Laboratory-confirmed influenza in Europe

Supplementary Tables and Figures

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Appendix A

Medline Search Strategy

1. Influenza.mp. or exp Influenza, Human/
2. exp Pneumonia/ or pneumonia.mp. or exp Pneumonia, Viral/
3. community acquired pneumonia.mp.
4. exp Respiratory Tract Infections/ or acute respiratory infection.mp.
5. respiratory tract illness.mp.
6. (influenza-like illness or influenza like illness or ARI or SARI or ILI).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
7. incidence.mp. or exp Incidence/
8. exp Prevalence/ or prevalence.mp.
9. exp Hospital Mortality/ or exp Mortality/ or exp Child Mortality/ or exp Maternal Mortality/ or Mortality.mp. or exp Infant Mortality/
10. death.mp. or exp "Cause of Death"/ or exp Death/
11. morbidity.mp. or exp Morbidity/
12. (burden or impact).mp.
13. epidemiology.mp. or exp Epidemiology/
14. exp Hospitalization/ or hospitalisation.mp. or exp "Length of Stay"/
15. 1 or 2 or 3 or 4 or 5 or 6
16. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
17. 15 and 16

Appendix B: TESSy participating countries and duration of participation

Country	First season of data contributing to review	
	ARI/ILI	SARI
Albania	2007-2008	2011-2012
Armenia	2010-2011	2009-2010
Austria	2004-2005	-
Azerbaijan	2008-2009	2015-2016
Belarus	2006-2007	2015-2016
Belgium	2004-2005	-
Bulgaria	2007-2008	-
Croatia	2013-2014	-
Czech Republic	2004-2005	-
Denmark	2004-2005	-
Estonia	2005-2006	-
Finland	2004-2005	-
France	2004-2005	-
Georgia	2008-2009	2010-2011
Germany	2004-2005	-
Greece	2004-2005	-
Hungary	2004-2005	-
Ireland	2004-2005	-
Israel	2004-2005	-
Italy	2004-2005	-
Kazakhstan	2008-2009	2009-2010
Kyrgyzstan	2008-2009	2009-2010
Latvia	2004-2005	-
Lithuania	2004-2005	-
Luxembourg	2004-2005	-
North Macedonia	2016-2017	-
Malta	2010-2011	-
Netherlands	2004-2005	-
Norway	2004-2005	-
Poland	2004-2005	-
Portugal	2004-2005	-
Republic of Moldova	2009-2010	2010-2011
Romania	2004-2005	-
Russian Federation	2009-2010	2010-2011
Serbia	2006-2007	2012-2013
Slovakia	2004-2005	-
Slovenia	2004-2005	-
Spain	2004-2005	-
Sweden	2006-2007	-
Switzerland	2004-2005	-
Tajikistan	2009-2010	2017-2018
Turkey	2008-2009	-
United Kingdom	2004-2005	-
Ukraine	2006-2007	2009-2010
Uzbekistan	2012-2013	2017-2018

Appendix C: Studies included in meta-analysis

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Supplemental Table 1. Sensitivity Analysis: RT-PCR confirmed influenza only (omitting studies in which influenza only confirmed by viral culture/IF)

Influenza virus	Pooled estimate of proportion positive %	% change from original estimate	Pooled estimate of proportion positive by age group (%) (95% CI, number of studies)					
			0-17yrs	% change	18-64yrs	% change	>65 yrs	% change
Any influenza virus								
Outpatient	36	n/a	26	0	41	n/a	33	n/a
Inpatient	24	n/a	9	n/a	-	-	-	-
Influenza A								
Outpatient	25	+1	14	n/a	22	n/a	18	n/a
Inpatient	20	n/a	6	n/a	-	-	-	-
Influenza B								
Outpatient	7	-2	9	+1	15	n/a	10	n/a
Inpatient	5	+1	3	n/a	-	-	-	-
Influenza A(H1N1): pre 2009 pandemic								
Outpatient	3	n/a	3	n/a	-	-	-	-
Inpatient	-	-	-	-	-	-	-	-
Influenza A(H1N1): post 2009 pandemic								
Outpatient	11	n/a	8	n/a	16	n/a	4	n/a
Inpatient	14	n/a	2	n/a	-	n/a	-	-
Influenza A(H3N2)								
Outpatient	13	n/a	9	-1	8	n/a	10	n/a
Inpatient	9	n/a	3	-1	-	-	-	n/a

n/a not applicable, no studies excluded in sensitivity analysis; - No data

Supplemental Table 2. Definitions of quality levels and numbers of studies included in meta-analyses

Quality indicator	Study Quality Level		
	High	**Intermediate**	**Low**
Geographic representativeness	Multi-city study (N=18)	Multiple centres in one city (N= 6)	One centre in a single city (N=16)
Age representativeness	Includes well defined and specified age groups from an entire child (0-17 years, 18-year span) to an adult (18-64 years, 47-year span) age span (N= 7)	One or two well defined age groups (N=23)	Age span not specified or includes <9 years for children or <23.5 years for adults (N= 10)
General representativeness	Randomly or systematically chosen subjects (N=2)	General population volunteers may exclude those with high risk of influenza complications (N=38)	Includes only members of a specific group (e.g., college students) (N= 0)
Sensitivity of symptoms prompting laboratory testing	Does not require any one specific symptom (N=24)	Requires one specific symptom; or includes URI without listing specific symptoms (N= 8)	Requires ≥2 specific symptoms (N= 8)
Laboratory method	RT-PCR with or without culture (N=35)	Viral culture without RT-PCR (N=5)	Methods other than RT-PCR or culture (N=0)

Supplemental Table 3. Quality levels for studies included in meta-analyses

First author, year published	Age-groups(years)	Number seasons	Geographic representativeness	Age representativeness	General representativeness	Sensitivity of symptoms	Laboratory method
Gasparini 2007	0-19, 0-3, 3-19	2	Low	Intermediate	Intermediate	Intermediate	High
Gooskens 2014	0-3, 3-19,0-19	1	Low	Intermediate	Intermediate	High	High
Esposito 2011 c	0-19	1	High	Intermediate	Intermediate	High	High
Esposito 2011b	0-19	2	High	Intermediate	Intermediate	High	High
Esposito 2005	0-19	1	Low	Intermediate	Intermediate	High	High
Silvennoinen 2009	0-19	2	Low	Intermediate	Intermediate	High	Intermediate
Ajayi-Obe 2008	0-7	2	Low	Intermediate	Intermediate	High	High
Paixao 2014	0-7	1	Intermediate	Intermediate	Intermediate	Low	High
Plymoth 2015	15-44, 45-65	2	Intermediate	High	High	Intermediate	High
Kouni 2013	0-19	1	Low	Intermediate	Intermediate	Intermediate	High
Pebody 2013	0-7,3-19, 15-44 ,45-64, ≥65, all	1	High	High	Intermediate	High	High
Meerhoff 2015	0-19, all	3	High	Intermediate	Intermediate	High	High
Tsolia 2006	3-19	2	High	Intermediate	Intermediate	Low	Intermediate
Harvala 2014	0-7, 3-19, 15-44, 37-65, ≥65, all	1	High	High	Intermediate	High	High
Heikkinen 2004	0-3, 0-7, 3-19, 0-19	2	Intermediate	Intermediate	Intermediate	High	Intermediate
Karadag-oncel 2014	0-19	1	Low	Intermediate	Intermediate	Low	High
Pebody 2015	0-19, 15-44, 45-64, ≥65, all	1	High	High	Intermediate	High	High
Castilla 2015	≥65	2	Low	Intermediate	Intermediate	Intermediate	High
Chatzopoulou 2012	0-7	1	Intermediate	Intermediate	Intermediate	Intermediate	High
Principi 2004	0-19	1	High	Intermediate	Intermediate	Low	Intermediate
Meury 2004	0-19y	2	Low	Intermediate	Intermediate	High	High
Beaute 2015	0-7, 3-19, 45-65, ≥65,all	1	High	High	Intermediate	High	High
Zambon 2001	0-7,3-19,15-44, 45-65, 65,all	3	High	High	Intermediate	High	High
Heikkinen 2003	0-19	1	Low	Intermediate	Intermediate	High	Intermediate
Bennet 2016	0-19	6	Low	Intermediate	Intermediate	Intermediate	High
Tsolia 2004	3-19	1	Low	Intermediate	Intermediate	Low	High
Pierangeli 2007	All	1	Low	Intermediate	Intermediate	High	High
Redlberger-Fritz 2012	All	10	Intermediate	High	Intermediate	Low	High
Zielinski 2013	All	1	High	Low	Intermediate	High	High
Rezza 2006	All	1	Intermediate	Low	Intermediate	Low	High
Mosnier 2015	All	9	High	Low	Intermediate	Intermediate	High
Puig- Barbera 2014	All	1	High	Low	Intermediate	High	High
Puig-Barbara 2015	All	1	High	Low	Intermediate	High	High
Puig-Barbara 2016	All	1	High	Low	Intermediate	High	High
Redlberger-Fritz 2016	All	1	High	Low	Intermediate	High	High

Boddington 2017	All	4	High	Low	High	Low	High
Der Heidan 2016	All	13	High	Low	Intermediate	Intermediate	High
Fajfr 2014	All	3	Low	Low	Intermediate	High	High

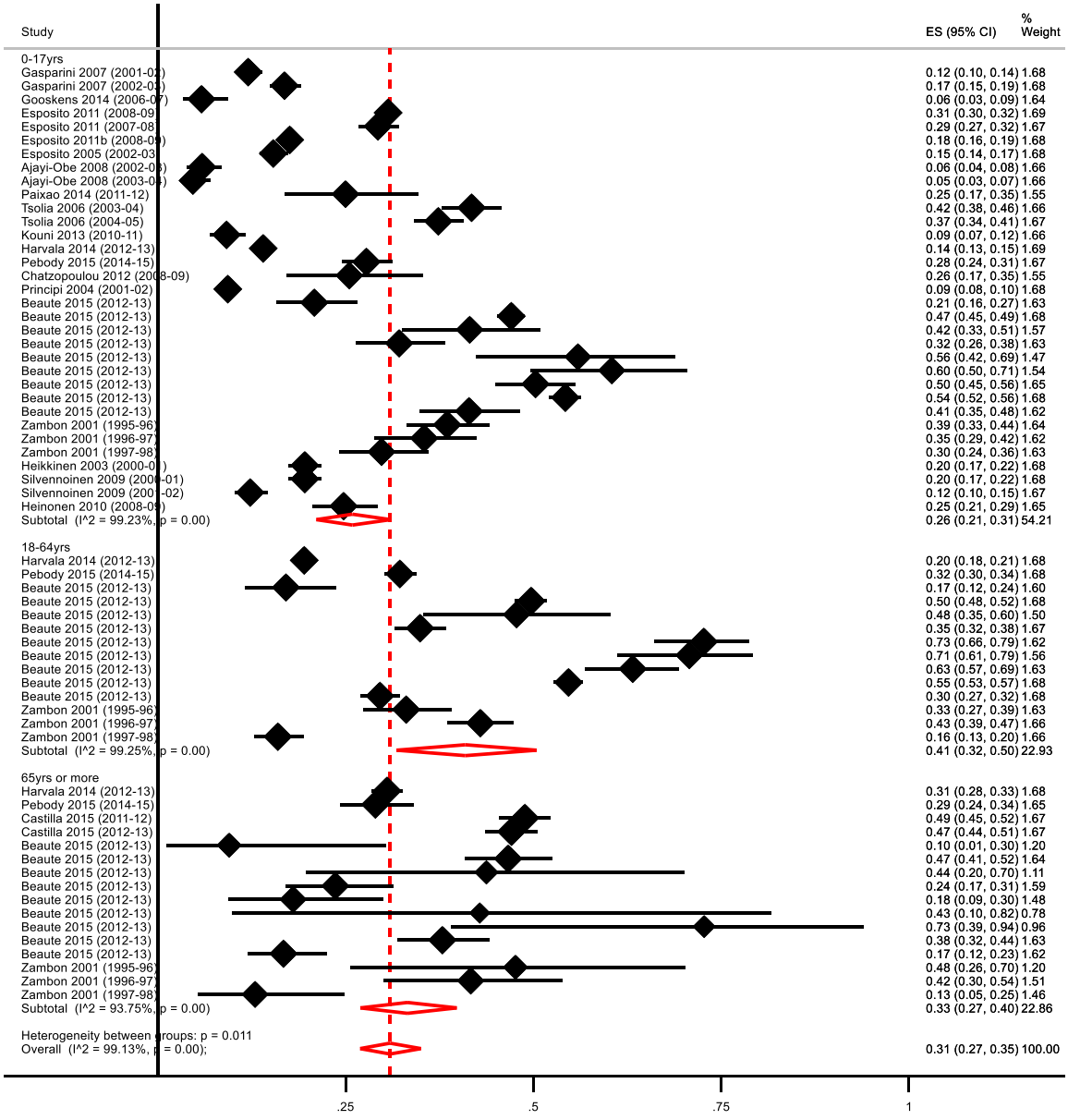
Supplemental Table 4: Proportion of confirmed influenza by type/subtype for influenza seasons between 1999-2000 and 2014-2015 (literature review)

Season	Proportion laboratory-confirmed influenza % (95% CI)			
	Influenza A	Influenza A(H1N1)	Influenza A(H3N2)	Influenza B
1999-2000	36 (31-42)	0 (0-1)	21 (17-26)	0 (0-0)
2000-2001	38 (33-44)	23 (18-28)	0 (0-2)	4 (2-7)
2001-2002	15 (13-16)	0 (0-0)	15 (13-16)	15 (14-16)
2002-2003	42 (40-43)	0 (0-0)	34 (32-25)	6 (6-7)
2003-2004	31 (20-43)	0 (0-0)	19 (17-20)	0 (0-0)
2004-2005	22 (17-27)	5 (5-6)	21 (20-22)	4 (1-8)
2005-2006	11 (5-18)	1 (1-1)	9 (8-10)	14 (6-26)
2006-2007	29 (17-43)	3 (2-3)	32 (31-33)	0 (0-0)
2007-2008	20 (16-24)	21 (20-22)	0 (0-1)	10 (3-20)
2008-2009	30 (23-37)	2 (2-3)	19 (7-33)	6 (3-9)
2010-2011	24 (23-25)	30 (28-32)	1 (0-1)	14 (9-20)
2011-2012	47 (18-77)	0 (0-0)	16 (10-23)	1 (0-2)
2012-2013	23 (18-27)	14 (12-17)	7 (4-11)	17 (12-23)
2013-2014	16 (12-21)	9 (1-24)	10 (6-16)	2 (0-5)
2014-2015	27 (22-28)	4 (3-4)	21 (13-30)	9 (6-10)

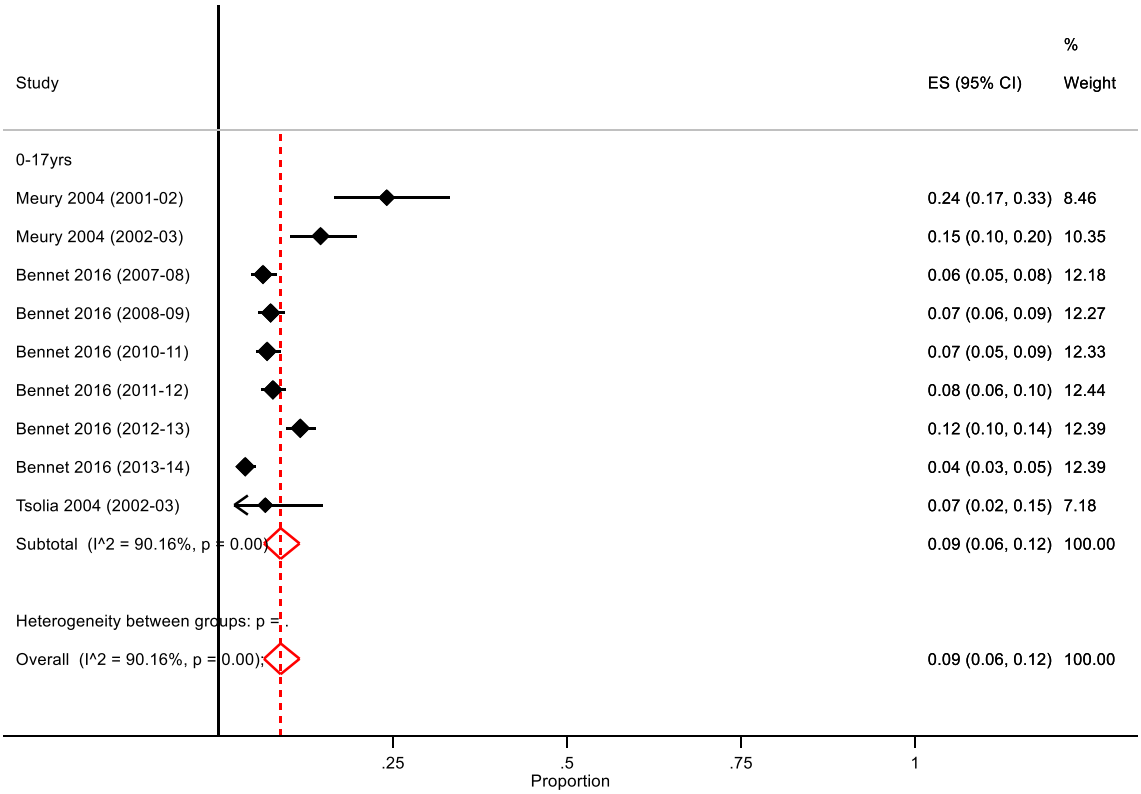
Supplemental Table 5: Proportion of confirmed influenza by type/subtype for influenza seasons between 2004-2005 and 2017-2018 (TESSy ILI/ARI data)

Season	Proportion laboratory-confirmed influenza % (95% CI)			
	Influenza A	Influenza A(H1N1)	Influenza A(H3N2)	Influenza B
2004-2005	24 (19-28)	2 (1-4)	15 (11-20)	7 (5-8)
2005-2006	8 (6-10)	1 (1-2)	3 (2-4)	15 (11-19)
2006-2007	30 (23-37)	1 (0-1)	18 (12-26)	1 (0-1)
2007-2008	20 (16-24)	13 (9-19)	0 (0-0)	10 (7-13)
2008-2009	26 (20-32)	1 (0-1)	15 (10-21)	6 (5-8)
2010-2011	21 (18-24)	16 (13-19)	1 (0-1)	13 (11-16)
2011-2012	23 (18-28)	0 (0-1)	19 (15-23)	3 (2-4)
2012-2013	20 (17-23)	10 (8-12)	5 (4-7)	17 (13-21)
2013-2014	21 (16-26)	8 (5-11)	10 (7-13)	1 (0-1)
2014-2015	23 (19-28)	4 (2-5)	15 (12-19)	11 (9-13)
2015-2016	22 (19-25)	17 (14-20)	1 (1-2)	12 (9-16)
2016-2017	32 (28-37)	0 (0-0)	27 (22-32)	3 (2-4)
2017-2018	12 (10-14)	6 (4-7)	3 (2-4)	25 (21-29)

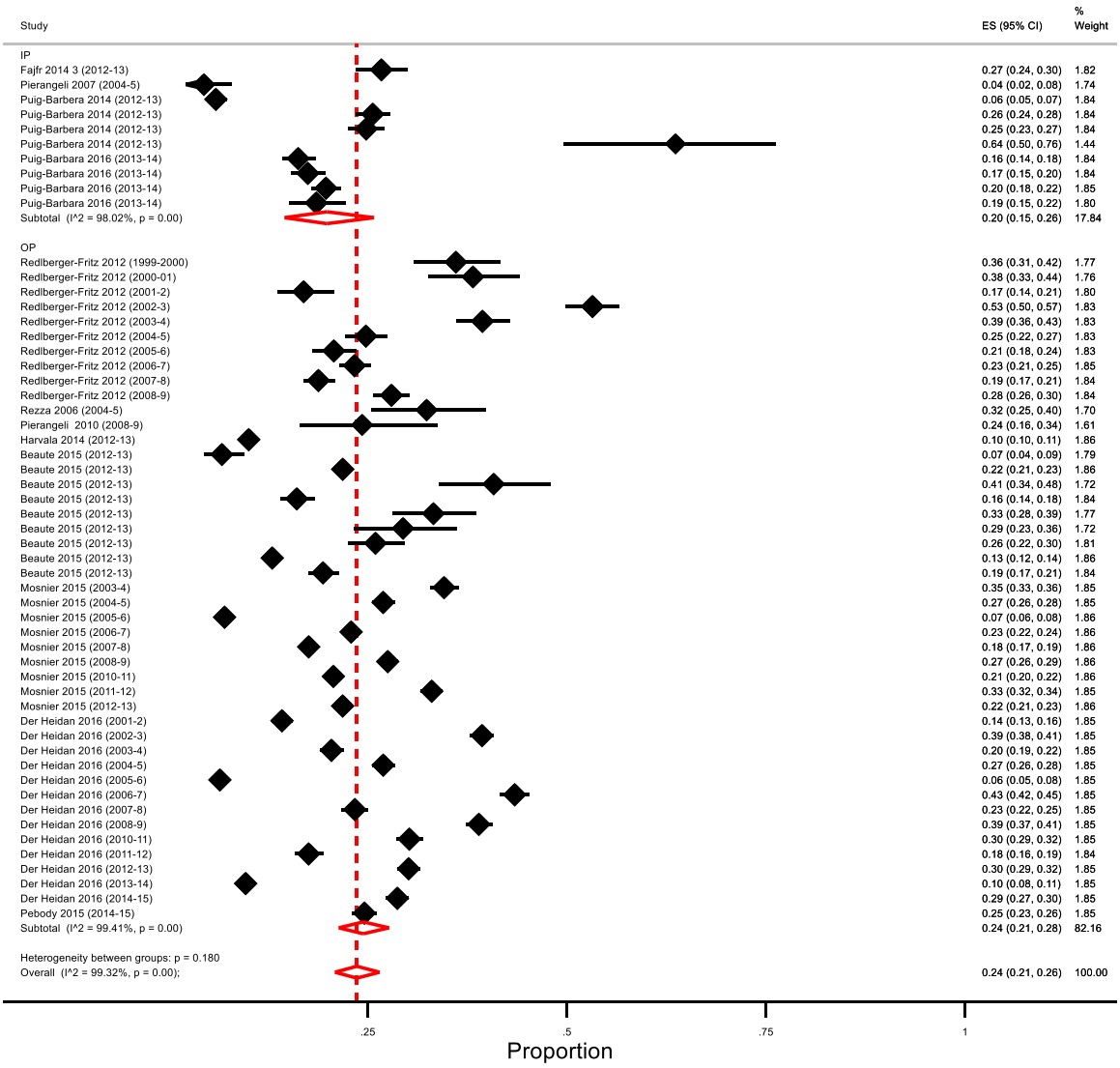
Supplemental Figure 1: Forest plot (studies from literature review): proportion of all influenza viruses by age groups in outpatients seeking care in Europe



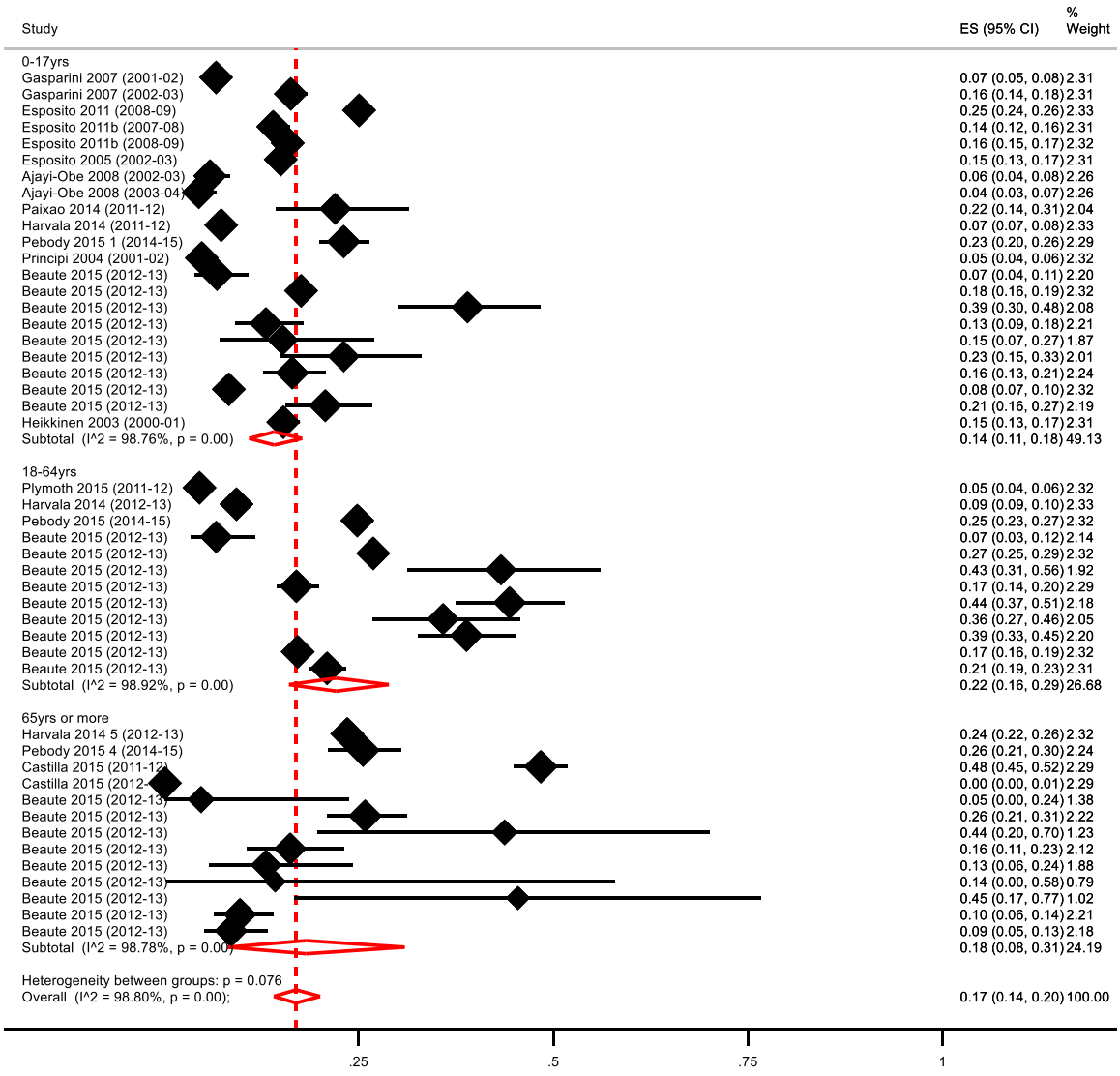
Supplemental Figure 2: Forest plot (studies from literature review): proportion of all influenza viruses by age groups in inpatients seeking care in Europe



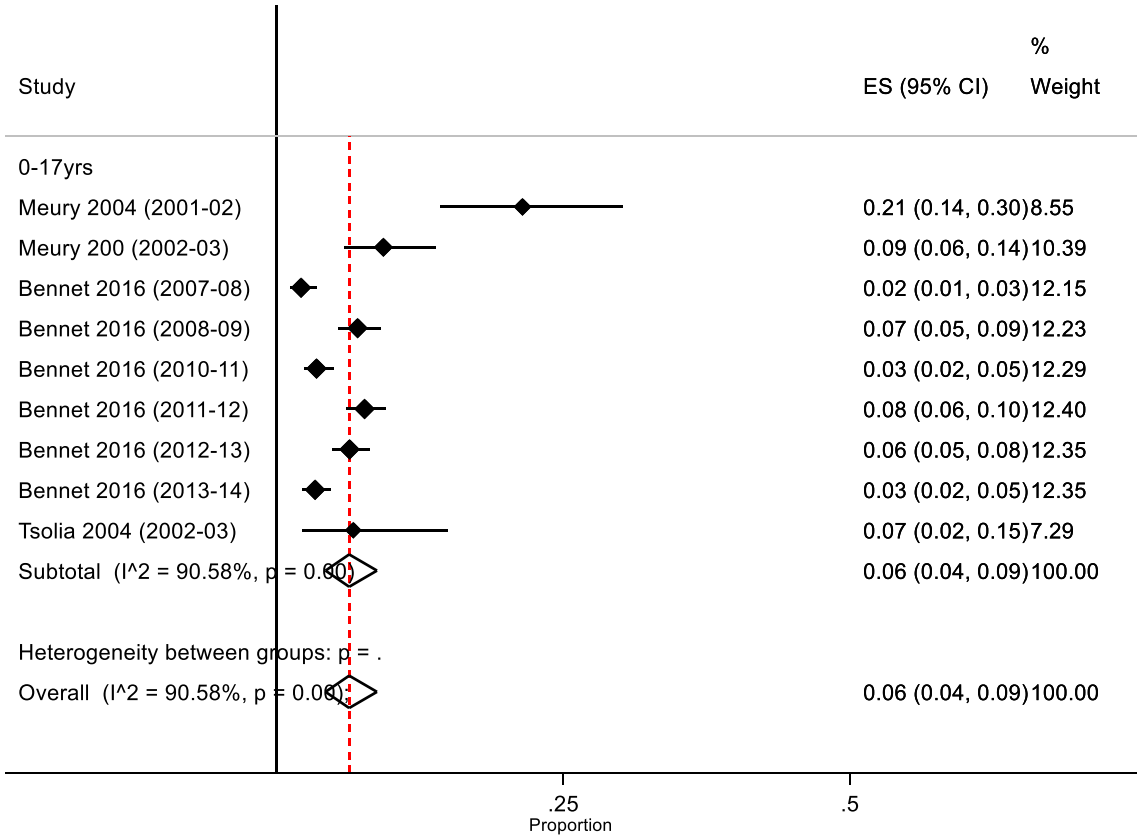
Supplemental Figure 3. Forest plot (studies from literature review): proportion of influenza A virus subgroup analysis by healthcare setting



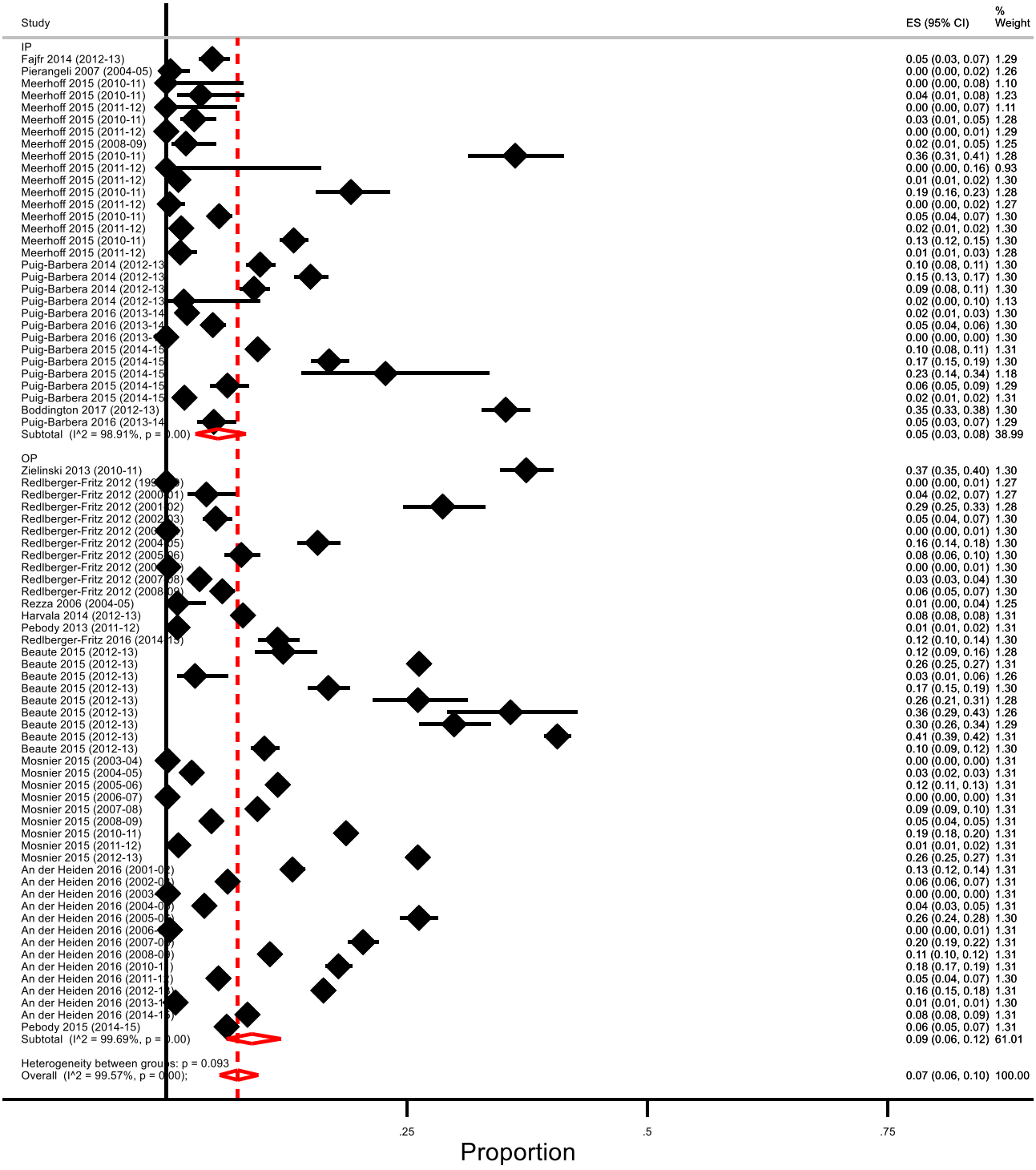
Supplemental Figure 4. Forest plot (studies from literature review): proportion of influenza A viruses by age groups in outpatients seeking care in Europe



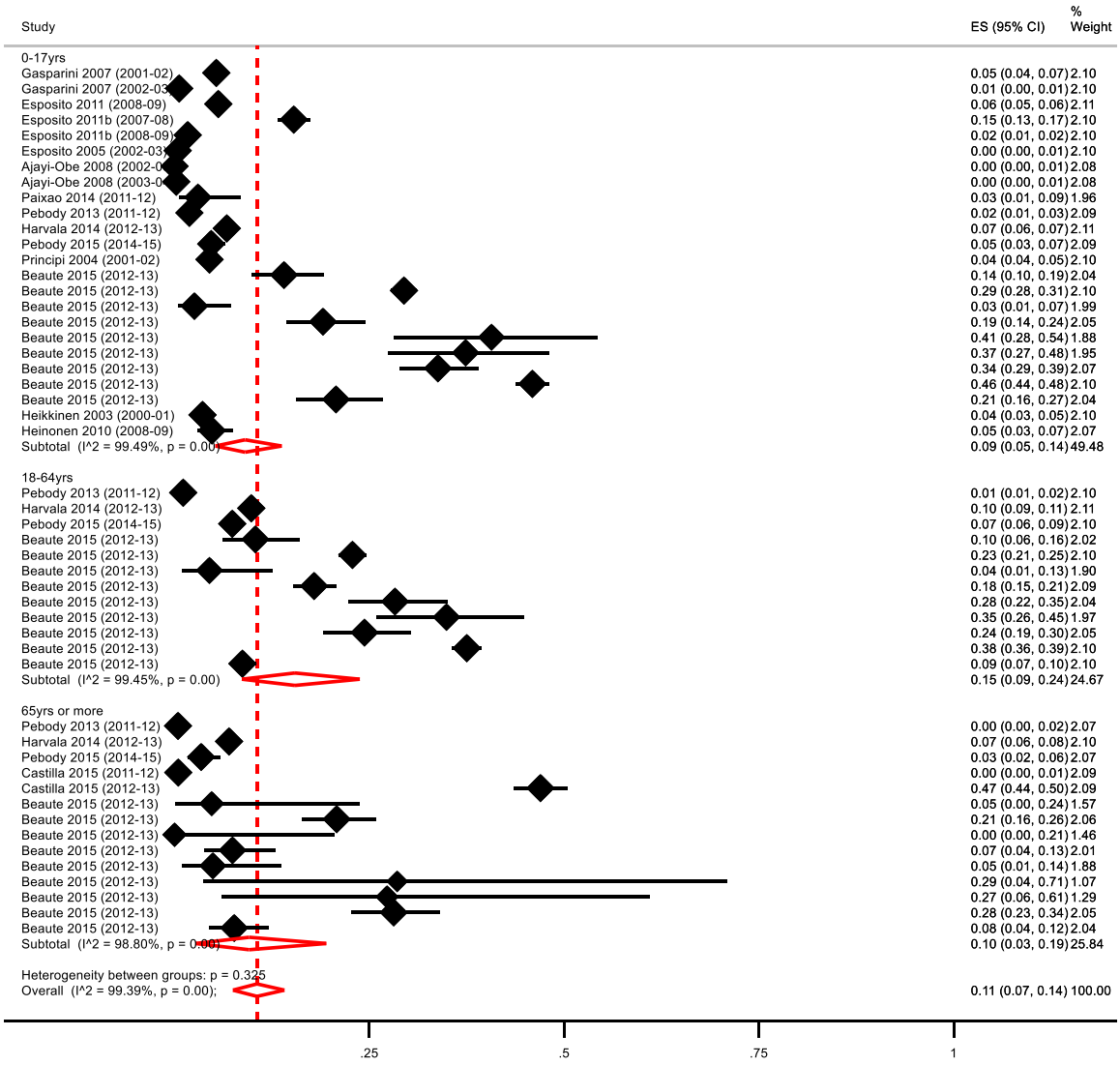
Supplemental Figure 5. Forest plot (studies from literature review): proportion of influenza A viruses by age groups in Inpatients seeking care in Europe



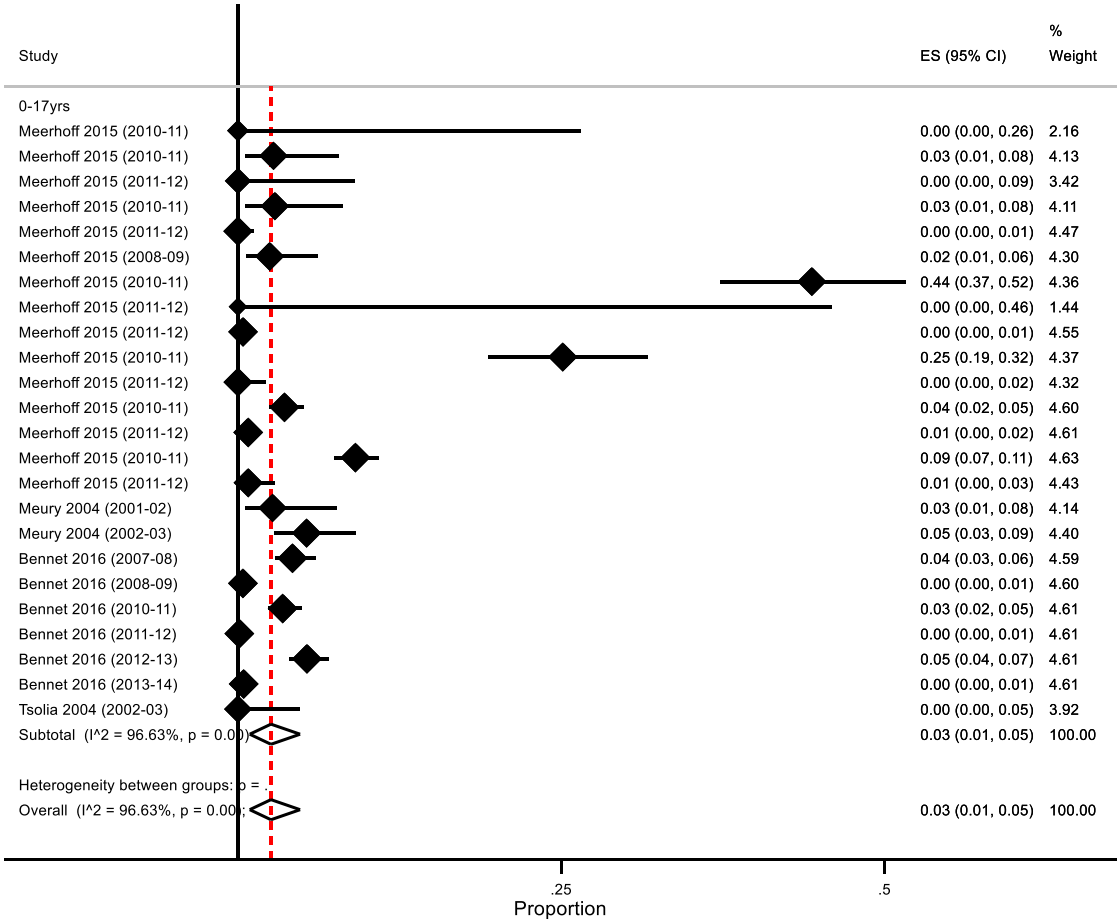
Supplemental Figure 6. Forest plot (studies from literature review): proportion of influenza B viruses subgroup analysis by healthcare setting in patients seeking care in Europe



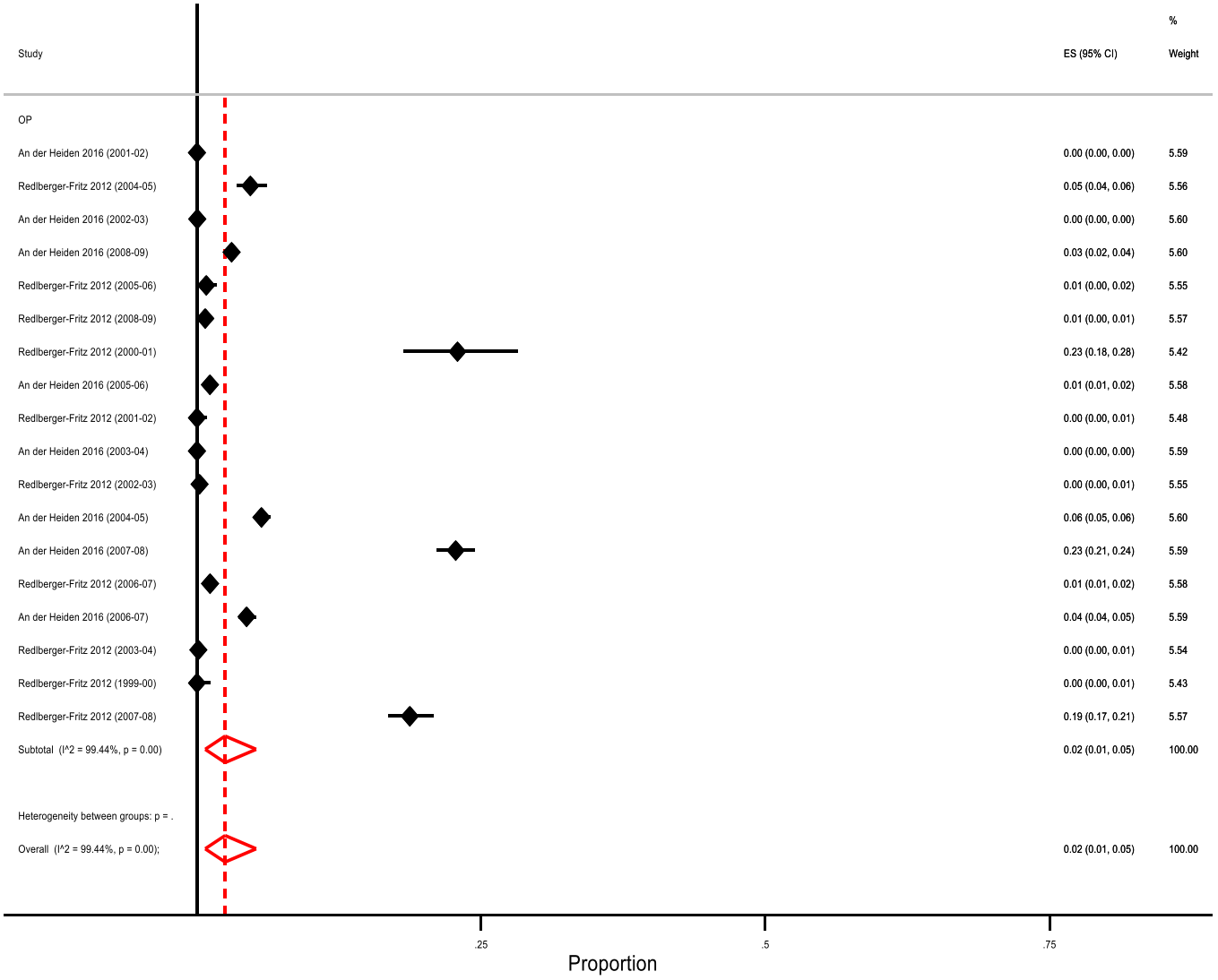
Supplemental Figure 7. Forest plot (studies from literature review): proportion of influenza B viruses by age groups in outpatients seeking care in Europe



Supplemental Figure 8. Forest plot (studies from literature review): proportion of influenza B viruses by age groups in Inpatients seeking care in Europe

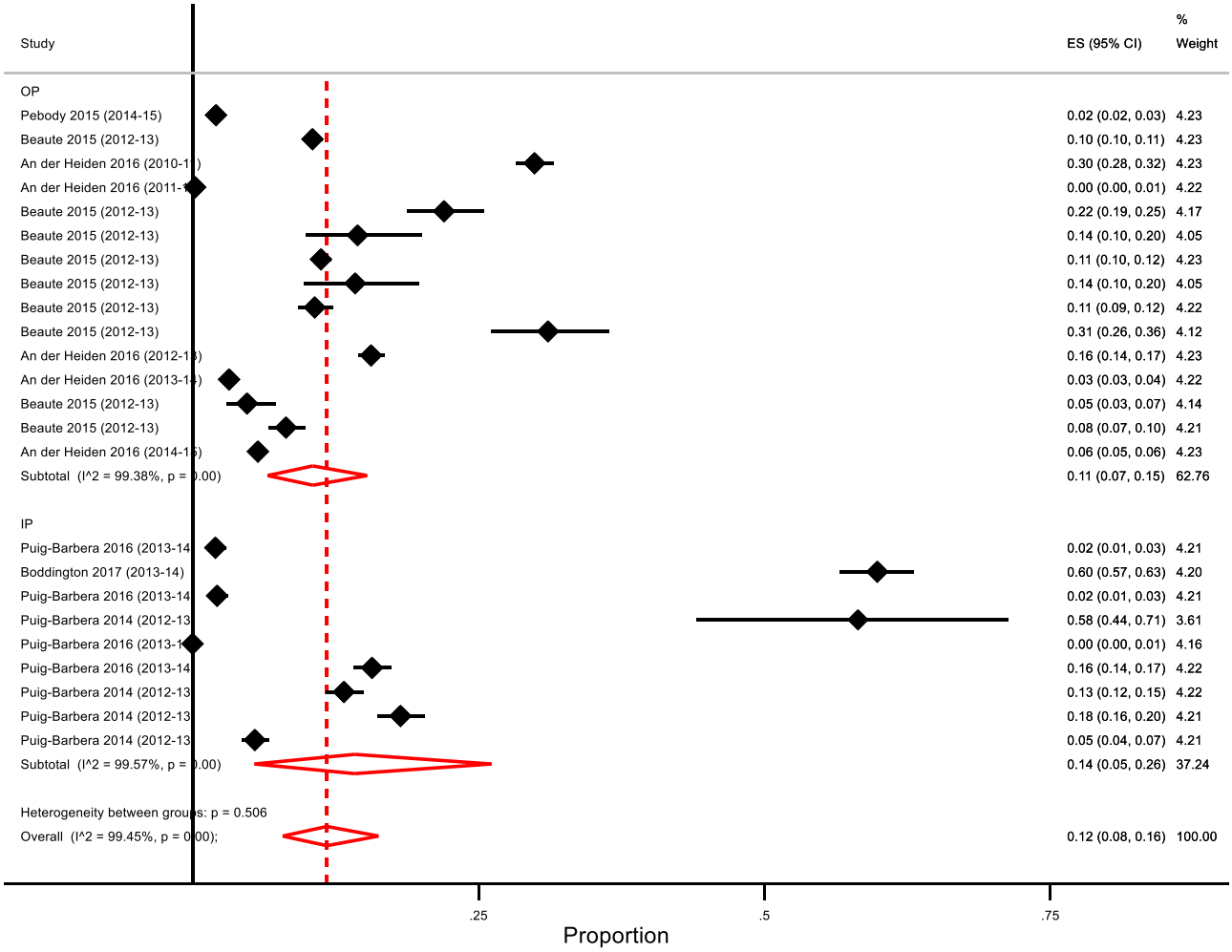


Supplemental Figure 9a. Forest plot (studies from literature review): proportion of pre-pandemic influenza A(H1N1) viruses subgroup analysis by healthcare setting in patients seeking care in Europe

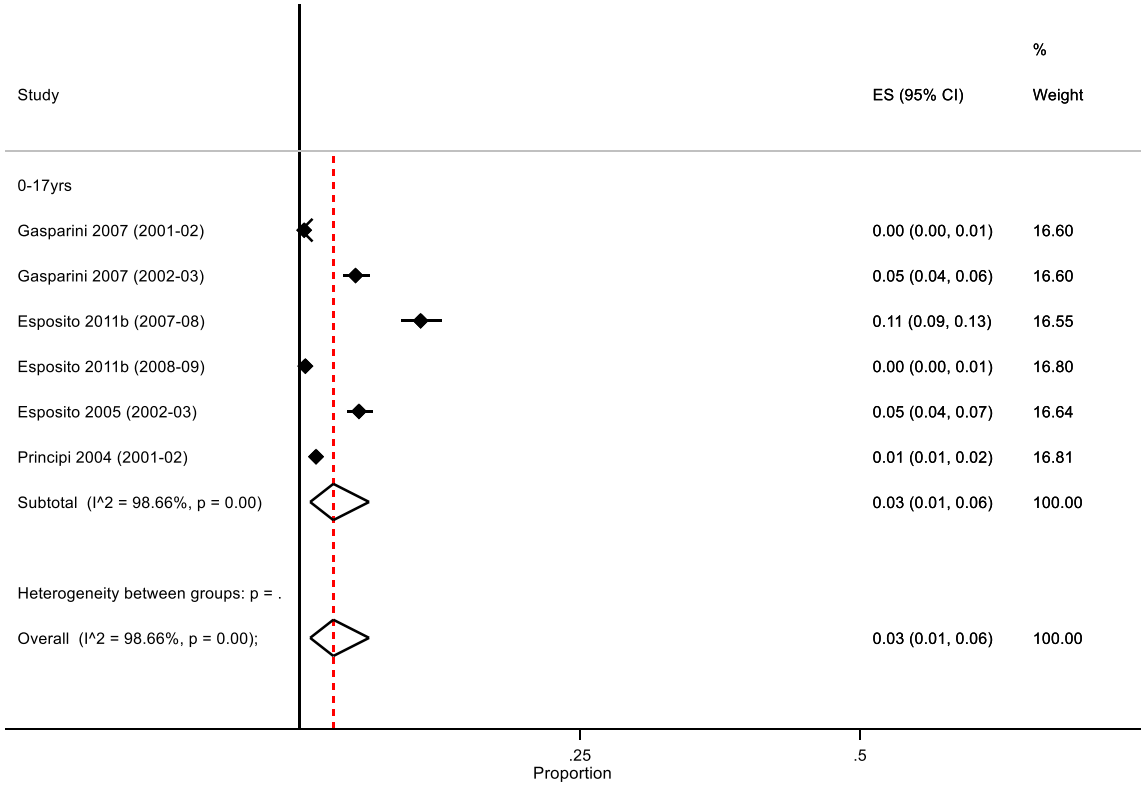


No studies of pre-pandemic H1N1 in in-patients.

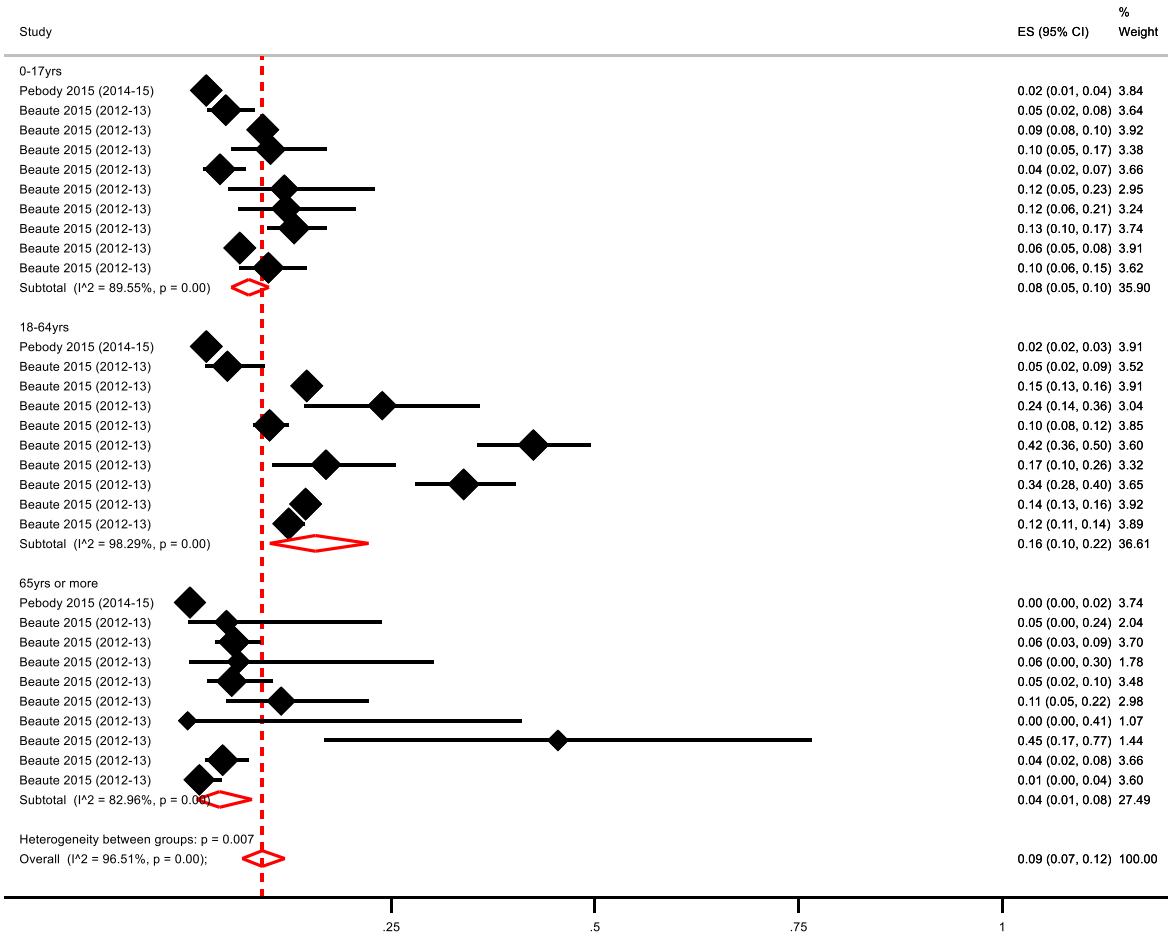
Supplemental Figure 9b. Forest plot (studies from literature review): proportion of post-pandemic influenza A(H1N1) viruses subgroup analysis by healthcare setting in patients seeking care in Europe



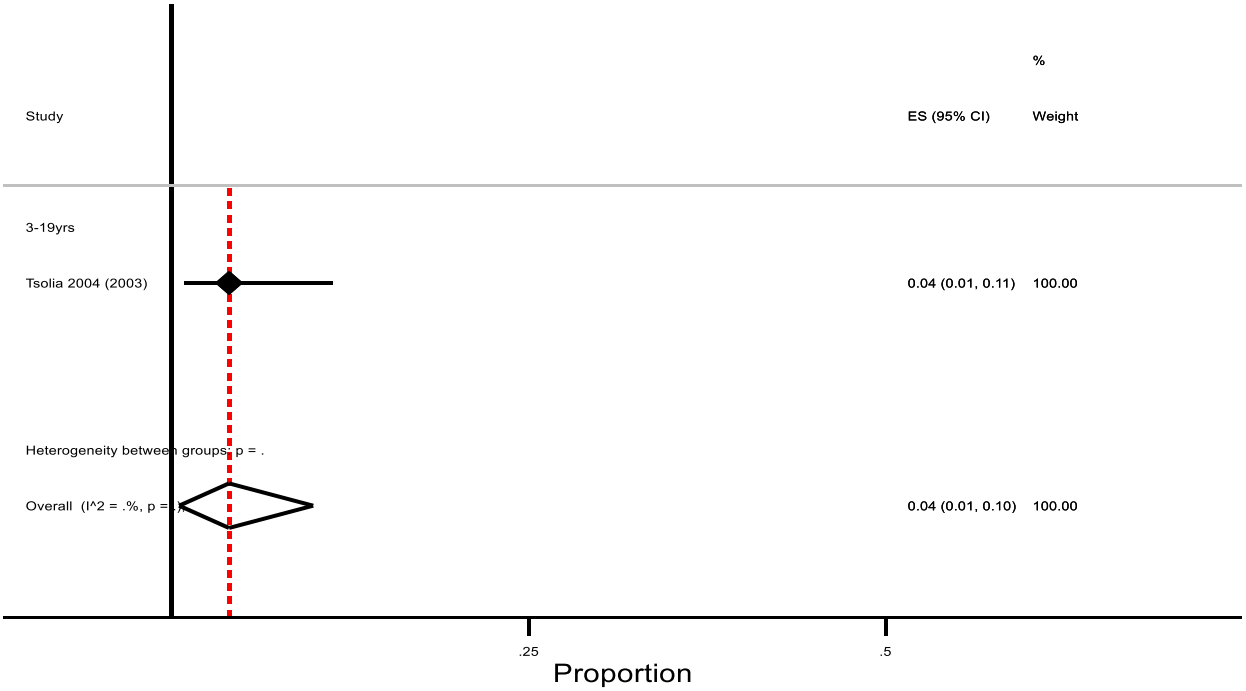
Supplemental Figure 10a. Forest plot (studies from literature review): proportion of pre-pandemic influenza A(H1N1) viruses by age groups in outpatients seeking care in Europe



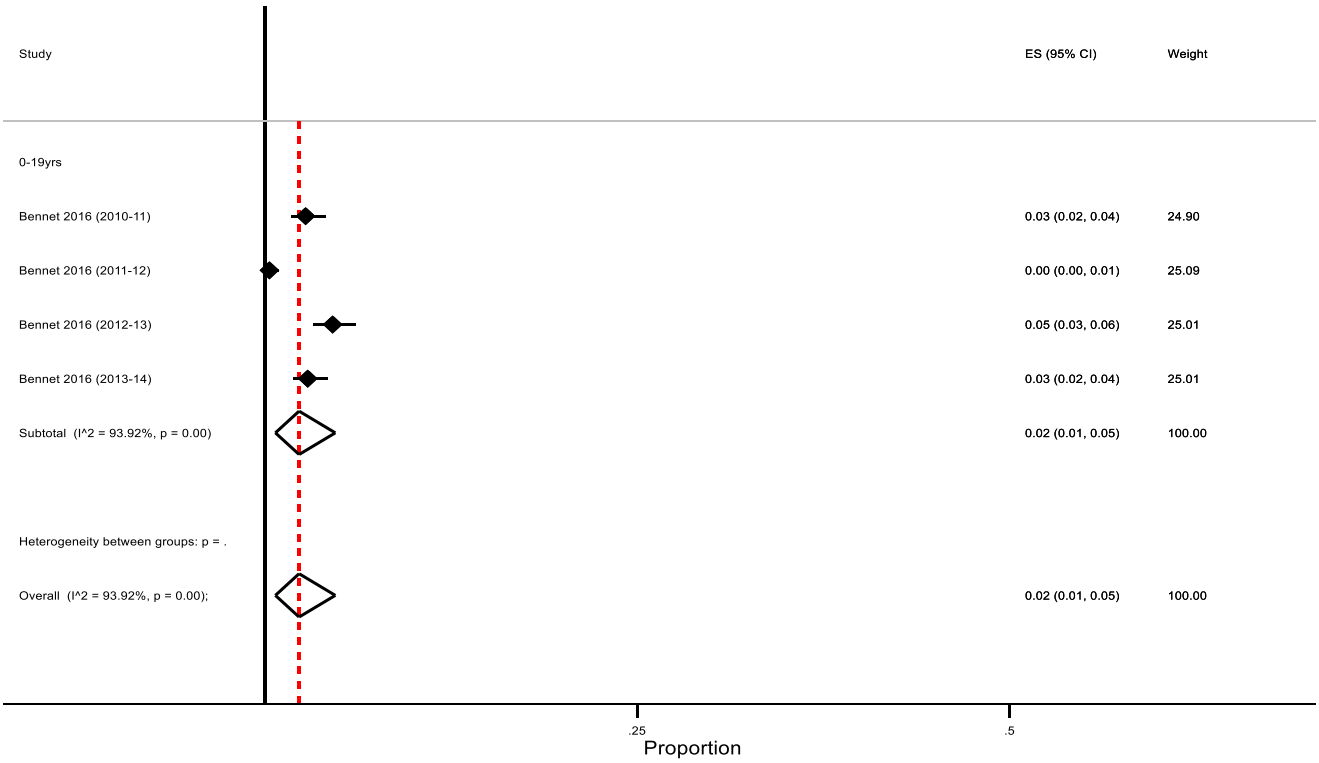
Supplemental Figure 10b. Forest plot (studies from literature review): proportion of post-pandemic influenza A(H1N1) viruses by age groups in out-patients seeking care in Europe



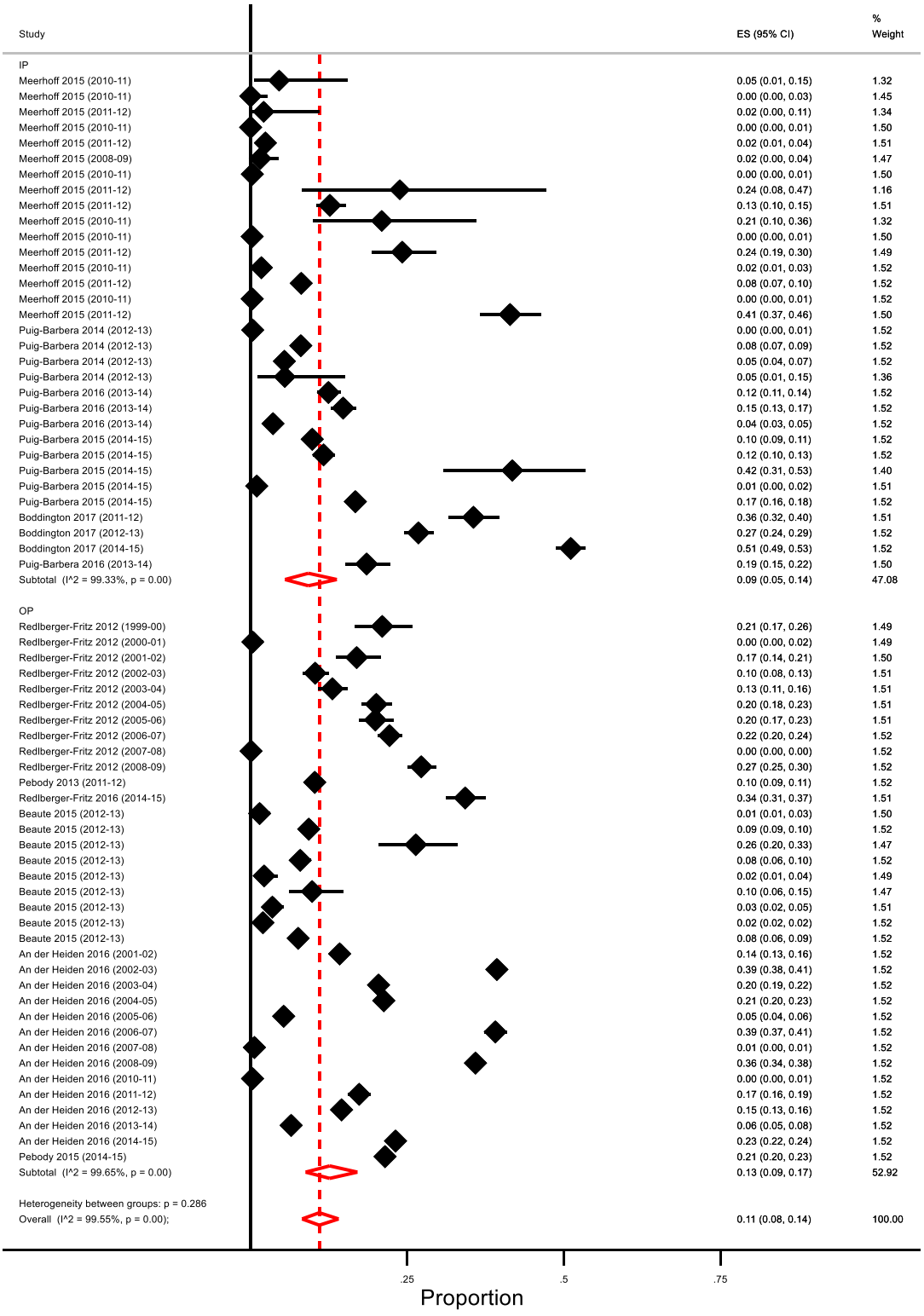
Supplemental Figure 11a. Forest plot (studies from literature review): proportion of pre-pandemic influenza A(H1N1) viruses by age groups in inpatients seeking care in Europe



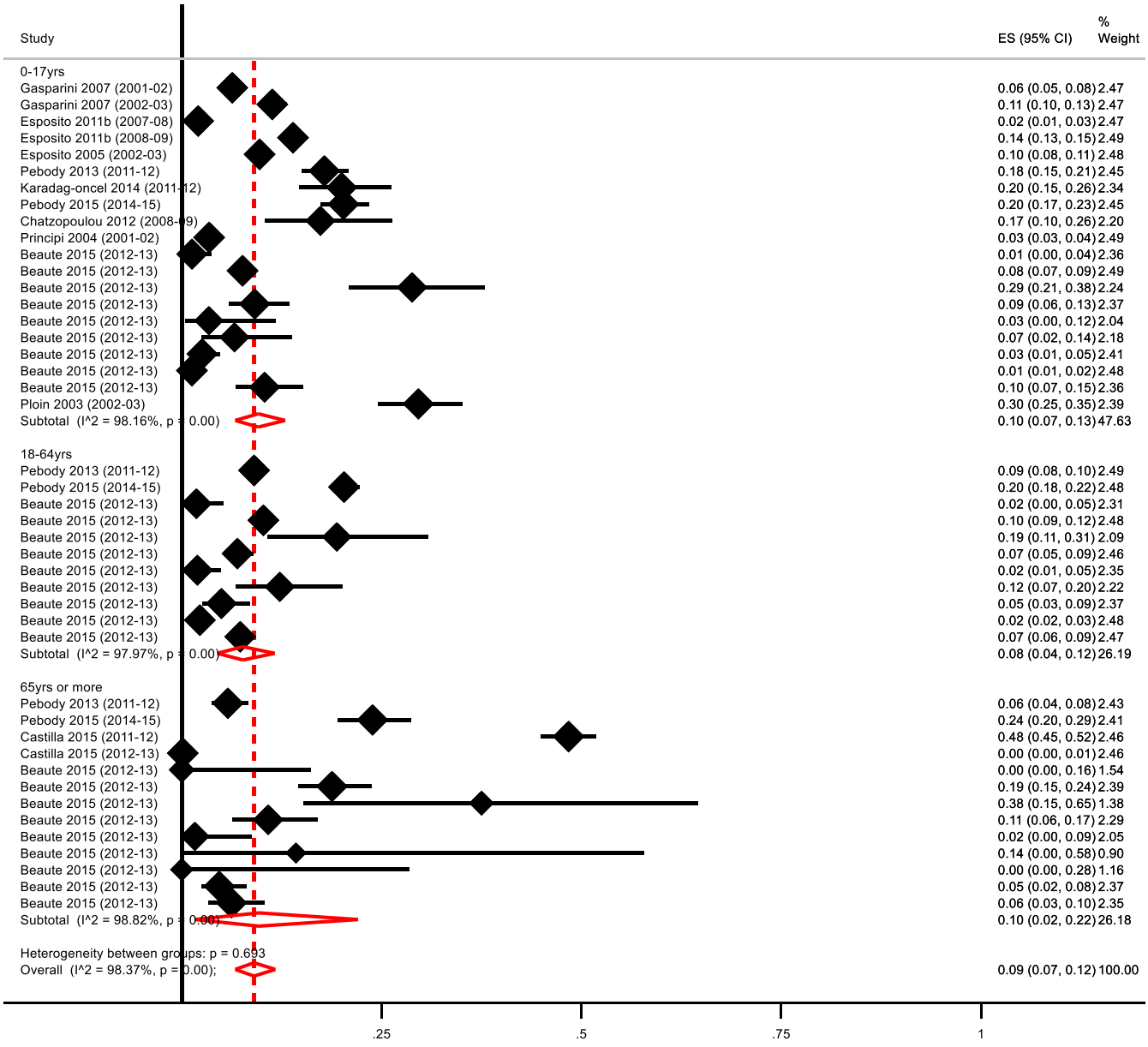
Supplemental Figure 11b. Forest plot (studies from literature review): proportion of post-pandemic influenza A(H1N1) viruses by age groups in inpatients seeking care in Europe



Supplemental Figure 12. Forest plot (studies from literature review): proportion of influenza A(H3N2) viruses subgroup analysis by healthcare setting in patients seeking care in Europe



Supplemental Figure 13. Forest plot (studies from literature review): proportion of Influenza A(H3N2) viruses by age groups in Outpatients seeking care in Europe



Supplemental Figure 14. Forest plot (studies from literature review): proportion of influenza A(H3N2) viruses by age groups in inpatients seeking care in Europe