|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cluster** | **Pairs (n)** | **Time between index and second**  **(years)** | **Pairs with exactly the same population (n, %)** | **Details for pairs with slightly different population** |
| Coronary artery disease (stents) | 11 | 1 (0.5 ; 6) † | 9 (81 %) | Divergent pair 1: Subgroup of diabetic patients  Divergent pair 2: subgroup of ST + patients |
| Rheumatoid arthritis | 9 | 3 (1 ; 4) † | 6 (67 %) | For the 3 divergent pairs: Subgroup of patients non naive of DMARD |
| Atrial fibrillation | 5 | 1 (1 ; 7) † | 5 (100 %) | . |
| Chron Disease | 2 | 0 and 0 | 1 (50 %) | Divergent pair: Subgroup of patients with surgery |
| Chronic Obstructive Pulmonary Disease | 2 | 0 and 5 | 2 (100 %) | . |
| Type 2 diabetes | 2 | 2 and 3 | 2 (100 %) | . |
| Ankylosing spondylitis | 1 | 2 | 1 (100 %) | . |
| Antifungal prophylaxis in liver transplantation | 1 | 8 | 1 (100 %) | . |
| Cardiovascular prevention | 1 | 2 | 1 (100 %) | . |
| Coronary artery disease (drugs) | 1 | 0 | 1 (100 %) | . |
| Hepatitis C | 1 | 0 | 1 (100 %) | . |
| Neuropathic Pain | 1 | 4 | 1 (100 %) | . |
| Obesity | 1 | 1 | 0 (0 %) | Divergent pair: Subgroup of primary care studies |
| Osteoporosis | 1 | 3 | 1 (100 %) | . |
| Ulcerative colitis | 1 | 0 | 1 (100 %) | . |
| **Total** | **40** | **1.5 (1 ; 4)** † | **33 (83 %)** | **.** |

**e-table 1: Description of the 40 pairs.** The description is presented by cluster. † data are summarised with median and interquartile range.

**e-table 2: Detail of the 28 studies of the rheumatoid arthritis cluster (3 pages)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **PMID** | **Publication year** | **Network geometry** | **Funding** | **Outcomes** | **Population** | **Number of partcipants** | **Number of nodes** | **Number of studies** |
| 25435923 | 2014 | Network no direct | No grant | ACR50 | Not naïve | 2846 | 5 | 7 |
| 25244021 | 2014 | Network at least one loop | Non-profit funding sources | Radiographic erosion score | Both naive and not naive | 12171 | 7 | 39 |
| 25068763 | 2014 | Network no direct | Non-profit funding sources | ACR20, 50, or 70 | Not naive | 6357 | 6 | 24 |
| 24988902 | 2014 | Network no direct | Company/Biotech | HAQ-DI, Pain, PGA, SF36, and fatigue. | Not naive | 6477 | 8 | 17 |
| 24832836 | 2014 | Network at least one loop | Company/Biotech | ACR20, 50 | Both naive and not naive | 15044 | 10 | 34 |
| 24480452 | 2014 | Network no direct | No mention | HAQ | Both naive and not naive separately | 12301 | 9 | 28 |
| 24332807 | 2014 | Network no direct | No mention | Radiographic progression | Both naive and not naive separately | 6389 | 8 | 14 |
| 23745516 | 2013 | Network at least one loop | Company/Biotech | ACR20, 50, or 70, DAS | Not naive | 7345 | 3 | 15 |
| 23269860 | 2012 | Network at least one loop | Company/Biotech | ACR20, 50, or 70 | Not naive | 9326 | 10 | 37 |
| 23092868 | 2012 | Network no direct | Non-profit funding sources | Withdrawal for lack of efficacy | Both naive and not naive | 20578 | 10 | 44 |
| 22859920 | 2012 | Indirect but failed | No grant | Radiographic progression | Both naive and not naive |  |  | 12 |
| 22696776 | 2012 | Network at least one loop | Non-profit funding sources | ACR20, 50, or 70, Withdrawals | Not naive | 10965 | 9 | 30 |
| 22505698 | 2012 | Network at least one loop | Company/Biotech | HAQ, ACR20, 50, or 70 | Not naive | 3762 | 7 | 11 |
| 22151924 | 2011 | Network at least one loop | Company/Biotech | HAQ, ACR-50 and Remission (DAS28 < 2.6) | Not naive | 5628 | 9 | 16 |
| 21960560 | 2012 | Network no direct | No mention | HAQ, ACR20, 50 | Not naive | 6566 | 6 | 16 |
| 21848493 | 2011 | Network no direct | Non-profit funding sources | ACR20, 50, or 70 | Not naive | 10941 | 10 | 27 |
| 21831256 | 2012 | Network no direct | No mention | ACR20, 50, or 70 | Not naive | 3267 | 8 | 10 |
| 21239748 | 2011 | Network no direct | Company/Biotech | ACR20, 50, or 70 | Not naive | 7158 | 8 | 19 |
| 21182357 | 2011 | Network no direct | No mention | ACR50 | Both naive and not naive | 15411 | 10 | 28 |
| 21097801 | 2011 | Network no direct | No grant | ACR50 | Not naive | 6138 | 5 | 20 |
| 20223500 | 2010 | Network no direct | Company/Biotech | ACR20, 50, or 70 | Not naive | 10419 | 5 | 18 |
| 20054439 | 2009 | Network no direct | Non-profit funding sources | ACR 50 | Both naive and not naive | 7614 | 5 | 22 |
| 19884297 | 2009 | Network no direct | Non-profit funding sources | ACR50 | Both naive and not naive | 7643 | 7 | 27 |
| 17943257 | 2008 | Network no direct | No mention | ACR20, 50, or 70, Withdrawals due to lack of efficacy | Not naive | 1040 | 4 | 3 |
| 17478472 | 2007 | Network no direct | No grant | ACR20, 50 | Both naive and not naive | 6994 | 5 | 13 |
| 17225293 | 2006 | Network no direct | Non-profit funding sources | ACR20, 50 | Not naive | 5248 | 5 | 17 |
| 15130461 | 2004 | Network no direct | Non-profit funding sources | ACR20 | Not naive |  | 3 | 4 |
| 14532140 | 2003 | Network no direct | No mention | ACR20, 50, or 70 | Not naive | 1053 | 4 | 4 |

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**e-figure 1:** Overview of study conduct

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**e-Figure 2: A: Cumulative number of NMA publications in the rheumatoid arthritis topic**

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**e-figure 3:** Number of nodes per meta-analysis as a function of years (the regression line and its 95 % confidence interval are obtained through locally weighted regression)

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**e-figure 4:** Completeness of NMAs in terms of references, in comparison with all available references 1/ the year the NMA was published and 2/ 2 years before publication of the NMA.

**Selection process for the references plotted in red in figure 3B**

(ADALIMUMAB OR GOLIMUMAB OR INFLIXIMAB OR OCRELIZUMAB OR CERTOLIZUMAB OR TOCILIZUMAB OR RITUXIMAB OR ABATACEPT OR ANAKINRA OR ETANERCEPT) AND rheumatoid arthritis AND ("1900/01/01"[PDAT] : "2015/01/01"[PDAT]) AND Randomized Controlled Trial[ptyp] AND (Randomized Controlled Trial[ptyp])

**568** trials, among these, 76 were included in at least one NMA. 2 already included with an initial PMID were not found by this search. The 4 that were included without a PMID were not found (of course).

It results in **492** trials that were checked. THE PMIDs USED IN THIS SEARCH ARE HERE:

26324784 26087654 25992914 25922848 25736355 25557658 25550338 25550337 25539805 25535985 25512675 25504080 25381560 25372086 25367713 25359150 25355728 25274892 25253199 25249397 25227967 25182696 25169728 25139667 25131223 25128520 25099160 25074688 25005467 25005327 24996416 24981319 24972708 24942540 24907147 24842476 24834925 24818633 24812287 24786931 24786925 24786016 24783914 24782192 24782115 24758073 24756903 24737786 24727841 24708204 24706006 24641941 24618266 24593170 24584926 24584918 24550168 24525910 24517212 24473673 24448345 24443001 24441150 24438039 24431394 24429167 24429164 24412895 24385202 24372225 25980298 24368514 24356481 24356474 24344160 24339699 24313916 24307478 24295403 24293583 24252035 24247368 24241487 24237999 24129130 24168956 24152421 24115082 24022747 24001888 23983039 23979914 23975656 23962455 23945134 23940214 23925361 23918037 23912798 23908187 23904473 23904470 23897769 23864239 23861303 23818718 23817631 23782588 23772084 23765873 23755969 23740460 23740226 23729804 23723317 23716067 23711100 23686414 23678153 23651756 23588946 23588939 23547848 23547212 23515142 23514433 23509040 23497111 23463543 23460074 23457387 23457383 23436260 23434570 23418046 23397148 23332236 23322466 23316080 23305631 23300117 23294908 23292882 23264555 23252525 23213004 23204515 23196701 23146660 23097311 23095282 23092868 23059810 23053688 23027887 23011358 22984272 22984173 22975754 22972745 22972168 22966146 22956167 22949223 22943199 22942403 22923753 22915624 22915617 22908326 22873531 22859346 22851468 22847212 22829691 22798265 22782640 22776409 22753773 22753402 22730343 22661646 22596211 22589265 22562983 22562980 22540770 22530354 22508468 22505702 22464340 22462423 22459542 22397953 22368231 22302136 22258482 22253903 22247354 22231904 22183975 22169051 22166255 22131049 22128078 22127693 22127692 22127691 22121130 22102701 22101760 22089463 22088414 22045836 22012969 22002809 21998118 21952978 21947196 21943782 21926186 21926153 21917824 21914628 21893583 21885491 21884601 21821865 21807781 21784729 21722499 21639907 21618201 21572151 21557525 21515916 21496415 21485024 21478189 21452294 21430660 21415052 21415050 21406499 21362764 21362762 21360491 21352592 21305524 21296603 21285171 21242235 21225699 21225693 21211205 21204103 21128258 21083889 21068104 20964833 20957659 20889601 20799264 20691795 20662070 20622199 20617358 20610444 20610442 20595536 20574648 20535801 20525844 20507292 20498212 20482894 20472597 20463186 20448287 20444749 20439295 20436073 20430577 20423835 20402381 20237125 20194448 20191568 20191522 20187135 20131246 20097931 20082236 20039425 20039397 19932542 19909548 19877104 19847430 19846407 19781326 19756557 19741011 19690125 19665644 19640853 19626391 19589891 19565475 19500335 19487269 19466423 19460761 19452245 19404938 19386610 19369462 19351624 19293160 19279507 19273451 19248130 19228659 19116965 19074911 19067101 19019888 18957487 18930988 18930987 18854518 18801760 18794178 18784373 18766426 18759293 18718986 18716298 18704426 18678578 18670735 18662933 18612923 18593759 18576334 18535115 18524792 18512710 18511473 18498922 18487628 18474811 18438876 18438853 18438829 18402714 18388156 18383415 18383390 18358909 18322991 18276741 18240203 18234715 18203764 18203329 18198195 18173917 18086727 18085743 18050385 18050378 18050208 18050196 18050189 17985420 17937474 17921185 17846044 17766699 17763439 17728331 17666447 17644545 17644537 17599726 17552048 17470434 17444589 17412737 17405834 17404783 17392352 17371885 17334829 17322150 17304653 17293364 17158431 17133559 17105853 17083767 17062648 17062431 17014006 16995864 16984942 16953150 16639484 16583466 16583424 16572441 16568505 16567357 16541481 16541213 16540554 16508932 16508926 16465653 16464988 16396977 16385521 16308341 16227416 16206346 16079172 16052582 15996057 15975966 15951469 15931231 15860509 15838068 15818699 15818697 15756499 15743471 15708879 15641062 15564721 15496641 15355744 15355743 15290731 15286005 15248223 15228184 15188350 15176649 15170922 15088288 15077311 15077292 15077287 14969077 14722203 14613288 14498766 12905468 12860493 12794815 12728284 12709725 12563672 12428223 12415583 12364632 12115174 12115173 12047962 12022323 11987981 11915973 11817593 11677200 11357169 11357168 11157143 11096166 10972371 10817552 10717011 10688396 10589362 10589361 10415055 9870877 9864837 9663484 8670316 7934491

Of these, **202** were retained (title and abstract) and **157** excluded studies after considering the full text.

Secondary publications: 81

Comparison is not relevant: 30

Comparisons of dosages: 12

Only safety: 8

Continuation design: 7

Pharmacokinetic/pharmacodynamics: 5

Not available (or language): 5

Published after 2014: 3

Children: 2

Very short term studies:2

Not RA: 1

Protocol:1

**45** additional studies were retained for the graph. THE PMIDs ARE HERE:

11915973 15077292 24618266 18050189 21572151 18203329 22972745 23097311 18759293 16464988 17158431 19741011 20662070 21452294 21807781 22462423 22984272 24356474 25131223 24429167 21952978 22247354 22508468 22661646 22753402 22873531 22915624 22923753 22984173 23011358 23059810 23146660 23316080 23434570 24313916 24339699 24431394 24641941 24942540 24972708 24981319 25074688 25355728 25367713 25512675

**+ 2** additional studies retrieved by cross checking this search with a previous search of CT.gov

22131049 22966146