

# Supplementary Material

## Drug survival of biologics in treating psoriasis: a meta-analysis of real-world evidence

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## **Figure legends for supplementary figures**

Supplementary Table S1: Included studies of drug survival of biologics for treating psoriasis.

Supplementary Figure S1: Forest plots of drug survival of biologics for treating psoriasis in all subjects (a-d) with etanercept (a); with adalimumab (b); (c) with infliximab (c); with ustekinumab (d).

Supplementary Figure S2: Forest plots of drug survival of biologics for treating psoriasis in biologic-naïve subjects (a-d) with etanercept (a); with adalimumab (b); (c) with infliximab (c); with ustekinumab (d).

Supplementary Figure S3: Forest plots of drug survival for discontinue due to loss of efficacy (a-d) with etanercept (a); with adalimumab (b); (c) with infliximab (c); with ustekinumab (d).

Supplementary Figure S4: Forest plots of drug survival for discontinue due to adverse effects (a-d) with etanercept (a); with adalimumab (b); with infliximab (c); with ustekinumab (d).

Supplementary Table S1. Included studies of drug survival of biologics for treating psoriasis

References	Patient population n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
<b>Etanercept</b>											
Arnold et al <sup>9</sup>	46	28	60	22	48	17	38	-	-	S****; C*; O**	
Bonafede et al <sup>10</sup>	1855	899	48.5	-	-	-	-	-	-	S****; C; O**	Biologic-naïve
Brunasso et al <sup>11</sup>	34	21	62.0	21	62.0	21	62.0	21	62.0	S****; C*; O**	Biologic-naïve
	13	4	30.0	2	14.0	2	14.0	2	14.0		Biologic-naïve
Chan et al <sup>12</sup>	1096	877	80.0	-	-	-	-	-	-	S****; C; O**	
Davila-Seijo et al <sup>13</sup>	672	388	82.9	258	49.2	168	38.0	129.0	20.5	S****; C*; O**	
Doshi et al <sup>14</sup>	1025	301	29.4	-	-	-	-	-	-	S****; C*; O**	
Esposito et al <sup>15</sup>	389	362	93.0	327	84.1	302	77.6	293	75.2	S****; C*; O**	
Gniadecki et al <sup>16</sup>	449	295	65.7	236	52.5	86	19.2	159	35.4	S****; C*; O**	
Gniadecki et al <sup>17</sup>	311	229	73.5	183	58.8	146	47.1	128	41.2	S****; C*; O**	
Inzinger et al <sup>18</sup>	501	355	70.8	305	60.8	281	56.0	-	-	S****; C*; O**	
Jacobi et al <sup>19</sup>	55	37	67.3	20	36.4	22	40.0	18	32.0	S****; C*; O**	
Kimball et al <sup>20</sup>	2510	1629	64.9	1329	52.9	1220	48.6	1076	42.9	S****; C; O**	
Di Lernia et al <sup>21</sup>	131	86	65.6							S****; C; O**	

References	Patient population n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
Di Lernia et al <sup>21</sup>	116			43	37.1					S****; C; O**	
Marinas et al <sup>22</sup>	175	123	82.6	90	68.7	60	56.3	33	47.5	S****; C; O**	
Menter et al <sup>23</sup>	289	196	67.7	168	58.1	154	53.2	140	48.4	S****; C**; O**	Biologic-naïve
	155	90	58.1	75	48.4	65	41.9	55	35.5		2 <sup>nd</sup> line therapy
	71	39	54.8	36	50.0	34	48.6	25	35.5		3 <sup>rd</sup> line therapy
Menting et al <sup>24</sup>	118	100	85.0	94	79.6	91	77.0	76	64.0	S***; C; O**	Biologic-naïve
	55	47	86.0	39	71.4	35	62.9	23	42.0		Biologic-experienced
Mercadal et al <sup>25</sup>	34	-	-	21	62	-	-	-	-	S****; C*; O**	
Mitratza et al <sup>26</sup>	58	37	64.0	-	-	15	26.0	-	-	S****; C*; O**	Biologic-naïve
Pogácsás et al <sup>27</sup>	330	241	72.9	195	59.2	156	47.4			S****; C*; O**	
Richter et al <sup>28</sup>	55	28	50.9	13	23.6	5	9.1	4	7.3	S****; C*; O**	
Ross et al <sup>29</sup>	21	12	59.3	11	52.5	10	49.2	10	49.2	S****; C**; O**	
Shalom et al <sup>30</sup>	646	167	25.87	82	12.7	41	6.35			S****; C**; O**	
Van den Reek et al <sup>31</sup>	82	56	68.0	-	-	-	-	-	-	S****; C*; O**	
Van den Reek et al <sup>32</sup>	148	106	71.8	85	57.7	69	46.8	51	34.6	S****; C*; O**	Biologic-naïve
	45	38	84.6	31	68.0	28	62.8	25	55.8		Biologic-experienced
Ventayol et al <sup>33</sup>	34	-	-	21	62.0	-	-	-	-	S****; C; O**	Biologic-naïve

References	Patient populatio n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
Vilarrasa et al <sup>34</sup>	248	176	70.9	130	52.6	97	39.1	76	30.5	S****; C*; O**	
Warren et al <sup>35</sup>	1098	769	70.0	560	51.0	439	40.0	-	-	S****; C*; O**	
Zweegers et al <sup>36</sup>	238	178	74.6	143	60.3	117	49.3	98	41.1	S****; C*; O**	
<b>Adalimumab</b>											
Arnold et al <sup>9</sup>	137	96	70	73	53	67	49	-	-	S****; C*; O**	
Bonafede et al <sup>10</sup>	1901	802	49.2	-	-	-	-	-	-	S****; C; O**	Biologic-naïve
Brunasso et al <sup>11</sup>	7	7	100.0	7	100.0	7	100.0	7	100.0	S****; C*; O**	Biologic-naïve
	8	6	74.0	6	74.0	-	-	-	-		Biologic-experienced
Davila-Seijo et al <sup>13</sup>	724	473	65.4	334	46.2	242	33.5	195	26.9	S****; C*; O**	
Doshi et al <sup>14</sup>	1084	438	40.4	-	-	-	-	-	-	S****; C*; O**	
Esposito et al <sup>15</sup>	114	99	86.5	80	70.1	67	58.4	56	49.5	S****; C*; O**	
Gniadecki et al <sup>16</sup>	774	524	67.7	481	62.1	414	53.5	379	49.0	S****; C*; O**	
Gniadecki et al <sup>17</sup>	427	289	67.7	214	50.0	163	38.2	151	35.3	S****; C*; O**	
Inzinger et al <sup>18</sup>	460	326	70.9	262	57.0	237	51.6	-	-	S****; C*; O**	
Jacobi et al <sup>19</sup>	37	22	59.5	14	37.8	20	55.2	16	43.2	S****; C*; O**	
Di Lernia et al <sup>21</sup>	78	51	65.4							S****; C; O**	
Di Lernia et al <sup>21</sup>	58			27	46.6					S****; C; O**	

References	Patient populatio n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
Lopez-Ferrer et al <sup>37</sup>	49	38	78.5	38	78.5	38	78.5	32	65.9	S****; C*; O**	Biologic-naïve
	70	42	60.3	33	47.7	32	45.8	32	45.8		Biologic-experienced
Marinas et al <sup>22</sup>	134	82	80.4	53	64.8	28	55	19	50.8	S****; C; O**	
Menter et al <sup>23</sup>	402	318	79.2	263	65.5	263	65.5	188	46.8	S****; C**; O**	Biologic-naïve
	622	441	71.0	371	59.7	341	54.8	311	50.0		2 <sup>nd</sup> line therapy
	197	130	66.1	108	54.8	95	48.4	79	40.3		3 <sup>rd</sup> line therapy
Menting et al <sup>24</sup>	29	22	77.0	22	77.0	22	77.0	22	77.0	S****; C; O**	Biologic-naïve
	58	49	84.0	43	74.3	35	60.0	32	56.0		Biologic-experienced
Mercadal et al <sup>25</sup>	37			18	48					S****; C*; O**	
Mitratza et al <sup>26</sup>	30	16	51.9	-	-	7	22.2	-	-	S****; C*; O**	Biologic-naïve
Pogácsás et al <sup>27</sup>	491	329	67.1	284	57.9	246	50			S****; C*; O**	
Richter et al <sup>28</sup>	106	68	64.1	52	49.1	34	32.1	24	22.6	S****; C*; O**	
Ross et al <sup>29</sup>	24	18	74.6	13	54.2	9	37.3	9	37.3	S****; C**; O**	
Shalom et al <sup>30</sup>	554	167	30.2	163	29.4	106	19.1			S****; C**; O**	
Spertino et al <sup>38</sup>	63	43	67.7	33	52.3	26	41.5	25	40.0	S****; C*; O**	
Suarez-Perez et al <sup>39</sup>	50	-	-	-	-	35	70.0	-	-	S****; C*; O**	
Umezawa et al <sup>40</sup>	59	47	79.7	-	-	-	-	-	-	S****; C; O**	

References	Patient populatio n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
Van den Reek et al <sup>41</sup>	459	362	78.8	275	60.0	253	55.1	243	53.0	S***; C*; O**	
Van den Reek et al <sup>42</sup>	116	88	76.0	66	57.0	65	56.0	60	52.0	S***; C*; O**	
Van den Reek et al <sup>31</sup>	101	75	74.0	-	-	-	-	-	-	S****; C*; O**	
Van den Reek et al <sup>43</sup>	116	-	-	-	-	-	-	58	50.0	S****; C*; O**	
Ventayol et al <sup>33</sup>	37	-	-	18	48.0	-	-	-	-	S****; C; O**	Biologic-naïve
Vilarrasa et al <sup>34</sup>	231	159	69.0	123	53.2	97	41.9	81	34.9	S****; C**; O**	
Warren et al <sup>35</sup>	1879	1484	79.0	1259	67.0	1109	59.0			S****; C*; O**	
Zweegers et al <sup>36</sup>	186	141	75.8	112	60.3	102	54.8	89	47.9	S****; C*; O**	
<b>Infliximab</b>											
Arnold et al <sup>9</sup>	140	74	53	52	37	52	37	-	-	S****; C*; O**	
Brunasso et al <sup>11</sup>	33	6	18.0	5	14.0	5	14.0	5	14.0	S****; C*; O**	Biologic-naïve
	2	2	100.0	2	100.0	2	100.0	2	100.0		Biologic-experienced
Davila-Seijo et al <sup>13</sup>	188	123	65.4	87	46.2	65	34.6	54	28.9	S****; C*; O**	
Doshi et al <sup>14</sup>	318	157	49.4	-	-	-	-	-	-	S****; C*; O**	
Esposito et al <sup>15</sup>	147	117	79.4	89	60.8	70	47.7	57	38.8	S****; C*; O**	
Gniadecki et al <sup>16</sup>	253	180	71.2	146	57.6	130	51.5	111	43.9	S****; C*; O**	
Gniadecki et al <sup>17</sup>	144	123	85.3	110	76.5	102	70.6	97	67.7	S****; C*; O**	

References	Patient populatio n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
Inzinger et al <sup>18</sup>	58	34	58.0	17	30.1	13	22.6	-	-	S****; C*; O**	
Jacobi et al <sup>19</sup>	13	7	7.0	3	3.0	-	-	-	-	S****; C*; O**	
Di Lernia et al <sup>21</sup>	98	70	64.6							S****; C; O**	
Di Lernia et al <sup>21</sup>	89			41	37.1					S****; C; O**	
Marinas et al <sup>22</sup>	160	40	83.8	30	66.4	25	55.4	19	48.5	S****; C; O**	
Menter et al <sup>23</sup>	63	53	83.9	49	77.4	43	67.7	34	53.2	S****; C**; O**	Biologic-naïve
	93	63	67.7	51	54.8	24	25.8	15	16.1		2 <sup>nd</sup> line therapy
	103	71	69.4	58	56.5	40	38.7	37	35.5		3 <sup>rd</sup> line therapy
Menting et al <sup>24</sup>	19	14	75.0	14	75.0	14	75.0	14	75.0	S****; C; O**	Biologic-naïve
	21	14	68.0	13	60.0	9	42.9	9	43.0		Biologic-experienced
Mitratza et al <sup>26</sup>	21	11	54.4	-	-	9	42.9	-	-	S*****; C*; O**	Biologic-naïve
Pogácsás et al <sup>27</sup>	266	182	68.4	144	54.0	91	34.2	-	-	S****; C*; O**	
Ross et al <sup>29</sup>	14	10	69.5	10	69.5	8	59.3	6	41.5	S****; C**; O**	
Shalom et al <sup>30</sup>	152	46	30.2	29	19.1	22	14.3			S****; C**; O**	
Umezawa et al <sup>40</sup>	38	28	73.3	-	-	-	-	-	-	S****; C; O**	
Vilarrasa et al <sup>34</sup>	84	58	68.8	46	54.2	38	45.5	36	42.4	S****; C**; O**	
Warren et al <sup>35</sup>	96	62	65.0	48	50.0	34	35.0	-	-	S****; C*; O**	



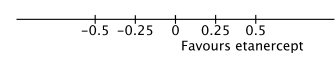
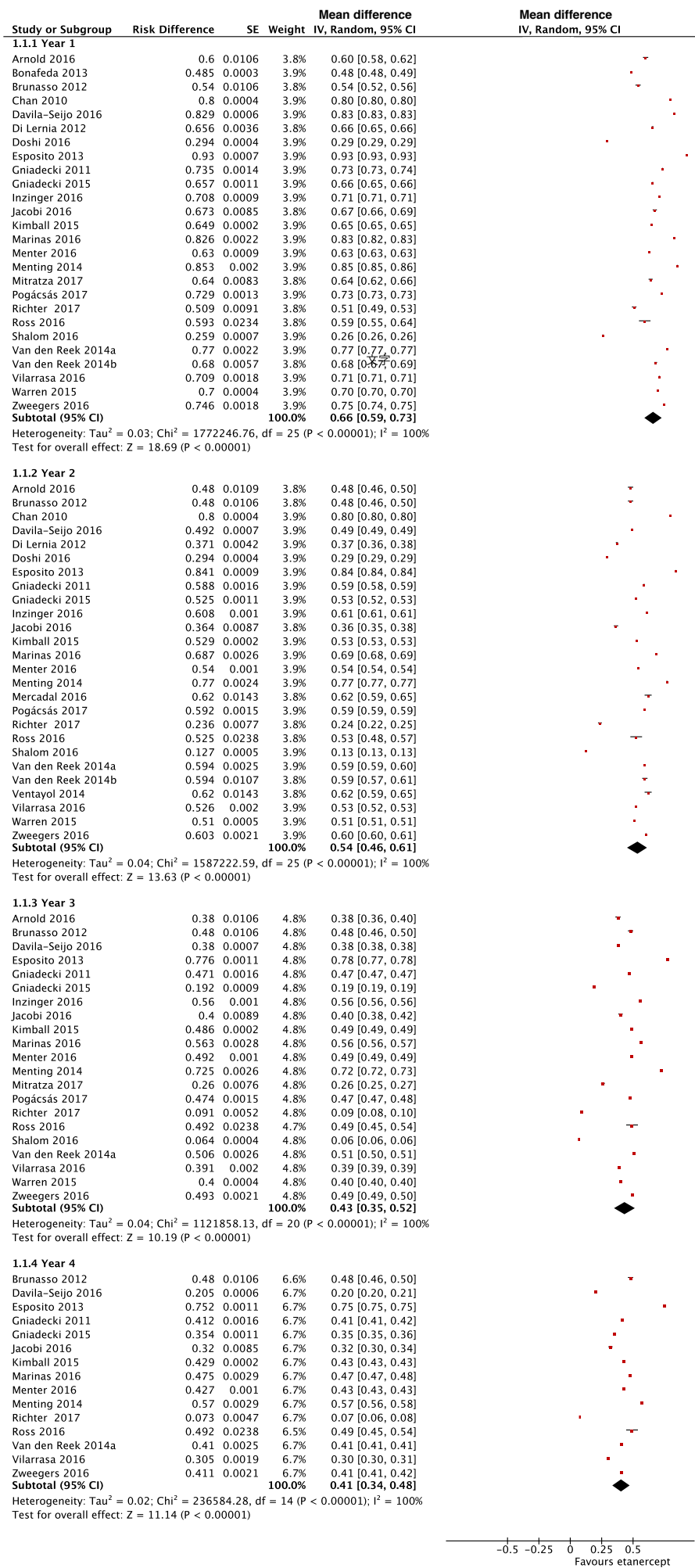
References	Patient populatio n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
<b>Ustekinumab</b>											
Arnold et al <sup>9</sup>	59	53	90.0	49	83.0	49	83.0	-	-	S****; C*; O**	
Davila-Seijo et al <sup>13</sup>	491	397	80.8	312	63.5	246	50.0	208	42.3	S****; C*; O**	
Doshi et al <sup>14</sup>	280	121	43.2	-	-	-	-	-	-	S****; C*; O**	
García-Martínez et al <sup>44</sup>	35	32	90.0	25	71.0	24	69.0	-	-	S****; C; O**	
Gniadecki et al <sup>16</sup>	391	308	78.8	278	71.2	271	69.2	263	67.2	S****; C*; O**	
Jacobi et al <sup>19</sup>	11	11	100.0	6	54.6	8	76.0	-	-	S****; C*; O**	
Marinas et al <sup>22</sup>	176	122	91.4	85	85.6	47	80.0	18	75.5	S****; C; O**	
Menter et al <sup>23</sup>	301	282	93.6	272	90.3	262	87.1	262	87.1	S****; C**; O**	Biologic-naïve
	566	493	87.1	456	80.7	438	77.4	438	77.4		2 <sup>nd</sup> line therapy
	551	462	83.9	427	77.4	391	71.0	373	67.7		3 <sup>rd</sup> line therapy
Menting et al <sup>24</sup>	1	-	-	-	-	-	-	-	-	S****; C; O**	Biologic-naïve
	21	18	84.0	14	65.7	12	57.0	-	-		Biologic-experienced
Mercadal et al <sup>25</sup>	41	-	-	33	81.0	-	-	-	-	S****; C*; O**	
Mitratza et al <sup>26</sup>	25	21	82.6	-	-	12	47.8	-	-	S*****; C*; O**	Biologic-naïve
Pogácsás et al <sup>27</sup>	487	410	84.2	352	72.3	320	65.8			S****; C*; O**	

References	Patient populatio n	Drug survival rate								NOS score <sup>a</sup>	Note
		1 year		2 years		3 years		4 year			
		N	%	n	%	n	%	n	%		
Richter et al <sup>28</sup>	48	34	70.8	18	37.5	7	14.6	2	4.2	S****; C*; O**	
Ross et al <sup>29</sup>	25	23	93.2	23	93.2	-	-	-	-	S****; C**; O**	
Shalom et al <sup>30</sup>	224	171	76.2	149	66.7	139	61.9			S****; C**; O**	
Suarez-Perez et al <sup>45</sup>	44	-	-	-	-	37	84.0	-	-	S***; C*; O**	
Umezawa et al <sup>40</sup>	30	29	96.7	-	-	-	-	-	-	S****; C; O**	
Van den Reek et al <sup>31</sup>	66	56	85.0	-	-	-	-	-	-	S****; C*; O**	
Ventayol et al <sup>33</sup>	41	-	-	33	81.0	-	-	-	-	S****; C; O**	Biologic-naïve
Vilarrasa et al <sup>34</sup>	140	108	77.2	96	68.5	87	61.8	81	57.8	S****; C**; O**	
Warren et al <sup>35</sup>	450	401	89.0	369	82.0	338	75.0	-	-	S****; C*; O**	
Zweegers et al <sup>36</sup>	102	86	84.0	75	73.6	73	71.2	73	71.2	S****; C*; O**	

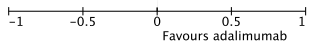
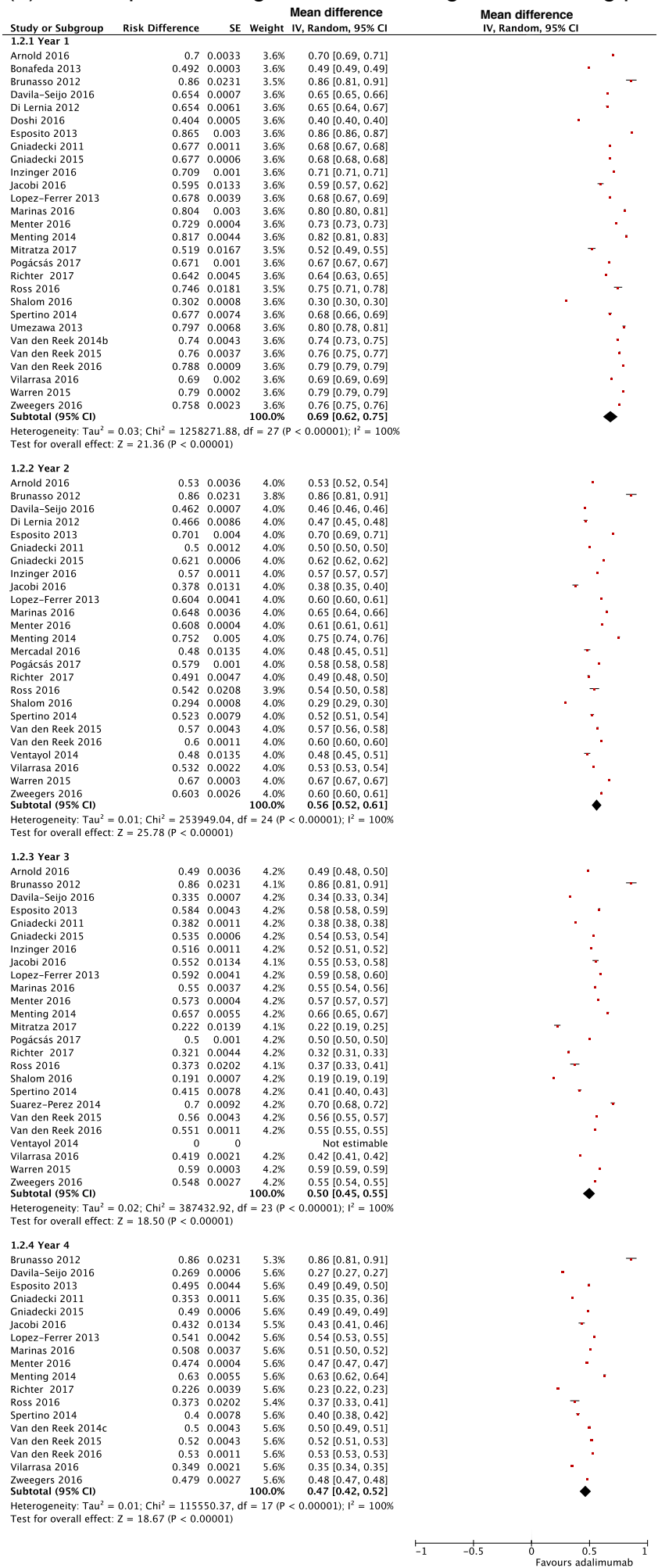
NOS Newcastle–Ottawa scale

<sup>a</sup> :Scale domains: S selection of study groups, C comparability, O outcome assessment

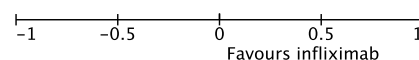
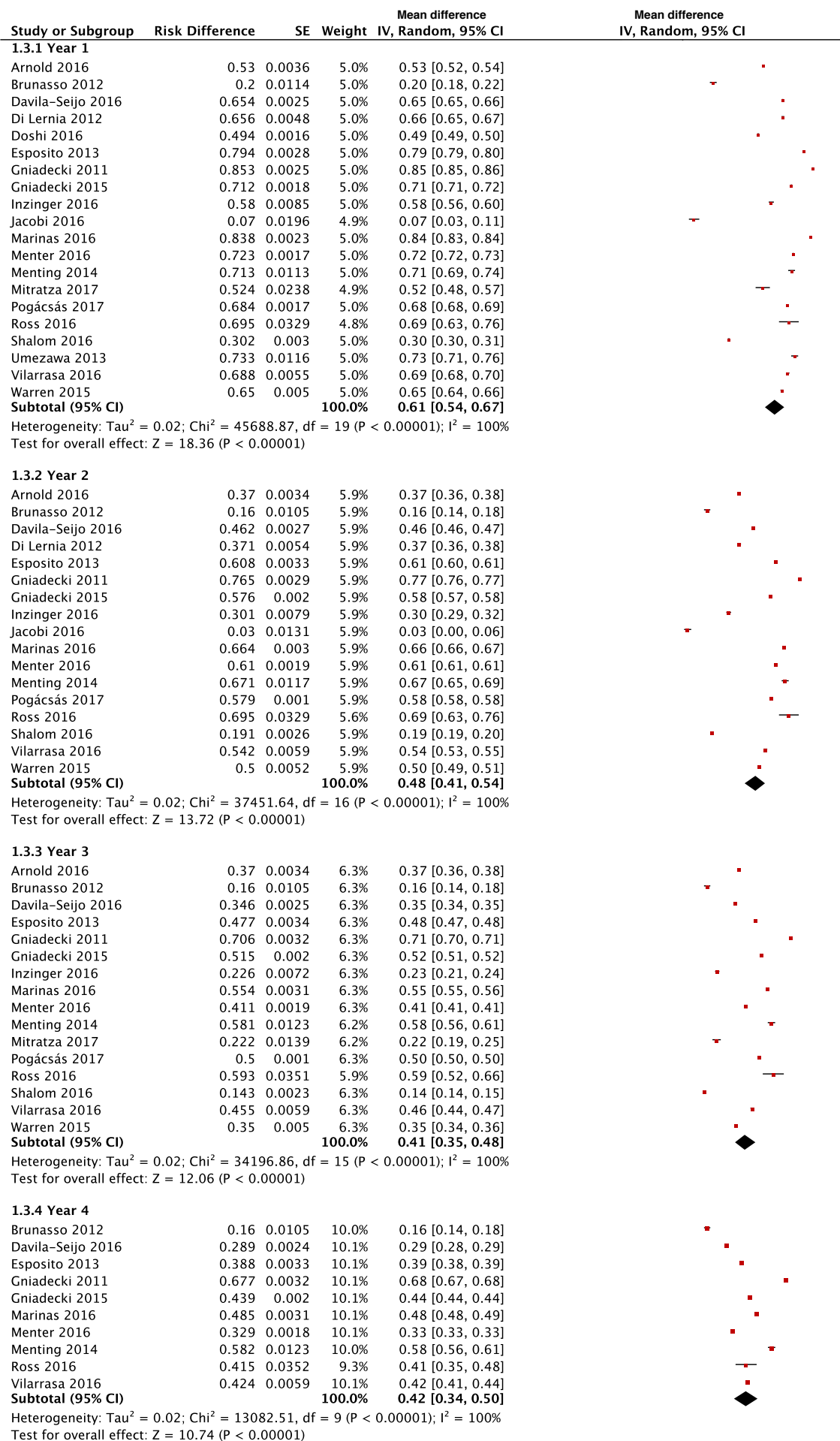
Supplemental Figure S1(a): Forest plots of drug survival of biologics for treating psoriasis in all subjects with etanercept.



# Supplementary Figure S1(b): Forest plots of drug survival of biologics for treating psoriasis in all subjects with adalimumab.

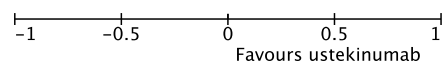
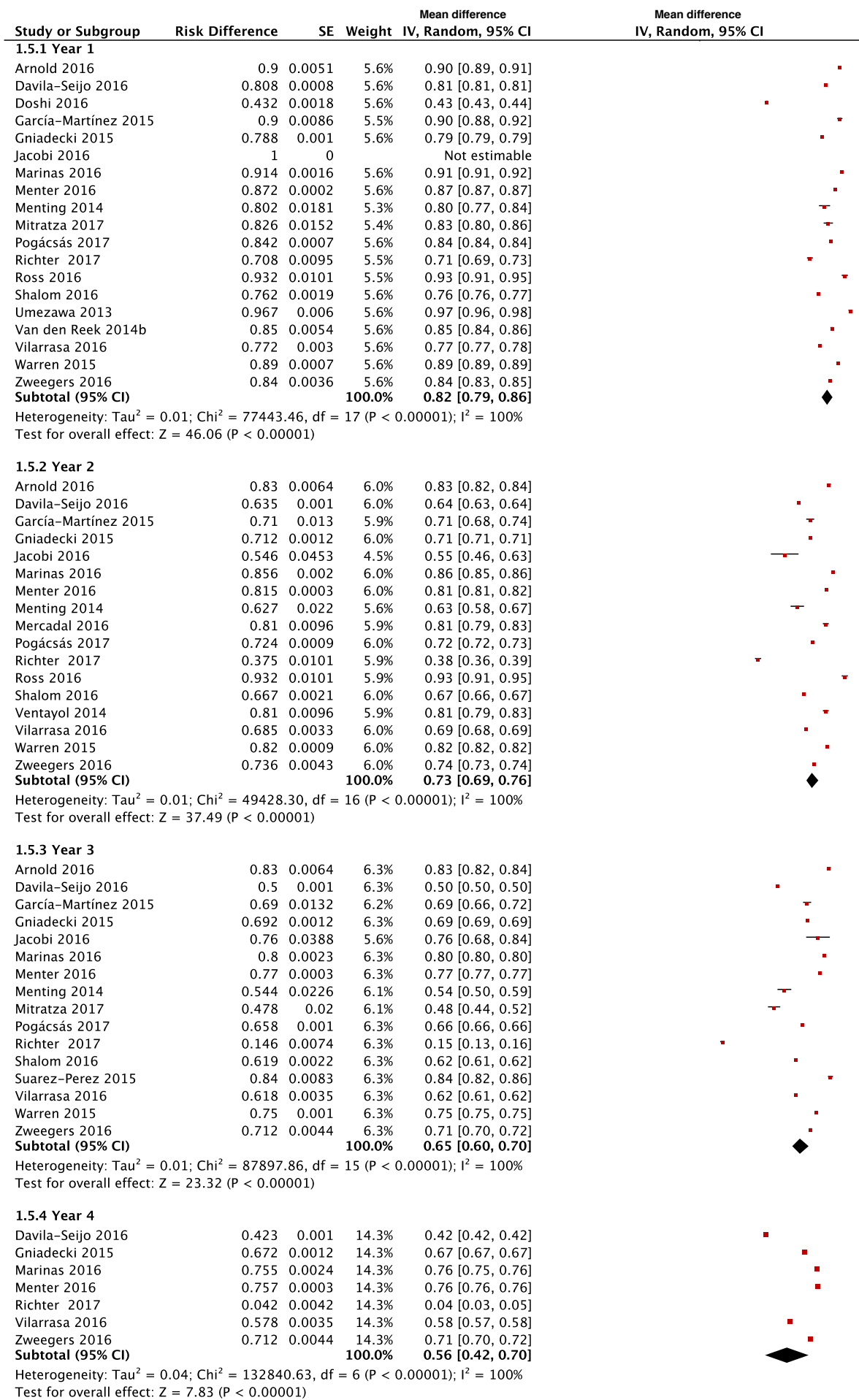


Supplementary Figure S1(c): Forest plots of drug survival of biologics for treating psoriasis in all subjects with infliximab.



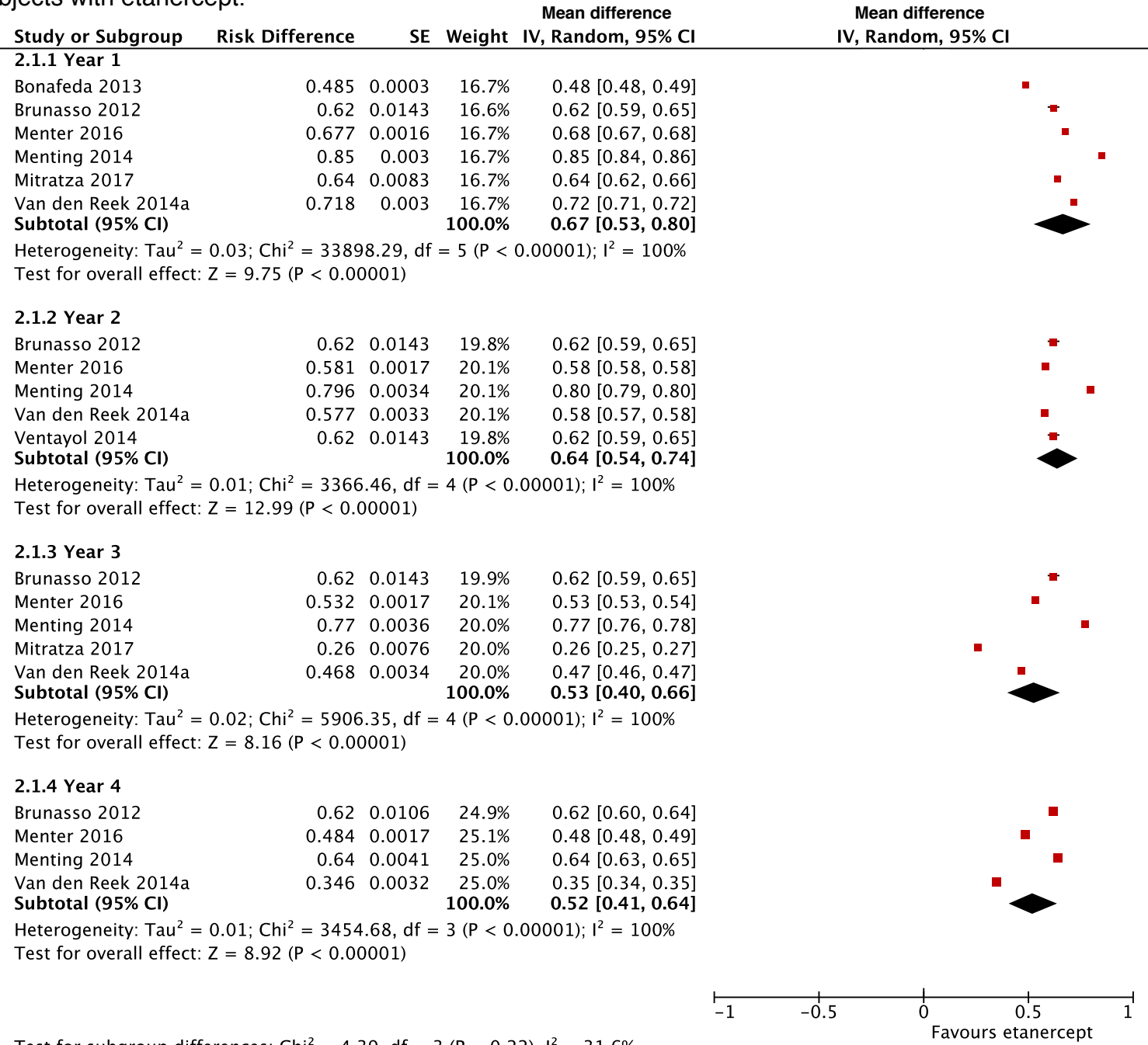
Test for subgroup differences: Chi<sup>2</sup> = 20.71, df = 3 (P = 0.0001), I<sup>2</sup> = 85.5%

Supplementary Figure S1(d): Forest plots of drug survival of biologics for treating psoriasis in all subjects with ustekinumab.



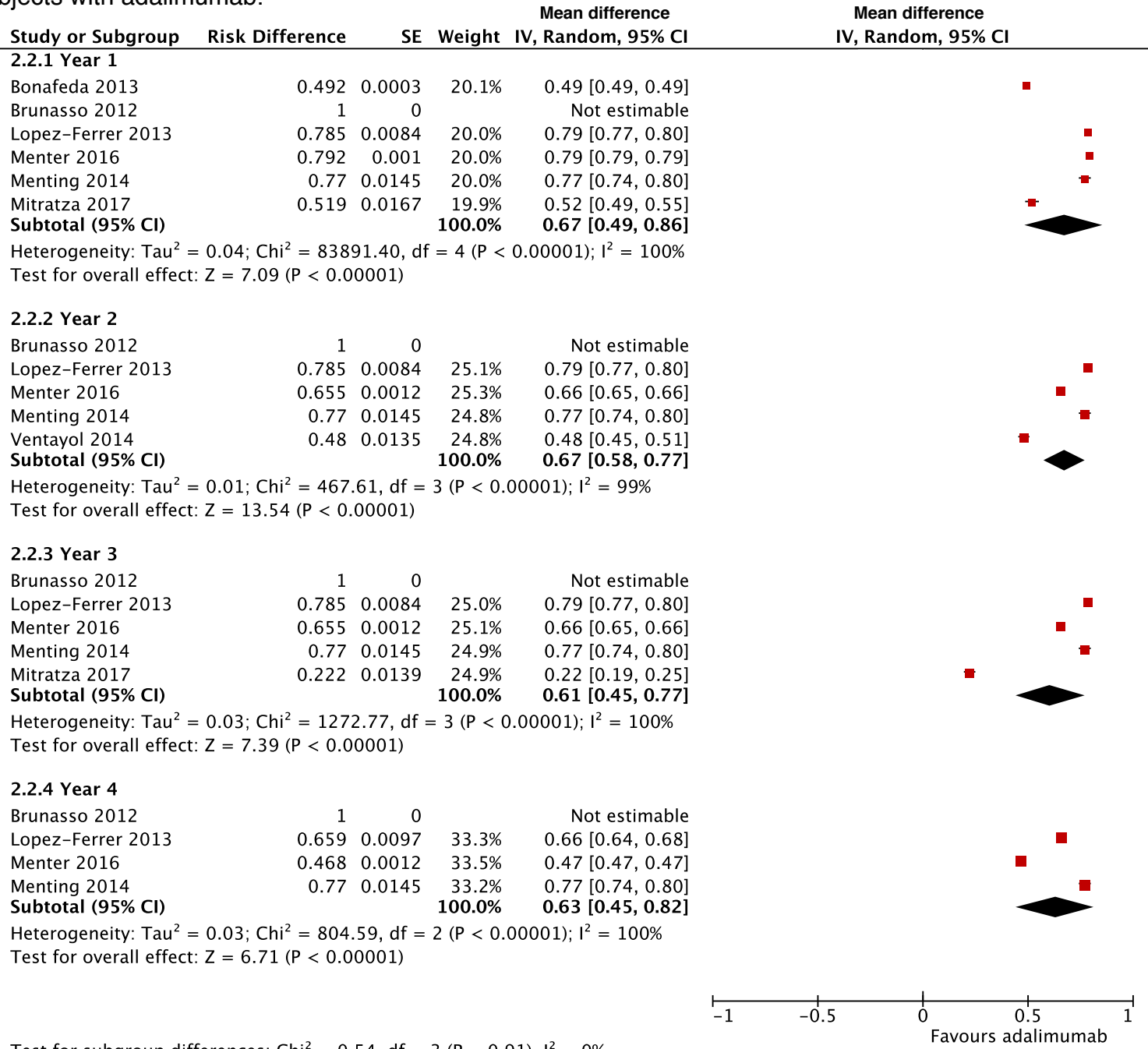
Test for subgroup differences: Chi<sup>2</sup> = 37.57, df = 3 (P < 0.00001), I<sup>2</sup> = 92.0%

Supplementary Figure S2(a): Forest plots of drug survival of biologics for treating psoriasis in biologic-naïve subjects with etanercept.

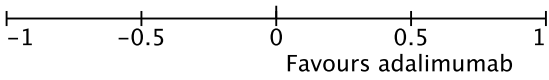


Test for subgroup differences: Chi<sup>2</sup> = 4.39, df = 3 (P = 0.22), I<sup>2</sup> = 31.6%

Supplementary Figure S2(b): Forest plots of drug survival of biologics for treating psoriasis in biologic-naïve subjects with adalimumab.

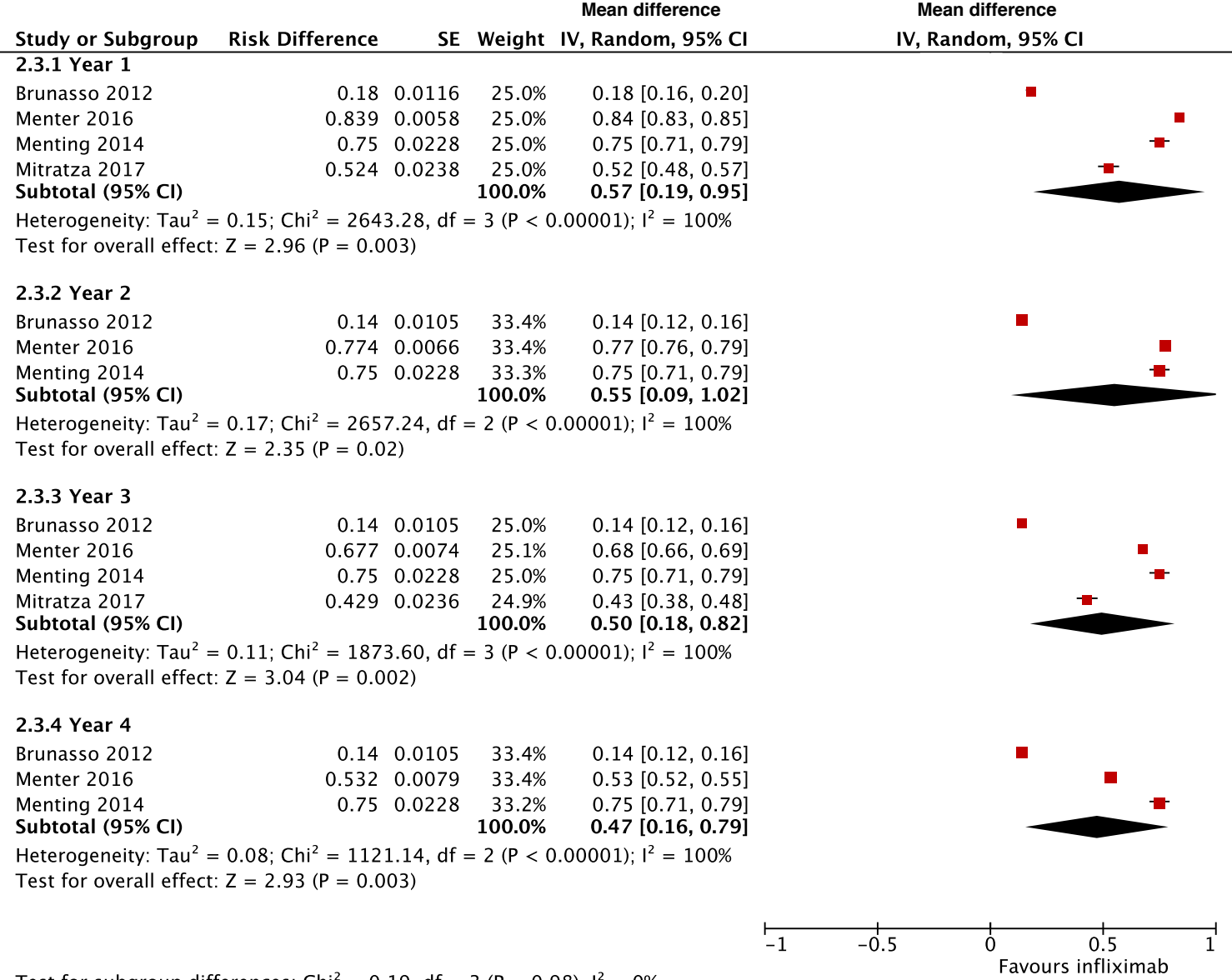


Test for subgroup differences: Chi<sup>2</sup> = 0.54, df = 3 (P = 0.91), I<sup>2</sup> = 0%

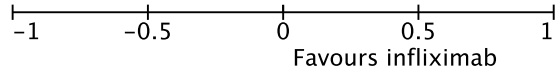




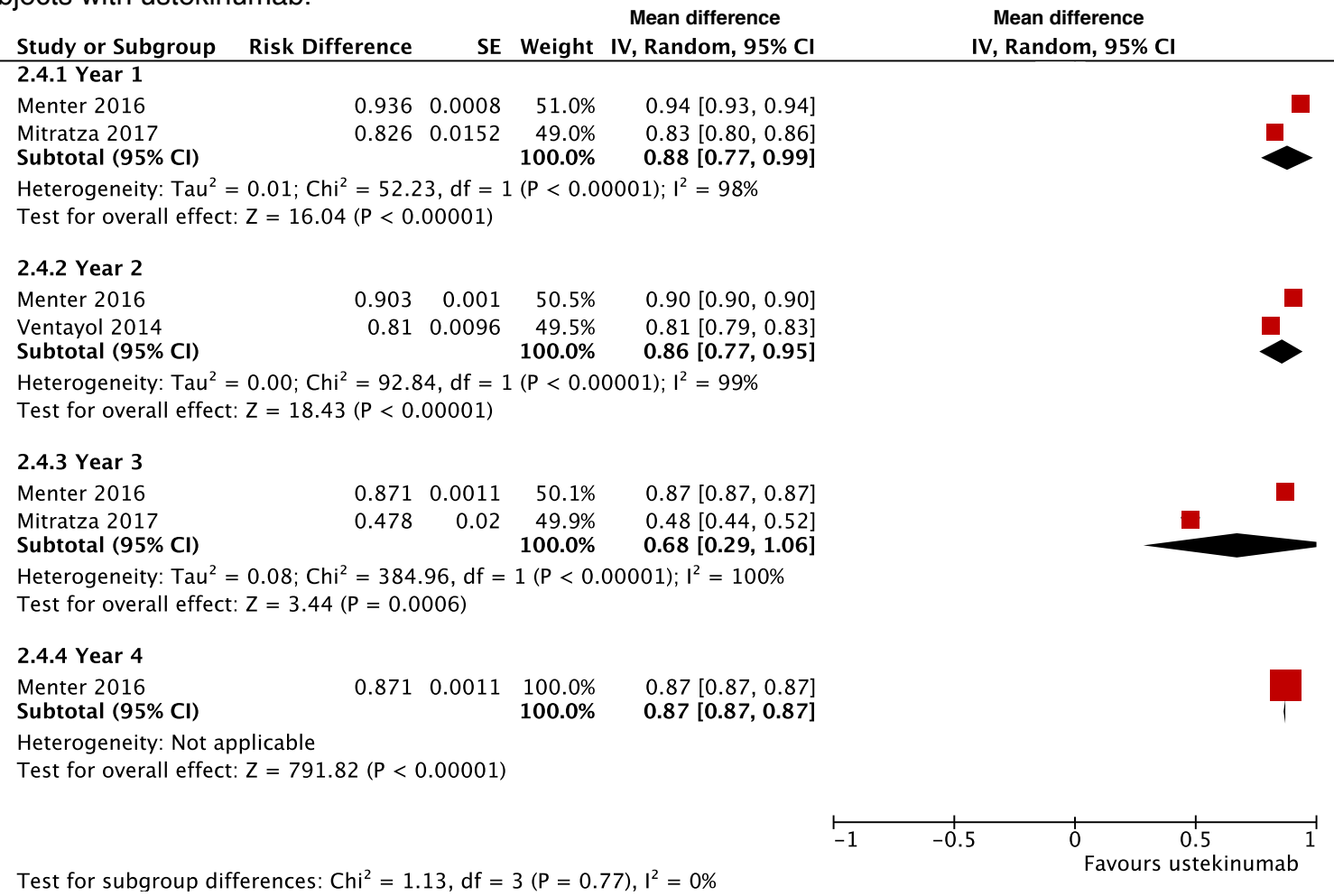
Supplementary Figure S2(c): Forest plots of drug survival of biologics for treating psoriasis in biologic-naïve subjects with infliximab.



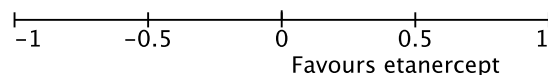
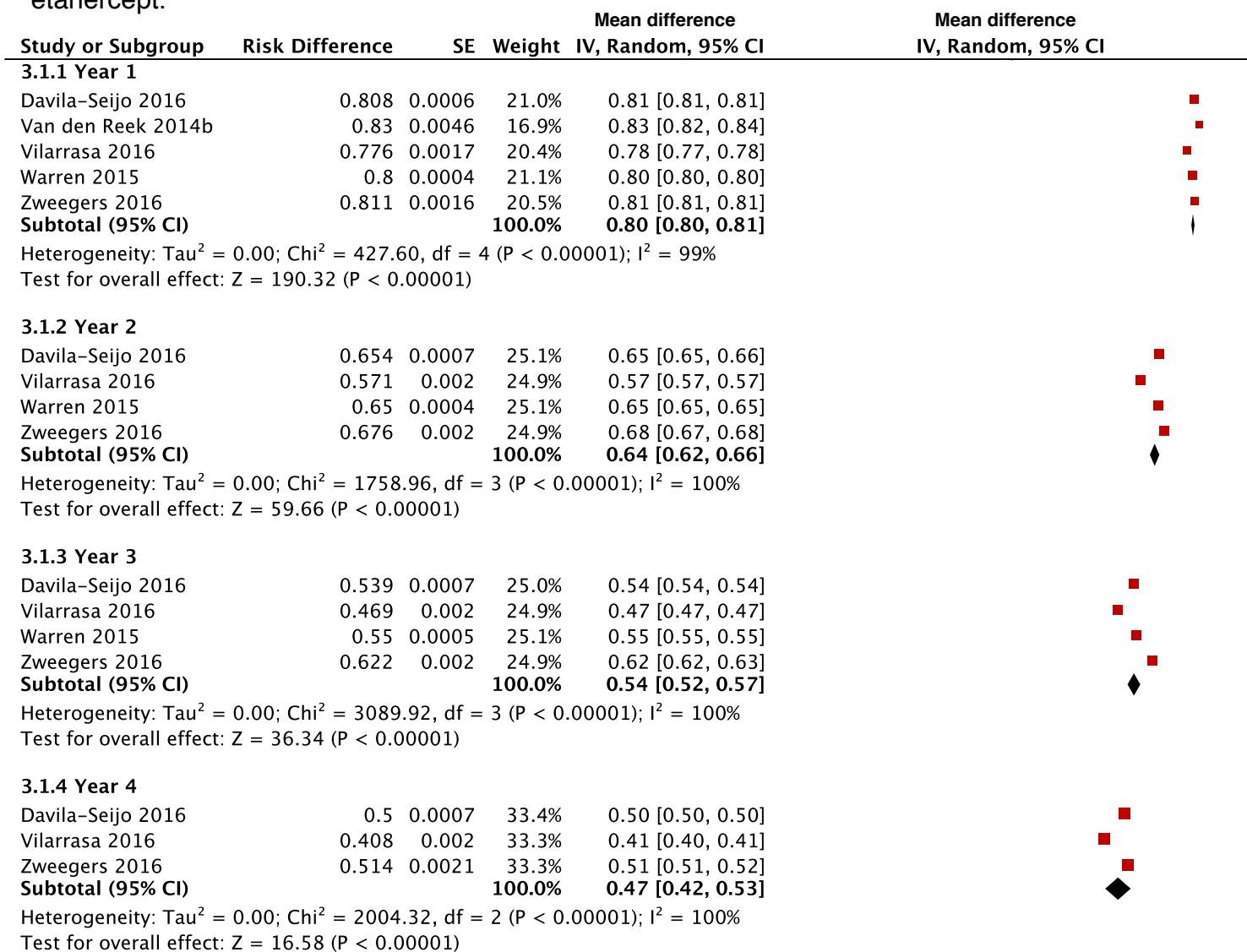
Test for subgroup differences: Chi<sup>2</sup> = 0.19, df = 3 (P = 0.98), I<sup>2</sup> = 0%



Supplemetnary Figure S2(d): Forest plots of drug survival of biologics for treating psoriasis in biologic-naïve subjects with ustekinumab.

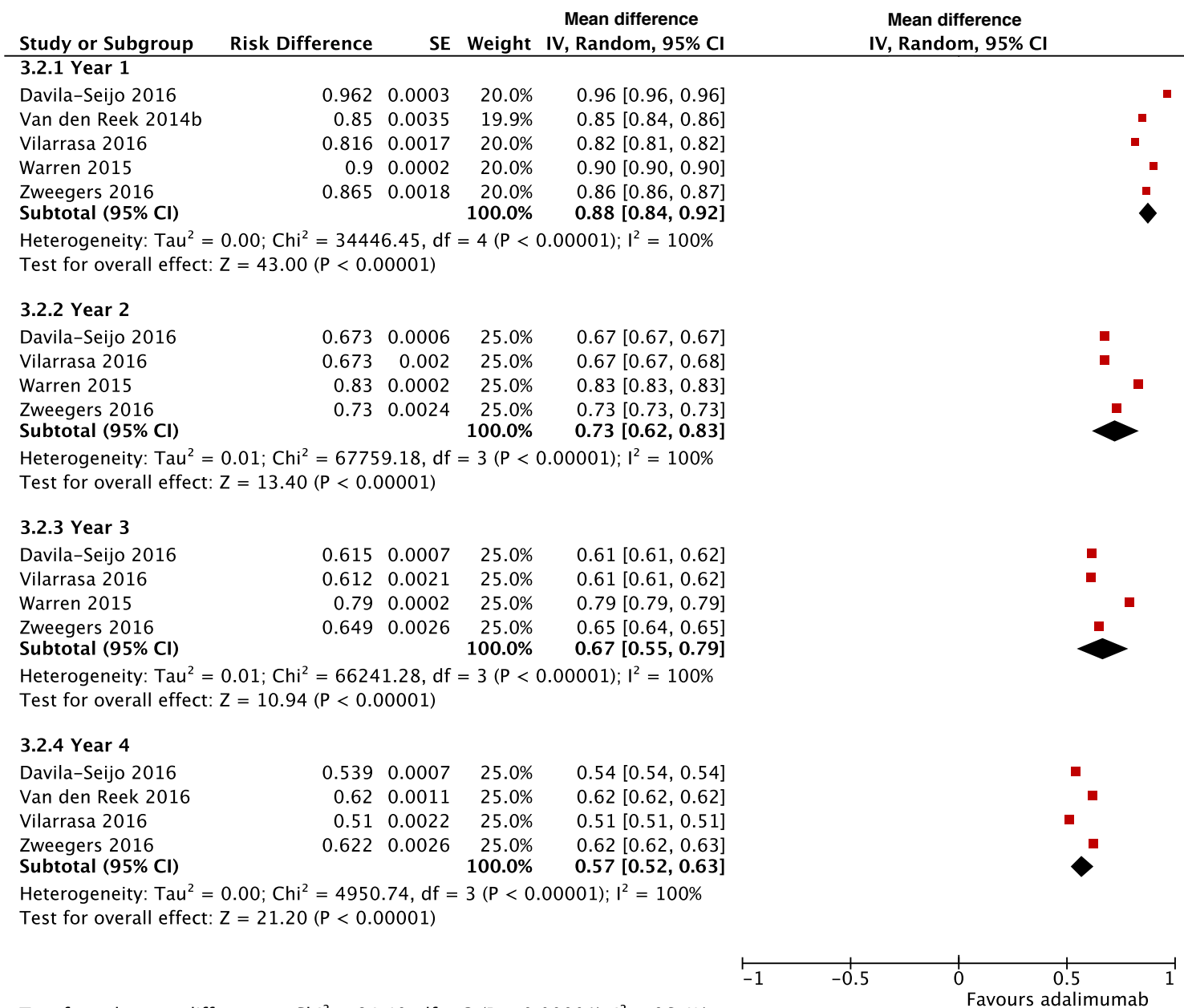


Supplementary Figure S3(a): Forest plots of drug survival for discontinue due to loss of efficacy with etanercept.

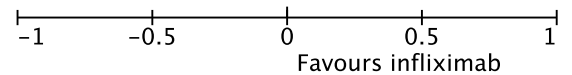
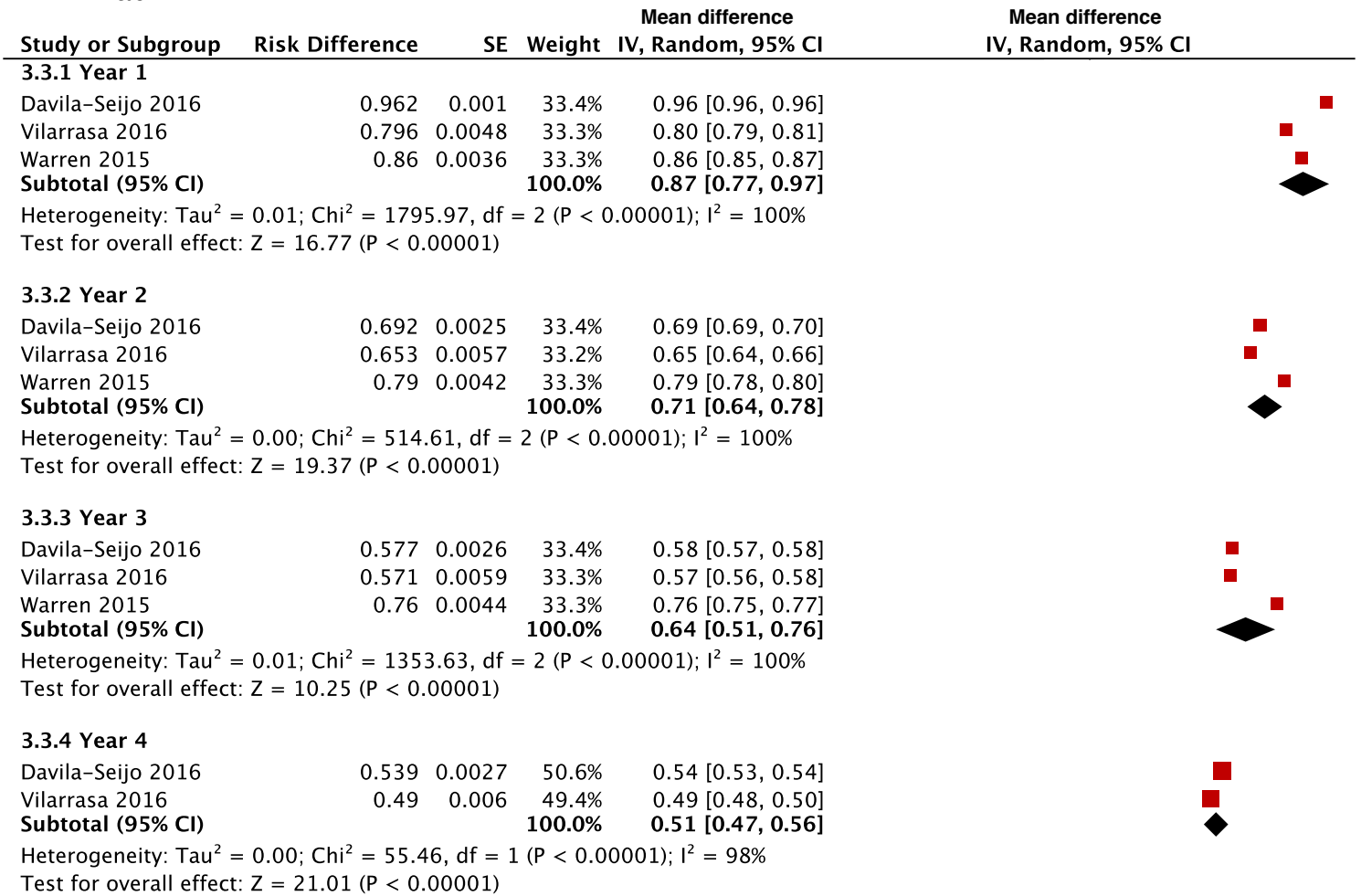


Test for subgroup differences: Chi<sup>2</sup> = 545.09, df = 3 (P < 0.00001), I<sup>2</sup> = 99.4%

Supplemetnary Figure S3(b): Forest plots of drug survival for discontinue due to loss of efficacy with adalimumab.

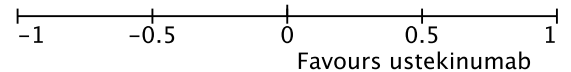
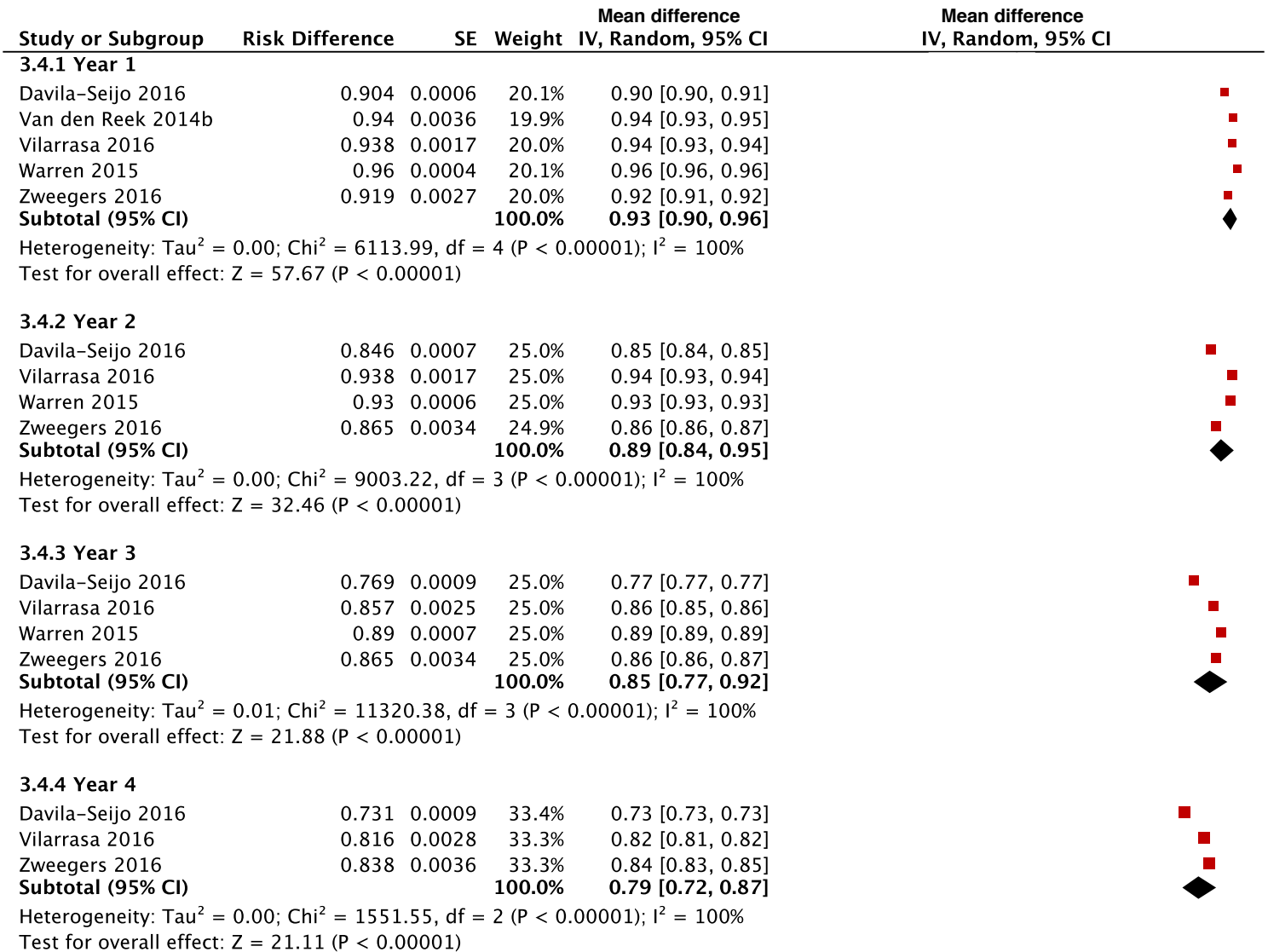


Supplemetnary Figure S3(c): Forest plots of drug survival for discontinue due to loss of efficacy with infliximab.



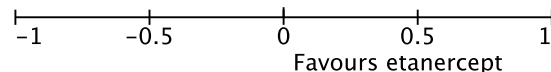
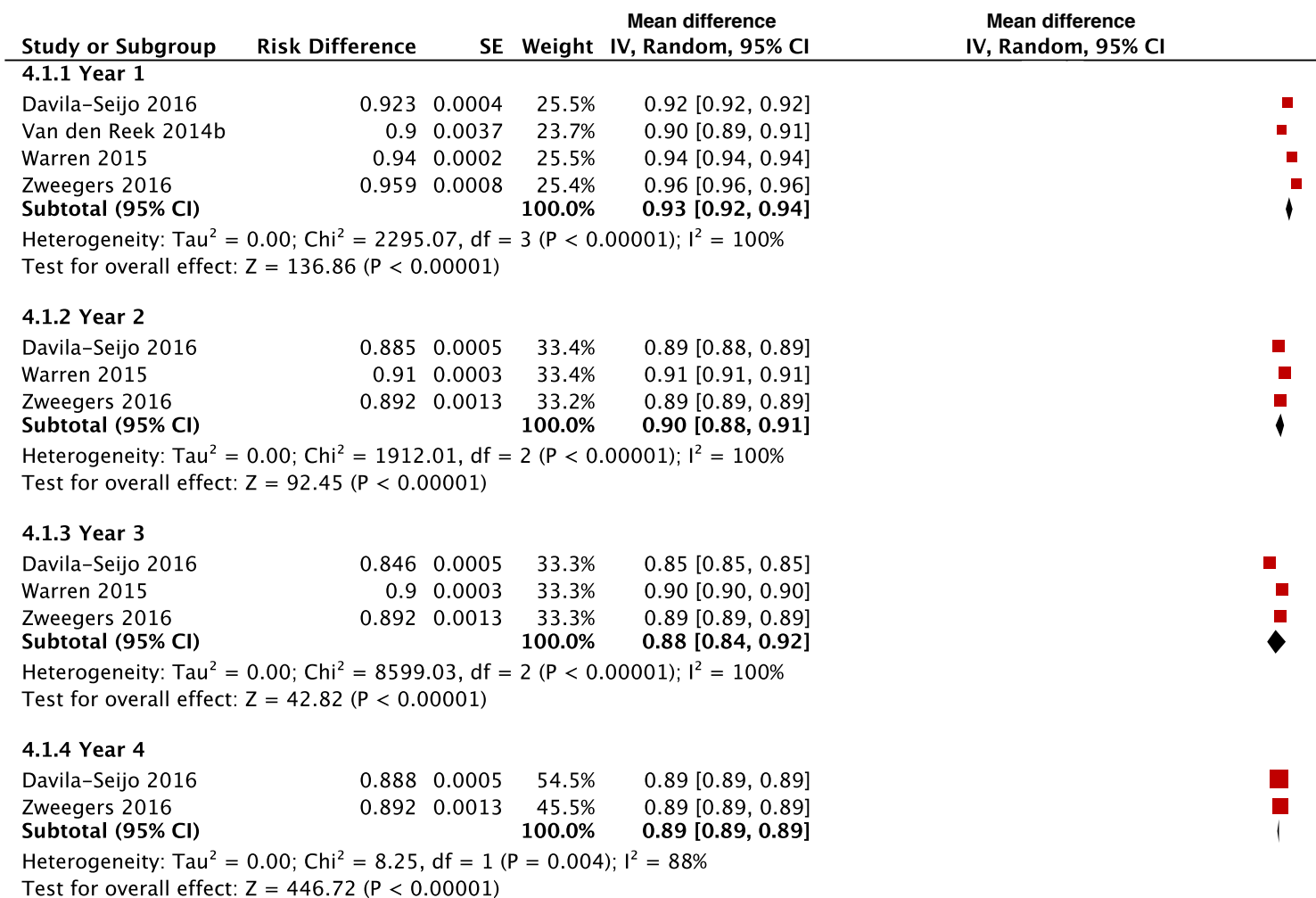
Test for subgroup differences: Chi<sup>2</sup> = 48.30, df = 3 (P < 0.00001), I<sup>2</sup> = 93.8%

Supplementry Figure S3(d): Forest plots of drug survival for discontinue due to loss of efficacy with ustekinumab.



Test for subgroup differences: Chi<sup>2</sup> = 13.79, df = 3 (P = 0.003), I<sup>2</sup> = 78.2%

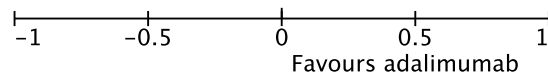
Supplementary Figure S4(a): Forest plots of drug survival for discontinue due to adverse effects with etanercept.



Test for subgroup differences: Chi<sup>2</sup> = 34.30, df = 3 (P < 0.00001), I<sup>2</sup> = 91.3%

Supplementary Figure S4(b): Forest plots of drug survival for discontinue due to adverse effects with adalimumab.

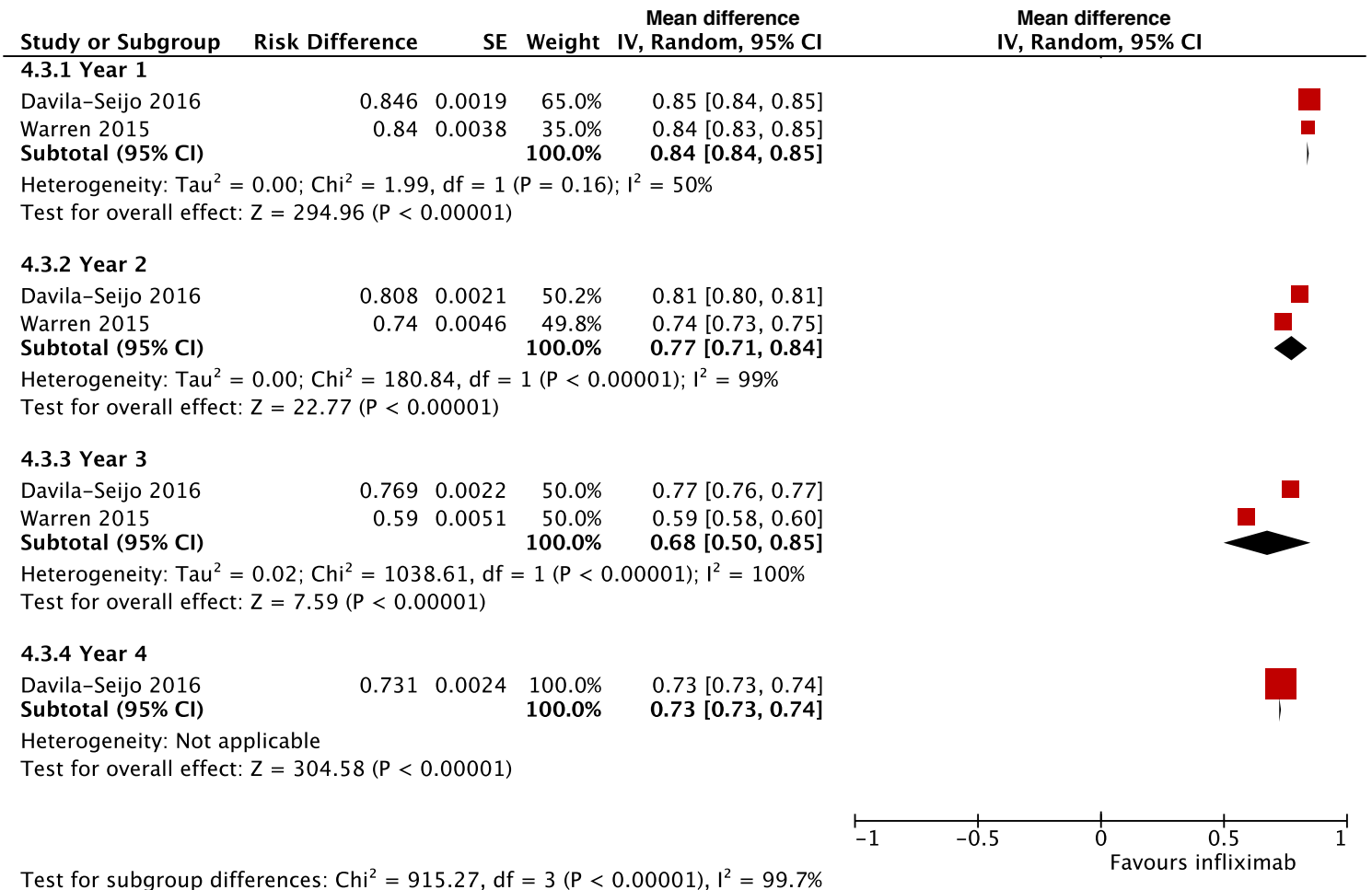
Study or Subgroup	Risk Difference	SE	Weight	Mean difference IV, Random, 95% CI	Mean difference IV, Random, 95% CI
<b>4.2.1 Year 1</b>					
Davila-Seijo 2016	0.923	0.0004	25.7%	0.92 [0.92, 0.92]	■
Van den Reek 2014b	0.95	0.0022	24.0%	0.95 [0.95, 0.95]	■
Warren 2015	0.93	0.0001	25.7%	0.93 [0.93, 0.93]	■
Zweegers 2016	0.892	0.0017	24.7%	0.89 [0.89, 0.90]	■
<b>Subtotal (95% CI)</b>			<b>100.0%</b>	<b>0.92 [0.92, 0.93]</b>	◆
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 862.48, df = 3 (P < 0.00001); I <sup>2</sup> = 100%					
Test for overall effect: Z = 222.32 (P < 0.00001)					
<b>4.2.2 Year 2</b>					
Davila-Seijo 2016	0.885	0.0004	33.5%	0.89 [0.88, 0.89]	■
Warren 2015	0.9	0.0002	33.6%	0.90 [0.90, 0.90]	■
Zweegers 2016	0.838	0.002	32.9%	0.84 [0.83, 0.84]	■
<b>Subtotal (95% CI)</b>			<b>100.0%</b>	<b>0.87 [0.86, 0.89]</b>	◆
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1988.34, df = 2 (P < 0.00001); I <sup>2</sup> = 100%					
Test for overall effect: Z = 109.30 (P < 0.00001)					
<b>4.2.3 Year 3</b>					
Davila-Seijo 2016	0.885	0.0004	33.6%	0.89 [0.88, 0.89]	■
Warren 2015	0.87	0.0002	33.6%	0.87 [0.87, 0.87]	■
Zweegers 2016	0.824	0.002	32.8%	0.82 [0.82, 0.83]	■
<b>Subtotal (95% CI)</b>			<b>100.0%</b>	<b>0.86 [0.85, 0.87]</b>	◆
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1720.49, df = 2 (P < 0.00001); I <sup>2</sup> = 100%					
Test for overall effect: Z = 115.48 (P < 0.00001)					
<b>4.2.4 Year 4</b>					
Davila-Seijo 2016	0.846	0.0005	33.8%	0.85 [0.85, 0.85]	■
Van den Reek 2016	0.84	0.0008	33.7%	0.84 [0.84, 0.84]	■
Zweegers 2016	0.811	0.0021	32.5%	0.81 [0.81, 0.82]	■
<b>Subtotal (95% CI)</b>			<b>100.0%</b>	<b>0.83 [0.82, 0.84]</b>	◆
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 282.26, df = 2 (P < 0.00001); I <sup>2</sup> = 99%					
Test for overall effect: Z = 137.66 (P < 0.00001)					



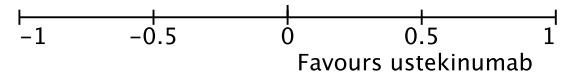
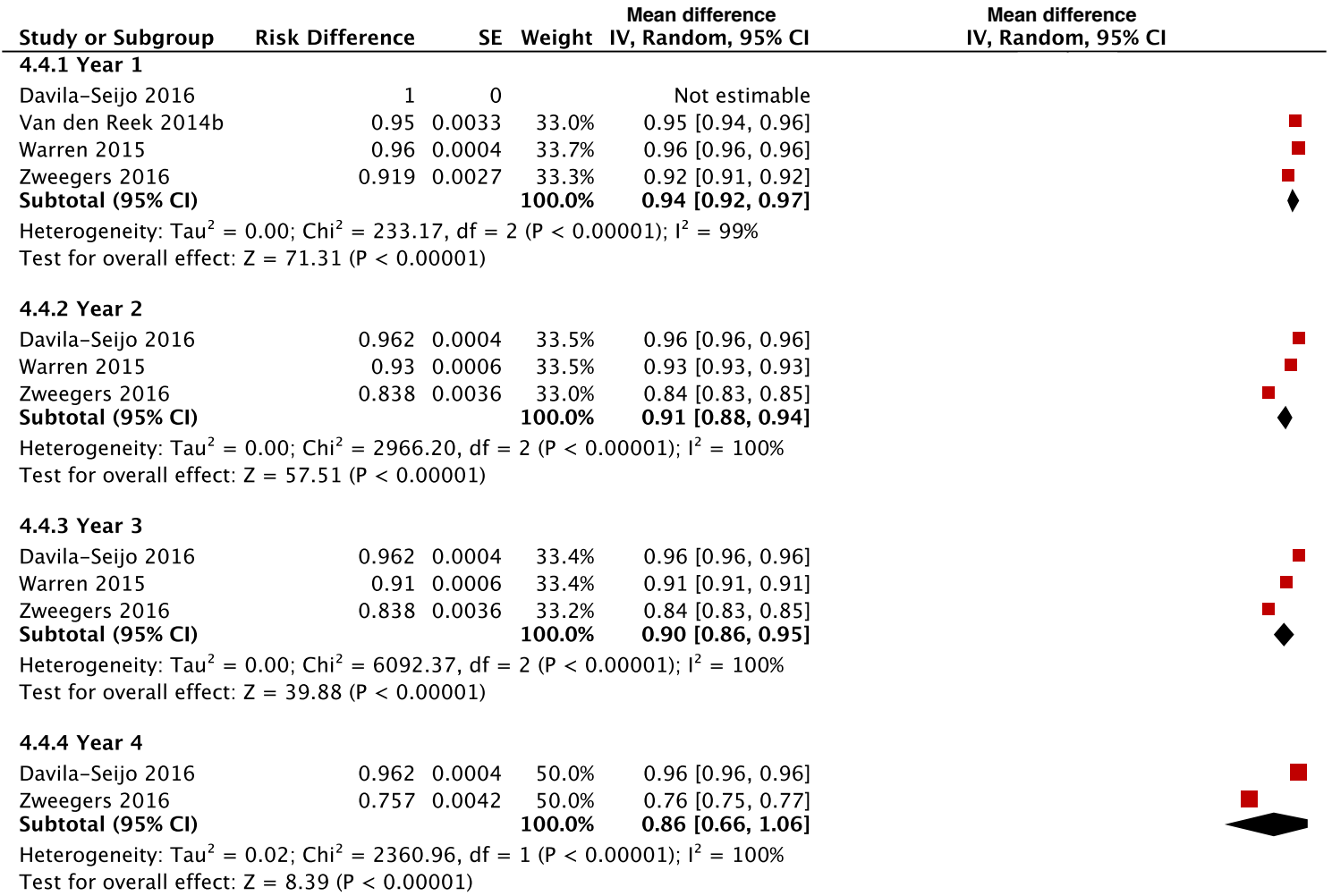
Test for subgroup differences: Chi<sup>2</sup> = 174.28, df = 3 (P < 0.00001), I<sup>2</sup> = 98.3%



Supplementary Figure S4(c): Forest plots of drug survival for discontinue due to adverse effects with infliximab.



Supplementry Figure S4(d): Forest plots of drug survival for discontinue due to adverse effects with ustekinumab.



Test for subgroup differences: Chi<sup>2</sup> = 4.02, df = 3 (P = 0.26), I<sup>2</sup> = 25.4%