**SUPPLEMENTARY APPENDIX**

**Supplemental table 1: Search strategy**

|  |  |
| --- | --- |
| **Search no.** | **Search terms** |
| **1** | ((earl\* or late\* or time\* or delay\* or duration or prolong\* or long\* or short\* or interval\*) adj3 (diagnos\* or detect\* or refer\* or treat\* or pathway\*)).tw,kf. |
| **2** | delayed diagnosis/ or exp early diagnosis/ |
| **3** | (symptom\* adj2 onset adj3 (diagnos\* or detect\* or refer\* or treat\* or pathway\*)).tw,kf. |
| **4** | "age of onset"/ |
| **5** | (diagnos\* adj2 error\*).tw,kf. |
| **6** | exp Diagnostic Errors |
| **7** | or/1-6 |
| **8** | (inflammatory bowel disease or IBD or crohn\* or ulcerative colitis).tw,kf |
| **9** | exp Inflammatory Bowel Diseases/ |
| **10** | 8 or 9 |
| **11** | 7 and 10 |
| **12** | exp child/ not exp adult/ |
| **13** | exp animals/ not exp humans/ |
| **14** | 11 not (12 or 13) |
| **15** | limit 14 to english language |
| **16** | limit 15 to dt=20221001-20221005 |
| **17** | 15 not 16 |

**Supplemental Table 2: Studies reporting the mean time to diagnosis in Crohn’s Disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Diagnostic interval** | **Study** | **Year** | **Country** | **Time to diagnosis (months)** | |
|  |  |  |  | **Mean** | **(SD; Range)** |
| **Patient Interval** |  |  |  |  |  |
|  | Maconi G et al.81 | 2015 | Spain | 2.66 | (3.95; 0.5 - 24) |
| Degen A et al.26 | 2016 | Germany | 2 | - |
| **Healthcare Interval** |  |  |  |  |  |
|  | Maconi G et al.81 | 2015 | Spain | 14.52 | (38.99; 0 - 272) |
| **Total time to diagnosis interval** |  |  |  |  |  |
|  | Brandes J et al.41 | 1976 | Germany | 43.2 | NR |
| Harper PC et al.62 ∞ | 1986 | USA | 76.8 | (NR; 18) |
| Harper PC et al.62 ∞ | 1986 | USA | 28.8 | (NR; 8.4) |
| Colombel JF et al.47 | 1990 | France | 15 | - |
| Wengrower D et al.110 | 1997 | Israel | 4 | (NR; 1- 36) |
| Latour P et al.73 | 1998 | Belgium | 6.5 | - |
| Segal I et al.99\* | 1988 | South Africa | NR | (NR; 1-252) |
| Jovanovic A.67 | 1999 | Croatia | 22.8 | - |
| Pimentel M et al.95 | 2000 | USA | 92.4 | (128.4; NR) |
| Wagtmans MJ et al.109 ∞ | 2001 | Netherlands | 37.2 | (NR; 0 - 436.8) |
| Wagtmans MJ et al.109 ∞ | 2001 | Netherlands | 36 | (NR; 0 - 271.2) |
| Pilar N et al.90 | 2002 | Spain | - | (NR; 0.25 - 104) |
| Piront P et al.96 ∞ | 2002 | France | NR | (NR; 1 -24) |
| Piront P et al.96 ∞ | 2002 | France | NR | (NR; 1- 24) |
| Oriuchi T et al.91 | 2003 | Japan | 29.9 | (43;NR) |
| Ge ZZ et al.55 \* | 2004 | China | 84 | (90; NR) |
| Aghazadeh R et al.29 | 2005 | Iran | 17.7 | - |
| Vind I et al.108 | 2006 | Denmark | - | (NR; 0 -576) |
| Jiang Li et al.66 \* | 2006 | China | 13.2 | (NR; NR) |
| Burgmann T et al.7 | 2006 | Canada | 150 | (NR; NR) |
| Tine J et al.65 ∞ | 2007 | Denmark | 121.2 | (NR; 0 - 324) |
| Tine J et al.65 ∞ | 2007 | Denmark | NR | (NR; 0 - 108) |
| Tine J et al.65 ∞ | 2007 | Denmark | NR | (NR; 0 -158) |
| Albert JG et al.30 | 2008 | Germany | NR | (NR; 0 - 281) |
| Semnani Sh.100 | 2008 | Iran | 5 | (NR; NR) |
| Das K et al.49 | 2009 | India | 36 | (NR; 1 - 432) |
| Munkholm P et al.87 | 2009 | Denmark | NR | (NR; 0 -324) |
| Ozin Y et al.92 \* | 2009 | Turkey | 19.2 | (38.8;NR) |
| Guariso G et al.60 | 2010 | Italy | 12.4 | (NR; 0 - 88) |
| Barrat S M.36 ∞ | 2011 | UK | 48 | (NR; 6 - 396) |
| Barrat S M.36 ∞ | 2011 | UK | 24 | (NR; 9.6 - 444) |
| Jain A.K et al.64 | 2012 | India | 15.3 | (NR ; 1- 72) |
| Belousova K et al.38 | 2012 | Russia | 42 | (NR;NR) |
| Schoepfer AM et al.98 | 2013 | Switzerland | - | (NR; 0 - 80) |
| Furfaro F et al.54 | 2014 | Italy | - | (NR; 0 - 324) |
| Li Y et al.76 \* | 2015 | China | 29 | (44.3; NR) |
| Maconi G et al.81 | 2015 | Spain | 32.9 | (57.92; 1 - 324) |
| Moon C M et al.85 | 2015 | Korea | 16 | (31.1; 0 - 412.4) |
| Basaranoglu M et al.37\* | 2015 | Turkey | 3 | (2.8; 0 - 18) |
| Zaharie R et al.113 | 2016 | Romania | - | (NR; 0 - 42) |
| Farkas K et al.52 | 2016 | Hungary | 16 | - |
| Degan A et al.26 | 2016 | Germany | 12 | - |
| Irving P et al.63 | 2018 | Multiple\*\*\* | NR | (NR; 564) |
| Giannelis P et al.57 \* | 2019 | Greece | 11.8 | (19.1; NR) |
| Nobrega V G et al.88 \* | 2018 | Brazil | 28 | (48; NR) |
| Lazdr D et al.70 | 2018 | Romania | 4.2 | (NR; 0.5 - 46) |
| Benchimol E I et al. 40 ∞ | 2018 | Canada | 6.3 | (7.8;NR) |
| Benchimol E I et al.40 ∞ | 2018 | Canada | 5.9 | (7.6;NR) |
| Juliao F et al.68 \* | 2019 | Columbia | 13.5 | (24.8;NR) |
| Yue Li et al.76\* | 2019 | China | 32 | (46.4;NR) |
| Halawani H et al.61 | 2020 | Saudi Arabia | 23.3 | (24.2;NR) |
| Halawani H et al.61 \* | 2020 | Saudi Arabia | 20.6 | (24.9; NR) |
| Mayorga A et al.82 | 2020 | Ecuador | 11.6 | (38.1; NR) |
| Banerjee R et al.34 \* ∞ | 2020 | India | 42.2 | (46.1; NR) |
| Banerjee R et al.34 \* ∞ | 2020 | India | 23 | (39; NR ) |
| Abraham BP et al.28 ∞ | 2020 | USA | 72 | (70.8; NR) |
| Abraham BP et al.28 ∞ | 2020 | USA | 272 | (133.1; NR) |
| Gomes TNF et al.59 \* | 2021 | Brazil | 44.8 | (69; NR) |
|  | Chaparro M et al.46 | 2021 | Spain | NR | (NR; 1 - 15) |
| **Median of Means (IQR)** |  |  | 23.2 (13 – 38.3) |  |
| **Median (IQR) of means**  **High-income countries** |  |  | 28.8 ( 15.5 - 45.6) |  |
| **Median (IQR) of means**  **Low-and middle-income countries** |  |  | 17.7 (11.8 - 29) |  |
| **Pooled Weighted**  **mean of means (S.D)** |  |  | 17.5 (33.8) |  |
| **Pooled Weighted**  **mean of means (S.D)**  **High-income countries** |  |  | 15.0 (35.9) |  |
| **Pooled Weighted**  **mean of means (S.D)**  **Low-and middle-income countries** |  |  | 30.7 (12.4) |  |

**\* Represents low- and middle-income countries; NR, Not reported; IQR, interquartile range; \*\*\* Finland, Italy, France, Canada, Germany, UK, Spain and Sweden; ∞ Data from different population groups in study**

**Supplemental Table 3: Studies reporting the mean time to diagnosis in Ulcerative Colitis**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Diagnostic Interval** | **Study** | **Year** | **Country** | **Time to diagnosis (months)** | |
|  |  |  |  | **Mean** | **(S.D; Range)** |
| **Patient Interval** |  |  |  |  |  |
| Degen A et al.26 |  |  | 1 | - |
|  |  | |  |  | |
| **Healthcare Interval** | NR |  |  | - | - |
|  |  | |  |  | |
| **Total time to diagnosis Interval** |  |  |  |  |  |
|  | Nordenvall B et al.89 | 1984 | Denmark | 27.6 | (NR; NR) |
|  | Colombel JF et al.47 | 1990 | France | 6.8 | - |
| Langholz E et al.72 | 1991 | Denmark | NR | (NR; 0 – 444) |
| Stewenius J et al.105 | 1996 | Sweden | 12.3 | - |
| Park SM et al.93 | 1996 | Korea | NR | (NR;2.75-75) |
| Latour P et al.73 | 1998 | Belgium | 4.8 | - |
| Yang SK et al.111 | 2000 | Korea | - | (NR: 1-120) |
| Pimentel M et al.95 | 2000 | USA | 14.4 | (21.6; NR) |
| Ling KL et al.79 | 2002 | Singapore | 7.5 | (NR; 1- 60) |
| Piront P et al.96 ∞ | 2002 | France | NR | (NR; 1 - 24) |
| Piront P et al.96 ∞ | 2002 | France | NR | (NR; 1 - 24) |
| Aghazadeh R et al.29 | 2005 | Iran | 13.9 | - |
| Jiang Li et al.66 \* | 2005 | China | 16.8 | - |
| Vind I et al.108 | 2006 | Denmark | - | (NR; 0 - 408) |
| Burgmann T et al.7 | 2006 | Canada | 150 | (NR; NR) |
| Semnani Sh et al.100 | 2008 | Iran | 2.2 | (1.4; NR) |
| Ozin Y et al.92 \* | 2009 | Turkey | 12.3 | (20.9; NR) |
| Roth L S et al.97 | 2010 | Canada | 184.8 | (54; 0 - 408) |
| Guariso G et al.60 | 2010 | Italy | - | (NR; 0 - 78) |
| Barrat S M et al.36 ∞ | 2011 | UK | 12 | (NR; 9.6 - 480) |
| Barrat S M et al.36 ∞ | 2011 | UK | 12 | (NR; 3 - 144) |
| Belousova K et al.38 | 2012 | Russia | 18 | (NR ; NR) |
| Zhang Z et al.115 | 2012 | Singapore | 17.8 | (NR; NR) |
| Jain A.K et al.64 \* | 2012 | India | 45 | (NR ; 4 - 145) |
| Basaranoglu M et al.37\* | 2015 | Turkey | 3.2 | (2.6; 0 - 15) |
| Zaharie R et al.113 | 2016 | Romania | NR | (NR; 0 - 52) |
| Degan A et al.26 | 2016 | Germany | 4 | - |
| Farkas K et al.52 | 2016 | Hungary | 8.8 | - |
| Lin WC et al.77 ∞ | 2016 | Taiwan | 4.8 | (9.6; 0 - 120) |
| Lin WC et al.77 ∞ | 2016 | Taiwan | 26.4 | (54; 0 - 288) |
| Benchimol E I et al.40 ∞ | 2018 | Canada | 4.34 | (7.0;NR) |
| Benchimol E I et al.40 ∞ | 2018 | Canada | 4.41 | (7.2;NR) |
| Nobrega VG et al.88 \* | 2018 | Brazil | 19 | (46; NR) |
| Irving P et al.63 | 2018 | Multiple\*\*\* | NR | (NR; 552) |
| Kang HS et al.16 | 2019 | Korea | 7.4 | (16.1; NR) |
| Armuzzi A et al.32 | 2019 | Global | 24 | (64.8; NR) |
| Molander et al.84 | 2019 | Finland | 27.6 | (66; NR) |
| Giannelis P et al.57 \* | 2019 | Greece | 7.3 | (13.6; NR) |
| Juliao F et al.68\* | 2019 | Columbia | 11.8 | (21.1;NR) |
| Mayorga A et al.82 \* | 2020 | Ecuador | 7.5 | (18;NR) |
| Banerjee R et al.34\*∞ | 2020 | India | 37.2 | (43.8; NR) |
| Banerjee R et al.34 \* ∞ | 2020 | India | 18 | (49; NR) |
| Zammarchi I et al.114 ∞ | 2020 | Italy | 69.6 | (55.2; NR) |
| Zammarchi I et al.114 ∞ | 2020 | Italy | 74.4 | (56.4; NR) |
| Connor SJ et al.48 | 2021 | Australia | 28.8 | (60;NR) |
| Gomes TNF et al.59\* | 2021 | Brazil | 24.7 | (37.8;NR) |
| Dubinski MC et al.50 | 2021 | Global | 24 | (64.8;NR) |
| Chaparro M et al.46 | 2021 | Spain | NR | (NR; 1 - 5) |
| Ling KL et al.70 | 2022 | Singapore | 7.5 | (NR; 60) |
|  | **Median of Means (IQR)** |  |  | **13.9 ( 7.5 - 25.6)** |  |
| **Median (IQR) of means**  **High-income countries** |  |  | **12.2 (7.2 - 26.7)** |  |
| **Median (IQR) of means**  **Low-and middle-income countries** |  |  | **16.8 (12 - 21.9)** |  |
| **Pooled Weighted**  **mean of means (S.D)** |  |  | **13.5 (17.6)** |  |
| **Pooled Weighted**  **mean of means (S.D)**  **High-income countries** |  |  | **11.4 (17.7)** |  |
| **Pooled Weighted**  **mean of means (S.D)**  **Low-and middle-income countries** |  |  | **24.9 (11.9)** |  |
|  |  |  |  |  |

**\* Represents low-and middle-income countries; NR, Not reported; IQR, interquartile range; \*\*\* Finland, Italy, France, Canada, Germany, UK, Spain, and Sweden; ∞ Data from different population groups in study**

**Supplemental Table 4: Characteristics of included studies amongst individuals diagnosed with Crohn’s Disease**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Year | Country | Study design/  Data Source | Centre | Study period | Population characteristics  Median age (years) and  Sex (Female %) | n | Time to diagnosis interval measured | Impact of delay on clinical outcomes |
| Brandes J et al. 41 | **1976** | **Germany** | **Retrospective cohort/**  **EPR** | **Single centre** | **1963 - 1975** | **NR**  **NR** | **52** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Kyle J et al.69 | **1971** | **Scotland** | **Cross-sectional cohort/**  **Health records** | **NR** | **1955 - 1969** | **NR**  **42%** | **174** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Lind E et al.78 | **1985** | **Norway** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1975 - 1979** | **Range 7 - 68**  **44%** | **214** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Segal I et al.99 | **1988** | **South Africa** | **Prospective case series/EPR** | **Single centre** | **1975 – 1988** | **Mean 37**  **(Range 8 – 86)**  **74%** | **46** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Donald M et al.53 | **1986** | **UK** | **Retrospective cohort/**  **EPR** | **Single centre** | **1975 – 1983** | **NR\*\***  **NR\*\*** | **30** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Colombel JF et al.47 | **1990** | **France** | **Prospective cohort/**  **Questionnaire** | **Multicentre** | **1988** | **34a**  **58%** | **281** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Wengrower D et al.110 | **1997** | **Israel** | **Retrospective cohort/**  **Questionnaire** | **Regional** | **NR** | **19.4 a**  **37.7%** | **53** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Loftus E V et al.80 | **1998** | **USA** | **Retrospective cohort/**  **EPR** | **Regional** | **1940 - 1993** | **29.5**  **54%** | **225** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Latour P et al.73 | **1998** | **Belgium** | **Retrospective cohort/ Questionnaire** | **Multicentre** | **1993 – 1996** | **30 a**  **62%** | **137** | **Total Time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Timmer A et al.106 | **1999** | **Germany** | **Retrospective cohort/**  **EPR** | **Regional** | **1980 – 1984** | **NR\*\***  **NR\*\*** | **288** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Jovanovic A et al.67 | **1999** | **Croatia** | **Retrospective cohort/**  **EPR** | **Regional** | **1973 - 1994** | **NR** | **197** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Pimentel M et al.95 | **2000** | **USA** | **Retrospective cohort/**  **Questionnaire** | **Single tertiary** | **2000** | **42.6 a**  **60%** | **45** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Wagtmans MJ et al.109 | **2001** | **Netherlands** | **Retrospective cohort/**  **EPR** | **Single tertiary** | **1934 – 2000** | **29.7**  **51%** | **541** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Piront P et al.96 | **2002** | **France** | **Prospective cohort/**  **Questionnaire** | **Multiple centres** | **1993 - 1996** | **67a/33%**  **30a/18%** | **23**  **114** | **Total time**  **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Pilar N et al.90 | **2002** | **Spain** | **Prospective cohort /**  **EPR** | **Single centre** | **1997 - 1999** | **26**  **48%** | **80** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Oriuchi T et al.91 | **2003** | **Japan** | **Retrospective cohort/**  **EPR** | **Tertiary single centre** | **1965 -1998** | **22**  **31%** | **149** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Ge ZZ et al.55 | **2004** | **China** | **Prospective cohort/**  **EPR** | **Single centre** | **2002 - 2003** | **44**  **15%** | **100** | **Total** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Aghazadeh R et al.29 | **2005** | **Iran** | **Retrospective cohort/**  **Questionnaire** | **2 centres** | **1992 - 2002** | **30.5**  **43%** | **47** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Edouard A et al.51 | **2005** | **West indies \*\*** | **Prospective cohort**  **EPR** | **Regional** | **1997 - 1999** | **29**  **62%** | **55** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Jiang Li et al.66 | **2005** | **China \*\*** | **Retrospective survery/**  **EPR** | **Multicentre** | **1990 – 2003** | **32.6 a**  **40%** | **63** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Vind I et al.108 | **2006** | **Denmark** | **Prospective cohort/**  **EPR** | **Regional** | **2003 - 2005** | **31**  **54%** | **209** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Burgmann T et al.7 | **2006** | **Canada** | **Prospective cohort**  **Questionnaire and EPR** | **Regional** | **2004 - 2005** | **NR**  **66%** | **65** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Abakar-Mahamat A et al. 27 | **2007** | **France** | **Prospective cohort/**  **EPR** | **Nationwide** | **2002 -2003** | **29**  **43%** | **20** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Tine J et al.65 | **2007** | **Denmark** | **Retrospective cohort**  **EPR** | **Regional** | **1962 - 1987**  **1991 - 1993**  **2003 - 2004** | **33 (Ratio F:M 58:42)**  **35 (Ratio F:M 66:34)**  **32 (Ratio F:M 54:46)** | **374**  **58**  **209** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Albert JG et al.30 | **2008** | **Germany** | **Cross-sectional cohort/Patient organisation** | **Questionnaire** | **2005 - 2007** | **28a F**  **31a M**  **65%** | **112** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Semnani Sh.100 | **2008** | **Iran** | **Retrospective cohort/**  **EPR** | **Multiple regions** | **2001 - 2004** | **33 a**  **75%** | **4** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Munkholm P et al.87 | **2009** | **Denmark** | **Prospective cohort/**  **EPR** | **Multicentre** | **1962 - 1987** | **33**  **58%** | **373** | **Total time** | **Not reported** |
|  |  |  |  |  |  |  |  |  |  |
| Das K et al.49 | **2009** | **India \*\*** | **Retrospective cohort/**  **EPR** | **3 tertiary centres** | **2000 - 2006** | **34.5 a**  **36%** | **182** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Ozin Y et al.92 | **2009** | **Turkey** | **Retrospective cohort/**  **Questionnaire** | **Tertiary single centre** | **1993 -2007** | **40**  **F:M Ratio 1.6:1** | **195** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Romberg-Camps et al.12 | **2009** | **Netherlands** | **Retrospective cohort/**  **Questionnaire** | **3 centres**  **1 tertiary** | **1991 - 2003** | **34 a**  **65%** | **448** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Guariso G et al.60 | **2010** | **Italy** | **Retrospective cohort/**  **EPR** | **Tertiary single centre** | **1994 - 2008** | **NR \*\***  **40%** | **65** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Barrat SM et al.36 | **2011** | **UK** | **Retrospective cohort/**  **Questionnaire** | **Single tertiary** | **2006 - 2009** | **NR**  **62%** | **216** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Jain A.K et al.64 | **2012** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Single tertiary** | **2005 - 2010** | **40 a**  **64** | **12** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Belousova K et al.38 | **2012** | **Russisa** | **Retrospective cohort/ EPR** | **Multicentre**  **EPR** | **2009 - 2010** | **32.3**  **50%** | **543** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Vavricka et al SR.107 | **2012** | **Switzerland** | **Retrospective cohort/**  **Questionnaire** | **Nationwide secondary care centres**  **62% tertiary** | **2006 - 2009** | **41 a**  **53%** | **932** | **Patient**  **Healthcare**  **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Goel A et al.58 | **2013** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Single tertiary** | **1995 - 2008** | **35 a**  **58%** | **223** | **Total time** | **Not Examined** |
|  |  |  |  |  |  |  |  |  |  |
| Schoepfer AM et al.98 | **2013** | **Switzerland** | **Retrospective cohort/**  **Questionnaire** | **Nationwide secondary care**  **68% tertiary** | **2006 - 2011** | **26**  **53%** | **905** | **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Pezerovic D et al.94 | **2013** | **Croatia** | **Retrospective cohort/**  **EPR** | **Selective regional cohort** | **1991 - 2019** | **NR**  **NR** | **31** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Nahon et al.11 | **2014** | **France** | **Prospective cohort/**  **EPR** | **2 tertiary centres** | **2002 - 2012** | **29 a**  **59%** | **364** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Furfaro F et al.54 | **2014** | **Italy** | **Prospective case series/**  **EPR** | **Single tertiary centre** | **2012 - 2013** | **NR**  **NR** | **351** | **Total time** | **Examined** |
|  |  |  |  |  |  |  |  |  |  |
| Sjoberg D et al.102 | **2014** | **Sweden** | **Retrospective cohort/**  **EPR** | **Multiple centres** | **2004 - 2009** | **36**  **48%** | **214** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Li Y et al.75 | **2015** | **China \*\*** | **Retrospective cohort/**  **EPR** | **Single tertiary Centre** | **2010 - 2014** | **31.8 a**  **30%** | **343** | **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Burisch et al.42 | **2014** | **Eastern Europe** | **Retrospective**  **cohort/**  **EPR** | **31 centres** | **2010** | **34**  **49%** | **430** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Burisch et al.42 | **2014** | **Western Europe** | **Retrospective cohort/**  **EPR** | **31 centres** | **2010** | **32**  **40%** | **105** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Basaranoglu M et al.37 | **2015** | **Turkey** | **Retrospective cohort/**  **EPR** | **Single tertiary centre** | **1995 - 2007** | **36**  **48%** | **98** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Mickael C et al.83 | **2015** | **France** | **Retrospective**  **Cohort/**  **EPR** | **Multicentre** | **1990 - 2010** | **NR**  **57%** | **8704** | **Total time** | **Examined** |
|  |  |  |  |  |  |  |  |  |  |
| Pellino G et al.14 | **2015** | **Italy** | **Retrospective**  **Cohort/**  **EPR** | **Tertiary** | **2000 - 2009** | **32.5 a**  **NR** | **396** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Maconi G et al.81 | **2015** | **Spain** | **Retrospective cohort/**  **Questionnaire** | **Unclear**  **Single Centre** | **2012 - 2013** | **37 a**  **51%** | **83** | **Patient**  **Healthcare**  **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Moon C M et al.85 | **2015** | **Korea** | **Retrospective cohort/**  **EPR** | **Multicentre**  **30/32 tertiary centres** | **2000 – 2008** | **28 a**  **28%** | **1047** | **Total time a** | **Examined** |
|  |  |  |  |  |  |  |  |  |  |
| Zaharie R et al.113 | **2016** | **Romania** | **Retrospective cohort/**  **Questionnaire** | **Regional Tertiary centres only** | **2006 - 2014** | **33**  **52%** | **478** | **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Nahon S et al.11 | **2016** | **France** | **Prospective cohort/**  **Questionnaire** | **Three referral centres** | **2002 - 2014** | **26**  **53%** | **497** | **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Benchimol E et al.40 | **2016** | **Canada** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1994 - 2009** | **NR\*\***  **NR\*\*** | **10714** | **Healthcare** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Degan A et al.26 | **2016** | **Germany** | **Retrospective cohort/**  **Questionnaire** | **Single Tertiary Centre** | **NR** | **NR\*\***  **NR\*\*** | **200** | **Patient a**  **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Farkas K et al.52 | **2016** | **Hungary** | **Retrospective cohort/**  **EPR** | **Multicentre** | **2007 - 2015** | **NR**  **NR** | **428** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Cantoro L et al.44 | **2017** | **Italy** | **Retrospective cohort/**  **EPR** | **4 referral centres** | **1955 - 2014** | **NR\*\***  **NR\*\*** | **1537** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Hong Z et al.13 | **2017** | **China** | **Retrospective cohort/**  **EPR** | **Single Centre** | **2013 - 2016** | **33 a**  **39%** | **215** | **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Nguyen VQ et al.19 | **2017** | **USA** | **Retrospective cohort/**  **EPR** | **Single tertiary Centre** | **2008 - 2015** | **38 a**  **59%** | **110** | **Patient**  **Healthcare**  **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Lee DW et al.74 | **2017** | **South Korea** | **Retrospective cohort/**  **EPR** | **Single tertiary Centre** | **2000 - 2015** | **28 a**  **76%** | **165** | **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Irving P et al.63 | **2018** | **Multiple\*\*\*** | **Cross-sectional cohort/**  **Questionnaire** | **Multiple nations** | **2013 - 2014** | **NR**  **NR** | **4097** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Lazdr D et al.70 | **2018** | **Romania** | **Retrospective cohort/**  **EPR** | **Multicentre** | **NR** | **39**  **51.6%** | **149** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Szanto K et al.104 | **2018** | **Hungary** | **Retrospective cohort/**  **EPR** | **Single tertiary Centre** | **2007 - 2015** | **27a**  **45%** | **428** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Nobegra V G et al.88 | **2018** | **Brazil** | **Cross sectional observational cohort/**  **EPR** | **Single tertiary Centre** | **2015 - 2016** | **33 a**  **89%** | **141** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Banerjee R et al.34 | **2018** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Regional** | **NR\*** | **28**  **40%** | **720** | **Total time b** | **Examined** |
|  |  |  |  |  |  |  |  |  |  |
| Novacek G et al.33 | **2019** | **Austria** | **Cross sectional cohort/**  **Questionnaire** | **18 centres** | **2014 - 2015** | **40**  **52%** | **830** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Giannelis P et al.57 | **2019** | **Greece** | **Retrospective cohort/**  **EPR** | **Single Centre** | **1980 - 2018** | **NR**  **NR** | **243** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Chaparro M et al.46 | **2018** | **Spain** | **Nationwide cohort/**  **EPR** | **Multicentre** | **2017** | **40**  **NR** | **1106** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Chaisidhivej N et al.45 | **2019** | **Thailand** | **Retrospective cohort**  **EPR** | **Multicentre** | **2000 – 2006**  **2007 – 2012**  **2013 - 2018** | **39 mean /49%**  **46 mean/49%**  **48 mean/49%** | **190** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Schoepfer A et al.98 | **2019** | **Switzerland** | **Retrospective cohort/**  **Questionnaire** | **Nationally representative cohort** | **2006 - 2016** | **29**  **53%** | **1163** | **Patient**  **Healthcare**  **Total time** | **Examined d** |
|  |  |  |  |  |  |  |  |  |  |
| Yue Li et al.76 | **2019** | **China \*\*** | **Prospective cohort/**  **EPR** | **Multicentre** | **2015 - 2017** | **32.3**  **30%** | **499** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Song E M et al.103 | **2019** | **South Korea** | **Prospective case series/**  **EPR** | **Single Centre** | **1989- 2016** | **NR\*\*** | **2600** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Juliao F et al.68 | **2019** | **Columbia \*\*** | **Retrospective cohort/**  **EPR** | **Single Tertiary Centre** | **2001 - 2017** | **NR**  **NR** | **159** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Ghosh K et al.56 | **2019** | **Bangladesh \*\*** | **Retrospective cohort/**  **Questionnaire** | **Single tertiary** | **NR** | **NR**  **NR** | **47** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Qiao L.C et al.71 | **2019** | **China \*\*** | **Retrospective cohort/**  **Questionnaire** | **Tertiary Single** | **2014 - 2018** | **NR**  **NR** | **218** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Banerjee R et al.34 | **2020** | **India (AIG) \*\*** | **Retrospective cohort/**  **EPR** | **Regional** | **2019** | **34 a**  **40%** | **1606** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Banerjee R et al.34 | **2020** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Regional** | **2012** | **35.9 a**  **NR\*** | **409** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Yzet C et al.112 | **2020** | **France** | **Retrospective cohort/**  **EPR** | **Single Centre** | **2008 - 2017** | **NR**  **NR** | **7** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Mayorga A et al.82 | **2020** | **Ecuador \*\*** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1990 -2018** | **42 a**  **46.6%** | **58** | **Total time a** | **Examined** |
|  |  |  |  |  |  |  |  |  |  |
| Halawani H et al.61 | **2020** | **Saudi Arabia** | **Retrospective cohort/**  **EPR** | **Single Tertiary Centre** | **2010 - 2018** | **28 a**  **51%** | **83** | **Total time a** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Walker GJ et al.17 | **2020** | **UK** | **Retrospective cohort/**  **EPR** | **Regional** | **2014 - 2017** | **NR\*** | **94** | **Patient c**  **Healthcare c**  **Total time c** | **Examined c** |
|  |  |  |  |  |  |  |  |  |  |
| Abraham, BP et al.28 | **2020** | **USA** | **Retrospective cohort**  **EPR** | **Multiple centres** | **2017 - 2020** | **42/57%**  **49/56%** | **372**  **392** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Gomes, TNF et al.59 | **2021** | **Brazil \*\*** | **Retrospective cohort/**  **EPR** | **Single Centre** | **1997-2017** | **32 a**  **50%** | **249** | **Total time b** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Chaparro M et al.46 | **2021** | **Spain** | **Prospective cohort/**  **EPR** | **Multiple centres** | **2017** | **41**  **50%** | **1647** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Alourifi M et al.31 | **2022** | **Saudi Arabia** | **Retrospective cohort/**  **EPR** | **Single centre** | **unclear** | **NR**  **NR** | **75** | **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |
| Robles LS et al.101 | **2022** | **Spain** | **Prospective cohort/**  **EPR and questionnaire** | **Multicentre** | **NR** | **NR**  **53%** | **100** | **Patient**  **Healthcare**  **Total time** | **Not examined** |
|  |  |  |  |  |  |  |  |  |  |

**\*\* - Low-and middle-income countries; \* NR – Not Reported ; \*\* NR – Not reported as required breakdown; EPR – Electronic patient record**

**a Only mean reported; b Only median reported; c Only presented combined time intervals for CD and UC; d Studies included in meta-analysis that examined the impact of diagnostic delay, defined as per study criteria (i.e., above the 75th centile of longest time to diagnosis)**

**Supplemental Table 5: Characteristics of included studies amongst individuals diagnosed with Ulcerative Colitis**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Year | Country | Study Design/  Data Source | Centre | Study period | Population characteristics  Median age (years) and Sex (Female %) | | n | Time to diagnosis interval measured | Impact of delay on clinical outcomes |
| Nordenvall B et al.89 | **1984** | **Denmark** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1955 – 1979** | | **NR**  **47%** | **1274** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Colombel JF et al.47 | **1990** | **France** | **Prospective cohort/**  **Questionnaire** | **Multicentre** | **1998** | | **40**  **47%** | **207** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Langholz E et al.72 | **1991** | **Denmark** | **Retrospective cohort/**  **EPR** | **Regional** | **1962 - 1987** | | **34 F**  **33 M**  **53%** | **1161** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Stewenius J et al.105 | **1996** | **Sweden** | **Retrospective cohort/**  **EPR** | **Regional** | **1958 – 1982** | | **37.2**  **41%** | **354** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Park SM et al.93 | **1996** | **Korea** | **Retrospective cohort/**  **EPR** | **Single centre** | **1989 - 1995** | | **NR**  **48%** | **66** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Latour P et al.73 | **1998** | **Belgium** | **Prospective cohort/**  **Questionnaire** | **Multicentre** | **1993 - 1996** | | **39**  **33%** | **111** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Timmer A et al.106 | **1999** | **Germany** | **Retrospective**  **Cohort/**  **EPR** | **Regional** | **1980 – 1984** | | **NR\*\***  **NR\*\*** | **75** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Pimentel M et al.95 | **2000** | **USA** | **Retrospective cohort/**  **Questionnaire** | **Single tertiary** | **2000** | | **46 a**  **38%** | **21** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Yang SK et al.111 | **2000** | **Korea** | **Retrospective**  **Cohort/**  **EPR** | **Multicentre** | **1986 - 1987** | | **35**  **52%** | **94** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Piront P et al.96 | **2002** | **France** | **Prospective cohort/**  **Questionnaire** | **Multicentre** | **1993 - 1996** | | **69/F:M Ratio 0.7:1**  **34/F: M Ratio 0.5:1** | **30**  **81** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Ling KL et al.79 | **2002** | **Singapore** | **Retrospective cohort/**  **EPR** | **Single tertiary** | **1971 - 2000** | | **Range 11 -78**  **36%** | **235** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Aghazadeh R et al.29 | **2005** | **Iran** | **Retrospective cohort/**  **Questionnaire** | **2 centres** | **1992 - 2002** | | **31. 9 a**  **56%** | **401** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Edouard A et al.51 | **2005** | **West indies \*\*** | **Prospective cohort/**  **EPR** | **Multicentre** | **1997 - 1999** | | **34**  **60%** | **66** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Jiang Li et al.66 | **2005** | **China \*\*** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1990 – 2003** | | **42 a**  **40%** | **389** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Vind I et al.108 | **2006** | **Denmark** | **Prospective cohort/EPR** | **Regional** | **2003 - 2005** | | **38**  **51%** | **326** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Burgmann T et al.7 | **2006** | **Canada** | **Prospective cohort/**  **EPR** | **Regional** | **2004 - 2005** | | **NR**  **NR** | **42** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Romberg-Camps et al.12 | **2009** | **Netherlands** | **Retrospective cohort/**  **Questionnaire** | **3 centres** | **1991 - 2003** | | **42 a**  **47%** | **600** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Tine J et al.65 | **2007** | **Denmark** | **Retrospective cohort/**  **EPR** | **Regional** | **1962 - 1987**  **1991 - 1993**  **2003 - 2004** | | **34/F:M Ratio 53:47**  **40/ F:M Ratio 57:43**  **38/ F:M Ratio 51:49** | **1160**  **89**  **326** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Abakar-Mahamat A et al.  27 | **2007** | **France** | **Prospective cohort/**  **EPR** | **Nationwide** | **2002 -2003** | | **44 a**  **39%** | **49** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Ozin Y et al.92 | **2009** | **Turkey** | **Prospective cohort/**  **Questionnaire** | **Tertiary single centre** | **1993 -2007** | | **42**  **1.2:1** | **507** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Moum B et al.86 | **2009** | **Norway** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1990 - 1993** | | **39**  **1: 1.22** | **525** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Guariso G et al.60 | **2010** | **Italy** | **Retrospective**  **Cohort/**  **EPR** | **Single tertiary Centre** | **1994 - 2008** | | **NR \*\***  **40%** | **186** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Roth L S et al.97 | **2010** | **UK** | **Retrospective cohort/**  **EPR** | **Tertiary**  **Single centre** | **1996 – 2001** | | **39 a**  **49%** | **201** | **Total time a** | **Examined (did not declare data)** |
|  |  |  |  |  |  | |  |  |  |  |
| Barrat SM et al.36 | **2011** | **UK** | **Retrospective cohort/**  **Questionnaire** | **Single tertiary** | **2006 - 2009** | | **NR**  **57%** | **110** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Vavricka et al SR.107 | **2012** | **Switzerland** | **Retrospective cohort/**  **Questionnaire** | **Nationwide secondary care centres**  **62% tertiary** | **2006 - 2009** | | **42 a**  **46%** | **625** | **Patient**  **Healthcare**  **Total time** | **Examined d** |
|  |  |  |  |  |  | |  |  |  |  |
| Jain A.K et al.64 | **2012** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Single tertiary** | **2005 - 2010** | | **49 a**  **51%** | **160** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Belousova K et al.38 | **2012** | **Russia** | **Retrospective cohort/**  **EPR** | **Multicentre** | **2009 -2010** | | **33.8**  **62.7%** | **1254** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Zhang Z et al.115 | **2012** | **Singapore** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1970 - 2011** | | **NR**  **40%** | **606** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Pezerovic D et al.94 | **2013** | **Croatia** | **Retrospective cohort/**  **EPR** | **Selective regional cohort** | **1991 - 2019** | | **NR**  **NR** | **119** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Burisch et al.42 | **2014** | **Eastern Europe** | **Retrospective cohort/**  **EPR** | **31 centres** | **2010** | | **36 a**  **43%** | **145** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Burisch et al.42 | **2014** | **Western Europe** | **Retrospective cohort/**  **EPR** | **31 centres** | **2010** | | **29 a**  **44%** | **668** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Basaranoglu M et al.37 | **2015** | **Turkey** | **Retrospective cohort/**  **EPR** | **Single tertiary centre** | **1995 - 2007** | | **41**  **29%** | **184** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Zaharie R et al.113 | **2016** | **Romania** | **Retrospective cohort/**  **EPR** | **Regional Tertiary centres only** | **2016 - 2014** | | **38 a**  **45%** | **682** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Lin WC et al.77 | **2016** | **Taiwan** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1991 - 2014** | | **37 mean/41%**  **68 mean/40%** | **459**  **77** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Degen A et al.26 | **2016** | **Germany** | **Retrospective cohort/**  **Questionnaire** | **Single Centre university hospital** | **NR** | | **NR\*\***  **NR\*\*** | **186** | **Patient a**  **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Benchimol E et al.40 | **2016** | **Canada** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1994 - 2009** | | **NR\*\***  **NR\*\*** | **12185** | **Healthcare** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Farkas K et al.52 | **2016** | **Hungary** | **Retrospective cohort/**  **EPR** | **Multicentre** | **2007 - 2015** | | **NR**  **NR** | **483** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Cantoro L et al.44 | **2017** | **Italy** | **Retrospective cohort/**  **EPR** | **4 referral centres** | **1955 - 2014** | | **NR\*\***  **NR\*\*** | **1855** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Nguyen VQ et al.19 | **2017** | **USA** | **Retrospective cohort/**  **EPR** | **Single tertiary Centre** | **2008 - 2015** | | **45 a**  **55%** | **67** | **Patient**  **Healthcare**  **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Lee DW et al.74 | **2017** | **South Korea** | **Retrospective cohort/**  **EPR** | **Single tertiary Centre** | **2000 – 2015** | | **40 a**  **59%** | **130** | **Total time** | **Examined d** |
|  |  |  |  |  |  | |  |  |  |  |
| Szanto K et al.104 | **2018** | **Hungary** | **Retrospective cohort/**  **EPR** | **Single tertiary centres** | **2007 - 2015** | | **31 a**  **51%** | **483** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Nobrega VG et al.88 | **2018** | **Brazil \*\*** | **Cross sectional cohort/**  **EPR** | **Single tertiary Centre** | **2015 - 2016** | | **36 a**  **39%** | **165** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Irving P et al.63 | **2018** | **Multiple\*\*\*** | **Cross-sectional cohort/**  **Questionnaire** | **Multiple nations** | **2013 - 2014** | | **NR** | **NR** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Novacek G et al.33 | **2019** | **Austria** | **Cross sectional cohort/**  **Questionnaire** | **18 centres** | **2014 - 2015** | | **41**  **49%** | **435** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Giannelis P et al.57 | **2019** | **Greece** | **Prospective cohort/**  **EPR** | **Single Centre** | **1980 - 2018** | | **NR**  **NR** | **240** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Kang HS et al.16 | **2019** | **South Korea** | **Retrospective cohort/**  **EPR** | **6 university hospitals** | **2006 - 2016** | | **54 a**  **41%** | **551** | **Patient**  **Healthcare**  **Total time** | **Examined d** |
|  |  |  |  |  |  | |  |  |  |  |
| Armuzzi A et al.32 | **2019** | **Global** | **Retrospective cohort/**  **Questionnaire** | **10 countries** | **2017 - 2018** | | **41 a**  **NR\*** | **2100** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Molander et al.84 | **2019** | **Finland** | **Retrospective cohort/**  **Questionnaire** | **Unclear** | **2018** | | **43.2 a**  **63%** | **508** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Juliao F et al.68 | **2019** | **Columbia \*\*** | **Retrospective cohort/**  **EPR** | **Single Tertiary Centre** | **2001 - 2017** | | **NR**  **NR** | **478** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Ghosh K et al.56 | **2019** | **Bangladesh \*\*** | **Retrospective cohort/**  **Questionnaire** | **Single tertiary** | **NR** | | **NR**  **NR** | **102** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Banerjee R et al.34 | **2020** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Regional** | **2019** | | **38 a**  **40%** | **2400** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Banerjee R et al.34 | **2020** | **India \*\*** | **Retrospective cohort/**  **EPR** | **Regional** | **2012** | | **39 a**  **NR\*** | **742** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Walker GJ et al.17 | **2020** | **UK** | **Retrospective cohort/**  **EPR** | **Regional** | **2014 - 2017** | | **NR\*** | **195** | **Patient c**  **Healthcare c**  **Total time c** | **Examined c** |
|  |  |  |  |  |  | |  |  |  |  |
| Mayorga A et al.82 | **2020** | **Ecuador \*\*** | **Retrospective cohort/**  **EPR** | **Multicentre** | **1990 – 2018** | | **42 a**  **48%** | **148** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Zammarchi I et al.114 | **2020** | **Italy** | **Retrospective cohort/**  **EPR** | **Single centre** | **2000 - 2019** | | **72/46%**  **50/46%** | **94**  **94** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Connor SJ et al.48 | **2021** | **Australia** | **Retrospective cohort/**  **Questionnaire** | **Nationwide** | **2017 - 2018** | | **41.1 a**  **41%** | **215** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Gomes TNF et al.59 | **2021** | **Brazil \*\*** | **Retrospective cohort/**  **EPR** | **Single Centre** | **1997 - 2017** | | **35.3 a**  **62%** | **249** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Dubinsky MC et al.50 | **2021** | **Global 10 countries** | **Retrospective cohort/**  **Questionnaire** | **Global Multicentre** | **2017 - 2018** | | **30**  **NR\*\*** | **2100** | **Total time a** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Chaparro M et al.46 | **2021** | **Spain** | **Prospective cohort/**  **EPR** | **Multiple centres** | **2017** | | **46**  **45%** | **1807** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Robles LS et al.101 | **2022** | **Spain** | **Prospective cohort**  **EPR and Questionnaire** | **Multicentre** | **NR** | | **NR**  **39%** | **90** | **Patient**  **Healthcare**  **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |
| Ling KL et al.79 | **2022** | **Singapore** | **Retrospective cohort/**  **EPR** | **Single centre** | **1971 - 2000** | | **Range 11 – 78**  **36%** | **235** | **Total time** | **Not examined** |
|  |  |  |  |  |  | |  |  |  |  |

**\*\* - Low-and middle-income countries; \* NR – Not Reported ; \*\* NR – Not reported as required ; EPR – Electronic patient record**

**a Only mean reported; b Only median reported; c Only presented combined time intervals for CD and UC; d Studies included in meta-analysis that examined the impact of diagnostic delay, defined as per study criteria, (i.e., above the 75th centile of longest time to diagnosis)**

**Supplemental Table 6: Study follow up period and covariates adjusted for amongst studies examining impact of delayed diagnosis**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Crohn’s Disease** | | | | | | | | | | |
| **Study author**  **country** | **Year** | **n** | **Follow up period** | **Outcome measure for disease course** | | | | | **Adjusted** | **Covariates** |
|  | | | | **Disease location** | **Disease severity/**  **phenotype** | **Medical treatment** | **Surgical intervention** | **Health care utilisation** |  | |
| **Vavricka et al SR.107**  **Switzerland** | 2012 | 932 | At diagnosis | √ | - | - | - | - | √ | 1. Age at diagnosis  2. Positive family history if IBD  3. Extra intestinal manifestations (EIM) |
| **Schoepfer AM et al.98**  **Switzerland** | 2013 | 905 | NR | - | √ | - | √ | - | √ | 1. Age at diagnosis ( < 40 vs. ≥ 40 years)  2. Gender (male vs. female)  3. Disease location at diagnosis  4. Cigarette smoking status at diagnosis  5. NSAID intake at first symptoms  6. Disease duration since CD diagnosis |
| **Li Y et al.75**  **China** | 2015 | 343 | NR | √ | - | √ | √ | - | X | NA |
| **Zaharie R et al.113**  **Romania** | 2016 | 478 | NR | √ | √ | - | √ | - | √ | 1.Sex (Male vs Female)  2.Ethnic group (Romanian vs other)  3.Age at diagnosis (<40 vs > 40)  4.Disease location  5.Provenance (Urban vs Rural)  6.Smoking status at diagnosis  7.Family history of IBD  8.Appendicectomy (No vs yes) |
| **Nahon S et al.**11  **France** | 2016 | 497 | Disease location  (at diagnosis) | √ | √ | √ | √ | - | X | NA |
| **Hong Z et al.**13  **China** | 2017 | 215 | NR | √ | - | √ | √ | - | X | NA |
| **Nguyen VQ et al.**19  **USA** | 2017 | 105 | NR | √ | √ | - | √ | - | √ | Adjusted only for stricturing disease  1.Age > 40 at diagnosis  2.Male vs Female  3.Smoker  4.NSAID use  5.Family history of IBD  6.Haematozoa  7.Ileal involvement only  8.Hospital diagnosis  9.EIM at diagnosis  10.Time to diagnosis |
| **Lee DW et al.74**  **South Korea** | 2017 | 177 | NR | √ | √ | - | √ | √ | √ | Disease phenotype and severity  1.Age  2.Sex |
| **Schoepfer A et al.**18  **Switzerland** | 2019 | 1163 | NR | - | √ |  | √ | - | X | NA |
| **Ghosh CK et al. 56**  **Bangladesh** | 2020 | 50 | At diagnosis | √ | - | - | √ | - | X | NA |
| **Ulcerative Colitis** | | | | | | | | | | |
| **Vavricka et al SR.107**  **Switzerland** | 2012 | 625 | NR | √ | - | - | - | - | X | NA |
| **Zaharie R et al.113**  **Romania** | 2016 | 682 | NR | √ | - | - | - | - | X | NA |
| **Lee DW et al.74**  **South Korea** | 2017 | 130 | NR | √   |  |  | | --- | --- | |  | **1.0037 - 5.2514** | | √ | - | √ | √ | √ | Disease location and severity  1.Age  2.Sex |
| **Kang HS et al.16**  **South Korea** | 2019 | 551 | NR | √ | √ | √ | √ | √ | X | NA |
| **Inflammatory Bowel Disease** | | | | | | | | | | |
| **Walker et al.17**  **United Kingdom** | 2020 | 304 | 1 year | - | - | √ | √ | √ | X | NA |

**Examined (√); Not examined (-); NA (Not applicable)**

**Supplemental Table 7: Quality assessment and risk of bias for studies reporting on the impact of delayed diagnosis in Crohn’s Disease evaluated with the Joanna Briggs Institute** **quality appraisal tool which uses 11 criteria (✓ criterion met; x criterion not met)**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Author** | **Year** | **Joanna Briggs Institute Criteria \*** | | | | | | | | | | | |
|  | | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **Total** |
| **1** | **Ghosh CK et al.56** | **2020** | √ | √ | √ | x | x | √ | √ | √ | v | x | √ | **8/11** |
| **3** | **Schoepfer A et al.**18 | **2019** | x | √ | √ | x | x | √ | √ | √ | √ | x | √ | **7/11** |
| **4** | **Lee DW et al.74** | **2017** | √ | √ | √ | √ | x | √ | √ | √ | x | x | √ | **8/11** |
| **5** | **Hong Z et al.13** | **2017** | x | √ | √ | √ | x | √ | √ | √ | √ | √ | √ | **9/11** |
| **6** | **Nguyen VQ et al.19** | **2017** | √ | √ | √ | √ | √ | √ | √ | √ | √ | x | √ | **10/11** |
| **7** | **Nahon S et al.**11 | **2016** | √ | √ | √ | √ | x | √ | √ | √ | x | x | √ | **8/11** |
| **8** | **Zaharie R et al.113** | **2016** | √ | √ | √ | √ | √ | √ | √ | x | x | x | √ | **8/11** |
| **9** | **Li Y et al.**76 | **2015** | √ | √ | √ | √ | √ | √ | √ | x | x | x | √ | **8/11** |
| **10** | **Schoepfer A et al.98** | **2013** | √ | √ | √ | √ | √ | √ | √ | √ | x | x | √ | **9/11** |
| **11** | **Vavricka SR.107** | **2012** | √ | x | x | √ | √ | √ | x | √ | √ | x | √ | **7/11** |

**\* 11 Joanna Briggs Institute Criteria**

**1.**Were the two groups similar and recruited from the same population? **2.**Were the exposures measured similarly to assign people to both exposed and unexposed groups? **3**.Was the exposure measured in a valid and reliable way? **4.**Were confounding factors identified? **5.**Were strategies to deal with confounding factors stated?

**6.** Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? **7.**Were the outcomes measured in a valid and reliable way?

**8**. Was the follow up time reported and sufficient to be long enough for outcomes to occur? **9**.Was follow up complete, and if not, were the reasons to loss to follow up described and explored? **10**.Were strategies to address incomplete follow up utilised? **11**.Was appropriate statistical analysis used?

**If it was unclear as to whether a criterion was met, we considered the study to have not met the criterion.**

**Supplemental Table 8: Quality assessment and risk of bias for studies reporting on the impact of delayed diagnosis in Ulcerative Colitis evaluated with the Joanna Briggs Institute quality appraisal tool which uses 11 criteria (✓ criterion met; x criterion not met)**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Author** | **Year** | **Joanna Briggs Institute Criteria\*** | | | | | | | | | | | |
|  |  | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **Total Score** |
| **2** | **Kang HS et al.**16 | **2019** | x | √ | √ | √ | √ | √ | √ | √ | x | x | √ | **8/11** |
| **3** | **Lee DW et al.**74 | **2017** | √ | √ | √ | √ | √ | √ | √ | √ | x | x | √ | **9/11** |
| **4** | **Vavricka SR et al.**107 | **2012** | √ | x | x | √ | √ | √ | x | √ | √ | x | √ | **7/11** |

**\* 11 Joanna Briggs Institute Criteria**

**1**.Were the two groups similar and recruited from the same population? **2.**Were the exposures measured similarly to assign people to both exposed and unexposed groups? **3.**Was the exposure measured in a valid and reliable way? **4.**Were confounding factors identified? **5.**Were strategies to deal with confounding factors stated?

**6.** Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? **7**.Were the outcomes measured in a valid and reliable way?

**8.** Was the follow up time reported and sufficient to be long enough for outcomes to occur? **9**.Was follow up complete, and if not, were the reasons to loss to follow up described and explored? **10.**Were strategies to address incomplete follow up utilised? **11**.Was appropriate statistical analysis used?

**If it was unclear as to whether a criterion was met, we considered the study to have not met that criterion.**

**Supplemental Table 9: Quality assessment of studies reporting on time to diagnosis interval in Crohn’s Disease**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Joanna Briggs Institute Criteria** | | | | | | | |  |
|  | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **Total** |
| **Kyle J et al.69** | **1971** | √ | x | √ | √ | x | x | √ | √ | **5** |
| **Lind E et al.78** | **1985** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Foxworthy D et al.53** | **1986** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Segal I et al.99** | **1988** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Loftus E V et al.80** | **1998** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Timmer A et al.106** | **1999** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Pilar N et al.90** | **2002** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Piront P et al.96** | **2002** | √ | x | √ | √ | √ | √ | √ | √ | **7** |
| **Edouard A et al.51** | **2005** | √ | √ | √ | x | x | x | x | √ | **4** |
| **Vind I et al.108** | **2006** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Burgmann T et al.7** | **2006** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Abakar-Mahamat A et al.27** | **2007** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Tine J et al.65** | **2007** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Albert JG et al.30** | **2008** | √ | √ | x | √ | √ | √ | √ | √ | **7** |
| **Romberg-Camps et al.12** | **2009** | √ | √ | x | √ | √ | √ | √ | √ | **7** |
| **Munkholm P et al.87** | **2009** | √ | √ | √ | √ | x | x | √ | √ | **5** |
| **Guariso G et al.60** | **2010** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Vavricka SR et al.107** | **2012** | √ | √ | x | x | √ | √ | √ | √ | **6** |
| **Goel A et al.58** | **2013** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Schoepfer AM et al.98** | **2013** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Pezerovic D et al.94** | **2013** | √ | √ | √ | √ | √ | √ | √ | √ |  |
| **Burisch et al.42** | **2014** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Nahon et al.11** | **2014** | √ | √ | x | √ | √ | √ | √ | √ | **7** |
| **Furfaro F et al.54** | **2014** | √ | √ | √ | √ | x | x | √ | √ | **5** |
| **Sjoberg D et al.102** | **2014** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Can G et al.43** | **2014** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Basaranoglu M et al.**37 | **2015** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Pellino G et al.**14 | **2015** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Mickael C et al.83** | **2015** | √ | √ | √ | x | √ | x | x | √ | **5** |
| **Li Y et al.76** | **2015** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Maconi G et al.81** | **2015** | √ | √ | x | √ | √ | x | √ | √ | **6** |
| **Zaharie R et al.113** | **2016** | √ | √ | x | x | √ | x | √ | √ | **5** |
| **Nahon S et al.11** | **2016** | √ | √ | x | x | √ | x | √ | √ | **5** |
| **Cantoro L et al.44** | **2017** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Hong Z et al.13** | **2017** | √ | √ | √ | √ | √ | x | √ | √ | **7** |
| **Nguyen VQ et al.**19 | **2017** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Lee DW et al.74** | **2017** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Szanto K et al.104** | **2018** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Banerjee R et al.34** | **2018** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Irving P et al.63** | **2018** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Chaisidhivej N et al.45** | **2019** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Song E M et al.103** | **2019** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Novacek G et al.33** | **2019** | √ | √ | x | x | √ | √ | √ | √ | **6** |
| **Ghosh K et al.56** | **2019** | √ | √ | x | x | √ | x | √ | √ | **5** |
| **Qiao L.C et al.71** | **2019** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Schoepfer A et al.98** | **2019** | √ | √ | x | x | √ | x | √ | √ | **5** |
| **Yzet C et al.112** | **2020** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Banerjee R et al.34** | **2020** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Walker GJ et al.17** | **2020** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Gomes, TNF et al.59** | **2021** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Chaparro M et al.46** | **2021** | √ | √ | x | √ | x | x | √ | √ | **5** |
| **Alourifi M et al.31** | **2022** | √ | √ | x | x | √ | √ | √ | √ | **6** |
| **Robles LS et al.101** | **2022** | √ | √ | x | x | √ | √ | √ | √ | **6** |

**\* 8 Joanna Briggs Institute Criteria**

**1.** Were the criteria for inclusion in the sample clearly defined? **2**. Were the study subjects and the setting described in detail? **3.** Was the exposure measured in a valid and reliable way? **4.** Were objective, standard criteria used for measurement of the condition? **5.** Were confounding factors identified? 6. Were strategies to deal with confounding factors stated? **7.** Were the outcomes measured in a valid and reliable way? **8.** Was appropriate statistical analysis used?

**If it was unclear as to whether a criterion was met, we considered the study to have not met that criterion.**

**Supplemental Table 10: Quality assessment of studies reporting on time to diagnosis interval in Ulcerative Colitis**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Joanna Briggs Institute Criteria \*** | | | | | | | |  |
|  | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **Total** |
| **Langholz E et al.72** | **1991** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Park SM et al.93** | **1996** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Stewenius J et al.105** | **1996** | √ | √ | √ | √ | √ | x | √ | √ | **7** |
| **Timmer A et al.106** | **1999** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Yang SK et al.111** | **2000** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Piront P et al.96** | **2002** | √ | x | √ | √ | √ | √ | √ | √ | **7** |
| **Ling KL et al.79** | **2002** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Edouard A et al.51** | **2005** | √ | √ | √ | x | x | x | x | √ | **4** |
| **Burgmann T et al.7** | **2006** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Vind I et al.108** | **2006** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Abakar-Mahamat A.et al.27** | **2007** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Tine J et al.65** | **2007** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Romberg-Camps et al.12** | **2009** | √ | √ | x | x | √ | √ | √ | √ | **6** |
| **Moum B et al.86** | **2009** | √ | √ | √ | √ | x | x | √ | √ | √ |
| **Guariso G et al.60** | **2010** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Vavricka et al SR.107** | **2012** | √ | √ | x | x | √ | √ | √ | √ | **6** |
| **Pezerovic D et al.94** | **2013** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Burisch et al.42** | **2014** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Basaranoglu M et al.37** | **2015** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Zaharie R et al.113** | **2016** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Cantoro L et al.44** | **2017** | √ | √ | √ | √ | x | x | √ | √ | **6** |
| **Nguyen VQ at al.19** | **2017** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Lee DW et al.75** | **2017** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Irving P et al.63** | **2018** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Szanto K et al.104** | **2019** | √ | √ | x | x | x | x | √ | √ | **4** |
| **Novacek G et al.33** | **2019** | √ | √ | √ | x | √ | √ | √ | √ | **7** |
| **Kang HS et al.16** | **2019** | √ | √ | x | x | √ | x | √ | √ | **5** |
| **Ghosh K et al.56** | **2019** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Banerjee R et al.56** | **2020** | √ | √ | √ | x | x | x | √ | √ | **5** |
| **Walker GJ et al.17** | **2020** | √ | √ | √ | √ | √ | x | √ | √ | **7** |
| **Gomes, TNF et al.59** | **2021** | √ | √ | √ | x | √ | x | √ | √ | **6** |
| **Benchimol E I et al.40** | **2016** | √ | √ | √ | √ | √ | √ | √ | √ | **8** |
| **Chaparro M et al.46** | **2021** | √ | √ | x | √ | x | x | √ | √ | **5** |
| **Robles LS et al.10** | **2022** | √ | √ | x | x | √ | √ | √ | √ | **6** |

**\* 8 Joanna Briggs Institute Criteria**

**1**. Were the criteria for inclusion in the sample clearly defined? **2.** Were the study subjects and the setting described in detail? **3**. Was the exposure measured in a valid and reliable way? **4.** Were objective, standard criteria used for measurement of the condition? **5**. Were confounding factors identified? **6.** Were strategies to deal with confounding factors stated? **7**. Were the outcomes measured in a valid and reliable way? **8.**Was appropriate statistical analysis used?

**If it was unclear as to whether a criterion was met, we considered the study to have not met that criterion.**

**Supplemental Table 11: Median of the median total time to diagnosis by era of study in IBD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Era of Study** | | |
| **<2010** | **2010 – 2015** | **>2015** |
| **Median (IQR)** | **Median (IQR)** | **Median (IQR)** |
| **Crohn’s Disease** |  |  |  |
| **All studies** | 8.3 ( 5 – 24) | 6.5 (4.2 – 9.8) | 8.6 (5.9 - 12.9) |
| **High-income countries** | 8.3 ( 5 -24) | 6 ( 4 – 9) | 6.2 (5.5 - 8.6) |
| **Low-and middle-income countries** | 19.5 (11.3 – 27.8) | 10 (8.3 – 18) | 12 ( 11 – 18) |
|  |  |  |  |
| **Ulcerative Colitis** |  |  |  |
| **All studies** | 4.8 ( 2.3 – 7.8) | 2.2 ( 2 -3) | 3.1 ( 2.2 -11.5) |
| **High-income countries** | 4.8 ( 3 – 8.5) | 2.2 (2 -3 ) | 2.7 (2.2 - 3.2) |
| **Low-and middle-income countries** | 2 (NA \*) | 1 (NA\*) | 16 (6.2 - 23.4) |

**Abbreviations: IQR – interquartile range; \* single study**

**Supplemental Table 12: Median of the mean total time to diagnosis by era of study in IBD**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Era of Study** | | |
| **<2010** | **2010 – 2015** | **>2015** |
| **Median (IQR)** | **Median (IQR)** | **Median (IQR)** |
| **Crohn’s Disease** |  |  |  |
| **All studies** | 29.4 (15.7 – 41.7) | 24 (15.3 – 32.9) | 20.6 (11.8 – 32) |
| **High-income countries** | 36 ( 22.8 – 76.8) | 28.4 (18 – 39.7) | 18.3 (10.6 -35.5) |
| **Low-and middle-income countries** | 17.7 (13.2 – 19.2) | 15.3 ( 9.2 – 22.1) | 23 (11.8 – 32) |
|  |  |  |  |
| **Ulcerative Colitis** |  |  |  |
| **All studies** | 9.9 (6.3 – 17.7) | 17.9 ( 13.5 - 38.3) | 12.3 (7.4 – 25.6) |
| **High-income countries** | 9.9 (6.3 – 17.7) | 17.8 (12 – 18) | 8.8 (6.05 – 27) |
| **Low-and middle-income countries** | 15.4 ( 14.6 – 16.1) | 45 (NA\*) | 15.2 (10.7 – 20.4) |

**Abbreviations: IQR – interquartile range; \* single study**

**Supplemental Table 13: Time to diagnosis interval in inflammatory bowel disease reported by sex**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **STUDY** | **COUNTRY** | **IBD SUBTYPE** | **Males vs Females** | **Median time (months)** | | **Mean time**  **(months)** | |
|  |  |  | **Odds Ratio**  **(95% Confidence Interval)** | **Males** | **Females** | **Males** | **Females** |
| **CROHN’S DISEASE** | | | | | | | |
| Vavricka SR et al.107 | Switzerland | CD | 0.89 (0.61 - 1.29) P = 0.53 | - | - | - | - |
| Cantoro L et al.44 | Italy | CD | 1.04 (0.81 - 1.35) P = 0.74 | - | - | - | - |
| Nguyen VQ et al.19 | USA | CD | **0.33 (0.13 - 0.81) P = 0.01** | - | - | - | - |
| Lee DW et al.74 | South Korea | CD | 0.72 (0.23 - 2.26) P = 0.58 | - | - | - | - |
| Banerjee R et al.34 | India | CD | 1.15 (0.86 - 1.56) P = 0.33 | - | - | - | - |
| Schoepfer AM et al.98 | Switzerland | CD | 0.91 (0.68 - 1.21) P = 0.51 | - | - | - | - |
| Hong Z et al.13 | China | CD | 1.15 (0.60 - 2.20) P = 0.67 | - | - | - | - |
| Banerjee R et al.34 | India 2020 | CD | - | - | - | 41.7 | 42.9 |
| Wagtmans MJ et al.109 | Netherlands | CD | - | - | - | 37.2 | 36 |
| Moon CM et al. 85 | Korea | CD | 0.76 (0.55 - 1.04) P = 0.10 | - | - | - | - |
| Robles LS et al.101 | Spain | CD | - | 4.5 | 12.6 | - | - |
| **ULCERATIVE COLITIS** | | | | | | | |
| Vavricka SR et al.107 | Switzerland | UC | 0.59 (0.34 - 1.05) P = 0.08 | - | - | - | - |
| Cantoro L et al.44 | Italy | UC | 0.86 (0.62 - 1.20) P = 0.38 | - | - | - | - |
| Lee DW et al.74 | South Korea | UC | 0.78 (0.30 - 2.04) P = 0.61 | - | - | - | - |
| Kang HS et al.16 | South Korea | UC | 1.08 (0.57 – 2.06) P = 0.81 | - | - | - | - |
| Zaharie R et al.113 | Romania | UC | 1.21 (0.85 - 1.71) P= 0.29 | - | - | - | - |
| Robles LS et al.101 | Spain | UC | - | 2.7 | 6.1 | - | - |
| **INFLAMMATORY BOWEL DISEASE** | | | | | | | |
| Walker GJ et al.17 | UK | IBD\*\* | **0.49 (0.28 - 0.83) P = 0.01** | - | - | - | - |
| Burgmann T et al.7 | Canada | IBD | - | 9.5 | 7 | **12.7** | 10.2 |
| Ghosh CK et al.56 | Bangladesh | IBD | **3.04 (1.05 - 8.76) P = 0.04** | - | - | - | - |
| Giannelis P et al.57 | Greece | IBD | - | 4.5 | **12.6** | 7.8 | **12** |

**\*\* Health-care related interval**

**Supplemental Table 14: Subgroup meta-analyses in Crohn’s Disease and Ulcerative Colitis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Crohn’s Disease** | | | | | **Ulcerative Colitis** | |
|  | **Disease phenotype** | | **Surgical Intervention** | | **Disease phenotype** | **Colectomy** |
|  | **Stricturing** | **Penetrating** | **Intestinal** | **Perianal** |  |  |
|  | OR (95% CI); I2 | OR (95% CI); I2 | OR (95% CI); I2 | OR (95% CI); I2 | OR (95% CI); I2 | OR (95% CI); I2 |
| **World bank economic class** |  |  |  |  |  |  |
| **High-income** | **1.94 (1.36 - 2.78); 60%** | **1.62 (1.30 - 2.02); 0%** | **1.72 (1.25 - 2.36); 38%** | 1.27 (0.90 - 1.80); 0% | 1.22 (0.69 - 2.15); 40% | **4.13 (1.04 - 16.40); 0%** |
| **Low-and middle-income** | 2.12 (0.45 - 9.92); 76% | 5.22 (0.24 - 297.65); 85% | **3.75 (1.88 - 7.46); 54%** | 0.89 (0.43 - 1.83); NA | NA | NA |
|  |  |  |  |  |  |  |
| **Year of study** |  |  |  |  |  |  |
| **< 2010** | NA | NA | NA | NA | NA | NA |
| **2010 - 2015** | 1.41 (0.90 - 2.22); 48% | 1.20 (0.66 - 2.15); 0% | **2.47 (1.53 - 4.00); 34%** | 1.00 (0.66 - 1.52);0% | 0.89 (0.69 - 2.15); NA | NA |
| **> 2015** | **2.24 (1.22 - 3.57); 63%** | **1.78 (1.25 - 2.55); 49%** | **2.21 (1.39 - 3.50); 65%** | 1.49 (0.93 - 2.40);0% | 1.46 (0.63 - 3.30); 57 % | **4.13 (1.04 – 16.40); 0%** |
|  |  |  |  |  |  |  |
| **Study quality (JBI Criteria)** |  |  |  |  |  |  |
| **0 – 3 points** | NA | NA | NA | NA | NA | NA |
| **4 – 7 points** | **1.55 (1.11 - 2.17); NA \*** | **1.78 (1.27 – 2.50); NA \*** | 1.48 (0.99 – 2.21); NA \* | 1.06 (0.64 -1.76); NA \* | 0.89 (0.69 - 2.15); NA \* | NA |
| **8 – 11 points** | **2.03 (1.33 – 3.11); 66%** | **1.62 (1.10 - 2.40); 44%** | **2.47 (1.63 – 3.75); 62%** | 1.28 (0.83 - 1.99); 15% | 1.46 (0.63 - 3.30); 57 % | **4.13 (1.04 – 16.40); 0%** |
|  |  |  |  |  |  |  |

**\* Single study only therefore pooled analyses not possible; OR – Odds Ratio; CI – Confidence Interval; NA – not applicable as no studies in sub-group**; **JBI - Joanna Briggs Institute**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Crohn’s Disease** | | | | | **Ulcerative Colitis** | |
|  | **Disease phenotype** | | **Surgical Intervention** | | **Disease phenotype** | **Colectomy** |
|  | **Stricturing** | **Penetrating** | **Intestinal** | **Perianal** |  |  |
|  | n | n | n | n | n | **n** |
| **World Bank economic class** |  |  |  |  |  |  |
| **High-income** | **6** | **6** | **6** | **3** | **3** | **2** |
| **Low-and middle-income** | **2** | **2** | **3** | **1** | **0** | **0** |
|  |  |  |  |  |  |  |
| **Year of study** |  |  |  |  |  |  |
| **< 2010** | **0** | **0** | **0** | **0** | **0** | **0** |
| **2010 - 2015** | **2** | **2** | **2** | **2** | **1** | **0** |
| **> 2015** | **6** | **6** | **7** | **2** | **2** | **2** |
|  |  |  |  |  |  |  |
| **Study quality (JBI Criteria)** |  |  |  |  |  |  |
| **0 – 3 points** | **0** | **0** | **0** | **0** | **0** | **0** |
| **4 – 7 points** | **1** | **1** | **1** | **1** | **1** | **0** |
| **8 – 11 points** | **7** | **7** | **8** | **3** | **2** | **2** |
|  |  |  |  |  |  |  |

**Supplemental Table 15: Number of studies included in subgroup meta-analyses for Crohn’s Disease and Ulcerative Colitis**

**JBI - Joanna Briggs Institute**

**Supplemental Table 16: Impact of delayed diagnosis on disease location, medical treatment, and health care utilisation in (A) Crohn’s Disease (B) Ulcerative Colitis**

**(A)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Number of studies included in analysis | Pooled Odds Ratio | 95% Confidence Interval | I2, % | p value |
| Disease location |  |  |  |  |  |
| L1 | **6** | 1.07 | 0.83 - 1.39 | 30 | 0.21 |
| L2 | 0.69 | 0.54 - 0.89 | 0 | 0.78 |
| L3 | 1.03 | 0.85 - 1.27 | 0 | 0.49 |
| L4 | 1.53 | 0.90 - 2.60 | 0 | 0.76 |
|  |  |  |  |  |  |
| Medical Treatment |  |  |  |  |  |
| 5 - ASA \* | **3** | 1.06 | 0.77 - 1.46 | NA | - |
| Prednisolone | 0.84 | 0.65 - 1.09 | 0 | 0.79 |
| Budesonide\* | 1.39 | 1.01 - 1.93 | NA | - |
| Immunomodulators | 1.00 | 0.78 - 1.29 | 0 | 0.90 |
| Methotrexate\* | 0.96 | 0.62 - 1.47 | NA | - |
| Anti-TNF | 1.25 | 0.99 - 1.58 | 0 | 0.83 |
| Enteral Nutrition\* | 2.20 | 0.49 - 9.96 | NA | - |
|  |  |  |  |  |  |
| Healthcare utilisation |  |  |  |  |  |
| CD-related hospitalisation | **1** | 1.60 | 0.93 - 2.75 | NA | - |
| Frequent hospitalisation | 2.06 | 0.84 - 5.05 | NA | - |
|  |  |  |  |  |  |

**(B)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Number of studies included in analysis | Pooled Odds Ratio | 95% Confidence Interval | I2, % | p value |
| Disease extent |  |  |  |  |  |
| Extensive vs proctitis | **3** | 1.22 | 0.69 – 2.15 | 40 | 0.19 |
|  |  |  |  |  |  |
| Disease severity |  |  |  |  |  |
| Mayo 3 | **2** | 1.14 | 0.68 - 1.91 | 6 | 0.30 |
|  |  |  |  |  |  |
| Medical Treatment |  |  |  |  |  |
| Anti-TNF\* | **1** | 2.60 | 1.01 - 6.71 | NA | - |
|  |  |  |  |  |  |
| Health care utilisation |  |  |  |  |  |
| UC related hospitalisation | **2** | 1.08 | 0.64 – 1.82 | 0 | 0.89 |
| Frequent hospitalisation | 1.07 | 0.26 – 4.42 | 59 | 0.12 |
|  |  |  |  |  |  |

**\* Single study only therefore pooled analyses not possible; NA – not applicable**

**PRISMA Checklist**

| **Section and Topic** | **Item #** | **Checklist item** | **Location where item is reported** |
| --- | --- | --- | --- |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review. | Page 1 and 8 |
| **ABSTRACT** | | |  |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Page 4 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Page 7 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page 7 and 8 |
| **METHODS** | | |  |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Page 9 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 9 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Page 9 and Supplemental table 1 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Pages 9-12 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Pages 9-12 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Pages 9-12 |
| 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Pages 9-12 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Pages 9-12 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Pages 9-12 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Pages 9-12 |
| 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Pages 9-12 |
| 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Page 12 |
| 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Page 12 |
| 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Page 12 |
| 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Page 12 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 12 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Page 12 |
| **RESULTS** | | |  |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 14 and Figure 2 |
| 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Page 13 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Supplemental tables 2 and 3 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Supplemental tables 7,8,9 and 10 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimates and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Page 14 - 18 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Page 14 - 18 |
| 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Page 14 - 18 |
| 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Page 14 - 18 |
| 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Page 14 - 18 |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Page 14 - 18 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Page 14 - 18 |
| **DISCUSSION** | | |  |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Page 19 -21 |
| 23b | Discuss any limitations of the evidence included in the review. | Page 20 -22 |
| 23c | Discuss any limitations of the review processes used. | Page 18 - 19 |
| 23d | Discuss implications of the results for practice, policy, and future research. | Page 20 |
| **OTHER INFORMATION** | | |  |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Not registered |
| 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 9 -11 |
| 24c | Describe and explain any amendments to information provided at registration or in the protocol. | NA |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | **St Georges University of London’s librarians, Mr Stephen Reid, and Ms Karen John - Pierre, for helping us with the literature search.** |
| Competing interests | 26 | Declare any competing interests of review authors. | None to declare |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Data extracted from included studies; data used for all analyses available upon reasonable request |

**PRISMA Abstract Checklist**

| **Section and Topic** | **Item #** | **Checklist item** | **Reported (Yes/No)** |
| --- | --- | --- | --- |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review. | Y |
| **BACKGROUND** | | |  |
| Objectives | 2 | Provide an explicit statement of the main objective(s) or question(s) the review addresses. | Y |
| **METHODS** | | |  |
| Eligibility criteria | 3 | Specify the inclusion and exclusion criteria for the review. | Y |
| Information sources | 4 | Specify the information sources (e.g., databases, registers) used to identify studies and the date when each was last searched. | Y |
| Risk of bias | 5 | Specify the methods used to assess risk of bias in the included studies. |  |
| Synthesis of results | 6 | Specify the methods used to present and synthesise results. | Y |
| **RESULTS** | | |  |
| Included studies | 7 | Give the total number of included studies and participants and summarise relevant characteristics of studies. | Y |
| Synthesis of results | 8 | Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e., which group is favoured). | Y |
| **DISCUSSION** | | |  |
| Limitations of evidence | 9 | Provide a brief summary of the limitations of the evidence included in the review (e.g., study risk of bias, inconsistency and imprecision). |  |
| Interpretation | 10 | Provide a general interpretation of the results and important implications. | Y |
| **OTHER** | | |  |
| Funding | 11 | Specify the primary source of funding for the review. | N |
| Registration | 12 | Provide the register name and registration number. | N |