**Supplementary table 1**: Details on adjustment of numbers to avoid repetition in studies which were an extension or long-term follow-up of initial studies

|  |  |  |  |
| --- | --- | --- | --- |
| Author/ Year | Number in the study | Adjusted number | Remarks |
| Colombel 2007(23) (CHARM trial) | 854 | 189 | Adjusted for ADHERE and extension trial of CHARM and ADHERE |
| Colombel 2014(25) (ULTRA 1,2, 3 long term extension) | 588 | 588 | Same |
| Hanauer 2006(44) (CLASSIC I trial) | 225 | 225 | Same |
| Lichtiger 2010(65) (CHOICE trial) | 673 | 673 | Same |
| Pannacione 2010(80) (ADHERE) |  | 138 | Adjusted for CHARM and extension trial of CHARM and ADHERE |
| Pannacione 2013(82) (CHARM and ADHERE extension) | 329 | 329 | Same |
| Reinisch 2011(92) (ULTRA 1) | 353 | 353 | 130 patients in 80/40 and 223 patients in 160/80 mg groups |
| Reinisch 2013(94) (ULTRA 1 extension) | 576 | 223 | Only patients in placebo arm of initial study, who received ADA later included (130+93=223) |
| Rutgeert 2012(98) (EXTEND trial) | 129 | 129 | Same |
| Sandborn 2007(99) (GAIN trial) | 159 | 159 | Same |

**Supplementary Table 2**: Quality of studies included in the meta-analysis as assessed by the New castle Ottawa scale

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author/ year** | | **Study design** | Selection | Comparability | Assessment | Total |
| Abreu 2017(1) | | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Agarwal 2018(2) | | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Akyuz 2015(3) | | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Alawneh 2014(4) | | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Algabav 2014(5) | | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Andersen 2015(6) | | Cohort study | \*\*\* | 1 | \*\*\* | 7 |
| Angelison 2016(7) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Balint 2016(8) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Bau 2017(9) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Belderbos 2013(10) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Belousova 2014(11) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Bermejo 2013(12) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Byun 2014(13) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Byun 2015(14) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Cagatay 2018(15) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Carbone 2007(16) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Carrillo 2013(17) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Caspersen 2008(18) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Cekic 2015(19) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Choi 2005(20) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Choi 2016(21) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Colombel 2004(22) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Colombel 2007(23) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Colombel 2010(24) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Colombel 2014(25) | Open labeled extension studies | \*\*\* | 0 | \*\*\* | 6 |
| Cordero-Ruiz 2011(26) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Cottone 2011(27) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| D'Haens 2017(28) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Didia 2014(29) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Duncan 2013(30) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Fidder 2008(31) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Fragaki 2014(32) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Freund 2018(33) | Cohort study | \*\*\* | 0 | \* | 4 |
| Gagniere 2018(34) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Garcia-Bosch 2016(35) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Garcia-Vidal 2009(36) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Gheorghe 2003(37) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Gies 2010(38) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| González-Lama 2008(39) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Greveson 2012(40) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Greveson 2013(41) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Hamzouglu 2010(42) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Hanauer 2002(43) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Hanauer 2006(44) | Randomized control trial | \*\*\* | 0 | \*\* | 5 |
| Hernandez Camba 2013(45) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Hong 2016(46) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Hou 2017(47) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Jauregui-Amezaga 2013(48) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Jung 2012(49) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Jung 2015(50) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Kamat 2019(51) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Kang 2018(52) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Keane 2001(53) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Kim 2013(54) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Kim 2014(55) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Kim 2015(56) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lawrance 2010(57) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lawrance 2014(58) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Lee 2013(59) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lee 2016(60) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lee 2017(61) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lee 2018(62) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lemann 2006(63) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Lichtenstein 2018(64) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lichtiger 2010(65) | Open labeled extension studies | \*\*\* | 0 | \*\* | 5 |
| Liu 2015(66) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Lofberg 2012(67) | Open labeled extension studies | \*\*\* | 0 | \*\* | 5 |
| Lonnkvist 2009(68) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Meghji 2017(69) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Meyer 2019(70) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Midha 2018(71) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Ministro 2011(72) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Motoya 2018(73) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Ng SC 2017(74) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Ochsenkuhn 2004(75) | Randomized control trial | \*\*\* | 0 | \*\* | 5 |
| Ogata 2016(76) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Oršić Frič 2014(77) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Ousslah 2010(78) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Pagliaro 2013(79) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Panaccione 2010(80) | Open labeled extension studies | \*\*\* | 0 | \*\*\* | 6 |
| Panaccione 2011(81) | Open labeled extension studies | \*\*\* | 0 | \*\* | 5 |
| Panaccione 2013(82) | Open labeled extension studies | \*\*\* | 0 | \*\*\* | 6 |
| Pannacione 2014(83) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Papay 2012(84) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Park 2015(85) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Pereira 2017(86) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Present 1999(87) | Randomized control trial | \*\*\* | 0 | \*\* | 5 |
| Puri 2017(88) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Qumseya 2011(89) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Ramos 2018(90) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Regueiro 2016(91) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Reinisch 2011(92) | Randomized control trial | \*\*\* | 0 | \*\* | 5 |
| Reinisch 2012(93) | Open labeled extension studies | \*\*\* | 0 | \*\*\* | 6 |
| Reinisch 2013(94) | Open labeled extension studies | \*\*\* | 0 | \*\*\* | 6 |
| Riis 2012(95) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Rodrigo 2004(96) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Rutgeerts 2005(97) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Rutgeerts 2012(98) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Sandborn 2007(99) | Randomized control trial | \*\*\* | 0 | \*\* | 5 |
| Sandborn 2007a(100) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Sandborn 2012(101) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Sands 2001(102) | Randomized control trial | \*\*\* | 0 | \*\* | 5 |
| Sands 2004(103) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Saoula 2014(104) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Schnitzler 2009(105) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Seiderer 2004(106) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Seminerio 2013(107) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Seo 2017(108) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Serghini 2009(109) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Sprakes 2012(110) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Suzuki 2013(111) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Swoger 2010(112) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Taxonera 2018(113) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Thi 2018(114) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Travis 2017(115) | Open labeled extension studies | \*\*\* | 0 | \*\* | 5 |
| Tweed 2015(116) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Van der Have 2014(117) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Wang 2018(118) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Watanabe 2012(119) | Randomized control trial | \*\*\* | 0 | \*\*\* | 6 |
| Watanabe 2014(120) | Open labeled extension studies | \*\*\* | 0 | \*\*\* | 6 |
| Wenzi 2004(121) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Winthrop 2013(122) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Yang 2015(123) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Ye 2014(124) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Yoo 2014(125) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Zabana 2008(126) | Cohort study | \*\*\* | 0 | \*\*\* | 6 |
| Zhou 2014(127) | Cohort study | \*\*\* | 0 | \*\* | 5 |
| Zhou 2015(128) | Cohort study | \*\*\* | 0 | \*\* | 5 |

References for the table are attached as supplementary file

**Supplementary Table 3**: Characteristics of studies included in meta-analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author/ year** | **Country** | **TB incidence/100000** | **Abstract/ Full-text** | **Study design** | **Study type** | **Mean age at anti-TNF** | **Males (n)** | **Duration of follow-up after anti-TNF** |
| Abreu 2017(1) | Portugal | 20 | Full-text | Cohort study | Prospective | 36.7 | 18 | 26 |
| Agarwal 2018(2) | India | 204 | Full-text | Cohort study | Retrospective | 35.6 | 35 | 19 |
| Akyuz 2015(3) | Turkey | 17 | Abstract | Cohort study | Retrospective | |  |  |
| Alawneh 2014(4) | Jordan | 6.8 | Full-text | Cohort study | Retrospective | 39.2 |  | 26.2 |
| Algabav 2014(5) | Spain | 10 | Abstract | Cohort study | Prospective |  |  |  |
| Andersen 2015(6) | Denmark | 5.1 | Full-text | Cohort study | Retrospective | 44.6 | 606 | 12 |
| Angelison 2016(7) | Sweden | 5.7 | Full-text | Cohort study | Retrospective | 33.9 | 153 | 34.8 |
| Balint 2016(8) | Hungary | 7.4 | Full-text | Cohort study | Prospective |  | 40 | 12 |
| Bau 2017(9) | Brazil | 44 | Full-text | Cohort study | Retrospective | 35.6 | 62 | 47 |
| Belderbos 2013(10) | Netherlands | 5.2 | Abstract | Cohort study | Retrospective | | 220 | 24 |
| Belousova 2014(11) | Russia | 60 | Abstract | Cohort study | Prospective | 37.5 | 31 |  |
| Bermejo 2013(12) | Spain | 10 | Full-text | Cohort study | Prospective | 42 | 33 | 30 |
| Byun 2014(13) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 33 | 579 | 27 |
| Byun 2015(14) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 28.5 | 108 | 76.3 |
| Cagatay 2018(15) | Turkey | 17 | Full-text | Cohort study | Retrospective | |  |  |
| Carbone 2007(16) | Spain | 10 | Full-text | Cohort study | Prospective | 37 | 27 | 56 |
| Carrillo 2013(17) | Spain | 10 | Abstract | Cohort study | Retrospective | |  | 17.5 |
| Caspersen 2008(18) | Denmark | 5.1 | Full-text | Cohort study | Retrospective | 31.6 | 266 | 29.1 |
| Cekic 2015(19) | Turkey | 17 | Full-text | Cohort study | Retrospective | 42 | 53 | 15 |
| Choi 2005(20) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 25.3 | 8 | 13.1 |
| Choi 2016(21) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 29.5 | 206 | 30 |
| Colombel 2004(22) | USA | 10 | Full-text | Cohort study | Retrospective | 37 | 219 | 17 |
| Colombel 2007(23) | USA, Canada, Europe, South Africa, Australia | 3.1 | Full-text | Randomized control trial | Prospective | 37.1 | 326 | 14 |
| Colombel 2010(24) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 34.5 | 172 |  |
| Colombel 2014(25) | North America, Europe, Australia, New Zealand | 3.1 | Full-text | Open labeled extension studies | Prospective | 39.6 | 358 | 48 |
| Cordero-Ruiz 2011(26) | Spain | 10 | Full-text | Cohort study | Retrospective | 38.3 | 10 | 12 |
| Cottone 2011(27) | Italy | 6.9 | Full-text | Cohort study | Prospective | 71 | 55 | 26 |
| Cottone 2011a(27) | Italy | 6.9 | Full-text | Cohort study | Prospective | 38.5 | 110 | 28 |
| D'Haens 2017(28) | USA, Canada, Europe | 3.1 | Full-text | Cohort study | Prospective | 37.8 | 2156 | 36 |
| Didia 2014(29) | Brazil | 44 | Abstract | Cohort study | Prospective |  |  |  |
| Duncan 2013(30) | UK | 8.9 | Abstract | Cohort study | Retrospective | |  |  |
| Fidder 2008(31) | Belgium | 9.8 | Full-text | Cohort study | Retrospective | 40 | 316 | 60 |
| Fragaki 2014(32) | Greece | 4.1 | Abstract | Cohort study | Prospective |  | 35 | 27 |
| Freund 2018(33) | France | 8 | Full-text | Cohort study | Retrospective | |  |  |
| Gagniere 2018(34) | Multiple | 3.1 | Full-text | Cohort study | Retrospective | | 401 | 111 |
| Garcia-Bosch 2016(35) | Spain | 10 | Full-text | Cohort study | Retrospective | 36.4 | 27 | 69.5 |
| Garcia-Vidal 2009(36) | Spain | 10 | Full-text | Cohort study | Retrospective | 49.3 |  | 17 |
| Gheorghe 2003(37) | Romania | 14 | Abstract | Cohort study | Retrospective | | 13 | 6 |
| Gies 2010(38) | Canada | 5.5 | Full-text | Cohort study | Retrospective | 32 | 32 | 13 |
| González-Lama 2008(39) | Spain | 10 | Full-text | Cohort study | Retrospective | 39 | 81 | 28 |
| Greveson 2012(40) | UK | 8.9 | Abstract | Cohort study | Prospective |  |  |  |
| Greveson 2013(41) | UK | 8.9 | Full-text | Cohort study | Retrospective | 35 | 64 | 24 |
| Hamzouglu 2010(42) | USA | 3.1 | Full-text | Cohort study | Retrospective | 40 | 119 | 14.3 |
| Hanauer 2002(43) | USA, Canada, Europe, Israel | 3.1 | Full-text | Randomized control trial | Prospective | 35 |  | 12 |
| Hanauer 2006(44) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 39 | 100 | 2 |
| Hernandez Camba 2013(45) | Spain | 10 | Abstract | Cohort study | Retrospective | | 47 | 21.6 |
| Hong 2016(46) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 40.7 | 1900 |  |
| Hou 2017(47) | USA | 3.1 | Full-text | Cohort study | Retrospective | 50.6 | 3013 | 26.4 |
| Jauregui-Amezaga 2013(48) | Spain | 10 | Full-text | Cohort study | Retrospective | |  |  |
| Jung 2012(49) | S. Korea | 70 | Full-text | Cohort study | Retrospective | |  | 38.5 |
| Jung 2015(50) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 27.7 | 697 | 4.7 |
| Kamat 2019(51) | India | 204 | Full-text | Cohort study | Retrospective | | 45 | 23 |
| Kang 2018(52) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 33.1 | 487 | 12 |
| Keane 2001(53) | USA | 10 | Full-text | Cohort study | Retrospective | |  |  |
| Kim 2013(54) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 28.5 | 55 | 34 |
| Kim 2014(55) | S. Korea | 70 | Full-text | Cohort study | Retrospective | |  | 10 |
| Kim 2015(56) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 32.5 | 255 | 81.6 |
| Lawrance 2010(57) | Australia & NZ | 6.8 | Full-text | Cohort study | Retrospective | 33.6 | 289 | 33 |
| Lawrance 2014(58) | Australia & NZ | 6.8 | Abstract | Cohort study | Retrospective | |  |  |
| Lee 2013(59) | S. Korea | 70 | Full-text | Cohort study | Retrospective | |  |  |
| Lee 2016(60) | S. Korea | 70 | Full-text | Cohort study | Retrospective | |  |  |
| Lee 2017(61) | Malaysia | 93 | Full-text | Cohort study | Retrospective | |  |  |
| Lee 2018(62) | China | 70 | Full-text | Cohort study | Retrospective | 36.5 |  | 16 |
| Lemann 2006(63) | France | 8 | Full-text | Randomized control trial | Prospective | 26.5 | 27 | 12 |
| Lichtenstein 2018(64) | North America | 3.1 | Full-text | Cohort study | Prospective | 40.5 | 1389 | 73.2 |
| Lichtiger 2010(65) | USA | 3.1 | Full-text | Open labeled extension studies | Prospective | 40.8 | 275 | 4 |
| Liu 2015(66) | USA | 3.1 | Full-text | Cohort study | Retrospective | 39.3 | 471 | 17.5 |
| Lofberg 2012(67) | Begium, Austria, Germany, Sweden | 9.8 | Full-text | Open labeled extension studies | Prospective |  | 377 | 6 |
| Lonnkvist 2009(68) | Sweden | 5.7 | Full-text | Cohort study | Retrospective | 36 | 39 | 18 |
| Meghji 2017(69) | UK | 8.9 | Full-text | Cohort study | Retrospective | | 230 |  |
| Meyer 2019(70) | France | 8 | Full-text | Cohort study | Prospective |  | 2344 | 11 |
| Midha 2018(71) | India | 204 | Full-text | Cohort study | Retrospective | 34.9 | 18 | 2 |
| Ministro 2011(72) | Portugal | 20 | Abstract | Cohort study | Prospective |  |  | 18 |
| Motoya 2018(73) | Japan | 15 | Full-text | Cohort study | Prospective | 33.6 | 16 |  |
| Ng SC 2017(74) | China | 70 | Abstract | Cohort study | Prospective | 35 | 54 | 19 |
| Ochsenkuhn 2004(75) | Germany | 7.5 | Full-text | Randomized control trial | Prospective | 31 | 3 | 4 |
| Ogata 2016(76) | Japan | 15 | Full-text | Cohort study | Prospective | 35.5 | 1109 | 6 |
| Oršić Frič 2014(77) | Croatia | 10 | Abstract | Cohort study | Retrospective | |  | 36.5 |
| Ousslah 2010(78) | France | 8 | Full-text | Cohort study | Retrospective | 38 | 93 | 18 |
| Pagliaro 2013(79) | Italy | 6.9 | Abstract | Cohort study | Retrospective | |  |  |
| Panaccione 2010(80) | USA, Canada, Europe | 3.1 | Full-text | Open labeled extension studies | Prospective |  |  |  |
| Panaccione 2011(81) | Canada | 5.5 | Full-text | Open labeled extension studies | Prospective | 37 | 131 | 6 |
| Panaccione 2013(82) | USA, Canada, Europe | 3.1 | Full-text | Open labeled extension studies | Prospective |  |  | 48 |
| Pannacione 2014(83) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 38 | 91 | 4 |
| Papay 2012(84) | Austria | 7.3 | Full-text | Cohort study | Prospective | 36.1 | 109 | 39 |
| Park 2015(85) | S. Korea | 70 | Full-text | Cohort study | Prospective | 38 | 116 | 7 |
| Pereira 2017(86) | Portugal | 20 | Full-text | Cohort study | Retrospective | |  | 45.6 |
| Present 1999(87) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 37.2 | 27 | 2 |
| Puri 2017(88) | India | 204 | Full-text | Cohort study | Retrospective | |  |  |
| Qumseya 2011(89) | USA | 3.1 | Full-text | Cohort study | Retrospective | 41 | 155 | 17 |
| Ramos 2018(90) | USA | 3.1 | Full-text | Cohort study | Retrospective | |  | 34.8 |
| Regueiro 2016(91) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 37.1 | 77 | 18 |
| Reinisch 2011(92) | North America, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 38.2 | 161 | 2 |
| Reinisch 2012(93) | USA, Canada, Europe | 3.1 | Full-text | Open labeled extension studies | Prospective | 40 | 134 | 26.4 |
| Reinisch 2013(94) | USA, Canada, Europe | 3.1 | Full-text | Open labeled extension studies | Prospective |  |  | 12 |
| Riis 2012(95) | Norway | 5.1 | Full-text | Cohort study | Retrospective | 29.7 | 45 | 11.4 |
| Rodrigo 2004(96) | Spain | 10 | Full-text | Cohort study | Retrospective | 36 | 44 | 9 |
| Rutgeerts 2005(97) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 42 | 150 | 12 |
| Rutgeerts 2005a(97) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 40 | 144 | 6 |
| Rutgeerts 2012(98) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 37.1 | 48 | 13 |
| Sandborn 2007(99) | USA, Canada, Belgium, France | 3.1 | Full-text | Randomized control trial | Prospective | 39 | 50 | 1 |
| Sandborn 2007a(100) | USA, Canada, Europe | 3.1 | Full-text | Randomized control trial | Prospective | 36 | 16 | 13 |
| Sandborn 2012(101) | North America, Europe, Australia, New Zealand | 3.1 | Full-text | Randomized control trial | Prospective | 39.6 | 142 | 13 |
| Sands 2001(102) | USA | 3.1 | Full-text | Randomized control trial | Prospective |  |  |  |
| Sands 2004(103) | USA, Canada, Europe, Israel | 3.1 | Full-text | Randomized control trial | Prospective | 37 | 53 | 12 |
| Saoula 2014(104) | Algeria | 70 | Abstract | Cohort study | Retrospective | 35.2 | 117 | 12 |
| Schnitzler 2009(105) | Belgium | 9.8 | Full-text | Cohort study | Retrospective | 33.9 | 240 | 55 |
| Seiderer 2004(106) | Germany | 7.5 | Full-text | Cohort study | Retrospective | 36 | 54 | 26 |
| Seminerio 2013(107) | USA | 3.1 | Full-text | Cohort study | Retrospective | 37 | 281 | 75.6 |
| Seo 2017(108) | S. Korea | 70 | Full-text | Cohort study | Retrospective | 42.1 | 119 | 21.3 |
| Serghini 2009(109) | Tunisia | 34 | Full-text | Cohort study | Retrospective | 32.9 | 13 | 12 |
| Sprakes 2012(110) | UK | 8.9 | Full-text | Cohort study | Retrospective | | 86 | 24 |
| Suzuki 2013(111) | Japan | 15 | Full-text | Randomized control trial | Prospective | 43.5 | 111 | 12 |
| Swoger 2010(112) | USA | 3.1 | Full-text | Cohort study | Retrospective | 35.7 | 45 | 13.7 |
| Taxonera 2018(113) | Spain | 10 | Full-text | Cohort study | Prospective | 43 | 107 | 12 |
| Thi 2018(114) | UK | 8.9 | Full-text | Cohort study | Retrospective | 39 | 303 |  |
| Travis 2017(115) | USA, Canada, Europe | 3.1 | Full-text | Open labeled extension studies | Prospective | 41.8 | 255 | 6 |
| Tweed 2015(116) | UK | 8.9 | Abstract | Cohort study | Retrospective | |  |  |
| Van der Have 2014(117) | Netherlands | 5.2 | Full-text | Cohort study | Retrospective | 33 | 215 | 24 |
| Wang 2018(118) | China | 70 | Full-text | Cohort study | Retrospective | 32.3 |  | 24.9 |
| Watanabe 2012(119) | Japan | 15 | Full-text | Randomized control trial | Prospective | 31 | 36 | 12 |
| Watanabe 2014(120) | Japan | 15 | Full-text | Open labeled extension studies | Prospective | 30.9 | 47 | 36 |
| Wenzi 2004(121) | Austria | 7.3 | Full-text | Cohort study | Retrospective | 37 | 69 | 29 |
| Winthrop 2013(122) | USA | 3.1 | Full-text | Cohort study | Retrospective | |  |  |
| Yang 2015(123) | S. Korea | 70 | Full-text | Cohort study | Retrospective | |  | 31.7 |
| Ye 2014(124) | China | 70 | Abstract | Cohort study | Retrospective | |  | 13 |
| Yoo 2014(125) | S. Korea | 70 | Full-text | Cohort study | Retrospective | |  |  |
| Zabana 2008(126) | Spain | 10 | Full-text | Cohort study | Retrospective | 44 | 31 | 19 |
| Zhou 2014(127) | China | 70 | Full-text | Cohort study | Retrospective | 41.8 | 18 | 6 |
| Zhou 2015(128) | China | 70 | Full-text | Cohort study | Retrospective | 28.3 | 49 | 6 |

TB: tuberculosis; TNF: Tumor necrosis factor

**Supplementary Table 4:** Details on development of tuberculosis (TB) in patients with inflammatory bowel disease (IBD) exposed to adalimumab/ infliximab

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Total IBD on anti-TNF** | **Total No of TB cases diagnosed** | **Median Duration of anti-TNF after which TB developed** | **PTB** | **EPTB** | **Dissemi-nated** | **Screening for LTB done (Yes/ No)** | **Number of patients positive for LTB at baseline** | **No. of TB cases in patients positive for LTB at baseline** | **No. of TB cases in patients negative for LTB at baseline** |
| Abreu 2017(1) | 46 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Agarwal 2018(2) | 69 | 8 | 5 | 1 | 2 | 5 | Yes | 7 | 0 | 8 |
| Akyuz 2015(3) | 175 | 4 | 33 |  |  |  | Yes |  | 4 | 0 |
| Alawneh 2014(4) | 28 | 1 | 6 | 0 | 1 | 0 | Yes |  | 0 | 1 |
| Algabav 2014(5) | 133 | 3 | 48 | 1 | 0 | 2 | Yes |  | 3 | 0 |
| Andersen 2015(6) | 1444 | 0 |  |  |  |  | No |  | 0 | 0 |
| Angelison 2016(7) | 250 | 1 |  | 0 | 1 | 0 | No |  |  |  |
| Balint 2016(8) | 73 | 0 |  |  |  |  | No |  |  |  |
| Bau 2017(9) | 130 | 4 |  |  |  |  | Yes |  | 0 | 4 |
| Belderbos 2013(10) | 611 | 3 |  |  |  |  | Yes | 15 | 1 | 2 |
| Belousova 2014(11) | 71 | 5 |  | 5 | 0 | 0 | Yes |  |  |  |
| Bermejo 2013(12) | 74 | 0 |  |  |  |  | Yes | 0 | 0 | 0 |
| Byun 2014(13) | 873 | 25 | 23 | 21 | 4 | 0 | Yes | 73 | 3 | 22 |
| Byun 2015(14) | 160 | 5 | 7 | 4 | 1 | 0 | Yes | 17 | 0 | 5 |
| Cagatay 2018(15) | 127 | 7 |  | 4 | 3 | 0 | Yes |  |  |  |
| Carbone 2007(16) | 34 | 1 | 1 | 1 | 0 | 0 | No |  |  |  |
| Carrillo 2013(17) | 345 | 3 |  |  |  |  | No |  |  |  |
| Caspersen 2008(18) | 651 | 2 |  |  |  |  | No |  |  |  |
| Cekic 2015(19) | 76 | 3 | 5 | 1 | 2 | 0 | Yes | 45 | 1 | 2 |
| Choi 2005(20) | 13 | 0 |  |  |  |  | No |  |  |  |
| Choi 2016(21) | 317 | 7 | 2 | 7 | 0 | 0 | Yes |  | 1 | 6 |
| Colombel 2004(22) | 500 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Colombel 2007(23) | 189 | 2 | 19 | 2 | 0 | 0 | Yes |  | 0 | 2 |
| Colombel 2010(24) | 338 | 1 | 3 |  |  |  | Yes |  | 0 | 1 |
| Colombel 2014(25) | 600 | 1 |  |  |  |  | No |  |  |  |
| Cordero-Ruiz 2011(26) | 25 | 1 |  | 0 | 1 | 0 | Yes |  |  |  |
| Cottone 2011(27) | 95 | 1 |  |  |  |  | Yes |  |  |  |
| Cottone 2011a(27) | 190 | 0 |  |  |  |  | Yes |  |  |  |
| D'Haens 2017(28) | 77 | 3 |  | 1 | 2 | 0 | Yes |  | 0 | 3 |
| Didia 2014(29) | 5025 | 10 |  |  |  |  | Yes |  | 0 | 10 |
| Duncan 2013(30) | 69 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Fidder 2008(31) | 743 | 2 | 24 | 0 | 2 | 0 | Yes | 16 | 0 | 2 |
| Fragaki 2014(32) | 68 | 0 |  |  |  |  | Yes | 19 | 0 | 0 |
| Freund 2018(33) | 91 | 0 |  |  |  |  | Yes |  |  |  |
| Gagniere 2018(34) | 551 | 4 | 16 | 2 | 0 | 2 | Yes |  |  |  |
| Garcia-Bosch 2016(35) | 53 | 2 |  | 1 | 1 | 0 | Yes |  | 1 | 1 |
| Garcia-Vidal 2009(36) | 25 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Gheorghe 2003(37) | 24 | 0 |  |  |  |  | No |  |  |  |
| Gies 2010(38) | 53 | 0 |  |  |  |  | No |  |  |  |
| González-Lama 2008(39) | 169 | 0 |  |  |  |  | No |  |  |  |
| Greveson 2012(40) | 148 | 0 |  |  |  |  | Yes | 1 | 0 | 0 |
| Greveson 2013(41) | 125 | 0 |  |  |  |  | Yes | 2 | 0 | 0 |
| Hamzouglu 2010(42) | 297 | 0 |  |  |  |  | Yes |  |  |  |
| Hanauer 2002(43) | 225 | 1 | 4.5 |  |  |  | No |  |  |  |
| Hanauer 2006(44) | 225 | 0 |  |  |  |  | No |  |  |  |
| Hernandez Camba 2013(45) | 99 | 2 |  | 1 | 0 | 1 | Yes | 5 | 0 | 2 |
| Hong 2016(46) | 3730 | 64 | 16.4 |  |  |  | Yes |  |  |  |
| Hou 2017(47) | 3357 | 2 | 13 | 2 | 0 | 0 | Yes | 46 | 2 | 0 |
| Jauregui-Amezaga 2013(48) | 423 | 7 | 3 | 3 | 4 | 0 | Yes | 30 | 1 | 6 |
| Jung 2012(49) | 42 | 0 |  |  |  |  | Yes |  |  |  |
| Jung 2015(50) | 1046 | 21 | 9.3 |  |  |  | Yes | 31 |  |  |
| Kamat 2019(51) | 70 | 3 | 8 | 3 | 0 | 0 | Yes |  | 0 | 3 |
| Kang 2018(52) | 740 | 8 | 4 | 4 | 0 | 4 | Yes | 84 | 1 | 7 |
| Keane 2001(53) | 76000 | 18 | 3 |  |  |  | Yes |  |  |  |
| Kim 2013(54) | 80 | 2 |  | 2 | 0 | 0 | Yes | 7 |  |  |
| Kim 2014(55) | 211 | 3 | 12 | 0 | 0 | 3 | Yes |  | 0 | 3 |
| Kim 2015(56) | 376 | 16 | 7.5 | 3 | 4 | 9 | Yes | 30 | 4 | 12 |
| Lawrance 2010(57) | 626 | 0 |  |  |  |  | Yes | 3 | 0 | 0 |
| Lawrance 2014(58) | 591 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Lee 2013(59) | 93 | 3 | 4 | 3 | 0 | 0 | Yes |  | 2 | 1 |
| Lee 2016(60) | 821 | 10 | 3 | 8 | 0 | 2 | Yes |  | 4 | 6 |
| Lee 2017(61) | 74 | 3 |  | 2 | 0 | 1 | Yes |  |  |  |
| Lee 2018 | 83 | 1 | 20 | 1 | 0 | 0 | Yes | 5 | 0 | 1 |
| Lemann 2006(63) | 57 | 0 |  |  |  |  | Yes |  |  |  |
| Lichtenstein 2018(64) | 3440 | 3 |  |  |  |  | Yes |  |  |  |
| Lichtiger 2010(65) | 673 | 0 |  |  |  |  | No |  |  |  |
| Liu 2015(66) | 1030 | 4 |  |  |  |  | No |  |  |  |
| Lofberg 2012(67) | 945 | 0 |  |  |  |  | No |  |  |  |
| Lonnkvist 2009(68) | 103 | 0 |  |  |  |  | No |  |  |  |
| Meghji 2017(69) | 471 | 1 |  |  |  |  | Yes | 15 |  |  |
| Meyer 2019(70) | 5050 | 12 |  |  |  |  | No |  |  |  |
| Midha 2018(71) | 29 | 4 | 8 | 2 | 2 | 0 | Yes |  |  |  |
| Ministro 2011(72) | 18 | 0 |  |  |  |  | Yes |  |  |  |
| Motoya 2018(73) | 28 | 0 |  |  |  |  | Yes |  |  |  |
| Ng SC 2017(74) | 81 | 1 | 15 |  |  |  | Yes | 18 | 1 | 0 |
| Ochsenkuhn 2004(75) | 6 | 0 |  |  |  |  | Yes |  |  |  |
| Ogata 2016(76) | 1693 | 1 | 3 | 1 | 0 | 0 | Yes | 116 | 0 | 1 |
| Oršić Frič 2014(77) | 82 | 2 |  |  |  |  | No |  |  |  |
| Ousslah 2010(78) | 191 | 1 | 5 | 0 | 1 | 0 | No |  |  |  |
| Pagliaro 2013(79) | 63 | 2 |  |  |  |  | Yes | 11 | 2 | 0 |
| Panaccione 2010(80) | 138 | 1 |  |  |  |  | No |  |  |  |
| Panaccione 2011(81) | 304 | 0 |  |  |  |  | No |  |  |  |
| Panaccione 2013(82) | 329 | 0 |  |  |  |  | No |  |  |  |
| Pannacione 2014(83) | 159 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Papay 2012(84) | 203 | 0 |  |  |  |  | Yes | 39 | 0 | 0 |
| Park 2015(85) | 173 | 1 |  |  |  |  | No |  |  |  |
| Pereira 2017(86) | 177 | 5 |  | 2 | 3 | 0 | Yes | 8 | 1 | 4 |
| Present 1999(87) | 63 | 0 |  |  |  |  | No |  |  |  |
| Puri 2017(88) | 79 | 7 | 2 | 1 | 2 | 4 | Yes |  | 0 | 7 |
| Qumseya 2011(89) | 340 | 1 | 9 | 0 | 1 | 0 | Yes | 5 | 0 | 1 |
| Ramos 2018(90) | 25 | 1 | 6 | 0 | 0 | 1 | Yes | 35 | 1 | 0 |
| Regueiro 2016(91) | 147 | 1 |  |  |  |  | No |  |  |  |
| Reinisch 2011(92) | 260 | 0 |  |  |  |  | No |  |  |  |
| Reinisch 2012(93) | 229 | 0 |  |  |  |  | Yes |  |  |  |
| Reinisch 2013(94) | 223 | 0 |  |  |  |  | No |  |  |  |
| Riis 2012(95) | 83 | 1 |  | 0 | 1 | 0 | Yes |  | 0 | 1 |
| Rodrigo 2004(96) | 81 | 3 |  | 3 | 0 | 0 | Yes |  | 0 | 3 |
| Rutgeerts 2005(97) | 243 | 1 |  |  |  |  | Yes |  |  |  |
| Rutgeerts 2005a(97) | 241 | 0 |  |  |  |  | Yes |  |  |  |
| Rutgeerts 2012(98) | 129 | 0 |  |  |  |  | No |  |  |  |
| Sandborn 2007(99) | 159 | 0 |  |  |  |  | No |  |  |  |
| Sandborn 2007a(99) | 37 | 0 |  |  |  |  | No |  |  |  |
| Sandborn 2012(101) | 248 | 0 |  |  |  |  | No |  |  |  |
| Sands 2001(102) | 8 | 0 |  |  |  |  | No |  |  |  |
| Sands 2004(103) | 96 | 0 |  |  |  |  | No |  |  |  |
| Saoula 2014(104) | 214 | 4 | 18 | 1 | 1 | 2 | Yes | 28 | 2 | 2 |
| Schnitzler 2009(105) | 614 | 1 |  | 0 | 1 | 0 | No |  |  |  |
| Seiderer 2004(106) | 100 | 0 |  |  |  |  | Yes | 2 | 0 | 0 |
| Seminerio 2013(107) | 492 | 0 |  |  |  |  | No |  |  |  |
| Seo 2017(108) | 195 | 1 |  | 0 | 1 | 0 | No |  |  |  |
| Serghini 2009(109) | 20 | 1 |  | 0 | 1 | 0 | Yes | 13 | 0 | 1 |
| Sprakes 2012(110) | 210 | 1 |  | 1 | 0 | 0 | Yes |  | 0 | 1 |
| Suzuki 2013(111) | 240 | 1 | 2.5 |  |  |  | Yes |  | 0 | 1 |
| Swoger 2010(112) | 118 | 1 |  | 1 | 0 | 0 | No |  |  |  |
| Taxonera 2018(113) | 188 | 0 | 16 | 0 | 0 | 0 | Yes | 37 | 0 | 0 |
| Thi 2018(114) | 596 | 6 | 13 | 1 | 3 | 2 | Yes | 31 | 0 | 6 |
| Travis 2017(115) | 463 | 0 |  |  |  |  | No |  |  |  |
| Tweed 2015(116) | 116 | 0 |  |  |  |  | Yes | 14 | 0 | 0 |
| Van der Have 2014(117) | 611 | 3 |  | 2 | 0 | 1 | Yes | 15 | 1 | 2 |
| Wang 2018 | 263 | 5 | 14 |  |  |  | No |  |  |  |
| Watanabe 2012(119) | 67 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Watanabe 2014(120) | 79 | 0 |  |  |  |  | Yes |  | 0 | 0 |
| Wenzi 2004(121) | 153 | 0 |  |  |  |  | No |  |  |  |
| Winthrop 2013(122) | 1220 | 2 |  |  |  |  | Yes |  |  |  |
| Yang 2015(123) | 57 | 1 | 1.5 | 1 | 0 | 0 | Yes |  | 1 | 0 |
| Ye 2014(124) | 1233 | 12 |  |  |  |  | Yes | 89 | 5 | 7 |
| Yoo 2014(125) | 422 | 5 | 12.1 |  |  |  | Yes |  |  |  |
| Zabana 2008(126) | 67 | 0 |  |  |  |  | Yes | 67 | 0 | 0 |
| Zhou 2014(127) | 24 | 1 |  |  |  |  | No |  |  |  |
| Zhou 2015(128) | 70 | 2 |  |  |  |  | No |  |  |  |

IBD: inflammatory bowel disease; TB: tuberculosis; TNF: tumor necrosis factor; LTB: latent tuberculosis; PTB: pulmonary tuberculosis; EPTB: extra-pulmonary tuberculosis

**Supplementary Table 5**: Details on development of tuberculosis (TB) in patients with inflammatory bowel disease exposed to infliximab/ adalimumab, according to disease and treatment type

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author/ year** | **All patients** | | **Crohn’s disease** | | **Ulcerative colitis** | | **Patients who received infliximab** | | **Patients who received adalimumab** | |
| **Total** | **No. with TB** | **Total** | **No. with TB** | **Total** | **No. with TB** | **Total** | **No. with TB** | **Total** | **No. with TB** |
| Abreu 2017(1) | 46 | 0 | 39 | 0 | 7 | 0 | 46 | 0 |  |  |
| Agarwal 2018(2) | 69 | 8 | 47 | 7 | 22 | 1 | 69 | 8 |  |  |
| Akyuz 2015(3) | 175 | 4 | 137 | 3 | 38 | 1 | 151 |  | 24 |  |
| Alawneh 2014(4) | 28 | 1 |  |  |  |  |  |  |  |  |
| Algabav 2014(5) | 133 | 3 | 110 |  | 23 |  |  |  |  |  |
| Andersen 2015(6) | 1444 | 0 | 628 | 0 | 816 | 0 | 1243 | 0 | 201 | 0 |
| Angelison 2016(7) | 250 | 1 |  |  | 250 | 1 | 250 |  |  |  |
| Balint 2016(8) | 73 | 0 |  |  | 73 | 0 |  |  | 73 | 0 |
| Bau 2017(9) | 130 | 4 | 130 | 4 |  |  | 68 | 1 | 62 | 3 |
| Belderbos 2013(10) | 611 | 3 | 611 | 3 |  |  | 556 |  | 55 |  |
| Belousova 2014(11) | 71 | 5 | 26 |  | 45 |  | 71 |  |  |  |
| Bermejo 2013(12) | 74 | 0 | 62 | 0 | 12 | 0 | 47 | 0 | 27 | 0 |
| Byun 2014(13) | 873 | 25 | 643 | 19 | 230 | 6 | 759 | 25 | 181 | 0 |
| Byun 2015(14) | 160 | 5 | 128 | 3 | 32 | 2 | 133 | 5 | 29 | 0 |
| Cagatay 2018(15) | 127 | 7 |  | 4 |  | 3 |  |  |  |  |
| Carbone 2007(16) | 34 | 1 | 34 |  |  |  | 34 | 1 |  |  |
| Carrillo 2013(17) | 345 | 3 | 268 |  | 77 |  | 255 | 2 | 90 | 1 |
| Caspersen 2008(18) | 651 | 2 | 619 |  | 32 |  | 651 | 2 |  |  |
| Cekic 2015(19) | 76 | 3 | 51 | 2 | 25 | 1 | 44 | 2 | 32 | 1 |
| Choi 2005(20) | 13 | 0 | 13 | 0 |  |  | 13 | 0 |  |  |
| Choi 2016(21) | 317 | 7 | 317 | 7 |  |  | 317 | 7 |  |  |
| Colombel 2004(22) | 500 | 0 | 500 | 0 |  |  | 500 | 0 |  |  |
| Colombel 2007(23) | 189 | 2 | 189 | 2 |  |  |  |  | 189 | 2 |
| Colombel 2010(24) | 338 | 1 | 338 | 1 |  | 0 | 338 | 1 |  |  |
| Colombel 2014(25) | 588 | 1 |  |  | 588 | 1 |  |  | 588 | 1 |
| Cordero-Ruiz 2011(26) | 25 | 1 | 25 | 1 |  |  |  |  | 25 | 1 |
| Cottone 2011(27) | 95 | 1 | 58 | 0 | 37 | 1 | 78 |  | 17 |  |
| Cottone 2011a(27) | 190 | 0 | 116 |  | 74 |  | 158 |  | 32 |  |
| D'Haens 2017(28) | 5025 | 10 | 5025 | 10 |  |  |  |  | 5025 | 10 |
| Didia 2014(29) | 77 | 3 | 73 |  | 4 |  |  |  | 77 | 3 |
| Duncan 2013(30) | 69 | 0 |  |  |  |  |  |  |  |  |
| Fidder 2008(31) | 743 | 2 | 597 |  | 137 |  | 743 | 2 |  |  |
| Fragaki 2014(32) | 68 | 0 | 56 | 0 | 12 | 0 |  |  |  |  |
| Freund 2018(33) | 91 | 0 | 91 | 0 |  |  |  |  |  |  |
| Gagniere 2018(34) | 551 | 3 |  |  |  |  |  |  |  |  |
| Garcia-Bosch 2016(35) | 53 | 2 |  |  | 53 | 2 | 53 | 2 |  |  |
| Garcia-Vidal 2009(36) | 25 | 0 | 25 | 0 |  |  | 25 | 0 |  |  |
| Gheorghe 2003(37) | 24 | 0 | 24 | 0 |  |  | 24 | 0 |  |  |
| Gies 2010(38) | 53 | 0 |  |  | 53 | 0 | 28 |  | 25 |  |
| González-Lama 2008(39) | 169 | 0 | 169 | 0 |  |  | 169 | 0 |  |  |
| Greveson 2012(40) | 148 | 0 |  |  |  |  |  |  |  |  |
| Greveson 2013(41) | 125 | 0 | 102 | 0 | 16 | 0 |  | 0 |  | 0 |
| Hamzouglu 2010(42) | 297 | 0 | 297 | 0 |  |  | 297 | 0 |  |  |
| Hanauer 2002(43) | 225 | 1 | 225 | 1 |  |  | 225 | 1 |  |  |
| Hanauer 2006(44) | 225 | 0 | 225 | 0 |  |  |  |  | 225 | 0 |
| Hernandez Camba 2013(45) | 99 | 2 | 88 | 1 | 11 | 1 |  |  |  |  |
| Hong 2016(46) | 3730 | 64 | 2790 | 42 | 1130 | 22 |  |  |  |  |
| Hou 2017(47) | 3357 | 2 | 1954 |  | 775 |  | 2229 |  | 1097 |  |
| Jauregui-Amezaga 2013(48) | 423 | 7 | 329 | 4 | 94 | 3 | 354 | 6 | 201 | 1 |
| Jung 2012(49) | 42 | 0 | 42 | 0 |  |  |  | 0 |  |  |
| Jung 2015(50) | 1046 | 21 |  |  |  |  |  | 21 |  |  |
| Kamat 2019(51) | 70 | 3 | 49 | 1 | 21 | 2 |  |  | 70 | 3 |
| Kang 2018(52) | 740 | 8 | 597 | 5 | 143 | 3 | 507 | 6 | 227 | 2 |
| Keane 2001(53) | 76000 | 18 | 76000 | 18 |  |  | 76000 | 18 |  |  |
| Kim 2013(54) | 80 | 2 | 80 | 2 |  |  | 80 | 2 |  |  |
| Kim 2014(55) | 211 | 3 | 160 | 3 | 51 | 0 |  | 3 |  | 0 |
| Kim 2015(56) | 376 | 16 | 277 | 11 | 99 | 5 | 294 | 15 | 82 | 1 |
| Lawrance 2010(57) | 626 | 0 | 489 | 0 | 137 | 0 | 563 | 0 | 172 | 0 |
| Lawrance 2014(58) | 591 | 0 | 491 | 0 | 100 | 0 | 536 | 0 | 108 | 0 |
| Lee 2013(59) | 93 | 3 | 83 | 3 | 10 | 0 |  | 3 |  | 0 |
| Lee 2016(60) | 821 | 10 | 661 | 9 | 160 | 1 | 592 | 9 | 229 | 1 |
| Lee 2017(61) | 74 | 3 |  |  |  |  |  |  |  |  |
| Lee 2018(62) | 83 | 1 | 70 | 1 | 12 | 0 |  |  |  |  |
| Lemann 2006(63) | 57 | 0 | 57 |  |  | 0 | 57 | 0 |  |  |
| Lichtenstein 2018(64) | 3440 | 3 | 3440 | 3 |  |  | 3440 | 3 |  |  |
| Lichtiger 2010(65) | 673 | 0 | 673 | 0 |  |  |  |  | 673 | 0 |
| Liu 2015(66) | 1030 | 4 |  | 4 |  |  | 515 | 1 | 515 | 3 |
| Lofberg 2012(67) | 945 | 0 | 945 | 0 |  |  |  |  | 945 | 0 |
| Lonnkvist 2009(68) | 103 | 0 | 103 | 0 |  |  | 103 | 0 |  |  |
| Meghji 2017(69) | 471 | 1 | 354 |  | 117 |  |  |  |  |  |
| Meyer 2019(70) | 5050 | 12 | 5050 | 12 |  |  | 5050 | 12 |  |  |
| Midha 2018(71) | 29 | 4 |  |  | 29 | 4 |  |  | 29 | 4 |
| Ministro 2011(72) | 18 | 0 |  |  |  |  |  |  |  |  |
| Motoya 2018(73) | 28 | 0 | 28 | 0 |  |  |  |  | 28 | 0 |
| Ng SC 2017(74) | 81 | 1 | 68 |  | 13 |  | 63 |  | 21 |  |
| Ochsenkuhn 2004(75) | 6 | 0 |  |  | 6 | 0 | 6 | 0 |  |  |
| Ogata 2016(76) | 1693 | 1 | 1693 | 1 |  |  |  |  | 1693 | 1 |
| Oršić Frič 2014(77) | 82 | 2 | 60 |  | 22 |  | 57 |  | 40 |  |
| Ousslah 2010(78) | 191 | 1 |  |  | 191 | 1 | 191 |  |  |  |
| Pagliaro 2013(79) | 63 | 2 | 37 | 2 | 26 | 0 |  |  |  |  |
| Panaccione 2010(80) | 138 | 1 | 138 | 1 |  |  |  |  | 138 | 1 |
| Panaccione 2011(81) | 304 | 0 | 304 | 0 |  |  |  |  | 304 | 0 |
| Panaccione 2013(82) | 329 | 0 | 329 | 0 |  |  |  |  | 329 | 0 |
| Pannacione 2014(83) | 159 | 0 |  |  | 159 | 0 | 159 | 0 |  |  |
| Papay 2012(84) | 203 | 0 | 174 | 0 | 53 | 0 |  | 0 |  | 0 |
| Park 2015(85) | 173 | 1 | 95 | 1 | 78 | 0 | 173 | 1 |  |  |
| Pereira 2017(86) | 177 | 5 | 162 |  | 15 |  | 135 |  | 66 |  |
| Present 1999(87) | 63 | 0 | 63 | 0 |  |  | 63 | 0 |  |  |
| Puri 2017(88) | 79 | 7 |  |  | 79 | 7 | 79 |  |  |  |
| Qumseya 2011(89) | 340 | 1 | 296 |  | 44 |  | 268 | 1 | 158 | 0 |
| Ramos 2018(90) | 25 | 1 |  | 1 |  | 0 |  | 0 |  | 1 |
| Regueiro 2016(91) | 147 | 1 | 147 | 1 |  |  | 147 | 1 |  |  |
| Reinisch 2011(92) | 353 | 0 |  |  | 353 | 0 |  |  | 353 | 0 |
| Reinisch 2012(93) | 229 | 0 |  |  | 229 | 0 | 229 | 0 |  |  |
| Reinisch 2013(94) | 223 | 0 |  |  | 223 | 0 |  |  | 223 | 0 |
| Riis 2012(95) | 83 | 1 | 83 | 1 |  |  | 64 | 1 | 19 | 0 |
| Rodrigo 2004(96) | 81 | 3 | 81 | 3 |  |  | 81 | 3 |  |  |
| Rutgeerts 2005(97) | 243 | 1 |  |  | 243 | 1 | 243 | 1 |  |  |
| Rutgeerts 2005a(97) | 241 | 0 |  |  | 241 |  | 241 |  |  |  |
| Rutgeerts 2012(98) | 129 | 0 | 129 | 0 |  |  |  |  | 129 | 0 |
| Sandborn 2007(99) | 159 | 0 | 159 | 0 |  |  |  |  | 159 | 0 |
| Sandborn 2007a(100) | 37 | 0 | 37 | 0 |  |  |  |  | 37 | 0 |
| Sandborn 2012(101) | 248 | 0 |  |  | 248 | 0 |  |  | 248 | 0 |
| Sands 2001(102) | 8 | 0 |  |  | 8 | 0 | 8 | 0 |  |  |
| Sands 2004(103) | 96 | 0 | 96 | 0 |  |  | 96 | 0 |  |  |
| Saoula 2014(104) | 214 | 4 | 177 | 4 | 37 | 0 |  |  |  |  |
| Schnitzler 2009(105) | 614 | 1 | 614 | 1 |  |  | 614 | 1 |  |  |
| Seiderer 2004(106) | 100 | 0 | 92 | 0 | 8 | 0 | 100 | 0 |  |  |
| Seminerio 2013(107) | 492 | 0 | 492 | 0 |  |  | 492 | 0 |  |  |
| Seo 2017(108) | 195 | 1 |  |  | 195 | 1 | 195 | 1 |  |  |
| Serghini 2009(109) | 20 | 1 | 20 | 1 |  |  | 20 | 1 |  |  |
| Sprakes 2012(110) | 210 | 1 | 210 | 1 |  |  | 210 | 1 |  |  |
| Suzuki 2013(111) | 240 | 1 |  |  | 240 | 1 |  |  | 240 | 1 |
| Swoger 2010(112) | 118 | 1 | 118 | 1 |  |  |  |  | 118 | 1 |
| Taxonera 2018(113) | 188 | 0 | 137 | 0 | 54 | 0 | 120 |  | 68 |  |
| Thi 2018(114) | 596 | 6 | 453 | 5 | 143 | 1 |  | 3 |  | 3 |
| Travis 2017(115) | 463 | 0 |  |  | 463 | 0 |  |  | 483 | 0 |
| Tweed 2015(116) | 116 | 0 |  |  |  |  |  |  |  |  |
| Van der Have 2014(117) | 611 | 3 | 611 | 3 |  |  | 557 | 2 | 54 | 1 |
| Wang 2018(118) | 263 | 5 | 228 |  | 45 |  | 213 |  | 79 |  |
| Watanabe 2012(119) | 67 | 0 | 67 | 0 |  |  |  |  | 67 | 0 |
| Watanabe 2014(120) | 79 | 0 | 79 | 0 |  |  |  |  | 79 | 0 |
| Wenzi 2004(121) | 153 | 0 | 153 | 0 |  |  | 153 | 0 |  |  |
| Winthrop 2013(122) | 1220 | 2 | 761 | 1 | 459 | 1 |  |  |  |  |
| Yang 2015(123) | 57 | 1 | 43 | 1 | 14 | 0 |  | 1 |  | 0 |
| Ye 2014(124) | 1233 | 12 |  |  |  |  | 1233 | 12 |  |  |
| Yoo 2014(125) | 422 | 5 |  |  |  |  |  |  |  |  |
| Zabana 2008(126) | 67 | 0 | 67 | 0 |  |  | 67 | 0 |  |  |
| Zhou 2014(127) | 24 | 1 |  |  | 24 | 1 | 24 | 1 |  |  |
| Zhou 2015(128) | 70 | 2 | 70 | 2 |  |  | 70 | 2 |  |  |

References for the table are attached as supplementary file

**Supplementary Table 6:** Metaregression analysis to compare prevalence of tuberculosis (TB) between Crohn’s disease (CD) and ulcerative colitis (UC)

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Number of Studies\*** | **Coefficient (95%CI)** | **P value** |
| Disease type (CD vs UC) | 132 | 0.99 (0.92 – 1.08) | 0.99 |
| Local TB burden  Low vs intermediate  Low vs high | 132 | 0.99 (0.86 – 1.15)  3.24 (2.18 – 4.81) | 0.96  <0.001 |
| Study type (Retrospective vs Prospective) | 132 | 1.04 (0.97 – 1.12) | 0.28 |
| Mean age at which anti-TNF was started | 94 | 0.99 (0.98 – 1.01) | 0.44 |
| Duration of follow-up after anti-TNF was started | 107 | 1.00 (0.99 – 1.00) | 0.25 |
| Gender | 102 | 1.03 (0.87 – 1.23) | 0.70 |

\*Same study was counted twice, if it had reported separately for TB in patients with Crohn’s disease and ulcerative colitis

**Supplementary Table 7**: Metaregression analysis to compare prevalence of tuberculosis (TB) between patients who received infliximab (IFX) vs adalimumab (ADA)

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **No. of Studies\*** | **Coefficient (95%CI)** | **P value** |
| Treatment type (IFX vs ADA) | 103 | 1.05 (0.89 – 1.25) | 0.50 |
| Local TB burden  Low vs intermediate  Low vs high | 103 | 1.02 (0.86 – 1.21)  2.13 (1.40 – 3.26) | 0.86  0.001 |
| Study type (Retrospective vs Prospective) | 103 | 0.98 (0.85 – 1.24) | 0.84 |
| Mean age at which anti-TNF was started | 82 | 0.99 (0.98 – 1.01) | 0.69 |
| Duration of follow-up after which anti-TNF was started | 91 | 1.00 (0.99 – 1.00) | 0.30 |
| Gender | 86 | 0.89 (0.77 – 1.03) | 0.13 |

\*Same study was counted twice, if it had reported separately for TB in patients on Infliximab or Adalimumab

Supplementary table 8: Pooled prevalence of tuberculosis (TB) in the entire cohort and as per the disease and treatment type and local TB burden

|  |  |  |  |
| --- | --- | --- | --- |
|  | Categories | Pooled prevalence | No of studies |
| Entire cohort | Entire cohort | 0.08%(95% CI: 0.05%–0.10%) | 130 |
| Low TB burden | 0.02%(95% CI: 0.02%–0.03%) | 85 |
| Intermediate TB burden | 0.21%(95% CI: -0.02%–0.43%) | 13 |
| High TB burden | 1.59%(95% CI: 1.19%-2.00%) | 32 |
| CD patients | All CD patients | 0.07% (95% CI: 0.04% – 0.09%) | 80 |
| Low TB burden | 0.03% (95% CI: 0.02% – 0.04%) | 51 |
| Intermediate TB burden | 0.10% (95% CI: -0.03% – 0.24%), | 9 |
| High TB burden | 1.55% (95% CI: 1.04% - 2.06%) | 20 |
| UC patients | All UC patients | 0.06% (95% CI: 0.04% – 0.09%) | 52 |
| Low TB burden | 0.03% (95% CI: 0.001% – 0.05%) | 30 |
| Intermediate TB burden | 0.58% (95% CI: -0.51% – 1.67%) | 4 |
| High TB burden | 0.88% (95% CI: 0.33% - 1.43%) | 18 |
| Patients who received IFX | All IFX patients | 0.06% (95% CI: 0.03% – 0.09%) | 59 |
| Low TB burden | 0.02% (95% CI: 0.01% – 0.03%) | 40 |
| Intermediate TB burden | 0.13% (95% CI: -0.39% – 0.67%) | 4 |
| High TB burden | 1.96% (95% CI: 1.17% - 2.75%) | 15 |
| Patients who received ADA | All ADA patients | 0.03% (95% CI: 0.01% – 0.05%) | 44 |
| Low TB burden | 0.03% (95% CI: 0.01% – 0.05%) | 29 |
| Intermediate TB burden | 0.09% (95% CI: -0.05% – 0.23%) | 6 |
| High TB burden | 0.43% (95% CI: -0.14% - 1.01%) | 9 |

CD-Crohn’s disease; UC-ulcerative colitis; IFX-infliximab; ADA-adalimumab

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