

SEARCH STRATEGY

Embase

1. 'inflammatory bowel disease':ab,ti OR 'inflammatory bowel diseases':ab,ti OR ibd:ab,ti OR 'crohn disease':ab,ti OR crohn:ab,ti OR 'ulcerative colitis':ab,ti
2. nafld:ab,ti OR nafl:ab,ti OR 'non-alcoholic fatty liver disease':ab,ti OR 'nonalcoholic fatty liver disease':ab,ti OR 'fatty liver disease':ab,ti OR 'fatty liver':ab,ti OR steatosis:ab,ti OR nash:ab,ti OR steatohepatitis:ab,ti
3. #1 AND #2

PubMed

("inflammatory bowel disease"[Title/Abstract] OR "inflammatory bowel diseases"[Title/Abstract] OR "IBD"[Title/Abstract] OR "Crohn disease"[Title/Abstract] OR "Crohn's disease"[Title/Abstract] OR "ulcerative colitis"[Title/Abstract]) AND ("NAFLD"[Title/Abstract] OR "NAFL"[Title/Abstract] OR "non-alcoholic fatty liver disease"[Title/Abstract] OR "nonalcoholic fatty liver disease"[Title/Abstract] OR "fatty liver disease"[Title/Abstract] OR "fatty liver"[Title/Abstract] OR "steatosis"[Title/Abstract] OR "NASH"[Title/Abstract] OR "steatohepatitis"[Title/Abstract])

Web of Science

TOPIC: ("inflammatory bowel disease" OR "inflammatory bowel diseases" OR "IBD" OR "Crohn disease" OR "Crohn's disease" OR "ulcerative colitis") AND TOPIC: ("NAFLD" OR "NAFL" OR "non-alcoholic fatty liver disease" OR "nonalcoholic fatty liver disease" OR "fatty liver disease" OR "fatty liver" OR "steatosis" OR "NASH" OR "steatohepatitis")

Scopus

((TITLE ("inflammatory bowel disease" OR "inflammatory bowel diseases" OR "IBD" OR "Crohn disease" OR "Crohn's disease" OR "ulcerative colitis") OR ABS ("inflammatory bowel disease" OR "inflammatory bowel diseases" OR "IBD" OR "Crohn disease" OR "Crohn's disease" OR "ulcerative colitis"))) AND ((TITLE ("NAFLD" OR "NAFL" OR "non-alcoholic fatty liver disease" OR

"nonalcoholic fatty liver disease" OR "fatty liver disease" OR "fatty liver" OR "steatosis" OR "NASH" OR "steatohepatitis") OR ABS ("NAFLD" OR "NAFL" OR "non-alcoholic fatty liver disease" OR "nonalcoholic fatty liver disease" OR "fatty liver disease" OR "fatty liver" OR "steatosis" OR "NASH" OR "steatohepatitis")))

ProQuest

(ti("inflammatory bowel disease" OR "inflammatory bowel diseases" OR "IBD" OR "Crohn disease" OR "Crohn's disease" OR "ulcerative colitis") OR ab("inflammatory bowel disease" OR "inflammatory bowel diseases" OR "IBD" OR "Crohn disease" OR "Crohn's disease" OR "ulcerative colitis")) AND (ti("NAFLD" OR "NAFL" OR "non-alcoholic fatty liver disease" OR "nonalcoholic fatty liver disease" OR "fatty liver disease" OR "fatty liver" OR "steatosis" OR "NASH" OR "steatohepatitis") OR ab("NAFLD" OR "NAFL" OR "non-alcoholic fatty liver disease" OR "nonalcoholic fatty liver disease" OR "fatty liver disease" OR "fatty liver" OR "steatosis" OR "NASH" OR "steatohepatitis"))

Table 1. Six World Health Organisation (WHO) Regions with member states

| WHO region | Countries |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Africa Region | Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cabo Verde, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, South Africa, South Sudan, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, Zimbabwe. |
| Americas Region | Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, Uruguay, Venezuela. |
| Eastern Mediterranean Region | Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iran, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, Yemen. |
| Europe Region | Albania; Andorra; Armenia; Austria; Azerbaijan; Belarus; Belgium; Bosnia and Herzegovina; Bulgaria; Croatia; Cyprus; Czech Republic; Denmark; Estonia; Finland; France; Georgia; Germany; Greece; Hungary; Iceland; Ireland; Israel; Italy; Kazakhstan; Kyrgyzstan; Latvia; Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, United Kingdom, Uzbekistan. |

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|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| South-East Asia Region | Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste. |
| Western Pacific Region | Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam. |

Table 2. Characteristics of the studies included in the systematic review

| Study | Country | Diagnostic method of NAFLD | Disease type | Sample size | Prevalence of NAFLD (%) | Risk of bias score | Risk factors reported for NAFLD with an adjusted odds ratio |
|--------------------------------|----------------|-----------------------------------|---------------------|--------------------|--------------------------------|---------------------------|--------------------------------------------------------------------|
| Almohannadi, 2020 ¹ | Qatar | Imaging | IBD | 913 | 11.8 | 5 | Sex, diabetes |
| | | | CD | 383 | 11.7 | | |
| | | | UC | 530 | 11.9 | | |
| Andrade, 2016 ² | Portugal | Histopathology | IBD | 54 | 24.1 | 5 | - |
| Arias Loste, 2020 ³ | Spain | Histopathology | IBD | 795 | 44.0 | 4 | - |
| Balaban, 2017 ⁴ | Romania | Imaging | IBD | 62 | 37.1 | 3 | - |
| Bargiggia, 2003 ⁵ | Italy | Imaging | IBD | 511 | 38.0 | 2 | - |
| | | | CD | 311 | 39.5 | | |
| | | | UC | 200 | 35.5 | | |
| Bessissow, 2016 ⁶ | Canada | HSI | IBD | 321 | 33.6 | 2 | - |
| | | | CD | 217 | 37.3 | | |
| | | | UC | 104 | 26.0 | | |
| Bosch, 2017 ⁷ | USA | Histopathology | IBD | 93 | 36.6 | 3 | - |
| | | | CD | 39 | 61.5 | | |
| | | | UC | 54 | 18.5 | | |

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|-----------------------------------|-------------|----------------|-----|------|------|---|----------------------------|
| Carrillo-Palau, 2021 ⁸ | Spain | Imaging | IBD | 136 | 46.3 | 3 | - |
| Chhina, 2014 ⁹ | USA | Imaging | IBD | 1304 | 9.7 | 5 | - |
| Chicco, 2021 ¹⁰ | Italy | Imaging | IBD | 142 | 40.8 | 3 | - |
| | | | CD | 58 | 46.6 | | |
| | | | UC | 84 | 36.9 | | |
| De Boer, 2008 ¹¹ | Netherlands | Histopathology | IBD | 83 | 36.1 | 2 | - |
| Demir, 2020 ¹² | Turkey | Imaging | IBD | 539 | 31.9 | 5 | - |
| Di Girolamo, 2013 ¹³ | Italy | Imaging | IBD | 788 | 16.2 | 4 | - |
| Domislovic, 2019 ¹⁴ | Croatia | HSI | IBD | 250 | 36.4 | 5 | - |
| | | | CD | 167 | 36.5 | | |
| | | | UC | 83 | 36.1 | | |
| Dundulis, 2014 ¹⁵ | USA | Imaging | IBD | 70 | 41.4 | 5 | - |
| Erzin, 2015 ¹⁶ | Turkey | Imaging | IBD | 276 | 36.2 | 5 | - |
| | | | CD | 104 | 41.3 | | |
| | | | UC | 172 | 33.1 | | |
| Glassner, 2017 ¹⁷ | USA | Imaging | IBD | 421 | 13.3 | 3 | - |
| Hoffmann, 2020 ¹⁸ | Germany | Imaging | IBD | 455 | 46.8 | 3 | Age, BMI, dyslipidemia, |
| | | | CD | 302 | 48.0 | | |

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|-----------------------------------|--------|---------|-----|-----|------|---|-----------------------------------------------------------------------------------------------|
| | | | UC | 153 | 44.4 | | hypertension, prior surgery, biologics |
| Kang, 2020 ¹⁹ | Korea | Imaging | IBD | 443 | 11.1 | 4 | Sex, age, hypertension, diabetes, prior surgery, immunomodulators, corticosteroids, biologics |
| | | | CD | 274 | 7.3 | | |
| | | | UC | 169 | 17.2 | | |
| Kani, 2019 ²⁰ | Turkey | Imaging | IBD | 99 | 44.4 | 4 | - |
| | | | CD | 58 | 48.3 | | |
| | | | UC | 39 | 38.5 | | |
| Lee, 2019 ²¹ | USA | Imaging | IBD | 168 | 28.0 | 5 | - |
| Li, 2017 ²² | China | Imaging | IBD | 206 | 10.7 | 4 | - |
| | | | CD | 137 | 10.9 | | |
| | | | UC | 69 | 10.1 | | |
| Likhitsup, 2019 (A) ²³ | USA | Imaging | IBD | 70 | 44.3 | 4 | - |
| Likhitsup, 2019 (B) ²⁴ | USA | Imaging | IBD | 80 | 53.8 | 4 | Sex, BMI |
| | | | CD | 65 | 56.9 | | |
| | | | UC | 15 | 40.0 | | |
| Magrì, 2019 ²⁵ | Italy | Imaging | IBD | 178 | 40.4 | 3 | - |

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|---------------------------------|----------|-----------------|-----|-----|------|---|-----------------------------------------------------------------------------------|
| | | | CD | 83 | 43.4 | | |
| | | | UC | 95 | 37.9 | | |
| Mancina, 2020 ²⁶ | Italy | Imaging | IBD | 95 | 71.6 | 3 | - |
| | | | CD | 37 | 59.5 | | |
| | | | UC | 58 | 79.3 | | |
| McHenry, 2020 ²⁷ | USA | Imaging | CD | 311 | 37.9 | 3 | - |
| Mehrotra, 2018 ²⁸ | India | Imaging | UC | 128 | 18.0 | 3 | - |
| Navaneethan, 2009 ²⁹ | USA | Imaging | UC | 65 | 15.4 | 3 | - |
| Peixoto, 2017 ³⁰ | Portugal | Imaging | CD | 62 | 37.1 | 4 | - |
| Principi, 2018 ³¹ | Italy | Imaging | IBD | 465 | 28.0 | 2 | - |
| | | | CD | 258 | 24.4 | | |
| | | | UC | 207 | 32.4 | | |
| Quang Le, 2014 ³² | USA | Imaging and HSI | IBD | 232 | 40.9 | 4 | - |
| Restellini, 2017 ³³ | Canada | Imaging | IBD | 349 | 39.5 | 3 | Age, BMI, dyslipidemia, hypertension, prior surgery, immunomodulators |

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|----------------------------------------|---------|---------------------------|-----|------|------|---|------------------------------------------------|
| Ritaccio, 2021 ³⁴ | USA | Imaging or histopathology | IBD | 1672 | 12.4 | 2 | - |
| | | | CD | 897 | 14.6 | | |
| | | | UC | 453 | 8.6 | | |
| Sagami, 2017 ³⁵ | Japan | Imaging | CD | 303 | 21.8 | 2 | - |
| Saroli Palumbo, 2019 ³⁶ | Canada | Imaging | IBD | 384 | 32.8 | 1 | Sex, BMI, diabetes, immunomodulators |
| | | | CD | 248 | 31.5 | | |
| | | | UC | 136 | 35.3 | | |
| Schröder, 2015 ³⁷ | Germany | Imaging | IBD | 259 | 28.2 | 4 | - |
| | | | CD | 170 | 30.0 | | |
| | | | UC | 77 | 23.4 | | |
| Scrivo, 2020 ³⁸ | Italy | Imaging and HSI | IBD | 208 | 20.7 | 3 | - |
| Silva, 2019 ³⁹ | Brazil | Imaging | IBD | 306 | 6.9 | 5 | - |
| | | | CD | 141 | 7.1 | | |
| | | | UC | 165 | 6.7 | | |
| Simon, 2018 ⁴⁰ | USA | Imaging | CD | 462 | 52.4 | 0 | Age, diabetes |
| Sourianarayananane, 2013 ⁴¹ | USA | Imaging | IBD | 928 | 8.2 | 4 | Hypertension, prior surgery, immunomodulators, |

| | | | | | | | |
|-----------------------------------------|--------|---------|-----|-----|------|---|-------------------------------|
| | | | | | | | corticosteroids, biologics |
| Tirath, 2019 ⁴² | India | Imaging | CD | 100 | 42.0 | 3 | - |
| Yamamoto-Furusho, 2010 ⁴³ | Mexico | Imaging | IBD | 80 | 11.3 | 4 | - |
| Yen, 2021 ⁴⁴ | Taiwan | Imaging | IBD | 81 | 29.6 | 3 | Age, BMI |
| | | | CD | 36 | 30.6 | | |
| | | | UC | 45 | 28.9 | | |

Table 3. Pooled prevalence of non-alcoholic fatty liver disease (NAFLD) in patients with inflammatory bowel disease (IBD) according to different countries

| Disease type | Country | No. of studies | No. of IBD patients | Pooled prevalence of NAFLD, % (95% CI) | I² | P-value for χ^2 |
|---------------------|----------------|-----------------------|----------------------------|-----------------------------------------------|----------------------|----------------------------------------|
| IBD | Brazil | 1 | 306 | 6.9 (4.0-9.7) | NA | NA |
| | Canada | 3 | 1,054 | 35.3 (31.1-39.4) | 51.1% | 0.129 |
| | China | 1 | 206 | 10.7 (6.5-14.9) | NA | NA |
| | Croatia | 1 | 250 | 36.4 (30.4-42.4) | NA | NA |
| | Germany | 2 | 714 | 37.6 (19.3-55.8) | 96.2% | <0.001 |
| | India | 2 | 228 | 29.7 (6.2-53.3) | 93.8% | <0.001 |
| | Italy | 7 | 2,387 | 36.1 (25.1-47.2) | 97.2% | <0.001 |
| | Japan | 1 | 303 | 21.8 (17.1-26.4) | NA | NA |
| | Korea | 1 | 443 | 11.1 (8.1-14) | NA | NA |
| | Mexico | 1 | 80 | 11.3 (4.3-18.2) | NA | NA |
| | Netherlands | 1 | 83 | 36.1 (25.8-46.5) | NA | NA |
| | Portugal | 2 | 116 | 30.4 (17.7-43.2) | 57.8% | 0.124 |
| | Qatar | 1 | 913 | 11.8 (9.7-13.9) | NA | NA |
| | Romania | 1 | 62 | 37.1 (25.1-49.1) | NA | NA |
| | Spain | 2 | 931 | 44.4 (41.2-47.6) | 0.0% | 0.619 |
| | Taiwan | 1 | 81 | 29.6 (19.7-39.6) | NA | NA |
| | Turkey | 3 | 914 | 36.2 (30.2-42.2) | 66.6% | 0.050 |
| | USA | 13 | 5,876 | 29.6 (22.6-36.5) | 98.1% | <0.001 |
| | Worldwide | 44 | 14,947 | 30.7 (26.5-34.9) | 97.7% | <0.001 |
| CD | Brazil | 1 | 141 | 7.1 (2.9-11.3) | NA | NA |

| | | | | | | |
|----|-----------|----|-------|------------------|-------|--------|
| | Canada | 2 | 465 | 34.2 (28.5-40.0) | 43.6% | 0.183 |
| | China | 1 | 137 | 11.0 (5.7-16.2) | NA | NA |
| | Croatia | 1 | 167 | 36.5 (29.2-43.8) | NA | NA |
| | Germany | 2 | 472 | 39.1 (21.5-56.8) | 93.6% | <0.001 |
| | India | 1 | 100 | 42.0 (32.3-51.7) | NA | NA |
| | Italy | 5 | 747 | 41.3 (30.4-52.2) | 87.9% | <0.001 |
| | Japan | 1 | 303 | 21.8 (17.1-26.4) | NA | NA |
| | Korea | 1 | 274 | 7.3 (4.2-10.4) | NA | NA |
| | Portugal | 1 | 62 | 37.1 (25.1-49.1) | NA | NA |
| | Qatar | 1 | 383 | 11.8 (8.5-15) | NA | NA |
| | Taiwan | 1 | 36 | 30.6 (15.5-45.6) | NA | NA |
| | Turkey | 2 | 162 | 43.8 (36.2-51.4) | 0.0% | 0.395 |
| | USA | 5 | 1,774 | 44.2 (23.9-64.4) | 98.6% | <0.001 |
| | Worldwide | 25 | 5,223 | 34.4 (28.0-40.8) | 96.9% | <0.001 |
| UC | Brazil | 1 | 165 | 6.7 (2.9-10.5) | NA | NA |
| | Canada | 2 | 240 | 30.7 (21.6-39.9) | 59.5% | 0.116 |
| | China | 1 | 69 | 10.1 (3.0-17.3) | NA | NA |
| | Croatia | 1 | 83 | 36.1 (25.8-46.5) | NA | NA |
| | Germany | 2 | 230 | 34.1 (13.4-54.7) | 91.1% | 0.001 |
| | India | 1 | 128 | 18.0 (11.3-24.6) | NA | NA |
| | Italy | 5 | 644 | 44.1 (29.4-58.8) | 93.6% | <0.001 |
| | Korea | 1 | 169 | 17.2 (11.5-22.8) | NA | NA |
| | Qatar | 1 | 530 | 11.9 (9.1-14.6) | NA | NA |

| | | | | | | |
|--|-----------|----|-------|------------------|-------|--------|
| | Taiwan | 1 | 45 | 28.9 (15.7-42.1) | NA | NA |
| | Turkey | 2 | 211 | 34.1 (27.7-40.5) | 0.0% | 0.535 |
| | USA | 4 | 587 | 15.8 (7.3-24.3) | 72.2% | 0.013 |
| | Worldwide | 22 | 3,101 | 28.2 (22.0-34.3) | 95.1% | <0.001 |

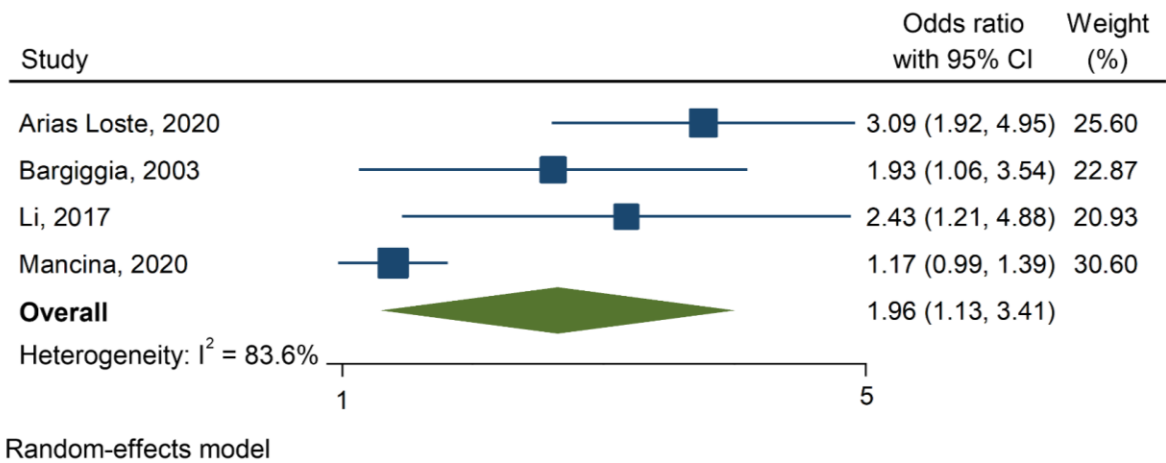


Figure 1. Forest plot of odds ratio for non-alcoholic fatty liver disease in IBD patients versus healthy controls

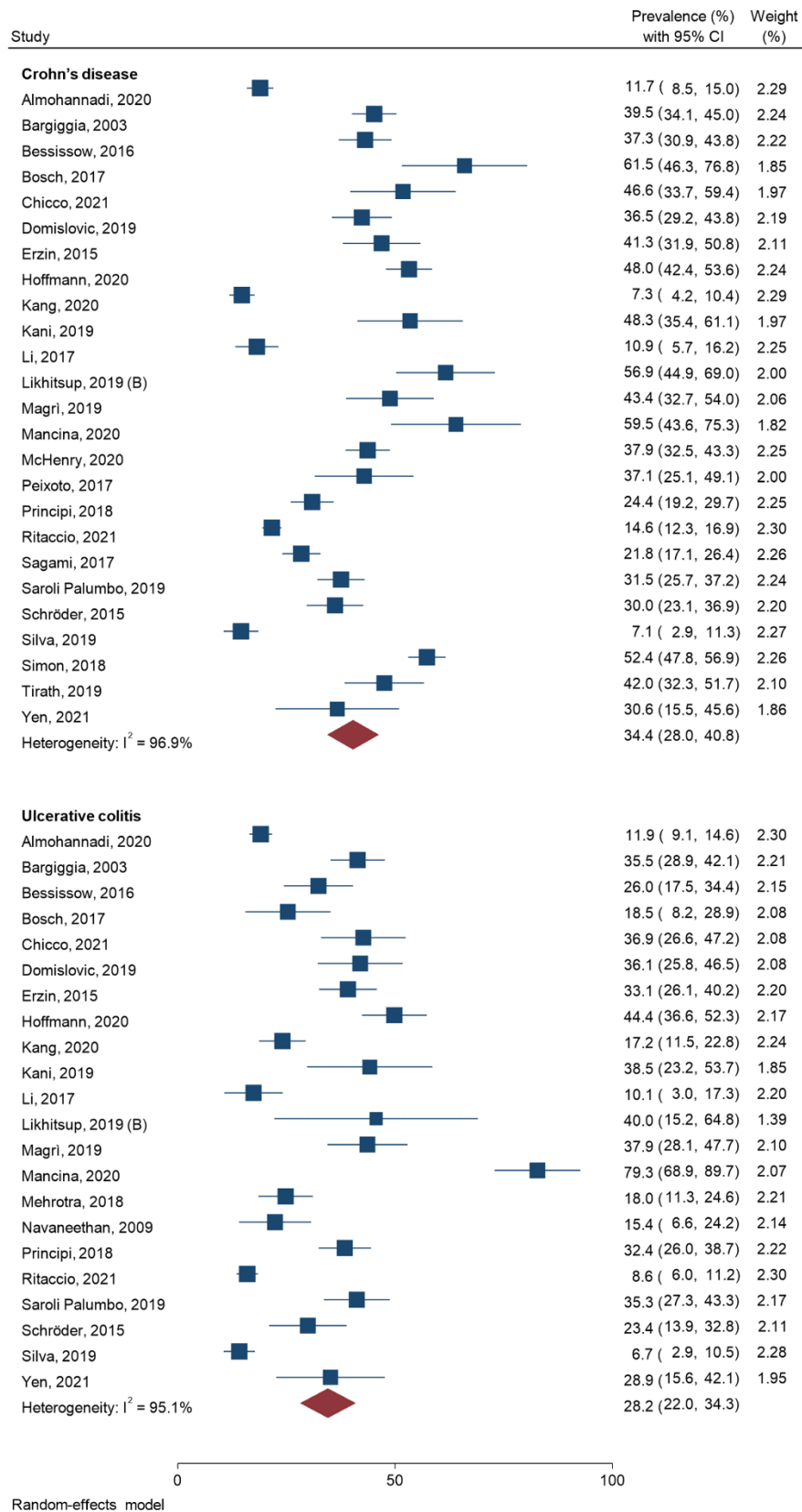


Figure 2. Forest plot of the pooled prevalence of non-alcoholic fatty liver disease in patients with Crohn's disease and ulcerative colitis

Table 4. Definition of IBD remission or activity used in the studies reporting the prevalence of NAFLD according to the disease activity

| Study | Definition |
|----------------|-----------------------------------------------------------------------------|
| Bessissow 2016 | CD: Harvey Bradshaw Index UC: Mayo score |
| Hoffmann, 2020 | CD: Harvey Bradshaw Index UC: Simple Clinical Colitis Activity Index |
| Magrì, 2019 | CD: Crohn’s disease activity index UC: Mayo score |
| Principi, 2018 | CD: Harvey Bradshaw Index UC: Mayo score |
| McHenry, 2020 | CD: Harvey Bradshaw Index |
| Sagami, 2017 | CD: Crohn’s disease activity index |

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