sup>	High ROB	Low ROB	Low ROB	Low ROB	Unclear	High ROB
Pinto, 2010 <sup>54</sup>	Low ROB	Low ROB	Low ROB	Low ROB	High ROB	High ROB
Priou, 2010 <sup>56</sup>	Low ROB	Low ROB	Unclear	Low ROB	Low ROB	Moderate ROB
Salturk, 2015 <sup>57</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB
Sancho, 2014 <sup>58</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB	Low ROB
Sancho, 2017 <sup>59</sup>	High ROB	Low ROB	Unclear	Unclear	Low ROB	High ROB
Sanjuan-López, 2014 <sup>60</sup>	Low ROB	High ROB	Low ROB	Low ROB	Low ROB	High ROB
Schonhofer, 2001 <sup>61</sup>	High ROB	Low ROB	Unclear	Unclear	Unclear	High ROB
Sivori, 2007 <sup>63</sup>	Low ROB	Low ROB	High ROB	Unclear	Low ROB	Moderate ROB
Tsolaki, 2008 <sup>65</sup>	High ROB	Low ROB	High ROB	Low ROB	Unclear	High ROB
Tsolaki, 2011 <sup>66</sup>	Low ROB	Low ROB	Low ROB	Low ROB	Unclear	Low ROB
Vasquez, 2017 <sup>67</sup>	Low ROB	Low ROB	Unclear	Unclear	Unclear	Moderate ROB
Vitacca, 2017 <sup>68</sup>	Low ROB	Unclear	Unclear	Low ROB	Low ROB	Moderate ROB
Windisch, 2006 <sup>69</sup>	Low ROB	Low ROB	Low ROB	Unclear	Unclear	Moderate ROB

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