Supplementary Table S1. Comparison of general study characteristics of 2006 with 2016 RCTs.

| Characteristics           | All       | Study year    |               | P     |
|---------------------------|-----------|---------------|---------------|-------|
|                           | (N = 76)  | 2006 (N = 34) | 2016 (N = 42) |       |
| Funding source            |           |               |               | 0.305 |
| Industry, full or partial | 42 (55.3) | 21 (61.8)     | 21 (50)       |       |
| Non-profit or unspecified | 34 (44.7) | 13 (38.2)     | 21 (50)       |       |
| Study phase               |           |               |               | 0.327 |
| Phase 2                   | 11 (14.5) | 3 (8.8)       | 8 (19)        |       |
| Non-phase 2/unspecified   | 65 (85.5) | 31 (91.2)     | 34 (81)       |       |
| Experimental intervention |           |               |               | 0.123 |
| Traditional DMARD         | 8 (10.5)  | 5 (14.7)      | 3 (7.1)       |       |
| Biologic DMARD            | 38 (50)   | 17 (50)       | 21 (50)       |       |
| Small molecule            | 4 (5.3)   | 0 (0)         | 4 (9.5)       |       |
| Others                    | 26 (34.2) | 12 (35.3)     | 14 (33.3)     |       |
| Number of study arms      |           |               |               | 0.381 |
| 2                         | 40 (52.6) | 16 (47.1)     | 24 (57.1)     |       |
| >2                        | 36 (47.4) | 18 (52.9)     | 18 (42.9)     |       |
| Placebo arm, yes          | 45 (59.2) | 15 (44.1)     | 30 (71.4)     | 0.016 |
| Study centers, multiple   | 57 (75)   | 26 (76.5)     | 31 (73.8)     | 0.790 |
| Study duration, months    | 6 (3-12)  | 9 (4.5-12)    | 6 (3-12)      | 0.275 |
| Efficacy, positive*       | 59 (80.9) | 28 (84.8)     | 31 (77.5)     | 0.427 |
|                           |           |               |               |       |

Values represent number (%) for categorical & median (25<sup>th</sup>-75<sup>th</sup> percentile) for the numeric variables. \*: N = 73, 3 RCTs excluded as were strategy trials with no intervention declared as experimental a priori. DMARD: disease modifying anti-rheumatic drug; N: total number; P: p-value; RCT: randomized controlled trial.

Supplementary Table S2. Differential attrition. Percentage of subjects in 2006 & 2016 RCTs not completing the trial in each study arm.

| Percent patients with | Experimental     | Active comparator | Placebo comparator |
|-----------------------|------------------|-------------------|--------------------|
| missing outcome       | intervention arm | arm               | arm                |
|                       | $(N = 68)^1$     | $(N = 26)^2$      | $(N=41)^3$         |
| < 5%                  | 13 (19.1)        | 4 (15.4)          | 4 (9.8)            |
| 5-10%                 | 9 (13.2)         | 7 (26.9)          | 4 (9.8)            |
| >10-20%               | 30 (44.1)        | 7 (26.9)          | 16 (39)            |
| >20%                  | 16 (23.5)        | 8 (30.8)          | 17 (41.5)          |

<sup>&</sup>lt;sup>1</sup>: Information about subjects completing trial missing for 8/73 RCTs in the experimental interventional arm (3 RCT had no missing data). <sup>2</sup>: Information about subjects completing trial missing for 5/31 RCTs with active comparator arm. <sup>3</sup>: Information about subjects completing trial missing for 4/45 for placebo control arm