

Supplemental Online Content

Egunsola O, Clement F, Taplin J, et al. Immunogenicity and safety of reduced-dose intradermal vs intramuscular influenza vaccines: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4(2):e2035693. doi:10.1001/jamanetworkopen.2020.35693

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. Search Strategy

MEDLINE

1. Influenza, Human/
2. exp influenzavirus a/ or exp influenzavirus b/ or influenzavirus c/
3. Influenza Vaccines/
4. (influenza* or flu).tw,kf.
5. 1 or 2 or 3 or 4
6. Injections, Intradermal/
7. (intradermal or intra-dermal).tw,kf.
8. ID injection*.tw,kf.
9. IDflu.tw,kf.
10. (inject* adj5 (dermal or dermis)).tw,kf.
11. mantoux.tw,kf.
12. dose sparing.tw,kf.
13. 6 or 7 or 8 or 9 or 10 or 11 or 12
14. 5 and 13
15. animals/ not humans/
16. 14 not 15
17. limit 16 to (case reports or editorial or letter)
18. 16 not 17
19. limit 18 to yr="2010 -Current"

EMBASE

1. influenza/ or exp influenza a/ or influenza b/ or influenza c/ or seasonal influenza/
2. influenza virus/ or exp influenzavirus a/ or exp influenzavirus b/ or exp influenzavirus c/

3. influenza vaccine/
4. (influenza* or flu).tw,kw.
5. 1 or 2 or 3 or 4
6. intradermal drug administration/
7. (intradermal or intra-dermal).tw,kw.
8. ID injection*.tw,kw.
9. IDflu.tw,kw.
10. (inject* adj5 (dermal or dermis)).tw,kw.
11. mantoux.tw,kw.
12. dose sparing.tw,kw.
13. 6 or 7 or 8 or 9 or 10 or 11 or 12
14. 5 and 13
15. exp influenza vaccine/dl [Intradermal Drug Administration]
16. 14 or 15
17. animals/ not human/
18. 16 not 17
19. limit 18 to (conference abstract or editorial or letter)
20. 18 not 19
21. limit 20 to yr="2010 -Current"

Cochrane Central Register of Controlled Trials

1. Influenza, Human/
2. exp influenzavirus a/ or exp influenzavirus b/ or influenzavirus c/
3. Influenza Vaccines/
4. (influenza* or flu).tw.

5. 1 or 2 or 3 or 4
6. Injections, Intradermal/
7. (intradermal or intra-dermal).tw.
8. ID injection*.tw.
9. IDflu.tw.
10. (inject* adj5 (dermal or dermis)).tw.
11. mantoux.tw.
12. dose sparing.tw.
13. 6 or 7 or 8 or 9 or 10 or 11 or 12
14. 5 and 13
15. animals/ not humans/
16. 14 not 15

eFigure 1. Quality Assessment of Randomized Clinical Trials

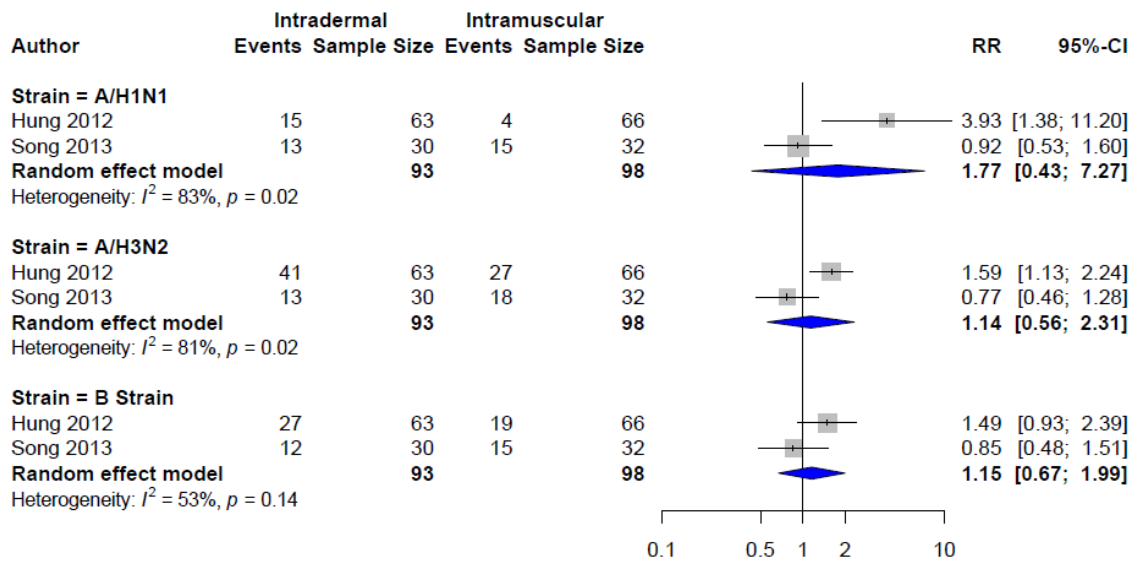
Author (Year)	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall Bias
Ansaldi et al. (2013) ¹⁸	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Ansaldi et al. (2012) ¹⁷	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Arnou et al. (2010) ¹⁹	Low Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Boonak et al. (2017) ²⁰	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Camiloni et al. (2014) ²¹	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Carter et al. (2019) ²²	Low Concern	Low Concern	Low Concern	Low Concern	Some Concern	Some Concern
Chan et al. (2014) ²³	Low Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Chi et al. (2010) ²⁴	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Chuaychoo et al.	Some Concern	Some Concern	Low	Low	Some Concern	Some Concern

Author (Year)	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall Bias
(2019) ²⁵			Concern	Concern		
Chuaychoo et al. (2016) ²⁶	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Chuaychoo et al. (2010) ²⁷	High Concern	Some Concern	Low Concern	Low Concern	Some Concern	High Concern
Della Cioppa et al. (2014) ²⁸	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Esposito et al. (2011) ²⁹	Low Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Frenck et al. (2011) ³⁰	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Garg et al. (2016) ³¹	Low Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Gorse et al. (2013) ³²	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Han et al. (2013) ³³	High Concern	Some Concern	Low Concern	High Concern	Some Concern	High Concern
Hung et al. (2016) ³⁴	Low Concern	Low Concern	Low Concern	Low Concern	Some Concern	Some Concern

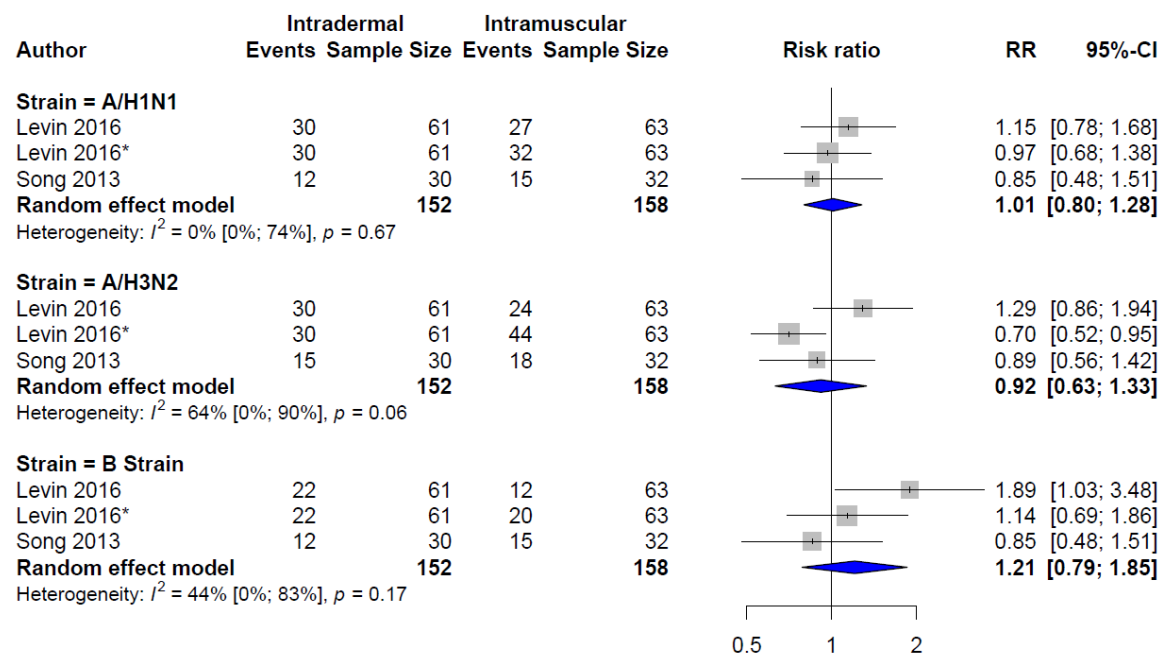
Author (Year)	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall Bias
Hung et al. (2014) ³⁶	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Hung et al. (2012) ³⁵	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Leung et al. (2017) ³⁷	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Levin et al. (2016) ⁴⁵	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Levin et al. (2014) ⁴⁴	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Nougaredet al. (2014) ³⁸	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Patel et al. (2010) ³⁹	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Seo et al. (2014) ⁴⁰	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Song et al. (2013) ⁴¹	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern
Tsang et al.	Some Concern	Some Concern	Low	Low	Some Concern	Some Concern

Author (Year)	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall Bias
(2014) ⁴²			Concern	Concern		
Van Damme et al. (2010) ⁴³	Some Concern	Some Concern	Low Concern	Low Concern	Some Concern	Some Concern

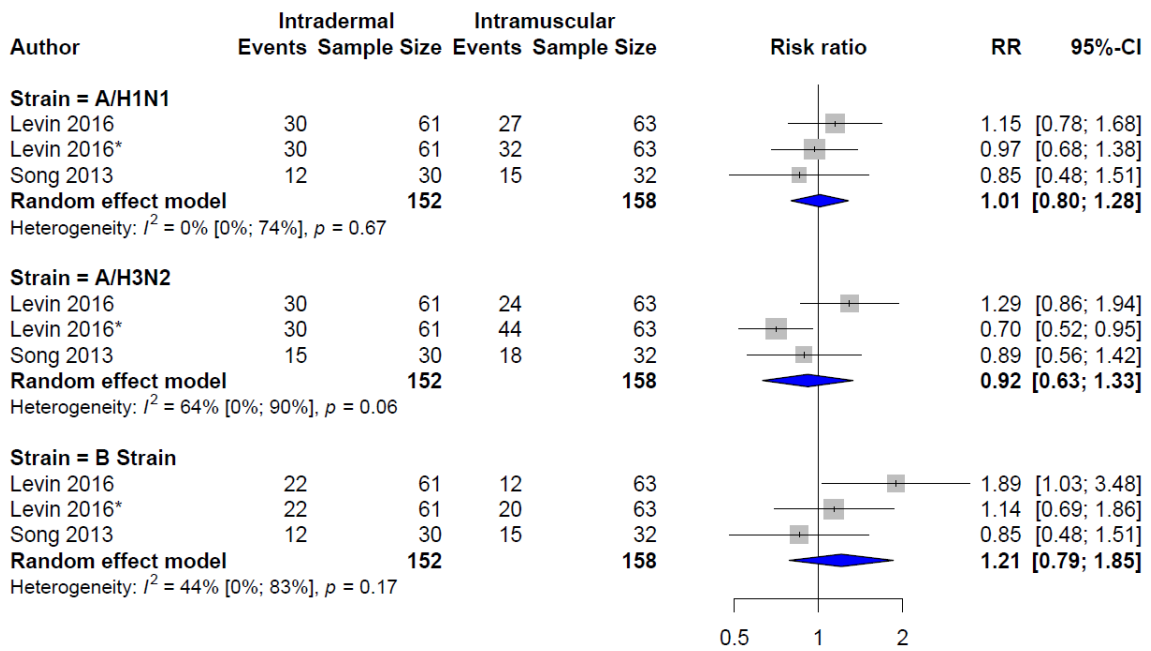
eFigure 2. Seroconversion: 3 µg ID vs 15 µg IM



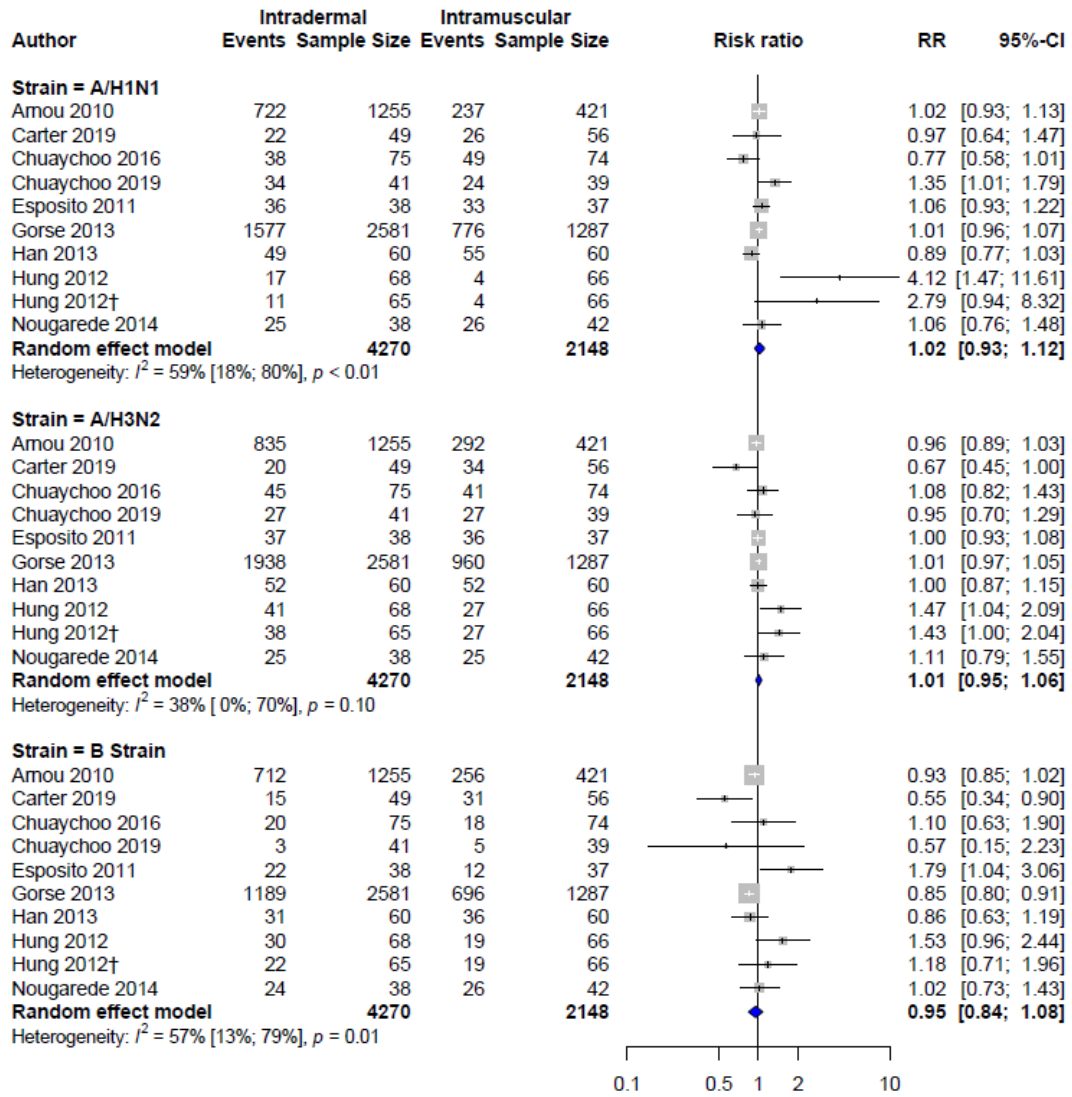
eFigure 3. Seroconversion: 6 µg ID vs 15 µg IM



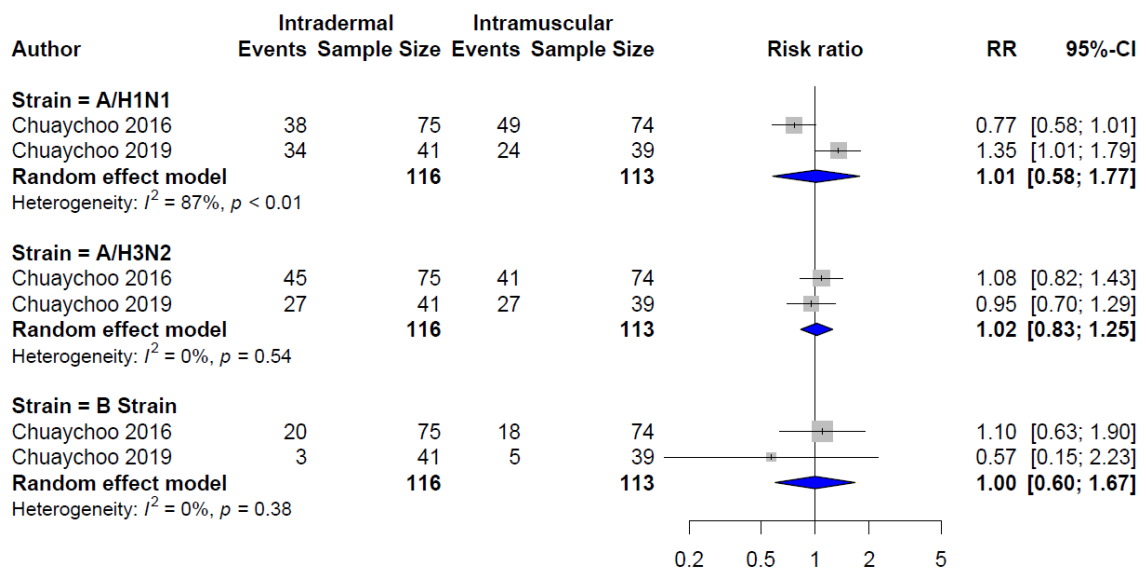
eFigure 4. Seroconversion: 7.5 µg ID vs 15 µg IM



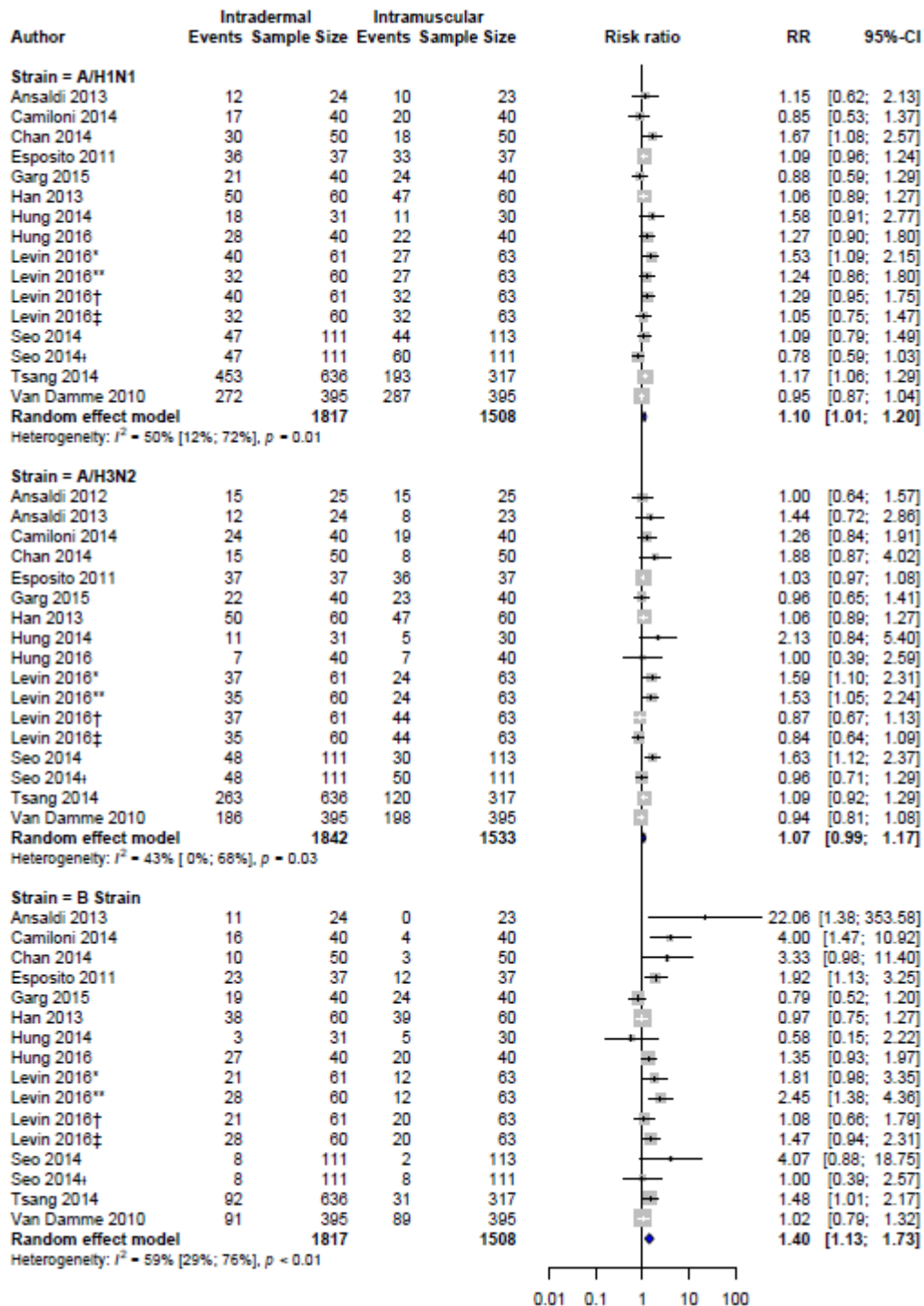
eFigure 5. Seroconversion: 9 µg ID vs 15 µg IM in All Population
 † Soluvia Microneedle



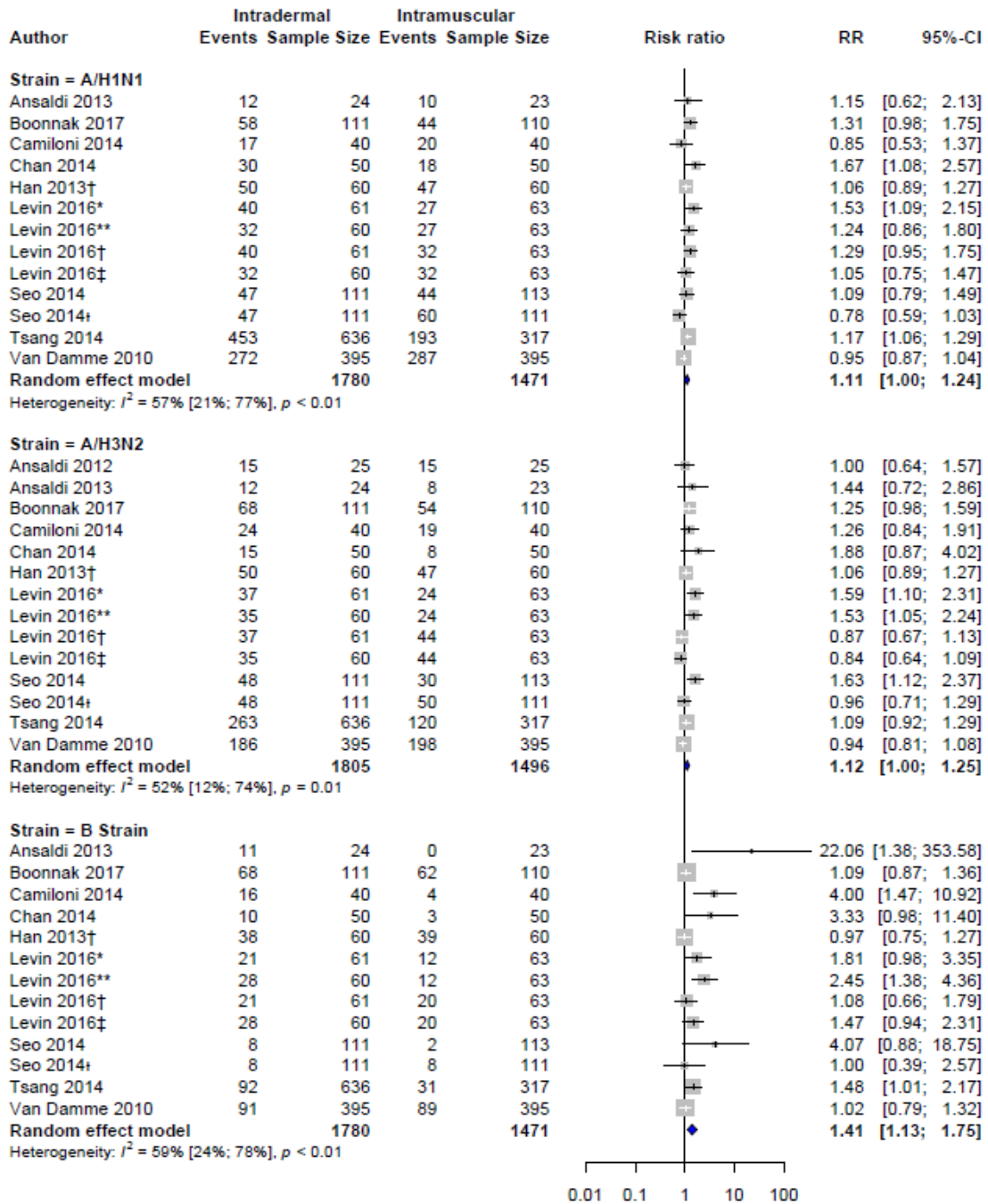
eFigure 6. Seroconversion: in Older Adults 9 µg ID vs 15 µg IM



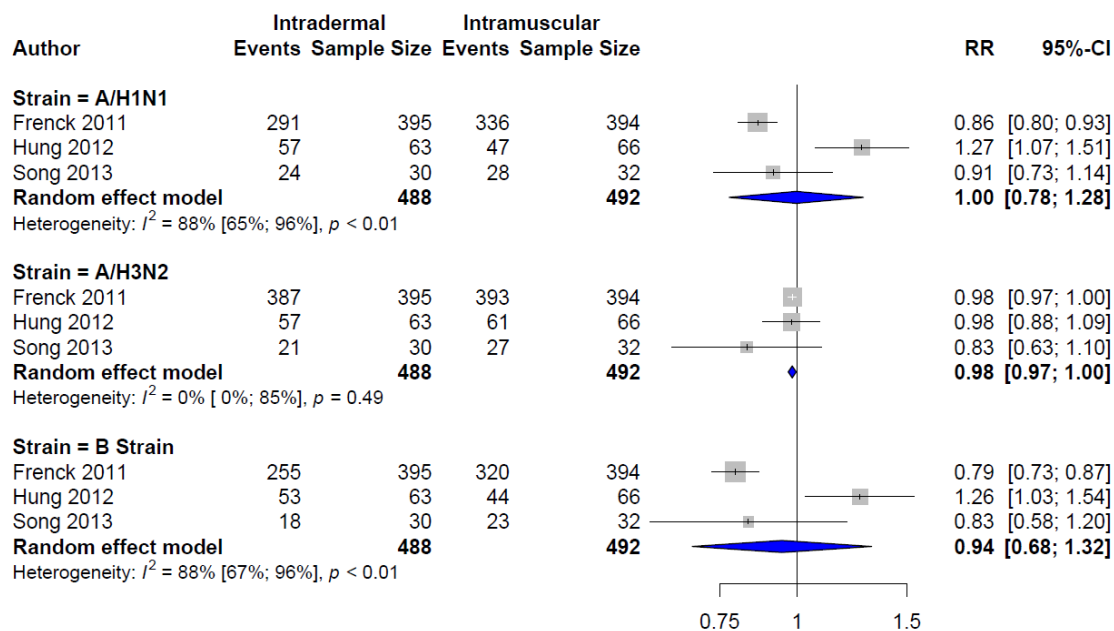
eFigure 7. Seroconversion: 15 µg ID vs 15 µg IM
 (*Inflexa vs Inflexa, ** Intanza vs Inflexa, †Inflexa vs Fluad, ‡Intanza vs Fluad, † Adjuvanted)



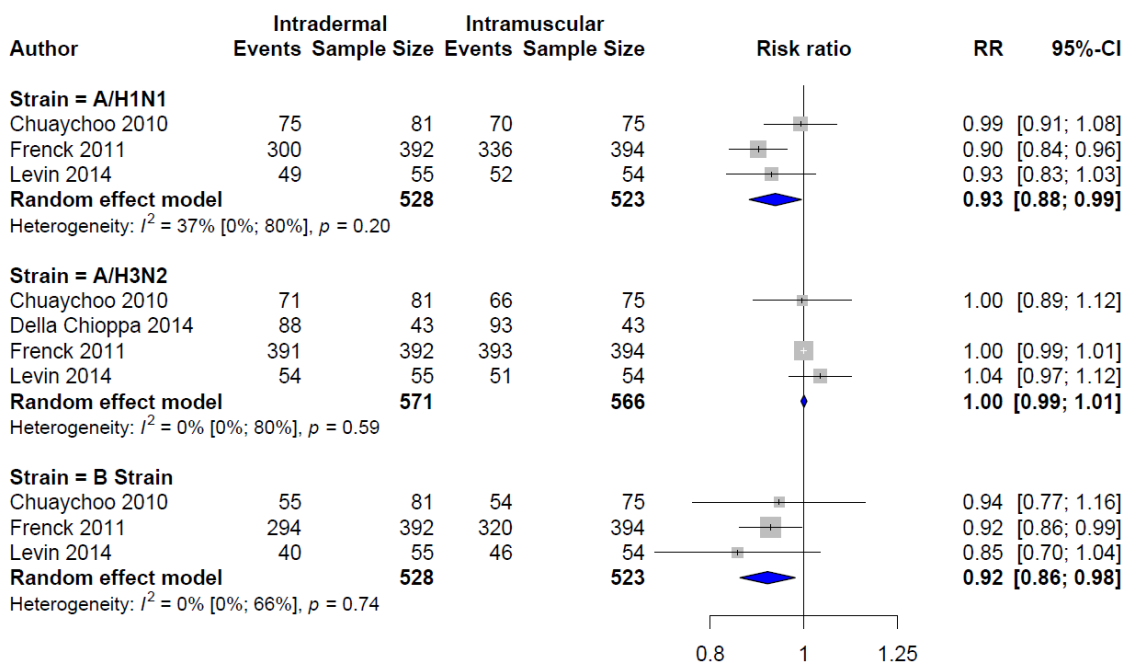
eFigure 8. Seroconversion: in Older Adults 15 µg ID vs 15 µg IM
 (*Inflexa vs Inflexa, ** Intanza vs Inflexa, †Inflexa vs Fluad, ‡Intanza vs Fluad, † Adjuvanted)



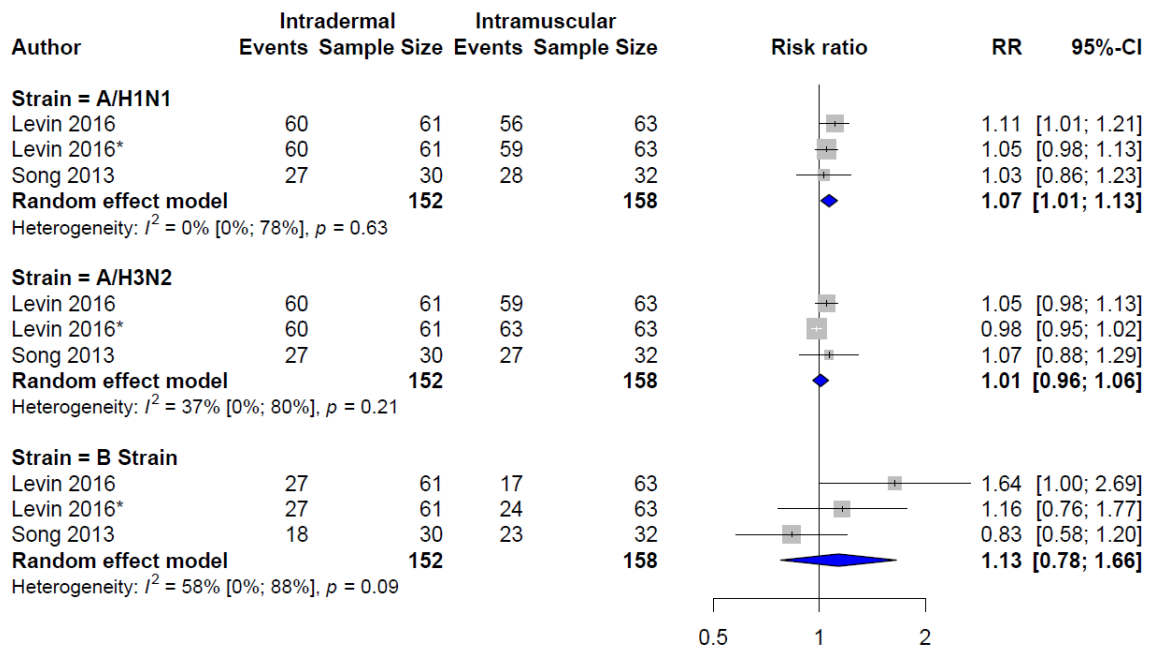
eFigure 9. Seroprotection: 3 µg ID vs 15 µg IM



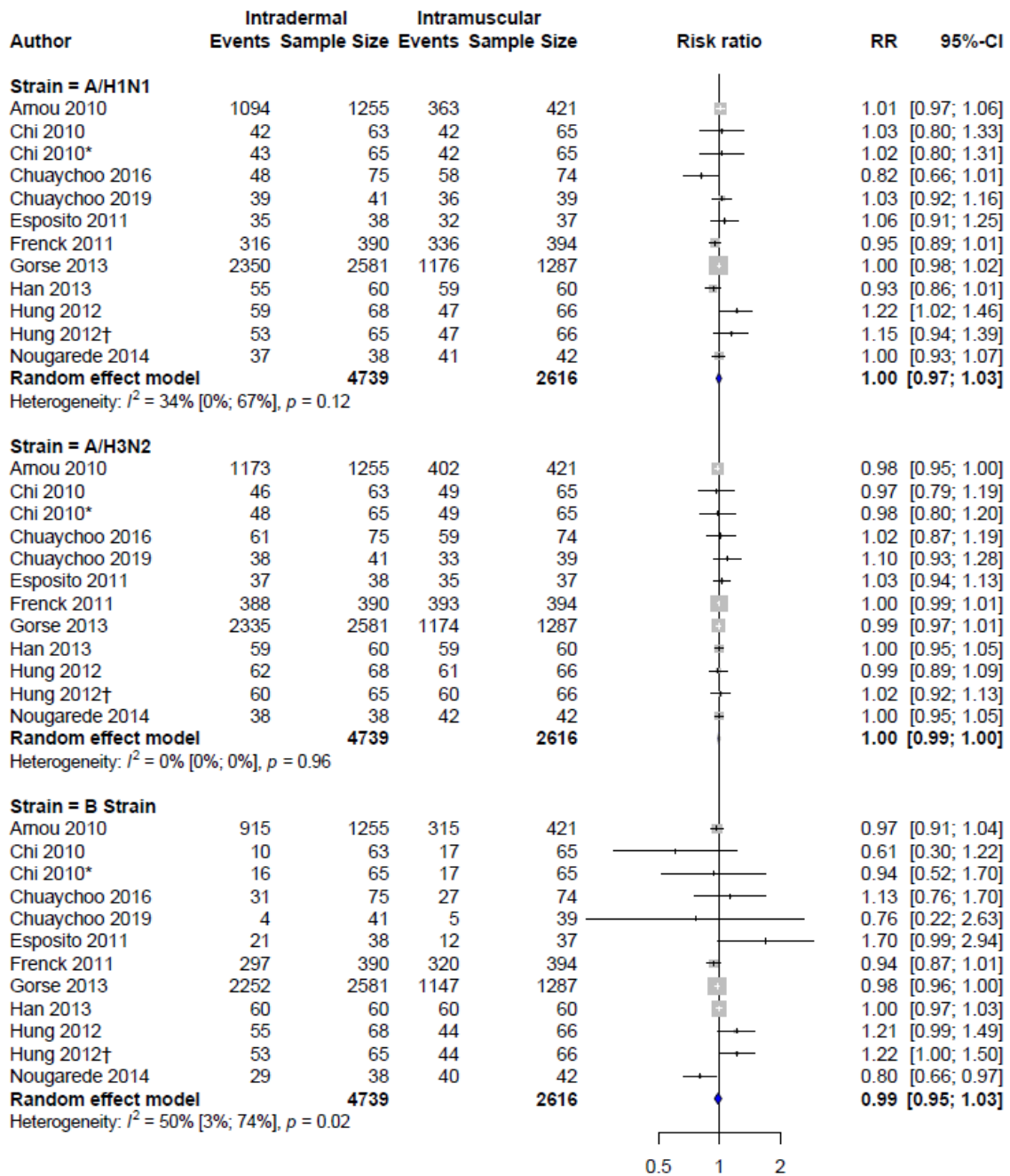
eFigure 10. Seroprotection: 6 µg ID vs 15 µg IM



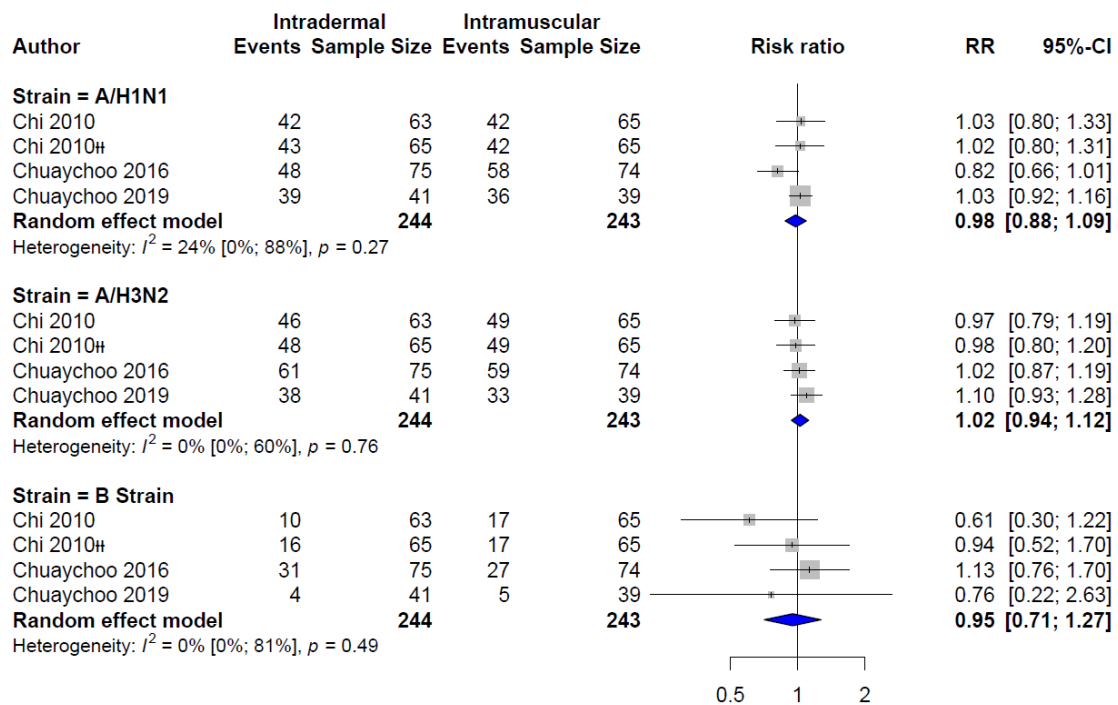
eFigure 11. Seroprotection: 7.5 µg ID vs 15 µg IM



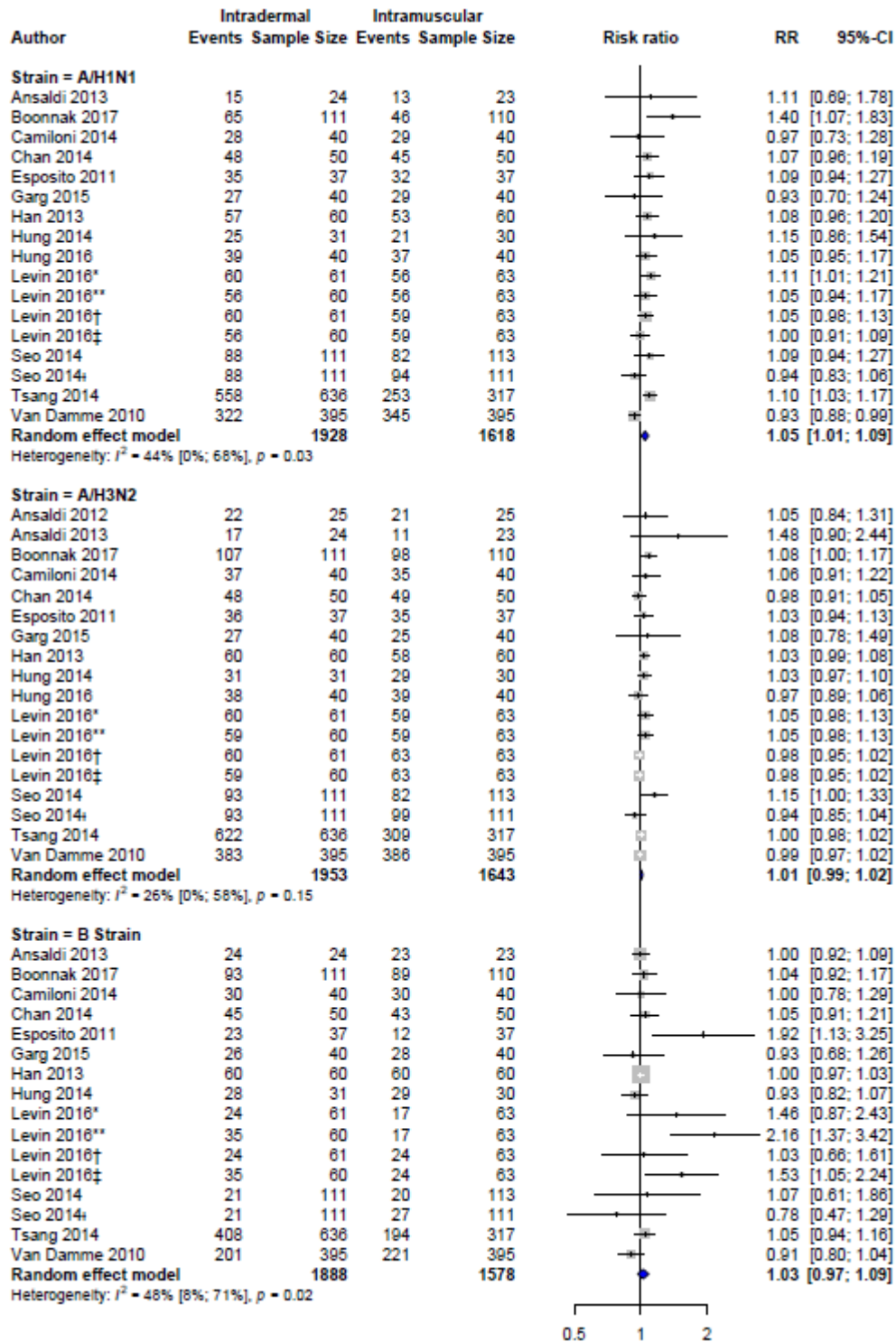
eFigure 12. Seroprotection: 9 µg ID vs 15 µg IM († Soluvia Microneedle, * Two Injections)



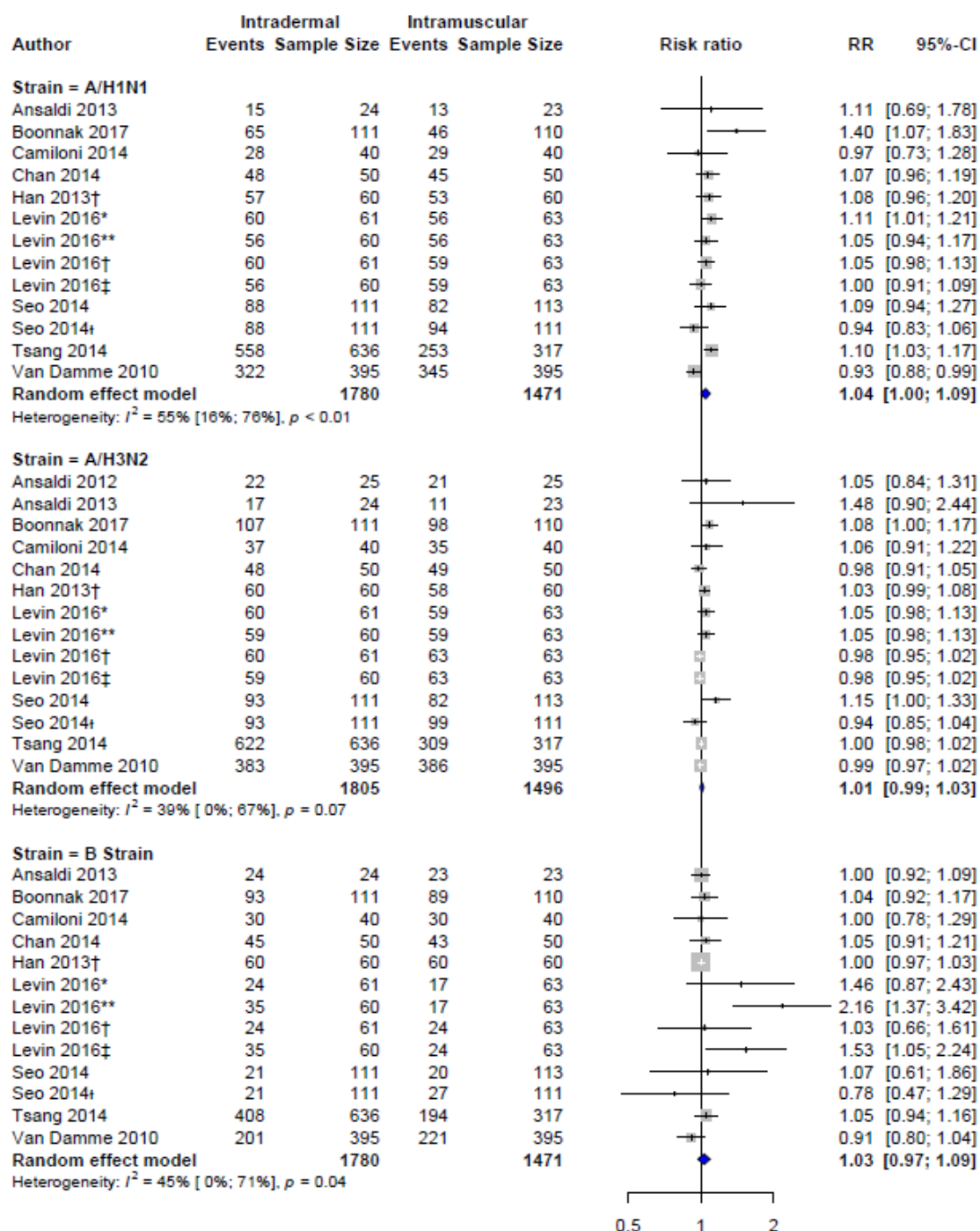
**eFigure 13. Seroprotection Older Adults: 9 µg ID vs 15 µg IM
 † Two Injections**



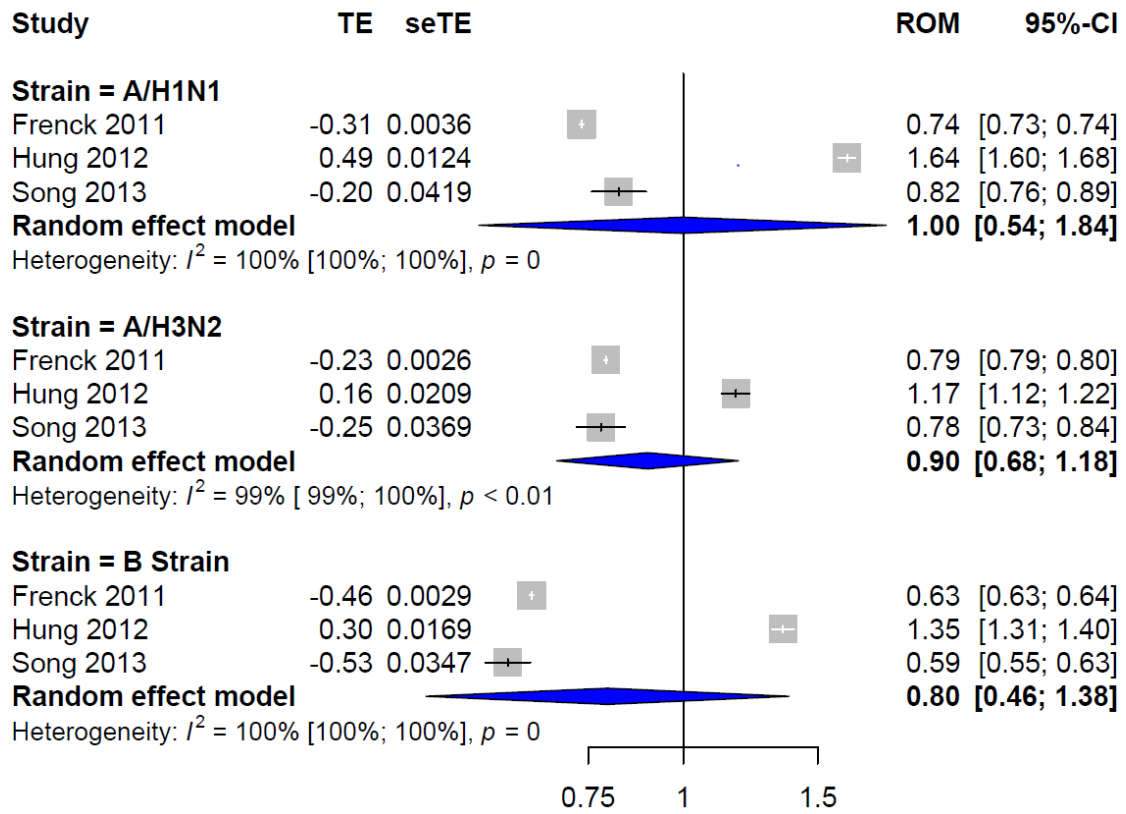
eFigure 14. Seroprotection: 15 µg ID vs 15 µg IM
 (*Inflexa vs Inflexa, ** Intanza vs Inflexa, †Inflexa vs Fluad, ‡Intanza vs Fluad, † Adjuvanted)



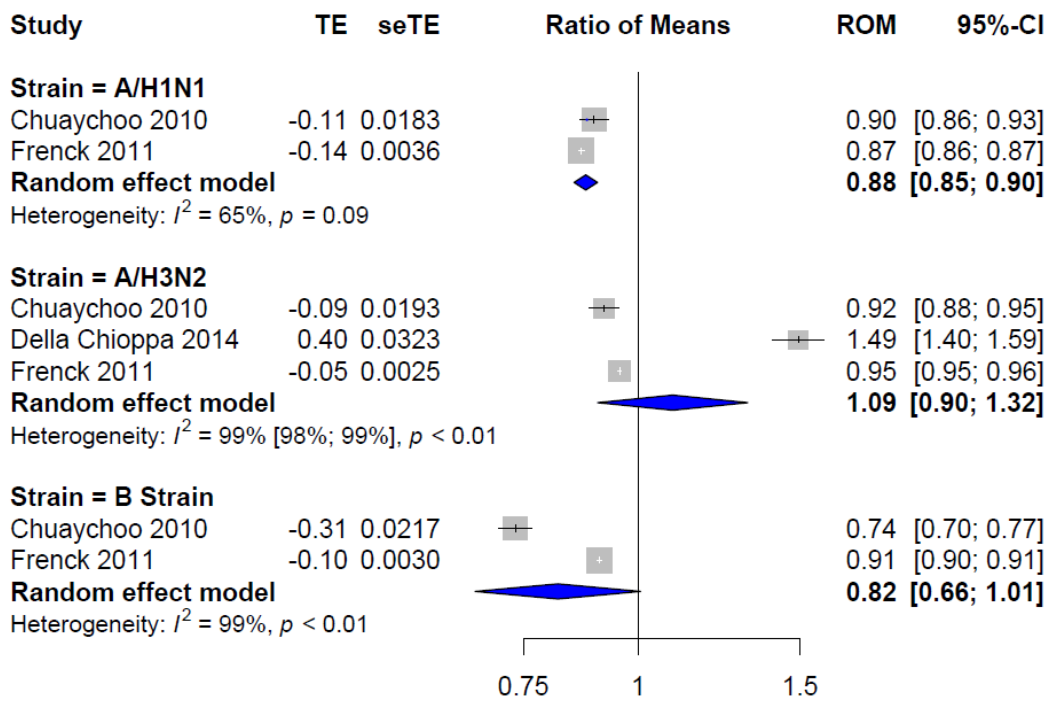
eFigure 15. Seroprotection in Older Adults: 15 µg ID vs 15 µg IM
 (*Inflexa vs Inflexa, ** Intanza vs Inflexa, †Inflexa vs Fluad, ‡Intanza vs Fluad, † Adjuvanted)



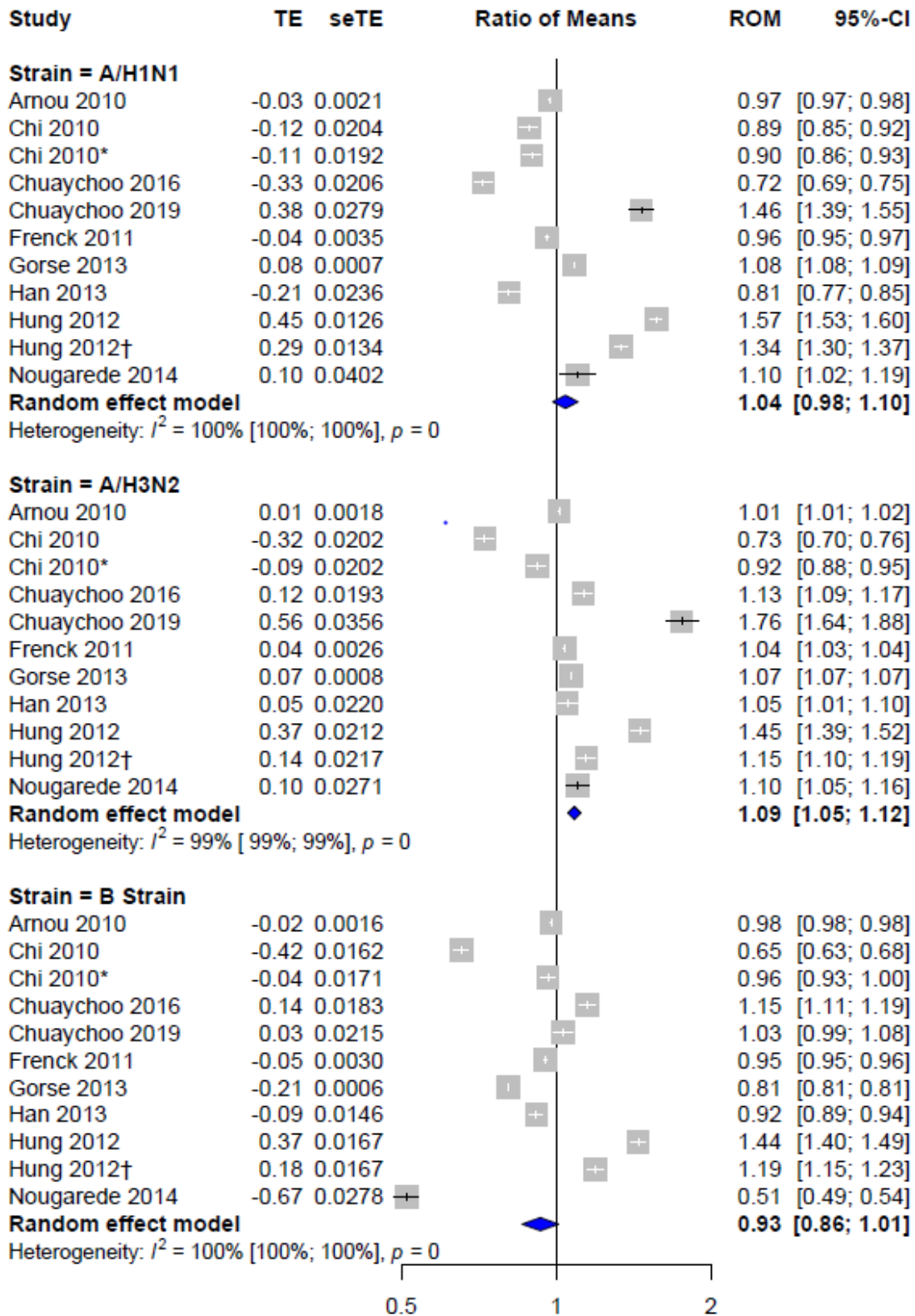
eFigure 16. GMT: 3 µg ID vs 15 µg IM



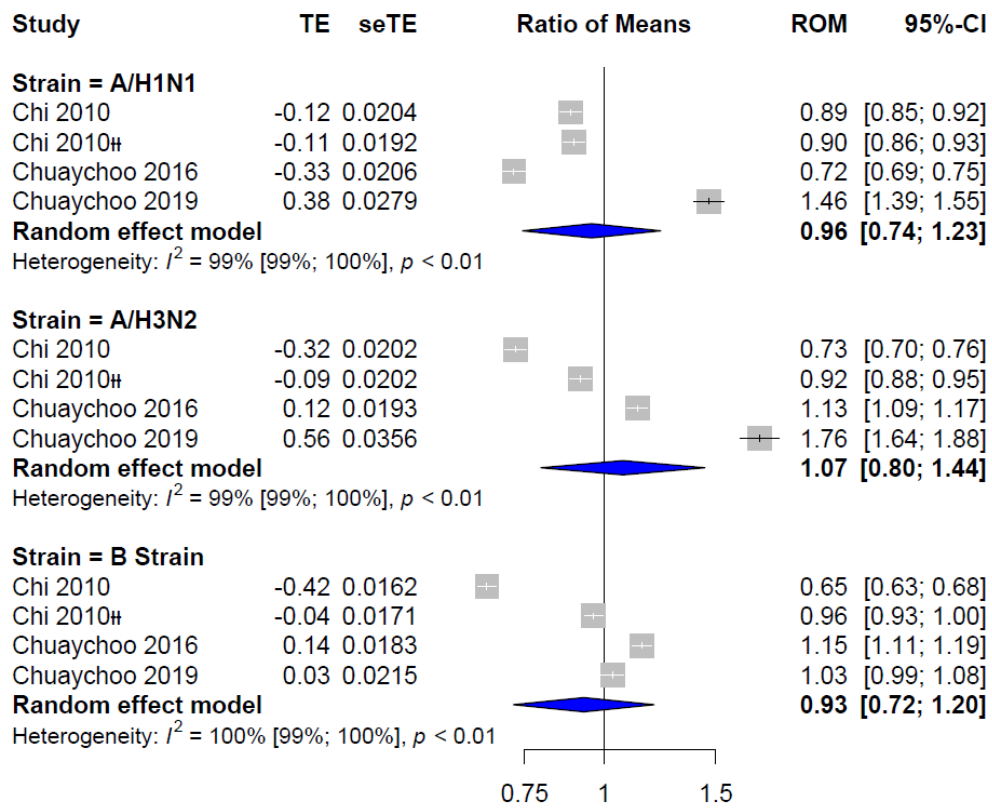
eFigure 17. GMT: 6 µg ID vs 15 µg IM



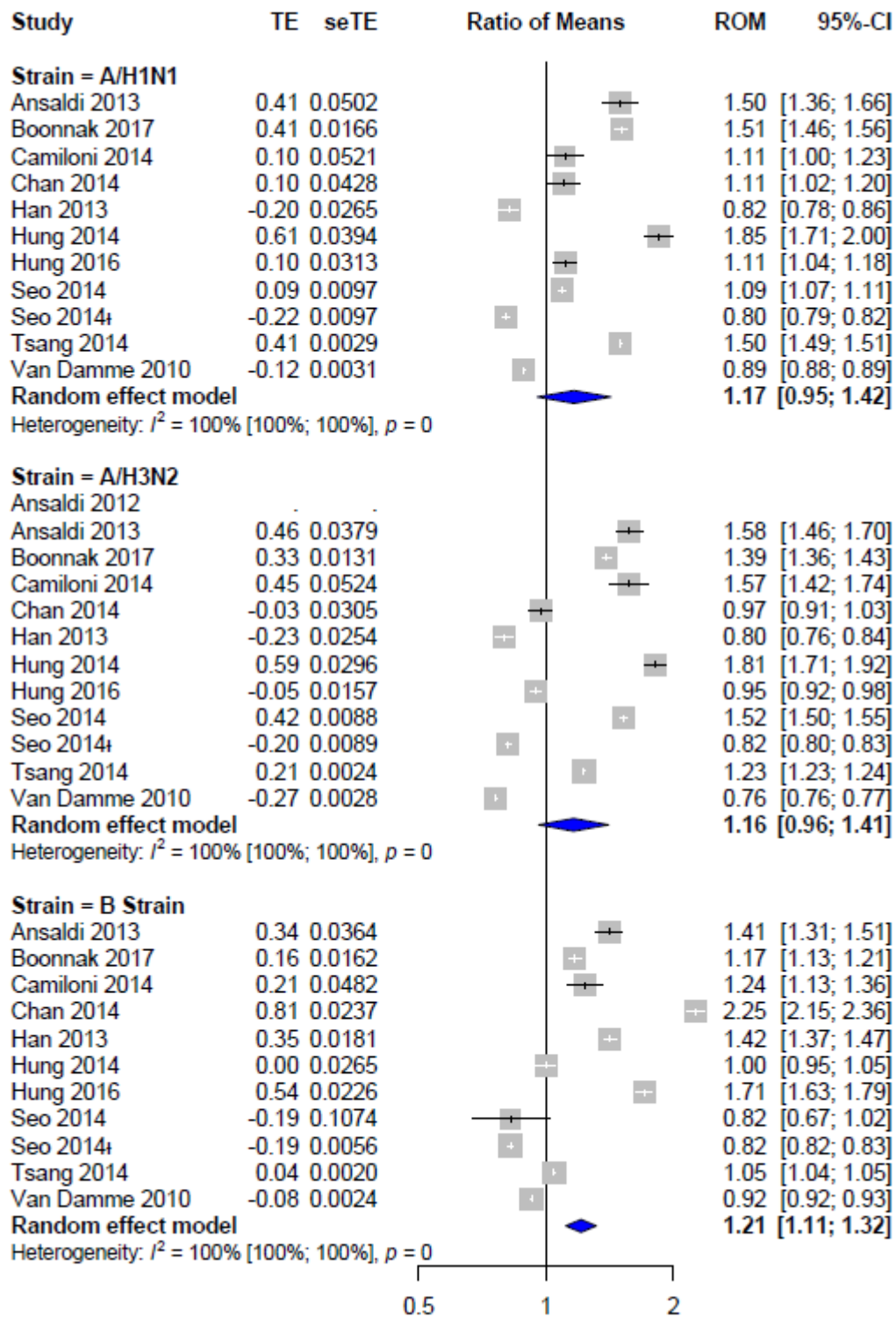
eFigure 18. GMT: 9 µg ID vs 15 µg IM
 (* Two Doses, †Soluvia Device)



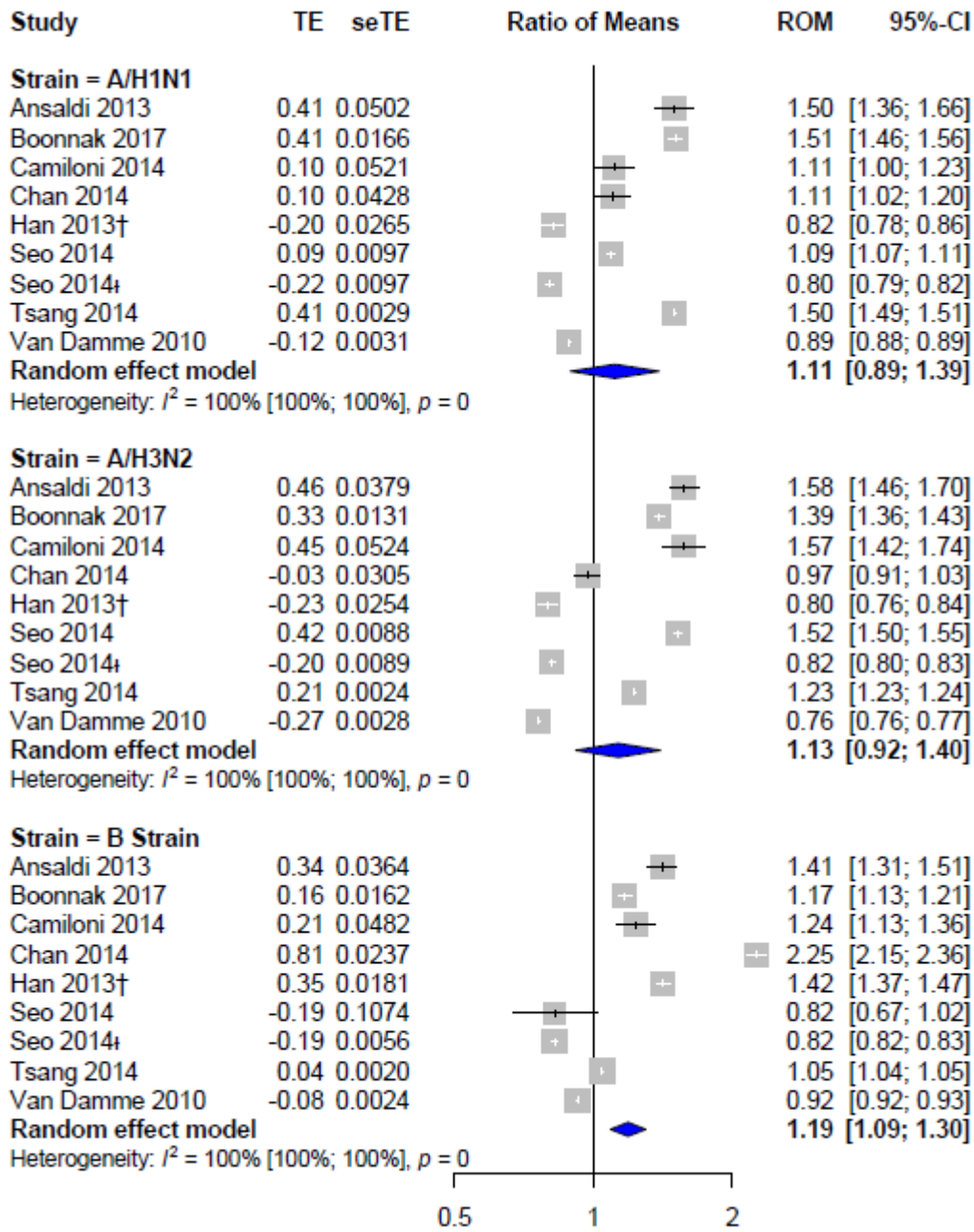
eFigure 19. GMT: in Older Adults 9 µg ID vs 15 µg IM



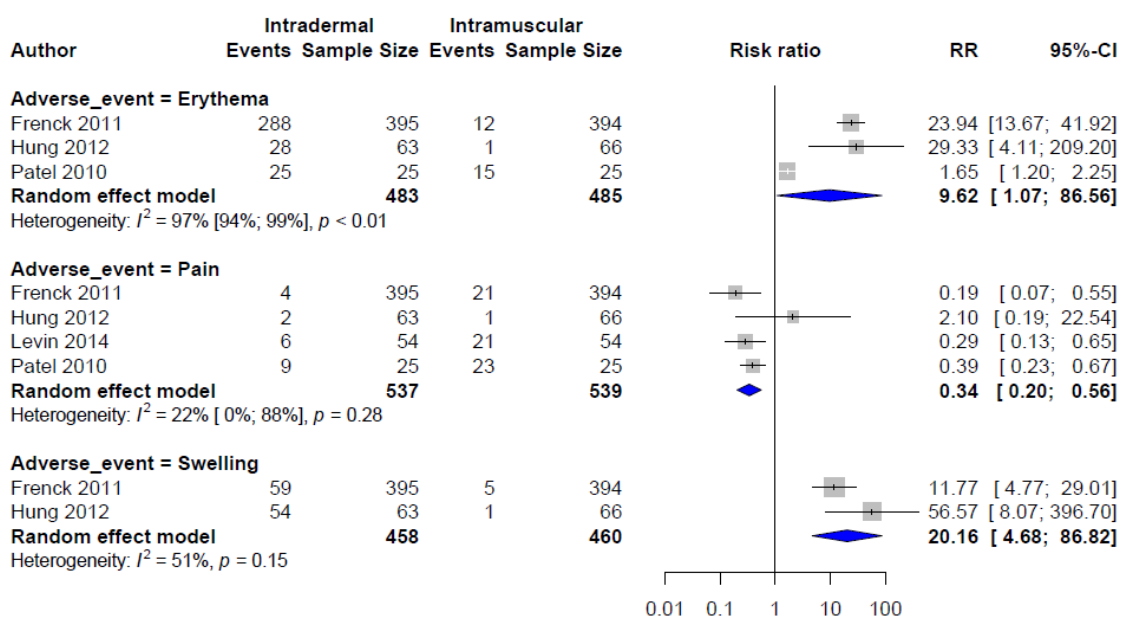
eFigure 20. GMT: 15 µg ID vs 15 µg IM



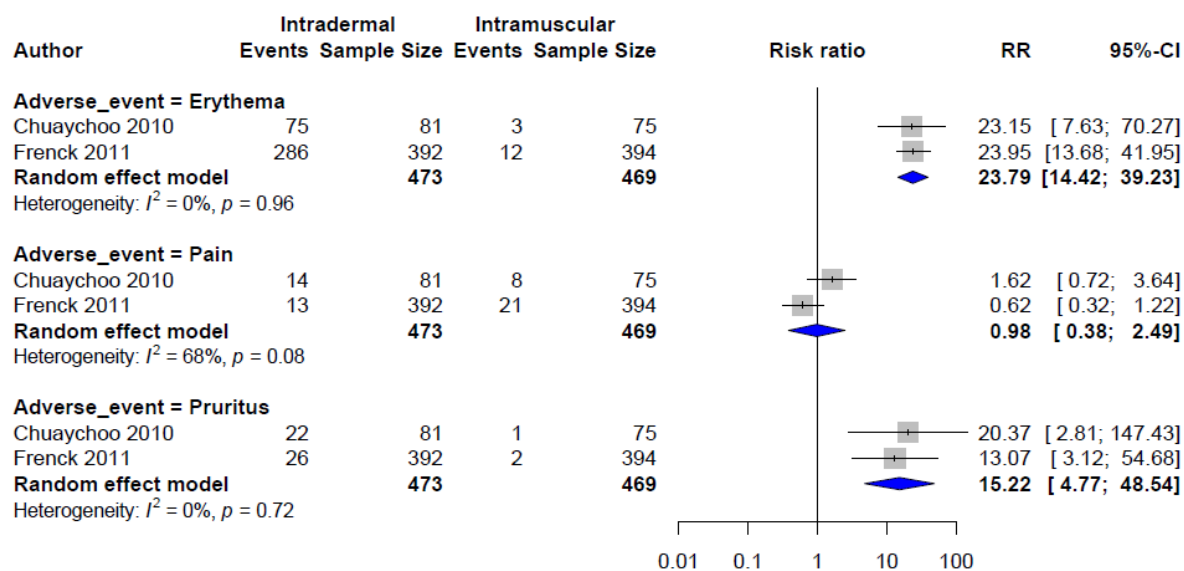
eFigure 21. GMT in Older Adults: 15 µg ID vs 15 µg IM (‡ Adjuvanted, †≥60 Years Old)



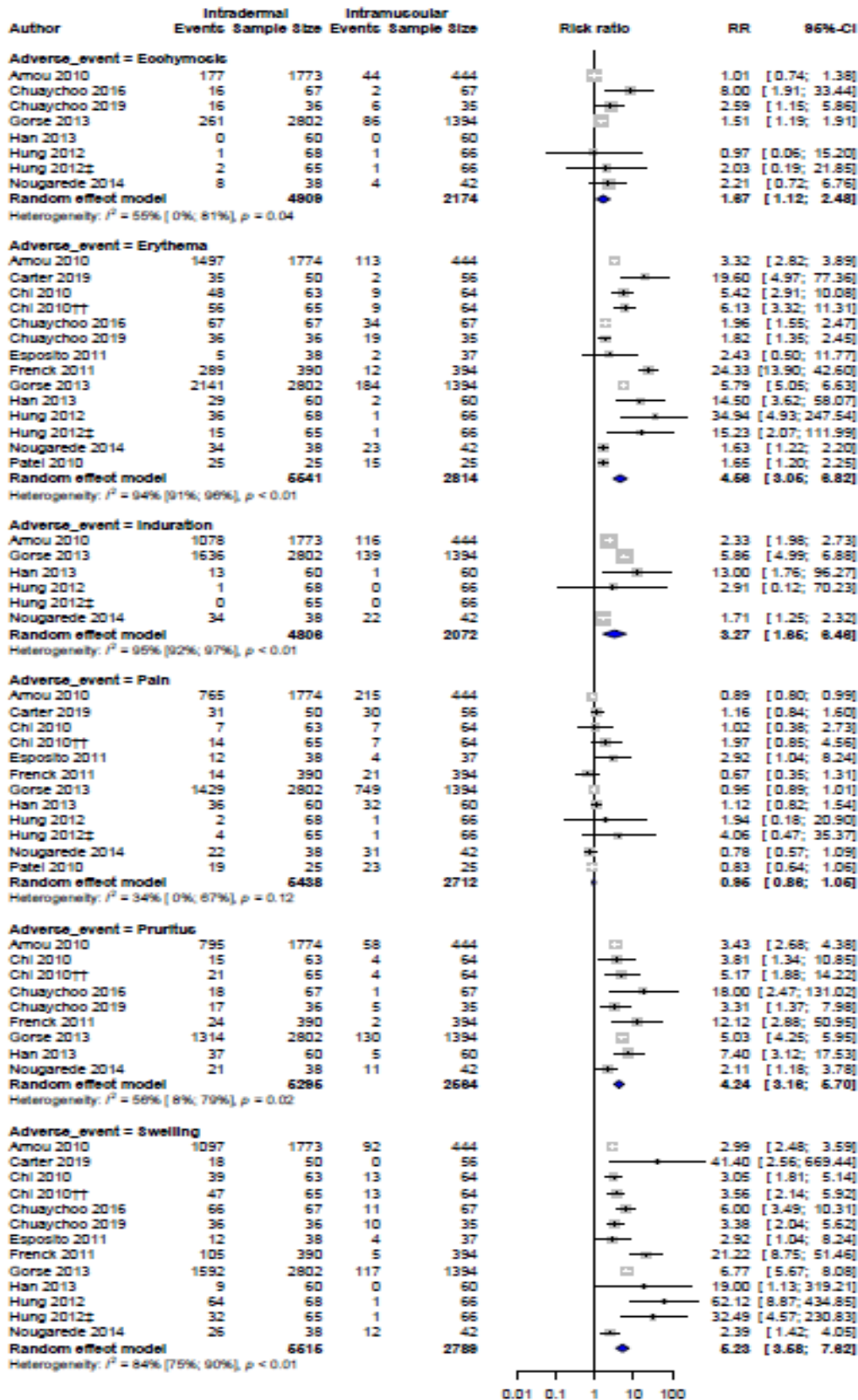
eFigure 22. Local Adverse Events: 3 µg ID vs 15 µg IM



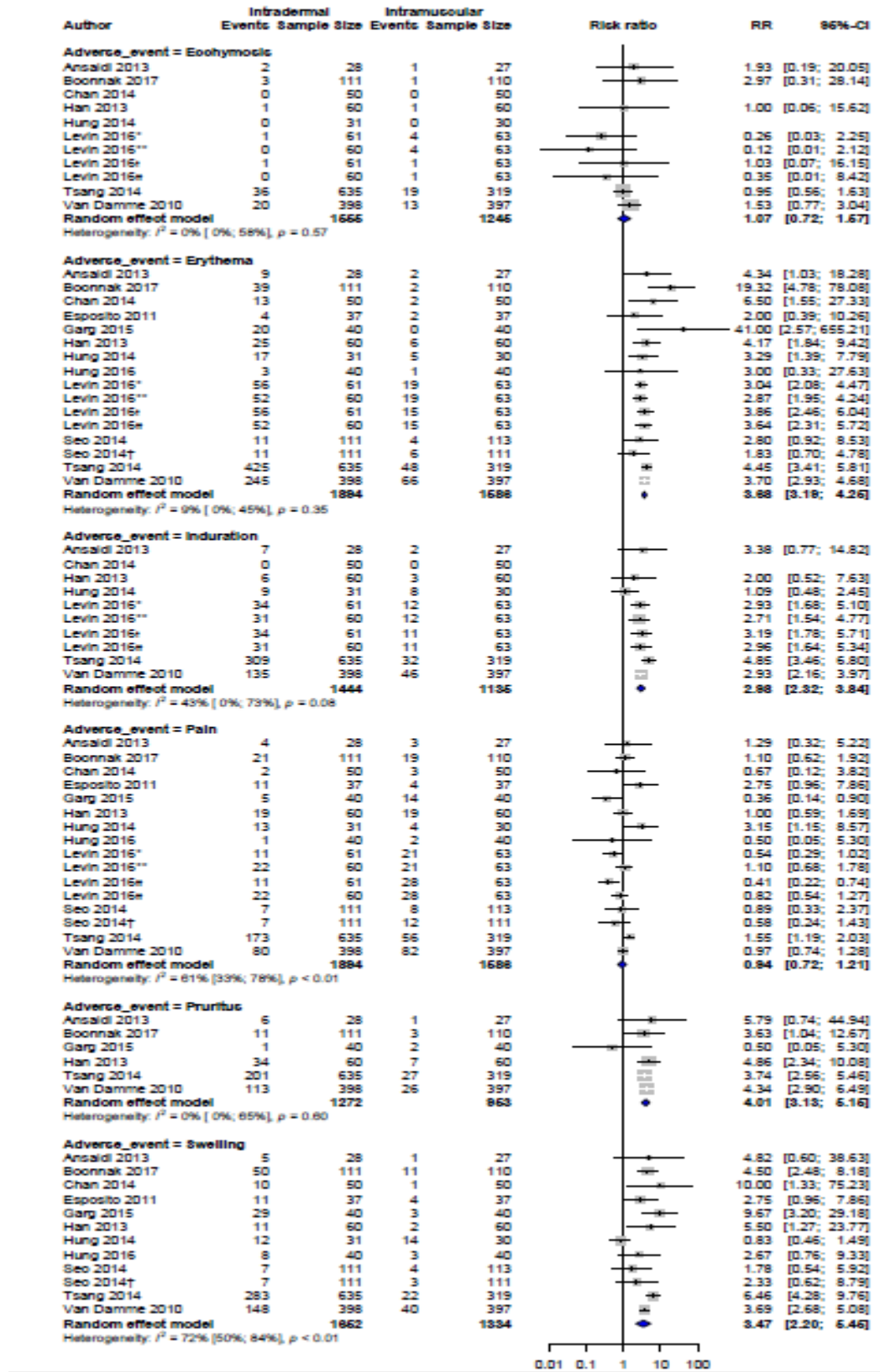
eFigure 23. Local Adverse Events: 6 µg ID vs 15 µg IM



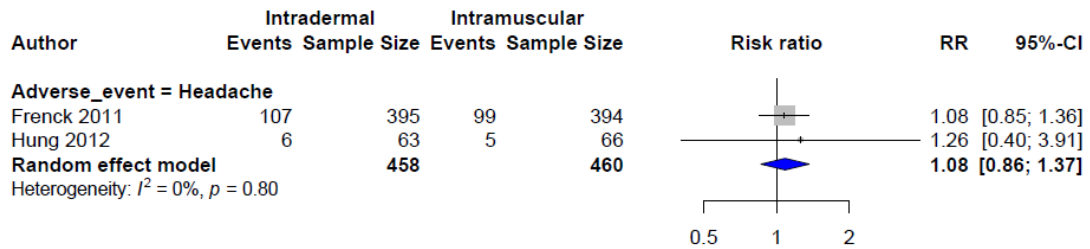
eFigure 24. Local Adverse Events: 9 µg ID vs 15 µg IM (††Two Doses, ‡Soluvia Device)



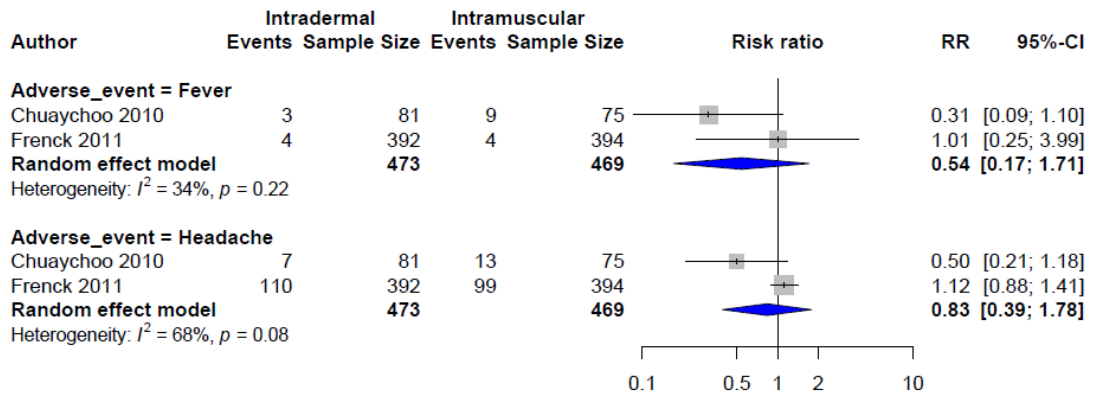
eFigure 25. Local Adverse Events: 15 µg ID vs 15 µg IM
 (*Inflexa vs Inflexa, ** Intanza vs Inflexa, †Inflexa vs Fluad, ‡Intanza vs Fluad, † Adjuvanted)



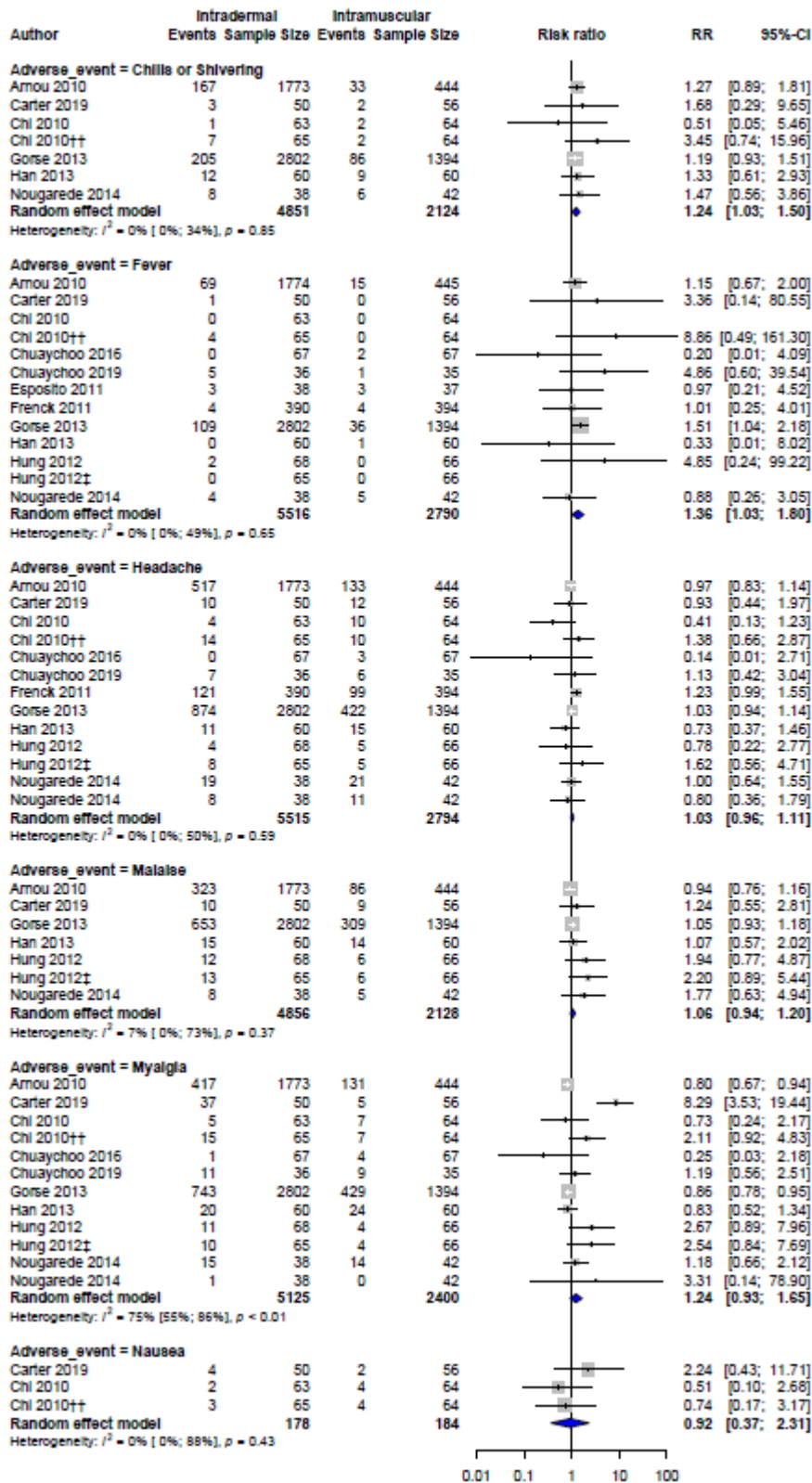
eFigure 26. Systemic Adverse Events: 3 µg ID vs 15 µg IM



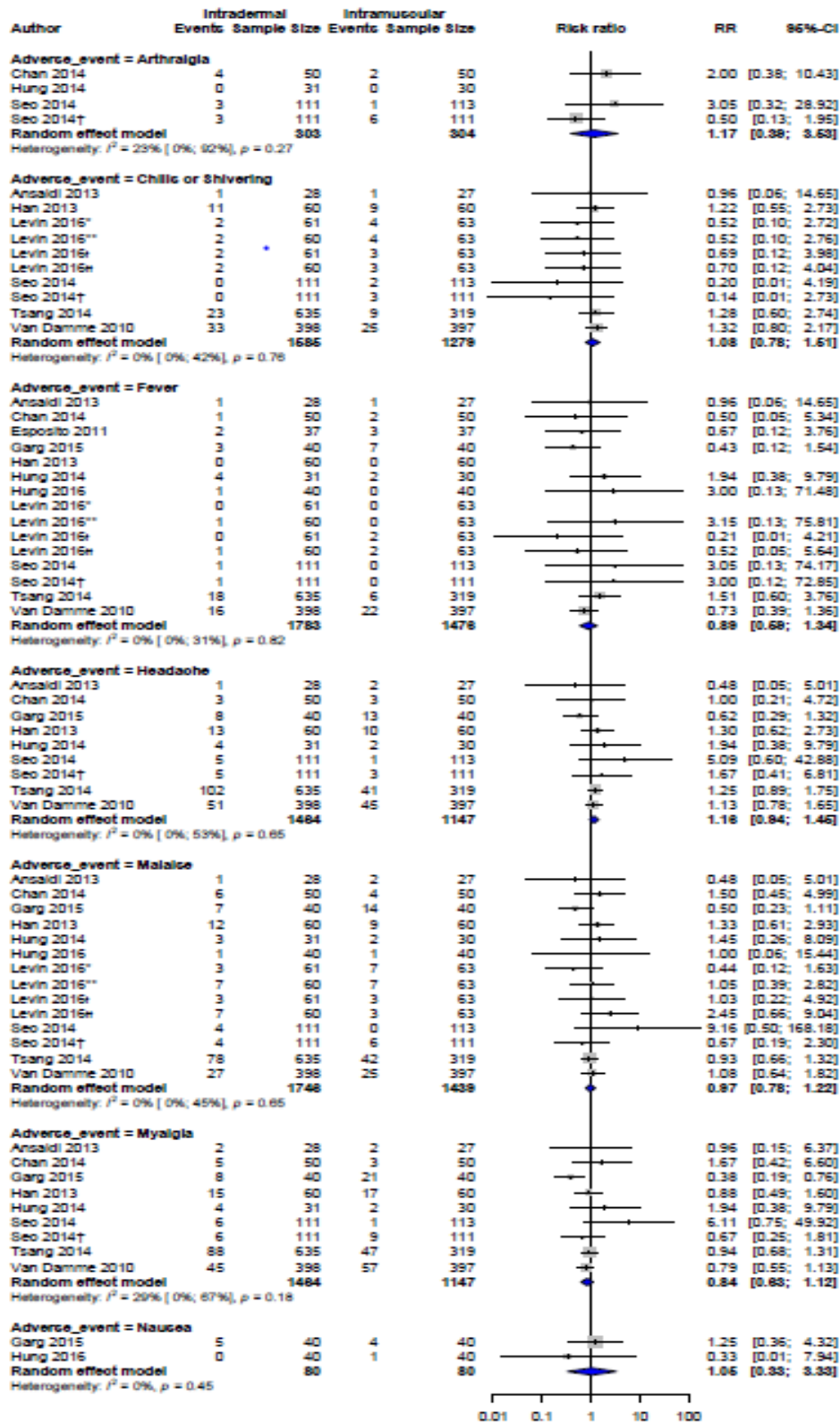
eFigure 27. Systemic Adverse Events: 6 µg ID vs 15 µg IM



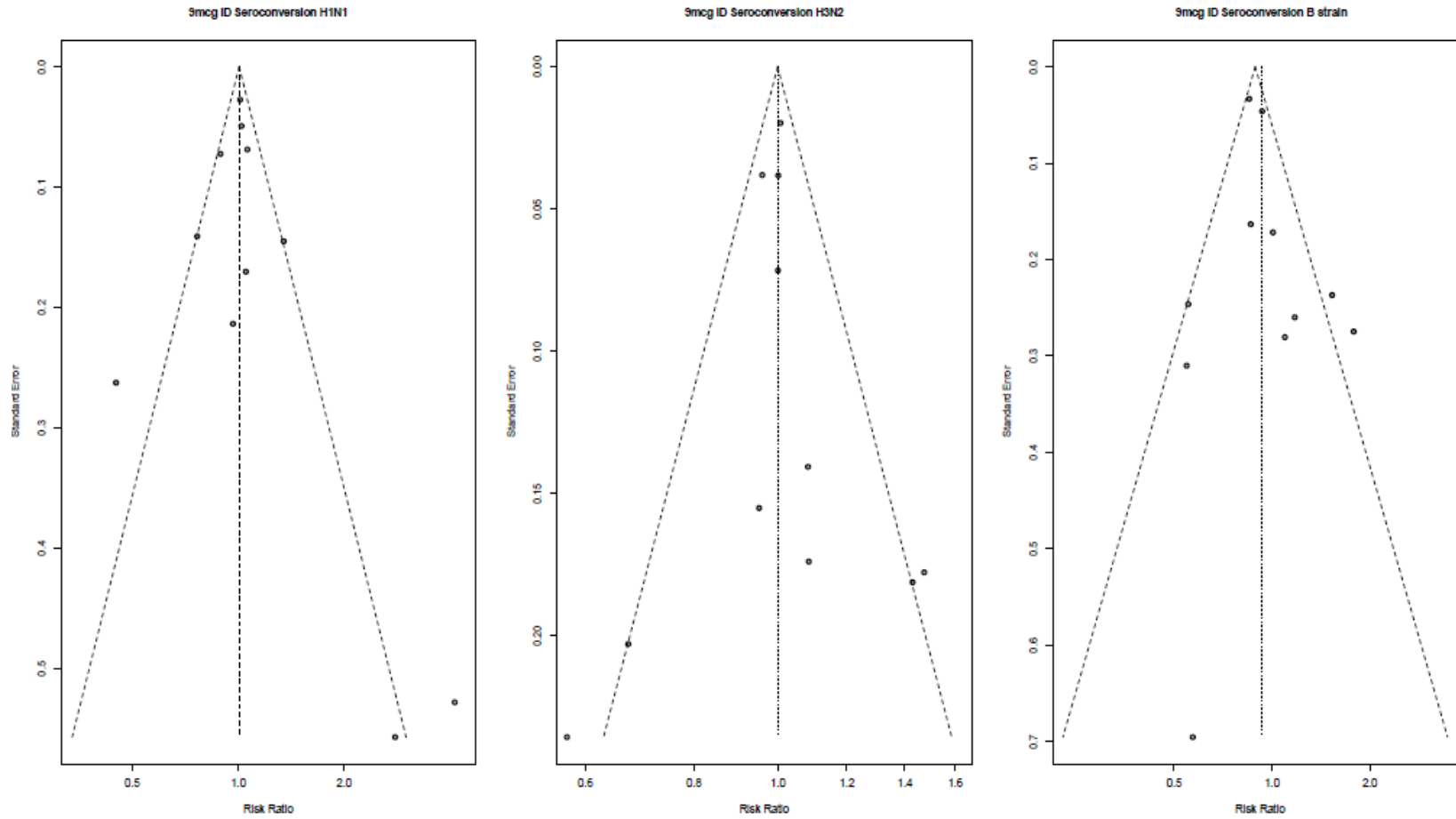
eFigure 28. Systemic Adverse Events: 9 µg ID vs 15 µg IM (‡ Soluvia, †† Two Doses)



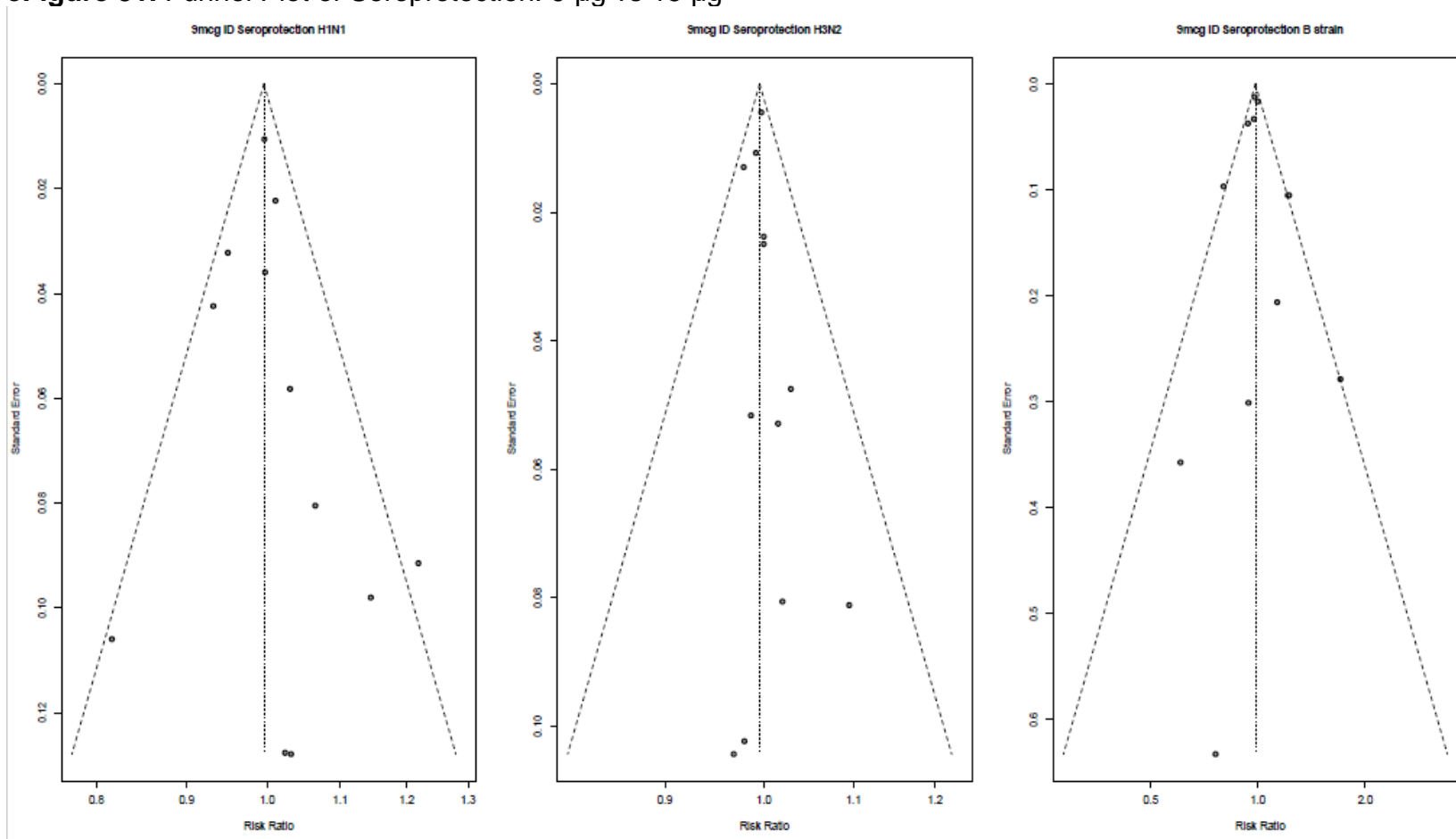
eFigure 29. Systemic Adverse Events: 15 µg ID vs 15 µg IM
 (*Inflexa vs Inflexa, ** Intanza vs Inflexa, †Inflexa vs Fluad, ‡Intanza vs Fluad, † Adjuvanted)



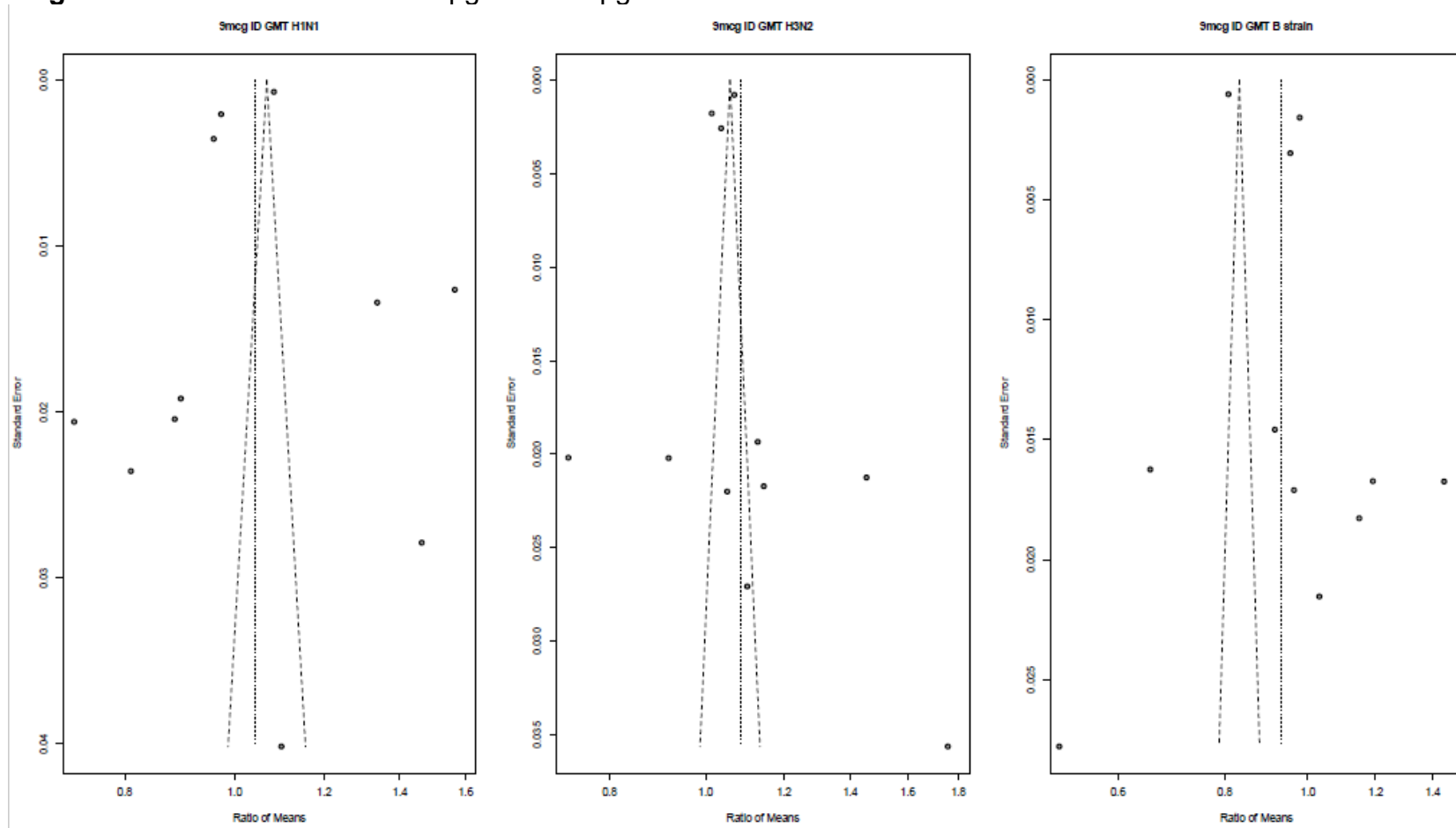
eFigure 30. Funnel Plot of Seroconversion: 9 µg ID vs 15 µg IM



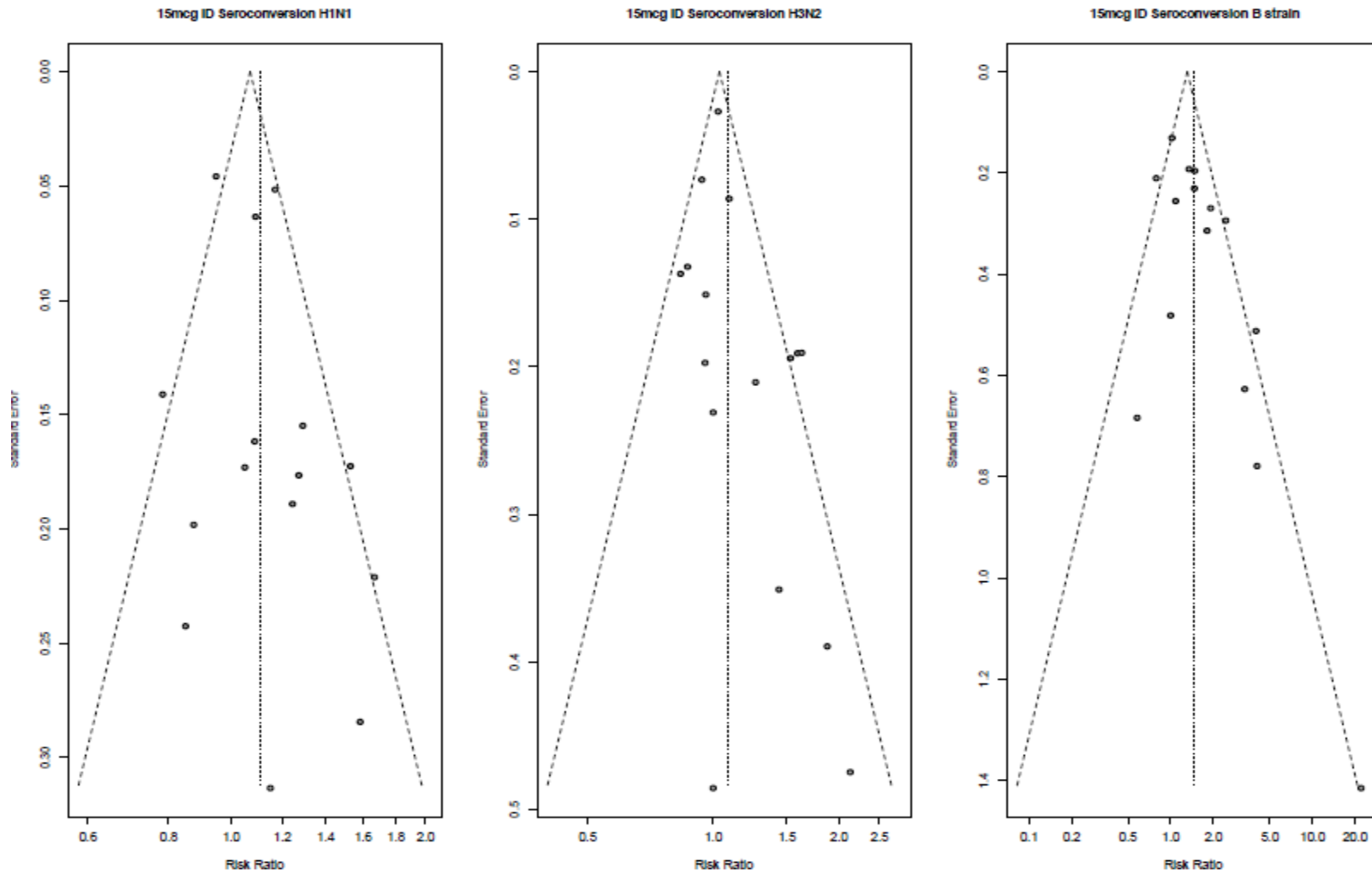
eFigure 31. Funnel Plot of Seroprotection: 9 µg vs 15 µg



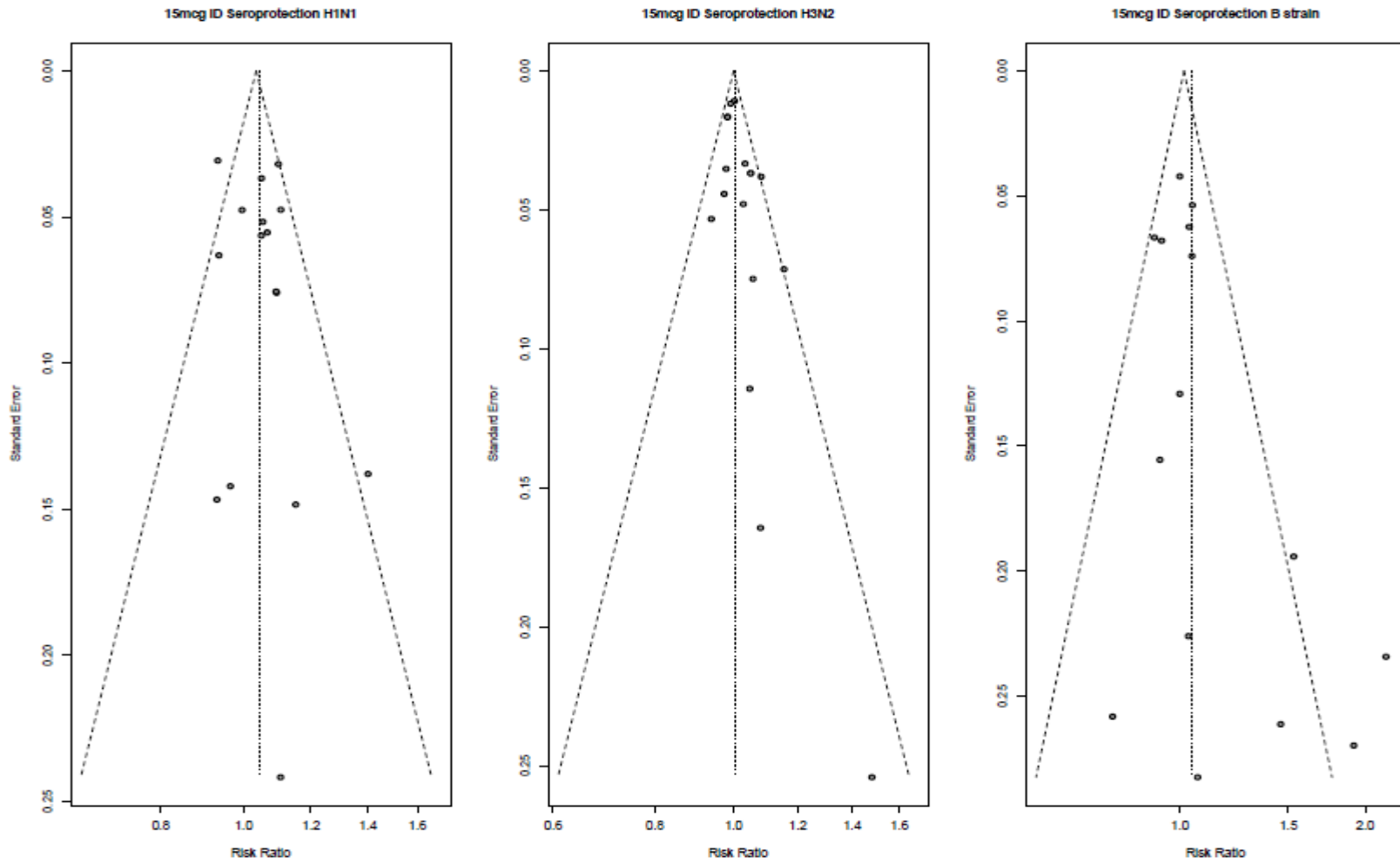
eFigure 32. Funnel Plot of GMT: 9 μg ID vs 15 μg IM



eFigure 33. Funnel Plot of Seroconversion: 15 µg ID vs 15 µg IM



eFigure 34. Funnel Plot of Seroprotection: 15 µg ID vs 15 µg IM



eFigure 35. Funnel Plot of GMT: 15 µg ID vs 15 µg IM

