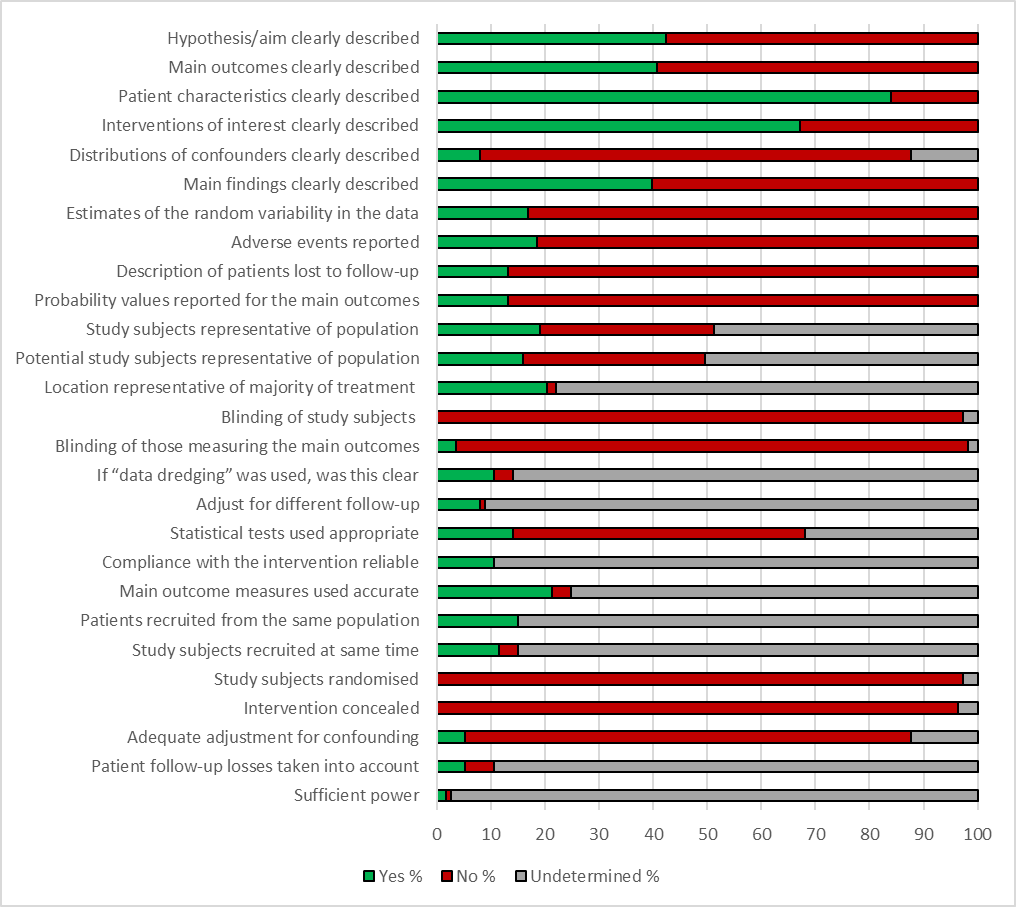
**Appendix Table 1.** Characteristics of All Included Studies.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Pub Year** | **Study Design** | **Study Location** | **Enrollment Period** | **Study Length (months)** | **N**  **Received Naloxone** | **Suspected/Confirmed Opioid Ingested** | **Setting of Opioid Use** | **Naloxone Initial Dose** | **Naloxone Cumulative Dose** | **Route of Administration** |
| Wong45 | 2018 | RS | USA | 2014-2016 | 36/36 | 42/42 | NR | NR | 0.4 \*/1.5 | NR | NR |
| Avetian46 | 2018 | RS | USA | 2016 | 4 | 261 | Heroin | OH | 4 † | 5.51 \* | IN |
| Bell42 | 2018 | RS | USA | 2013-2016 | 48 | 1072 | Fentanyl | NR | 0.4 † | 1.56 \* | IM |
| Gulec47 | 2018 | RS | USA | 2014-2016 | 20 | 986 | NR | NR | NR | 2.1 \* | NR |
| Scheuermeyer48 | 2018 | RS | Canada | 2016 | 4 | 827 | Fentanyl | OH | 0.4 \* | NR | IV, IM |
| Dudley49 | 2018 | RS | USA | 2016 | 4 | 1 | NR | NR | 2 † | 4 † | IN |
| Greenberg50 | 2018 | Case Report | USA | NR | NR | 1 | Heroin | OH | 2 † | 2 † | IV |
| Buxton51 | 2018 | Case Report | Canada | NR | NR | 1 | Fentanyl | OH | 0.4 † | 0.4 † | SC |
| Uddayasankar52 | 2018 | Case Report | Canada | NR | NR | 1 | Carfentanil | NR | 2 † | 4 † | IV |
| Gharehdaghi53 | 2017 | RS | Iran | 2011-2016 | 60 | 62 | Methadone | NR | NR | 0.4 \* + Inf | NR |
| Klebacher54 | 2017 | RS | USA | 2014-2016 | 14 | 2166 | NR | PR | 2 † | NR | IV, IN, IM, IO |
| Massey55 | 2017 | RS | USA | 2016 | <1 | 16 | Heroin | OH | 1.14 \* | 1.7 \* | IN, IV, IM |
| Somerville56 | 2017 | RS | USA | 2014-2015 | 6 | 196 | Fentanyl | PR | 2 † | NR | IN |
| Sutter33 | 2017 | Case series | USA | 2016 | >1 | 1 | Fentanyl | OH | 2 † | 2.8 † + Inf | IV, IN |
| Weiner57 | 2017 | RS | USA | 2006-2012 | 83 | 724 | Heroin | NR | 2 † | NR | IN |
| Khosravi58 | 2017 | RCT | Iran | 2015-2016 | 6/6 | 50/50 | Methadone | NR | 0.1 \*/0.04 † | 0.6 \* + Inf/0.44 \* | IV |
| Madah miri59 | 2017 | PS | Norway | 2014-2015 | 17 | 277 | Heroin | NR | NR | 1.28 \* | IN |
| Helander60 | 2017 | Case Series | Sweden | 2016 | 7 | 7 | Synthetic fentanyl | NR | 0.25 \* | 0.1-0.4 ‡ | NR |
| Tomassoni61 | 2017 | Case Series | USA | 2016 | <1 | 12 | Fentanyl | OH | NR | 3.7 \* | IN, IV, IO |
| Banta-Green62 | 2017 | Case Series | USA | 2011 | 6/6 | 71/43 | Heroin | Multiple | 0.46 \*/0.4 \* | NR | NR |
| Schneir63 | 2017 | Case Report | USA | NR | NR | 1 | U-47700 | PR | 2 † | 2 † | IV |
| Armenian64 | 2017 | Case Report | USA | NR | NR | 1 | U-47700 | OH | 0.4 † | 0.4 † | IV |
| Das65 | 2017 | Case Report | USA | NR | NR | 1 | Heroin | PR | 2 † | 2 † | IV |
| Jones66 | 2017 | Case Report | USA | NR | NR | 1 | U-47700 | OH | 2 † | 4 † | IN, IV |
| Ostwal67 | 2017 | Case Report | India | NR | NR | 1 | Morphine | OH | 0.04 † | 0.2 † | IV |
| Seyani68 | 2017 | Case Report | England | NR | NR | 1 | NR | OH | 0.4 † | NR | IV |
| Chan69 | 2016 | RS | China | 2016 | 12 | 1 | Carfentanil | NR | 0.8 † | 0.8 \* | NR |
| Fisher70 | 2016 | RS | USA | 2014-2015 | 17 | 126 | NR | PR | 2 † | NR | IN |
| Friedman71 | 2016 | RS | USA | NR | 17 | 24 | NR | OH | 0.4-0.8 ‡ | NR | IV, IM, IN |
| Levine72 | 2016 | RS | USA | 2011-2013 | 24 | 205 | NR | NR | 0.8-2 ‡ | NR | IM, IN |
| Helander73 | 2016 | Case Series | Sweden | 2015 | NR | 6 | Fentanyl | NR | 0.42 \* | 0.57 \* | IV, IM, SC |
| Kim74 | 2016 | Case Series | USA | 2012 | 10 | 15 | Methadone | NR | 0.04 † | 0.08 \* | IV |
| Klar75 | 2016 | Case Series | Canada | 2016 | <1 | 37 | Fentanyl | OH | NR | ≤ 3 \* | IV |
| Bazoukis76 | 2016 | Case Report | Greece | NR | NR | 1 | Heroin | OH | 1.2 † | NR; Inf | IV |
| Hamel77 | 2016 | Case Report | USA | NR | NR | 1 | NR | OH | 2 † | 2 † | IV |
| Rogers78 | 2016 | Case Report | USA | NR | NR | 1 | Acetyl-fentanyl | PR | 2 † | 6 † + Inf | IV |
| Rando79 | 2016 | Case Report | USA | NR | NR | 1 | Methadone | NR | NR | 6 † | NR |
| Rando80 | 2015 | PS | USA | 2013-2014 | 12 | 67 | NR | NR | 2 † | NR | IN |
| Eizadi-Mood81 | 2015 | RS CS | Iran | 2012-2013 | 12 | 253 | Methadone | NR | NR | 1.3 \* | NR |
| Backberg82 | 2015 | Case Series | Sweden | 2014-2015 | 8 | 1 | Butyr-fentanyl | OH | 0.4 † | 0.6 † | IV, IM |
| Kitch83 | 2016 | Case Series | USA | NR | NR | 4 | Multiple | PR | 2 † | 3 \* | IN, IV |
| Agrafiotis84 | 2015 | Case Report | Greece | NR | NR | 1 | Multiple | OH | 0.4 † | 0.8 † | IV |
| Congeni85 | 2015 | Case Report | USA | NR | NR | 1 | Heroin | Prison | 1 † | 3 † | IM, IV |
| Steynor86 | 2015 | Case Report | England | NR | NR | 1 | Dihydrocodeine | OH | 0.4 † | 0.8 † + Inf | IV |
| Winston87 | 2015 | Case Report | England | NR | NR | 1 | Heroin | OH | NR | NR | IM |
| Borg88 | 2015 | Case Report | England | NR | NR | 1 | Fentanyl | PR | 0.8 † | 0.8 † | NR |
| Sabzghabaee89 | 2014 | RCT | Iran | NR | NR | 50/50 | Multiple | NR | 0.4 †/0.4 † | NR | IN/IV |
| Eizadi-Mood90 | 2014 | PS | Iran | 2011-2012 | 12 | 19 | Tramadol | NR | 0.01-0.4 ‡ | NR | IV |
| Oluwajenyo91 | 2014 | RS CS | Canada | NR | NR | 64 | Heroin | PR | 0.4 † | 0.58 \* | IM |
| Green92 | 2014 | Case Series | USA | NR | NR | 2 | Heroin | PR | 1.5 \* | 3 \* | IN |
| Helander93 | 2014 | Case Series | Sweden | NR | 4 | 6 | MT-45 | OH | 0.41 \* | 0.81 \* | NR |
| Bosak94 | 2014 | Case Series | USA | NR | NR | 1 | Tramadol | NR | 0.4 † | 1.2 † | NR |
| Hendrickson95 | 2014 | Case Report | USA | NR | NR | 1 | Heroin | NR | 2 † | 43.5 † + Inf | IM, IV |
| Lameijer96 | 2014 | Case Report | The Netherlands | NR | NR | 1 | Methadone | OH | 0.4 † | 0.8 † | IO |
| Zuckerman97 | 2014 | Case Report | USA | NR | NR | 1 | Fentanyl | OH | 2 † | 3.8 † | IN, IV |
| Knowlton98 | 2013 | RS | USA | 2008-2009 | 24 | 1297 | NR | NR | NR | 1.3 \* | IN, IV, IM |
| Berling99 | 2013 | RS | Australia | 2001-2011 | 124 | 65 | Oxycodone | NR | NR | NR | IM, IV |
| Shadnia100 | 2013 | RS | Iran | 2000-2010 | 120 | 1072 | Methadone | NR | NR | NR | IV |
| Baumann101 | 2013 | PS | USA | 2007-2009 | 18 | 26 | Multiple | NR | 2 † | NR | Neb, IV, IN |
| Krayeva102 | 2013 | PS | Russia | 2009-2010 | 12 | 641 | NR | NR | NR | 0.8 \* | IV, IM |
| Rubin103 | 2013 | Case Report | NR | NR | NR | 1 | Morphine | PR | 3 † | NR | NR |
| Mansfield104 | 2013 | Case Report | USA | NR | NR | 1 | Fentanyl | PR | 0.4 † | 0.8 † | IV |
| Bennett105 | 2012 | PS | Wales | NR | 6 | 28 | Multiple | OH | 0.4 † | NR | NR |
| Kim106 | 2012 | PS | USA | NR | NR | 5 | Methadone | NR | 0.04 † | 0.08 \* + Inf | IV |
| D'Orazio107. | 2012 | Case Series | USA | NR | NR | 4 | Fentanyl | OH | 1.4 \* | 2.8 \* + Inf | IV |
| Cowley108 | 2012 | Case Report | England | NR | NR | 1 | Tramadol | PR | 0.4 † | 0.8 † | IV |
| Galante109 | 2012 | Case Report | USA | NR | NR | 1 | Oxycodone | PR | 1 † | 1 † | NR |
| Shaw110 | 2012 | Case Report | Canada | NR | NR | 1 | Codeine | PR | 0.4 † | 0.4 † | IM |
| Nielsen111 | 2012 | Case Report | USA | NR | NR | 1 | Oxycodone | PR | 2 † | 2 † | NR |
| Weber112 | 2012 | RS | USA | 2010 | 6 | 70 | NR | NR | 2 † | 1.63 \* | Neb, IV, IM |
| Rudolph113 | 2011 | RS | Denmark | 1994-2003 | 120 | 4762 | NR | OH | 0.8 † | NR | IV, IM, SC |
| Wampler114 | 2011 | RS | USA | 2007-2009 | 24 | 592 | Multiple | OH | 2 † | NR | IM, IV |
| Faust115 | 2011 | Case Report | USA | NR | NR | 1 | Fentanyl | OH | 2 † | 2 † + Inf | IV |
| Porter116 | 2011 | Case Report | Canada | NR | NR | 1 | Morphine | OH | 0.4 † | 0.4 † | IV |
| Kucuker117 | 2011 | Case Report | Turkey | NR | NR | 1 | Poppy | PR | 2 † | 2 † | NR |
| Shaw118 | 2011 | Case Report | USA | NR | NR | 1 | Morphine | PR | 0.4 † | 0.4 † | IV |
| Merlin119 | 2010 | RS | USA | 2005-2010 | 60 | 96 | Multiple | NR | 1.2 \* | NR | IV, IM |
| Saybolt120 | 2010 | RS | USA | 2003-2007 | 50 | 36 | NR | OH | 2.6 \* | NR | IV |
| Enteen121 | 2010 | PS | USA | 2003-2009 | 75 | 1942 | NR | OH | 0.4 † | NR | IM |
| Reid122 | 2010 | Case Report | Norway | NR | NR | 1 | Fentanyl | PR | 0.4 † | 0.8 † | IV, IM |
| Christenson123 | 2010 | Case Report | USA | NR | NR | 2 | Methadone | NR | 0.4 † | 0.4-0.8 ‡ | NR |
| Jankowske124 | 2010 | Case Report | USA | NR | NR | 1 | Fentanyl | NR | 0.8 † | 0.8 † | IV |
| Robertson125 | 2009 | RS | USA | 2003-2004 | 17/17 | 104/50 | NR | OH | 1 †/2 † | NR | IV, IN |
| Kerr126 | 2009 | RCT | Australia | 2006-2008 | 17/17 | 83/89 | Heroin | OH | 2 †/2 † | NR | IN, IM |
| D’Orazio127 | 2009 | Case Series | USA | NR | NR | 3 | Fentanyl | NR | 0.93 \* | NR | IV |
| Mangili128 | 2009 | Case Series | USA | 2006 | 1 | 3 | Multiple | NR | NR | 5.3 \* | IM |
| Cole129 | 2009 | Case Report | USA | NR | NR | 1 | Tramadol | PR | NR | 4 † | IV |
| Kalimullah130 | 2009 | Case Report | USA | NR | NR | 1 | Heroin | NR | 0.8 † | 1.2 † | NR |
| Tobin131 | 2009 | PS | USA | 2004-2005 | 6 | 19 | NR | NR | 0.4 † | 0.4-1.2 ‡ | IV |
| Martins132 | 2008 | Case Report | Brazil | NR | NR | 1 | Methadone | Hospital | 2 † | NR | IV |
| Simpson133 | 2008 | Case Report | USA | NR | NR | 1 | Heroin | NR | 2 † | 2 † | IM |
| Schumann32 | 2008 | RS | USA | 2006 | 9 | 43 | Heroin | NR | NR | 3.36 \* | IV, SL, neb |
| Augustine134 | 2007 | Case Report | USA | NR | NR | 1 | Morphine | PR | NR | 4 † | NR |
| Ridgway135 | 2007 | Case Report | England | NR | NR | 1 | Methadone | NR | 0.4 † | 1.6 † | IV |
| Wong136 | 2007 | Case Report | USA | NR | NR | 1 | Methadone | OH | 0.2 † | 0.6 † | IV |
| Boyd137 | 2006 | RS | Finland | 1995-2000 | 60 | 123 | Heroin | OH | 0.4 \* | NR | IV, IM,SC |
| Galea138 | 2006 | PS | USA | 2004 | 6 | 25 | NR | OH | 0.4 † | NR | IM |
| Belz139 | 2006 | Case Series | USA | 2004 | NR | 164 | NR | OH | 1 \* | 0.2-4 ‡ | IV, IM, IN |
| Mell140 | 2006 | Case Report | USA | NR | NR | 1 | Heroin | OH | 2 † | 2 † | IV |
| Kelly141 | 2005 | RCT | Australia | 2002-2003 | 12/12 | 84/71 | NR | OH | 2 †/2 † | NR | IN, IM |
| Barton142 | 2005 | PS Non-Randomised Controlled Trial | USA | 2001 | 6 | 95 | NR | OH | 2 † | NR | IN, IV |
| Miller143 | 2005 | Case Report | USA | NR | NR | 1 | Fentanyl | NR | NR | 6 † | IV |
| Buajordet144 | 2004 | PS | Norway | 1998-1999 | 12 | 1192 | Heroin | OH | 0.4-0.8 ‡ | 0.86 \* | IM, IV |
| Barrueto145 | 2004 | Case Report | USA | NR | NR | 1 | Fentanyl | OH | 0.4 † | 0.4 † | IV |
| Boyd146 | 2003 | RS | Finland | 1995-2002 | 87 | 11 | Buprenorphine | OH | 0.4 \* | NR | NR |
| Vilke147 | 2003 | RS | USA | 1996-2000 | 48 | 998 | Heroin | NR | 2 † | < 6 \* | IM, IV |
| Martin148 | 2003 | RS | USA | NR | NR | 366 | NR | NR | NR | 0.9 \* + Inf | NR |
| Mirakbari149 | 2003 | PS | Canada | 1997-1999 | 36 | 1155 | NR | NR | 0.4 † | NR | IV |
| Regnard150 | 2003 | Case Series | England | NR | NR | 2 | Fentanyl | NR | 0.24 \* | 0.24 \* + Inf | IV |
| Brink151 | 2003 | Case Report | South Africa | NR | NR | 1 | Etorphine (M99) | PR | NR | >1.2 \* | IV |
| Mycyk152 | 2003 | Case Report | USA | NR | NR | 1 | Methadone | OH | 2 † | 4 † + Inf | Neb |
| Kelly153 | 2002 | Case Series | Australia | NR | NR | 6 | Heroin | NR | 1.4 \* | NR | IN |
| Schneir154 | 2002 | Case Report | USA | NR | NR | 1 | Oxycontin | OH | 2 † | 44 † | IV |
| Reeves155 | 2002 | Case Report | Australia | NR | NR | 2 | Fentanyl | PR | 1.4 \* | 1.4 \* | IV |
| Wang156 | 2002 | Case Report | USA | NR | NR | 1 | Heroin, codeine | NR | 2 † | 2 † | IV |
| Dettmer157 | 2001 | PS | Germany | 1999-2000 | 16 | 29 | NR | PR | 0.4 † | 0.41 \* | IM, IV, SC |
| Christenson158 | 2000 | PS | Canada | 1997-1998 | 12 | 573 | Heroin | OH | 0.4-0.8 ‡ | 0.93 \* | IV, SC |
| Williams159 | 2000 | Case Report | USA | NR | NR | 1 | NR | OH | 0.4 † | 3 † | IV |
| Kaplan160 | 1999 | RCT | USA | NR | NR | 58 | Multiple | NR | 2 † | < 8 \* | IV |
| Watson161 | 1998 | RS | USA | 1987-1995 | 96 | 84 | Multiple | NR | 2 \* | NR | IV, ETT, IM |
| Wanger162 | 1998 | PS | Canada | 1996 | 4 | 122 | Heroin | OH | 0.8 † | NR | SC, IV |
| Hicks163 | 1998 | Case Report | USA | NR | NR | 2 | Heroin | OH | 2 † | 2 † | IM |
| Westerling164 | 1998 | Case Report | Sweden | NR | NR | 1 | Morphine | PR | 0.2 † | 0.52 \* | IV |
| Pedersen165 | 1997 | PS | Denmark | 1991 | 1.5 | 14 | NR | OH | NR | < 1 \* | NR |
| Sachdeva166 | 1997 | Case Report | USA | NR | NR | 1 | Tramadol | PR | 2 † | 6 † + Inf | IV |
| Sporer167 | 1996 | RS | USA | 1993 | NR | 16/609 | NR | OH | 2 †/2 † | 2.8 \*/2.5 \* | IM, IV, ETT |
| Osterwalder168 | 1996 | Case Series | Switzerland | 1991-1993 | 36 | 453 | Multiple | NR | NR | 0.2 \* | IV, IM |
| Hendra169 | 1996 | Case Report | England | NR | NR | 1 | Methadone | OH | 0.4 † | NR | IV |
| Marsden170 | 1996 | Case Report | Scotland | NR | NR | 1 | Dextropropoxyphene | PR | 0.4 † | 0.8 † | IV |
| Osterwalder171 | 1995 | PS | Switzerland | 1991-1992 | 36 | 142 | Heroin | NR | 0.2 † | 0.4 † | IV, IM |
| Gaddis172 | 1992 | Case Series | USA | NR | NR | 2 | Heroin | PR | 2 † | 2 † | IV |
| Kessler173 | 1991 | RS | Switzerland | NR | 12 | 125 | Heroin | OH | 0.2-0.4 ‡ | 0.55 \* | IV, IM |
| Schneider174 | 1991 | Case Report | USA | NR | NR | 1 | Dextromethorphan | OH | 1 † | 3 † | IV |
| Challoner175 | 1990 | RS | USA | 1977-1987 | 120 | 11 | Pentazocine | NR | NR | 0.8 \* | IV |
| Yealy176 | 1990 | RS | USA | 1986 | 12 | 813 | NR | OH | 0.4-0.8 ‡ | 0.9 \* | IV |
| Larpin177 | 1990 | RS | France | NR | 156 | 154 | Heroin | NR | 0.2-80 ‡ | 2.2+6.6 \* | NR |
| Leykin178 | 1989 | RS | Israel | 1982-1984 | 36 | 7 | NR | NR | 0.1-0.4 ‡ | NR | IV |
| Popper179 | 1989 | Case Report | USA | NR | NR | 1 | Heroin | OH | 2 † | 2 † | IV |
| Ruane180 | 1989 | Case Report | Northern Ireland | NR | NR | 1 | Dextropropoxyphene | PR | NR | 4 † | IV |
| Maio181 | 1987 | Case Report | USA | NR | NR | 1 | Heroin | OH | 0.4 † | 1.6 † | Intralingual, IM |
| Schwartz182 | 1987 | Case Report | USA | NR | NR | 1 | Codeine | OH | 0.4 † | 1.6 † | IV |
| Leslie183 | 1986 | Case Series | Scotland | NR | NR | 2 | Codeine | NR | 0.8 \* | 3.4 \* | IV |
| Arcangeli184 | 1986 | Case Report | Italy | NR | NR | 1 | Heroin | NR | 0.4 † | 0.4 † | IV |
| Durakovic185 | 1986 | Case Report | Croatia | NR | NR | 1 | Morphine | OH | 0.4 † | 1.6 † | IV |
| El-Mallakh186 | 1986 | Case Report | USA | NR | NR | 1 | Codeine | NR | 0.8 † | 1.6 † | IV |
| Romac187 | 1986 | Case Report | USA | NR | NR | 1 | Methadone | OH | 0.4 † | 4.8 † + Inf | NR |
| Blain188 | 1985 | Case Series | UK | NR | NR | 2 | Multiple | PR | NR | 1.4 \* | IV |
| Jackson189 | 1985 | Case Report | USA | NR | NR | 1 | Pentazocine | PR | 2 † | 2 † | IV |
| Cuss190 | 1984 | Case Report | England | NR | NR | 1 | Heroin | Hospital | 0.4 † | 1.6 \* | IV, IM |
| Paccaud191 | 1984 | Case Report | Switzerland | NR | NR | 1 | Heroin | OH | 0.4 † | NR | IV |
| Rupreht192 | 1983 | RCT | The Netherlands | NR | NR | 10 | Heroin | NR | NR | NR | IV |
| Parker193 | 1983 | Case Series | England | NR | NR | 2 | Dextropropoxyphene | OH | 0.6 \* | 1.4 \* + Inf | IV |
| Redfern194 | 1983 | Case Report | England | NR | NR | 1 | Dihydrocodeine | OH | 0.4 † | 2.4 † + Inf | IV |
| Stahl195 | 1983 | Case Report | USA | NR | NR | 1 | Pentazocine | OH | 0.4 † | 0.8 † | IV |
| Barraclough196 | 1982 | Case Report | England | NR | NR | 1 | Dextropropoxyphene | OH | 0.4 † | 0.8 † | IV |
| Tandberg197 | 1982 | Case Report | USA | NR | NR | 1 | Heroin | OH | 0.8 † | 1.6 † | ETT |
| Bradberry198 | 1981 | Case Series | USA | NR | NR | 2 | Multiple | OH | 0.4 \* | 1.6 \* | IV |
| Malizia199 | 1981 | Case Series | Italy | NR | NR | 20 | Heroin | NR | 0.4 \* | NR | IV |
| Cardan200 | 1981 | Case Report | Romania | NR | NR | 1 | Codeine | PR | 0.4 † | 0.8 † | IV |
| Starkey201 | 1978 | Case Report | Scotland | NR | NR | 1 | Dextropropoxyphene | OH | 1.2 † | NR | IV, SC |
| Wiseman202 | 1977 | Case Report | England | NR | NR | 1 | Dextropropoxyphene | OH | 0.4 † | 0.4 † | IV |
| Persky203 | 1976 | RS | USA | 1973-1974 | 8 | 81 | Methadone | NR | 0.4 † | 0.8-4 ‡ | IV |
| Gay204 | 1976 | Case Report | USA | NR | NR | 1 | NR | NR | 0.8 † | 0.8 † | NR |
| Lawrence205 | 1975 | Case Report | Scotland | NR | NR | 1 | Diamorphine | OH | 0.4 † | 0.4 † | IV |
| Gottlieb206 | 1974 | Case Series | USA | NR | NR | 1 | Heroin | OH | 0.4 † | 0.4 † | IV |
| Vlasses207 | 1974 | Case Series | USA | NR | NR | 2 | Propoxyphene | OH | 1.4 \* | NR | IV |
| Warren208 | 1974 | Case Report | USA | 1973 | NR | 1 | Propoxyphene | NR | 1 † | 1 † | NR |
| Kersh209 | 1973 | Case Report | USA | NR | NR | NR | NR | NR | 0.8 † | NR | NR |
| Evans210 | 1973 | Case Series | Scotland | NR | NR | 9 | Multiple | NR | 0.4 † | NR | IV |
| Kersh211 | 1973 | Case Report | USA | NR | NR | 1 | Propoxyphene | PR | 0.4 † | 1 \* | IM, IV |
| Tarala212 | 1973 | Case Report | Scotland | NR | NR | 1 | Dextropropoxyphene | OH | 0.8 † | NR | IV, IM |
| Waldron213 | 1973 | Case Report | USA | NR | NR | 1 | Methadone | NR | NR | 3.2 † + Inf | IV |
| Buchner214 | 1972 | Case Series | USA | NR | NR | 6 | Methadone | NR | NR | NR | IV |
| Kaufman215 | 1972 | Case Series | USA | NR | NR | 49 | Heroin | NR | 0.8 † | NR | IV |

**Footnote:** NR: not reported; RS=Retrospective study; PS=Prospective study; RCT=Randomized controlled trial; CS=Cross-sectional study; OH=Out of hospital; PR=Private residence; \*: Mean or median; †: Actual dose given; ‡: Dose range given; IV: Intravenous; IM: Intramuscular; IN: Intranasal; IO: Intraosseous; ETT: Endotracheal tube; SC: Subcutaneous; Neb: Nebulized; Inf: Infusion.

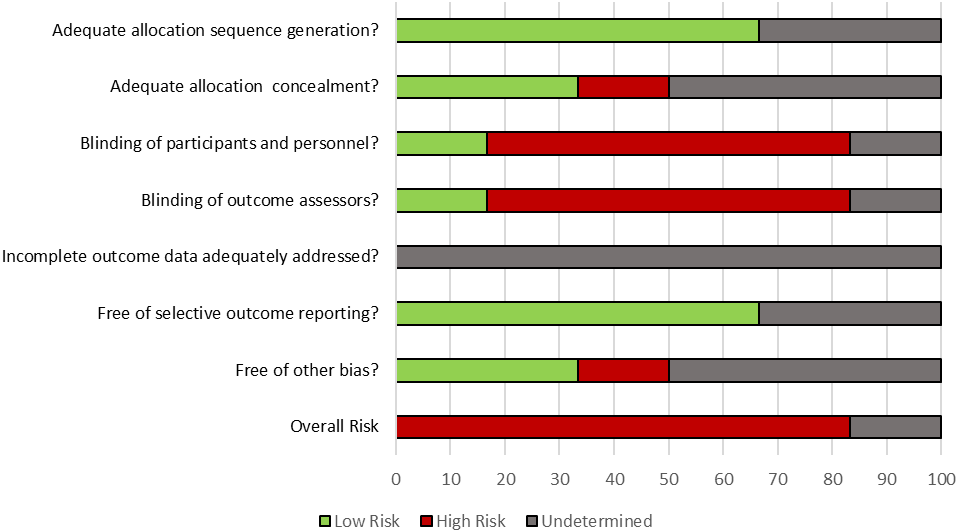
# Appendix Figure 1. Downs and Blacks Scores for Observational, Case Studies and Case Series.



Percentage of studies

**Appendix Figure 2.** Cochrane Risk of Bias Scores for Randomized Controlled Trials.

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Percentage of studies

**Appendix A: References**

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