Attachment 4: Included studies in individual sections

Medical publications taken into consideration

Table A4-1: Overview of study characteristics of included placebo-controlled LAIV studies

Study/ Publication(s)	Study period	Region	Target population	Age range	Blinded	Number of study participants	Study arms	Study quality
Studies reporting results on efficacy								
Belshe *et al.*(1998)[48]/ Belshe *et al.*(2000a)[52]/ Belshe *et al.* (2000b)[53]/ Longini *et al.* (2000)[54]/ Piedra *et al.* (2002)[55]	Year 1: Influenza season 1996/1997	USA	Healthy children	15 to 71 months	Yes	1,602	LAIV single dose LAIV dual dose Placebo	1+
	Year 2: Influenza season 1997/1998	USA	Healthy children	26 to 85 months	Yes	1,358	LAIV Placebo	1-
Bracco Neto *et al.* (2009)[49]	Year 1: Influenza season 2000	South Africa, South America	Healthy children	Six to 35 months	Yes	2,821	LAIV single dose LAIV dual dose Placebo 1 (including vaccine excipients) Placebo 2 (on sodium chloride base)	1+
	Year 2: Influenza season 2001	South Africa, South America	Healthy children	18 to 47 months	Yes	1,364	LAIV Placebo	1-
Forrest *et al.* (2008)[56]	Influenza season 2002	Asia (Phlippines, Thailand)	Healthy children	Six to 35 months	Yes	2,172	LAIV 10^5 FFU LAIV 10^6 FFU LAIV 10^7 FFU Placebo	1-
Lum *et al.* (2010)[57]	Influenza season 2002/2003	Europe, Asia, South America	Healthy children	Eleven to 23 months	Yes	1,150	LAIV (+MMR) Placebo (+MMR)	1+
Tam *et al.* (2007)[58]	Year 1: Influenza season 2000/2001	Asia	Healthy children	Twelve to 35 months	Yes	3,174	LAIV Placebo	1+
	Year 2: Influenza season 2001/2002	Asia	Healthy children	24 to 47 months	Yes	2,947	LAIV Placebo	1+

Study/ Publication(s)	Study period	Region	Target population	Age range	Blinded	Number of study participants	Study arms	Study quality
Vesikari *et al.* (2006a)[50]	Year 1: Influenza season 2000/2001	Europe, Israel	Healthy children	Six to 35 months	Yes	1,784	LAIV Placebo	1+
	Year 2: Influenza season 2001/2002	Europe, Israel	Healthy children	18 to 47 months	Yes	1,119	LAIV Placebo	1-
Studies not reporting results on efficacy, but only results on the tolerability/safety of LAIV								
Bergen *et al.* (2004)[59]	Oct to Dec 2000	USA	Healthy children and adolescents	One to 17 years	Yes	9,689	LAIV Placebo	1-
Breiman *et al.* (2009)[60]	Jan to May 2002	Bangladesh, Chile, Colombia, Malaysia, Peru, Philippines, Thailand	Healthy children	Six to 35 months	Yes (relevant study arms)	2,503	LAIV + OPV Placebo + OPV LAIV	1+
Halasa *et al.* (2011)[61]	Aug 2005 to Sep 2007 (outside of influenza seasons)	USA	Children with cancer	Five to 17 years	Yes	20	LAIV Placebo	1+
King *et al.* (2001)[62]	n.s.	USA	Children with and without HIV	One to 8 years	Yes	49	LAIV -> Placebo -> LAIV Placebo -> LAIV -> LAIV	1+
Nolan *et al.* (2008)[63]	2001; 2002 (outside of influenza season)	USA, Australia	Healthy children	Twelve to 15 months	Yes	1,245	MMR/VAR + Placebo -> LAIV -> LAIV MMR/VAR + LAIV -> LAIV -> Placebo LAIV -> LAIV -> MMR/VAR	1+
Redding *et al.* (2002)[64]	Autumn 1997	USA	Children and adolescents with asthma	Nine to 17 years	Yes	48	LAIV Placebo	1+
Vesikari *et al.* (2006b)[65]	Nov 1999	Finland	Healthy children	Nine to 36 months	Yes	197	LAIV Placebo	1+
Vesikari *et al.* (2008)[66]	Influenza season 2002/2003	Finland	Healthy children	Six to 23 weeks	Yes	120	LAIV Placebo	1+

Study/ Publication(s)	Study period	Region	Target population	Age range	Blinded	Number of study participants	Study arms	Study quality
Zangwill *et al.* (2001)[67]	Not stated	USA	Healthy children	Twelve to 36 months	Yes	500	LAIV (batch 1) LAIV (batch 2) LAIV (batch 3) LAIV (batch 4) Placebo	1+
FFU = fluorescent focus unit; LAIV = live-attenuated influenza vaccine; MMR=, Measles, mumps, rubella; OPV= oral polio vaccine; VAR= chickenpox (varicella) vaccine								

Table A4-2: Overview of study characteristics of included TIV-controlled LAIV studies

Study/ Publication(s)	Study period	Region	Target population	Age range	Blinded	Number of study participants	Study arms	Study quality
Studies reporting results on efficacy								
Ashkenazi *et al.* (2006)[16]	Influenza season 2002/2003	Europe, Israel	Children with repeated respiratory tract infections	Six to 71 months	No	2,187	LAIV TIV	1-
Belshe *et al.* (2007)[18]	Influenza season 2004/2005	Europe, Middle East, Asia, USA	Children without severe concomitant diseases	Six to 59 months	Yes	8,352	LAIV TIV	1+
Fleming *et al.* 2006)[15]	Influenza season 2002/2003	Europe, Israel	Children and adolescents with asthma	Six to 17 years	No	2,229	LAIV TIV	1-
Studies not reporting results on efficacy, but only results on the tolerability/safety of LAIV								
Hoft *et al.* (2011)[68]	Influenza seasons 2005/2006 and 2006/2007	USA	Healthy children	Six to 35 months	No	56	TIV -> TIV LAIV -> LAIV TIV -> LAIV LAIV -> TIV	1-
Levin *et al.* (2008)[69]	Sep to Nov 2004	USA	HIV-infected children and adolescents	Five to 17 years	No	243	LAIV TIV	1-
LAIV= live-attenuated influenza vaccine; TIV= trivalent inactivated vaccine								

Table A4-3: Overview of study characteristics of included LAIV studies with other comparators

Study Publication(s)	Study period	Region	Target population	Age range	Blinded	Number of study participants	Study arms	Study quality
Studies not reporting results on efficacy, but only results on the tolerability/safety of LAIV								
Block *et al.* (2007)[70]	2004/2005 (no reference to influenza season)	USA	Children and adults	Five to 49 years (report on sub-group five to eight years)	Yes	376 (age group five to eight years)	LAIV (frozen) LAIV (refrigerated)	1+
Block *et al.* (2012)[71]	March to May 2010	USA	Healthy children	Two to 17 years	Yes	2,305	Tetravalent LAIV LAIV (Yamagata) LAIV (Victoria)	1+
LAIV= live-attenuated influenza vaccine								

Epidemiological publications taken into consideration

Table A4-4: Epidemiological studies on effectiveness

Study/ Publication(s)	Study period	Region	Target population	Age range	Number of participants	Study arms	Study quality
Temple-Belton Working Group							
Gaglani *et al.* (2004)[72]	Influenza season 2000/2001	USA: Texas, Bell County, Temple-Belton area	Healthy children	18 months to 18 years	n =931 in the "Year 2–cumulative“ group n =2,281 in the "Year 3–cumulative“ group	LAIV-T versus no vaccination	2-
Halloran *et al.* (2003)[73]	Influenza season 2000/2001	USA: Texas, Bell County, Temple-Belton region	Healthy children	18 months to 18 years	Vaccinated 1999: n=931 2000: n=2,281 Not vaccinated: n =9,325	LAIV-T versus no vaccination	2-
Halloran *et al.* (2007)[74]	Influenza season 2003/2004	USA: Texas, Bell County, Temple-Belton region	Healthy children	Five to 18 years	n =1,706 in 2003 LAIV-T n=548 in 2003 TIV n=983 vaccinated in 1998–2001, but not 2002/2003 or 2003 n=3,166 never before vaccinated	LAIV-T versus TIV versus no vaccination	2-

Study/ Publication(s)	Study period	Region	Target population	Age range	Number of participants	Study arms	Study quality
Piedra *et al.* (2005a)[75]	Four influenza seasons 1997/1998 to 2000/2001 (1997/98 as baseline)	USA: Texas, Bell County, Temple-Belton region	Healthy children	18 months to 18 years	1998/1999: n=2,225 or n = 448 vaccinees 1999/2000: n=1,394 or n = 473 vaccinees 2000/2001: n=1,155 or n = 311 vaccinees	LAIV-T versus no vaccination	2-
Piedra *et al.* (2007)[76]	Influenza season 2003/2004	USA: Texas, Bell County, Temple-Belton region	Healthy children	Five to 18 years	n =4,961 with LAIV-T n =1,944 with IIV-T	LAIV-T or TIV versus no vaccination	2-
Other Working Groups							
King *et al.* (2005)[77]	Influenza season 2003/2004	USA: Maryland (exact location not specified)	Healthy school children and members of their households	≥ five years	One intervention school: n = 481 children vaccinated Two control schools: n = 565 and n=620 children not vaccinated	LAIV-T versus no vaccination	2-
King *et al.* (2006)[11]	Influenza season 2004/2005	USA: Maryland, Texas, Minnesota, Washington State	Healthy school children and members of their households	≥ five years	Eleven intervention schools: n=5,840 children vaccinated 17 control schools: n = 9,451 children not vaccinated	LAIV-T versus no vaccination	2-
Poehling *et al.* (2009)[78]	Influenza season 2006/2007	USA: Tennessee, Knox County, Davidson County	Children with ARI	<13 years	Knox County: n=443 vaccinated Davidson County: n=447 not vaccinated	LAIV-T versus no vaccination	2-
LAIV= live-attenuated influenza vaccine, -T= trivalent, TIV= trivalent inactivated influenza vaccine							

Table A4-5: Epidemiological studies on safety

Study/ Publication(s)	Study period	Region	Target population	Age range	Number of participants	Study arms	Study quality
Temple-Belton Working Group							
Gaglani *et al.* (2008)[79]	Five influenza seasons 1997/1998 to 2001/02 (1997/1998 as baseline)	USA: Texas, Bell County, Temple-Belton area	Healthy children	≥18 months	1998/1999: n=2,225 1999/2000: n=2,524 2000/2001: n=2,351 2001/2002: n=1,571 total: n=8,671	LAIV-T versus reference period	2-
Piedra *et al.* (2005b)[80]	Four influenza seasons from 1998/1999 to 2001/2002	USA: Texas, Bell County, Temple-Belton region	Healthy children	1.5 to 18 years	1998/1999: n=3,406 1999/2000: n=3,748 2000/2001: n=3,609 2001/2001: n=2,908	LAIV-T versus reference period	2-
Other Working Groups							
Baxter *et al.* (2012)[81]	Five influenza seasons from2003/2004 to 2007/2008	USA: Colorado, North California, Hawaii	Healthy children	Five to 17 years	n =43,702 persons with a total of n=53,369 vaccination doses	LAIV-T versus TIV versus no vaccination	2-
Mears *et al.* (2009)[82]	Influenza season 2006/2007	USA: Illinois, Chicago	Healthy children	Eleven to 17 years	n =127	LAIV-T	2-
Tennis *et al.* (2011)[83]	Two influenza seasons from 2007/2008 to 2008/2009	USA (without regional restrictions)	Children with asthma, wheezing or immune deficiency	24 to 59 months	(Not unambiguous)	LAIV-T versus TIV	2-
Tennis *et al.* (2012)[84]	Influenza season 2009/2010	USA (without regional restrictions)	Children with asthma, wheezing or immune deficiency	24 to 59 months	(Not unambiguous)	LAIV-T versus TIV	2-

Study/ Publication(s)	Study period	Region	Target population	Age range	Number of participants	Study arms	Study quality
Toback *et al.* (2013)[85]	Three influenza seasons from 2007/2008 to 2009/2010	USA: North California	Healthy children	Two to five years	Total n= 28,226 children 24-59 months, of which n = 8,126 children 24 to 35 months , n=20,100 children 36 to 59 months Received 33,443 doses	LAIV-T versus TIV versus no vaccination	2-
LAIV= live-attenuated influenza vaccine, -T= trivalent, TIV= trivalent inactivated influenza vaccine							

Table A4-6: Studies on effectiveness and safety/systematic reviews

Study/ Publication(s)	Study period	Region	Target population	Age range	Number of participants	Study arms	Study quality
Jefferson *et al.* (2012)[86]	In accordance with the included studies	Global	Healthy children	<16 years	In accordance with the included studies	In accordance with the included studies	-*
*No assessment presented, as the quality assessment would be based on the only relevant primary study (King *et al.* 2006[11]) included by Jefferson *et al.* 2012.							

Health-economic studies taken into consideration

Table A4-7: Object and methodological framework of included economic studies

Publication	Study object	Country	Study type	Form of health-economic evaluation	Consideration of indirect protective effects	Time horizon/ *Follow-up*	Perspective	Discounting (costs/effects)
Beutels *et al.* (2013a/2013b)[44;45]	Analysis of the cost effectiveness of vaccinating children (different age groups) with TIV or LAIV compared to the current situation (TIV with low vaccination coverage)	Belgium	Modelling (dynamic)	CEA; CUA	Yes	Ten years	Payer	3%/1,5%
Chen and Liao (2013)[20]	Analysis of the cost-effectiveness of vaccinating children against seasonal influenza compared to other interventions in a school setting	Taiwan	Modelling (dynamic)	CC	Yes	Not stated (probably one year)	Not stated	Not stated

Publication	Study object	Country	Study type	Form of health-economic evaluation	Consideration of indirect protective effects	Time horizon/ *Follow-up*	Perspective	Discounting (costs/effects)
Cohen and Nettleman (2000)[21]	Analysis of the cost-effectiveness of a routine vaccination of children (between six months and five years) with TIV in two settings compared to no vaccination	USA	Modelling	CC	Partially	Not stated	Society	Not stated
Dayan *et al.* (2001)[22]	Analysis of the cost-effectiveness of a vaccination of high-risk children (between six months and 15 years) compared to no vaccination	Argentina	Modelling	CC	No	One year	Society	Discounting not required
Esposito *et al.* (2006)[23]	Analysis of the cost-effectiveness of a vaccination of healthy children (between two and five years) compared to no vaccination	Italy	RCT	CC	Partially	Influenza season 2002/2003	Society	Discounting not required
Fitzner *et al.* (2001)[24]	Analysis of the cost-effectiveness of a vaccination of children (between one and 15 years) compared to no vaccination	Hong Kong	Modelling	CEA	No	One year	Individual; society	Discounting not required
Giglio *et al.* (2012)[25]	Analysis of the cost-effectiveness of a publicly funded vaccination of children (various age groups) compared to a situation with low vaccination coverage	Argentina	Modelling (dynamic)	CUA	Yes	Not stated	Payer	Not stated
Hall and Katz (2005)[26]	Analysis of hospital admissions treatment costs saved through the vaccination of children (between six and 23 months)	USA	Analysis of hospital data, modelling	CC	No	One year	Not stated	Discounting not required

Publication	Study object	Country	Study type	Form of health-economic evaluation	Consideration of indirect protective effects	Time horizon/ *Follow-up*	Perspective	Discounting (costs/effects)
Hibbert *et al.* (2007)[27]	Analysis of the cost-effectiveness of a vaccination of children (between six and 36 months) in day-care nurseries with LAIV compared to no vaccination	USA	Modelling	CC	Partially	Two influenza seasons (separate calculation)	Society	Discounting not required
Lee *et al.* (2012)[28]	Analysis of the cost-effectiveness of a general vaccination (providing several years of protection) of children (between two and 18 years) compared to the standard annual vaccination	USA	Modelling	CC; CUA	No	Life-time	Society	3%/3%
Luce *et al.* (2001)[29]	Analysis of the cost-effectiveness of a vaccination of healthy children with LAIV compared to no vaccination	USA	RCT, modelling	CEA	Partially	Influenza seasons 1996/1997 and 1997/1998	Payer; society	3%/3%
Luce *et al.* (2008)[46]	Analysis of the cost-effectiveness of a vaccination of children (between 24 and 59 months) with LAIV compared to vaccination with TIV	USA	Modelling	CC	No	One influenza season	Society	Discounting not required
Marchetti *et al.* (2007)[30]	Analysis of the cost-effectiveness of a vaccination of healthy children (between six and 60 months) with TIV (vriosomal and adjuvanted) compared to an exclusive vaccination of high-risk children	Italy	Modelling	CUA	Partially	Five years	Payer; society	3%/3%

Publication	Study object	Country	Study type	Form of health-economic evaluation	Consideration of indirect protective effects	Time horizon/ *Follow-up*	Perspective	Discounting (costs/effects)
Meltzer *et al.* (2005)[31]	Analysis of the cost-effectiveness of a vaccination of children (various age groups) compared to a situation without vaccination	USA	Modelling	CC	No	One year	Society	3% (production losses due to premature mortality)
Navas *et al.* (2007)[32]	Analysis of the cost-effectiveness of a vaccination of children (between three and 14 years) compared to no routine vaccination	Spain (Catalonia)	Modelling	CC; CEA; CUA	No	Six months	Payer; society	5% (production losses due to premature mortality)
Newall *et al.* (2013)[33]	Analysis of the cost-effectiveness of a vaccination of children (between five and 17 years) compared to a situation of low vaccination coverage in children	Australia	Modelling (dynamic)	CC; CEA	Yes	One year	Payer; society	5% (QALYs gained through the prevention of premature mortality)
Pitman *et al.* (2013)[34]	Analysis of the cost-effectiveness of a vaccination of children (two to four years; two to ten years; two to 18 years) with LAIV or TIV compared to an exclusive vaccination of persons at risk	England and Wales	Modelling (dynamic)	CUA	Yes	200 years	Payer	3.5%/3.5%
Prosser *et al.* (2006)[35]	Analysis of the cost-effectiveness of a vaccination of children (6-23 months; 2 years; 3-4 years; 5-11 years; 12-17 years) with LAIV or TIV compared to no vaccination	USA	Modelling	CUA/CEA	No	One year	Not stated	Discounting not required

Publication	Study object	Country	Study type	Form of health-economic evaluation	Consideration of indirect protective effects	Time horizon/ *Follow-up*	Perspective	Discounting (costs/effects)
Prosser *et al.* (2010)[47]	Analysis of the cost-effectiveness of a vaccination of children (six to 23 months; two years; three to four years) with LAIV or TIV compared to no vaccination under consideration of adverse events	USA	Modelling	CUA	No	One year	Society	3% (long-term effects of influenza and vaccination)
Salleras *et al.* (2009)[36]	Analysis of the cost-effectiveness of a vaccination of healthy children (between three and 14 years) compared to no vaccination	Spain (Catalonia)	Modelling	CC	No	Six months	Family	Discounting not required
Salo *et al.* (2006)[37]	Analysis of the cost-effectiveness of a vaccination of healthy children (between six months and 13 years) compared to no vaccination	Finland	Modelling	CC	No	One influenza season	Payer; society	Discounting not required
Schmier *et al.* (2008)[38]	Analysis of the cost-effectiveness of a school-based vaccination programme compared to a situation without school-base vaccination programme	USA	Modelling	CC	Partially	One influenza season	Society	Discounting not required
Skowronski *et al.* (2006)[39]	Analysis of the cost-effectiveness of a vaccination of children (between six and 23 months) compared to no vaccination	Canada	Modelling	CEA	Partially	One influenza season	Payer; society	3% (LYG)

Publication	Study object	Country	Study type	Form of health-economic evaluation	Consideration of indirect protective effects	Time horizon/ *Follow-up*	Perspective	Discounting (costs/effects)
Tarride *et al.* (2012)[40]	Analysis of the cost-effectiveness of a vaccination of children (between two and 17 years) with LAIV compared to vaccination with TIV	Canada	Modelling	CC; CUA	No (partially in sensitivity analyses)	One year	Payer; society	Discounting not required
Turner *et al.* (2003)[41]	Analysis of the cost-effectiveness of a vaccination of children (≤ twelve years) compared to no vaccination	UK	Modelling	CUA	No	Not stated	Payer	Discounting (probably) not required
Weycker *et al.* (2005)[42]	Analysis of the cost-effectiveness of a vaccination of children (between six months and 18 years) compared to a situation of low vaccination coverage in children	USA	Modelling (dynamic)	CC (without vaccination costs)	Yes	Not stated	Not explicitly stated (society)	3%/-
Yoo *et al.* (2013)[43]	Analysis of the cost-effectiveness of a school-based vaccination programme compared to a situation without school-base vaccination programme	USA	RCT, modelling	CC; CEA	Partially	Influenza season 2009/2010	Society	Discounting not required

CC= Cost Comparison; CEA= Cost-Effectiveness Analysis; CUA= Cost-Utility Analysis; LAIV= live-attenuated influenza vaccine; LYG= Life Year Gained, QALY= quality-adjusted life year; RCT= randomised controlled trial; TIV= trivalent inactivated influenza vaccine

Table A4-8: Data on analysed vaccination programmes

Publication	Vaccination	Target age group	Risk status	Efficacy and endpoint (for models)	Vaccination coverage (for models)	Cost of vaccination per dose
Beutels *et al.* (2013a/2013b)[44;45]	TIV and LAIV	Various age groups between six months and 17 years	Not considered	75% for one dose of LAIV; 81% for two doses of LAIV; influenza	20 to 90%	EUR 35.13 (including administrative costs)
Chen and Liao (2013)[20]	TIV	Four to 12 years (teaching staff between 25 and 24 years)	Not considered	70% (children); 62% (adults); 50% (elderly); endpoint not clearly stated	Not stated	USD 18.75 (including administrative costs)
Cohen and Nettleman (2000)[21]	TIV (LAIV in sensitivity analyses)	Six months to five years	Not considered	83% for TIV; 89% for LAIV; symptomatic infections	Not stated	USD 10.00
Dayan *et al.* (2001)[22]	Not stated	High-risk children from six months to 15 years	Model refers exclusively to high-risk children	70%	100%	USD 10.00
Esposito *et al.* (2006)[23]	TIV, virosomal	Two to five years	Not considered	No model	No model	EUR 19.38 (including administrative costs)
Fitzner *et al.* (2001)[24]	TIV	One to 15 years	Not considered	60%; ILI	60%	HKD 30 to 45
Giglio *et al.* (2012)[25]	Not stated	Six to 23 months; six to 36 months; six months to five years	Division into high- and low-risk children and adults	39% (children); ILI	50%	USD 6.29 to 10.19 (age-specific)
Hall and Katz (2005)[26]	Not stated	Six to 23 months	Division into high- and low-risk children	65%; endpoint not clearly stated	Information not required because the number of children is calculated who need to be vaccinated in order to avoid all hospitalisations within the study population.	USD 35 (including administrative costs)

Publication	Vaccination	Target age group	Risk status	Efficacy and endpoint (for models)	Vaccination coverage (for models)	Cost of vaccination per dose
Hibbert *et al.* (2007)[27]	LAIV	Six to 36 months	Not considered	83.8% (season 1) and 85.3% (season 2); symptomatic influenza infection	Not explicitly stated (100%)	USD 29.89 (including administrative costs)
Lee *et al.* (2012)[28]	Hypothetical universal vaccination (with several years of protection)	Two to 18 years	Not considered	50 to 75% (universal vaccination); 45% (annual standard vaccination); endpoint not clearly stated	Not stated	USD 100 to 200 for the universal vaccination and USD 20 for the annual standard vaccination
Luce *et al.* (2001)[29]	LAIV	15 to 71 months	Not considered	No model	No model	USD 20 (including administrative costs)
Luce *et al.* (2008)[46]	TIV and LAIV	24 to 59 months	Not considered	54.5% relative risk reduction of LAIV in comparison to TIV; uncomplicated influenza (culture-confirmed ILI)	Not stated	USD 27.85 for LAIV and USD 21.10 for TIV (including administrative costs)
Marchetti *et al.* (2007)[30]	TIV, virosomal and adjuvanted	Six to 24 months; six to 24 months	Vaccination of high-risk children in the comparison group	25.5% (6-24 months); 48% (25 to 60 months); ILI	30%	EUR 14.02 (including administrative costs)
Meltzer *et al.* (2005)[31]	Not stated	Six to 23 months; six to 59 months; five to 14 years	0%; 10%; 100% (ratio of children of high-risk status)	69% (mean of probability distribution used)	Not stated	USD 30; USD 60 (including administrative costs)
Navas *et al.* (2007)[32]	TIV, virosomal	Three to 14 years	Not considered	58.6%; acute febrile respiratory episode	Not explicitly stated (probably 100%)	EUR 9.35 (including administrative costs)
Newall *et al.* (2013)[33]	TIV	Five to 17 years	Not considered	60% (five to 64 years); 30% (65+ years); 40% (children under five years of age)	60%	AUD 20.60 (including administrative costs for a school-based vaccination programme)

Publication	Vaccination	Target age group	Risk status	Efficacy and endpoint (for models)	Vaccination coverage (for models)	Cost of vaccination per dose
Pitman *et al.* (2013)[34]	LAIV and TIV	Two to four; two to ten; two to 18 years	Vaccination of high-risk children in the comparison group	80% (LAIV); 60% (TIV)	50%	GBP 38.60 (including administrative costs)
Prosser *et al.* (2006)[35]	LAIV and TIV	Six to 23 months; two years; three to four years; five to eleven years; twelve to 17 years	Analyses of children with or without high-risk status	83.8% (LAIV); 69% (TIV); symptomatic influenza infection	Not stated	USD 31.86-34.56 for TIV and USD 37.89 for LAIV (including administrative costs)
Prosser *et al.* (2010)[47]	LAIV and TIV	Six to 23 months; two years; three to four years	Model refers exclusively to low-risk children	83.8% (LAIV); 69% (TIV); symptomatic influenza infection	Not stated	USD 41.52-42.32 for TIV and USD 45.90 for LAIV (including administrative costs)
Salleras *et al.* (2009)[36]	TIV, virosomal	Three to 14 years	Model refers exclusively to healthy children	58.6%; acute febrile respiratory episode	Not explicitly stated (probably 100%)	EUR 18.73 (including administrative costs)
Salo *et al.* (2006)[37]	TIV	Six months to 13 years	Model refers exclusively to healthy children	80%; influenza	Not explicitly stated (probably 100%)	EUR 5.38 (including administrative costs)
Schmier *et al.* (2008)[38]	LAIV	School children; no explicit age stated	Not considered	Intervention group 17% of households with one child with ILI; control group: 26% of households with one child with ILI; main focus on the assessment of resource consumption per household	47% in the intervention group; 2% in the control group	USD 20.70 (including administrative costs if administered as part of the school vaccination programme)
Skowronski *et al.* (2006)[39]	TIV	Six to 23 months	5% of children have pre-existing condition	66%; influenza infection	100%	CAD 15 (including administrative costs)
Tarride *et al.* (2012)[40]	LAIV and TIV	Two to 17 years	Not considered	Probability of influenza with LAIV: 4.9%; probability of influenza with TIV: 10.5%	Not stated	CAD 17.59 for LAIV and CAD 13.18 for TIV (including administrative costs)

Publication	Vaccination	Target age group	Risk status	Efficacy and endpoint (for models)	Vaccination coverage (for models)	Cost of vaccination per dose
Turner *et al.* (2003)[41]	Not stated	≤ twelve years	Not considered	OR for influenza prevention through vaccination 0.199	Not stated	GBP 8.40 (including administrative costs)
Weycker *et al.* (2005)[42]	Not stated	Six months to 18 years	Division into high- and low-risk children and adults	70% (children and young adults); 50% elderly adults; susceptibility	20 to 80%	No consideration of vaccination costs
Yoo *et al.* (2013)[43]	TIV and LAIV (no separate analysis)	School children; no explicit age stated	Not stated	No model	42.7% in the intervention group; 29.5% in the control group	USD 67.13 (including administrative costs and c information and coordination costs)
ILI= influenza-like infection; LAIV= live-attenuated influenza vaccine; TIV= trivalent inactivated influenza vaccine						

Table A4-9: Results from included economic studies

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
Beutels *et al.* (2013a/2013b)[44;45]	Vaccination of children between two and 17 years with LAIV with a vaccination coverage of 50%	Current situation (TIV with low vaccination coverage)	ICER: EUR 44,280/QALY	Not stated
	Vaccination of children between five and 17 years with LAIV with a vaccination coverage of 50%	Current situation (TIV with low vaccination coverage)	ICER: EUR 44,260/QALY	Not stated
	Vaccination of children between twelve and 17 years with LAIV with a vaccination coverage of 50%	Current situation (TIV with low vaccination coverage)	ICER: EUR 42,046/QALY	Not stated
	Vaccination of children under two years of age with TIV and children between two and 17 years with LAIV with a vaccination coverage of 50%	Current situation (TIV with low vaccination coverage)	ICER: EUR 44,415/QALY	Not stated

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
Chen and Liao (2013)[20]	Vaccination	No intervention	USD 86/per year per person	Not stated
Cohen and Nettleman (2000)[21]	Routine vaccination of children between six months and twelve years with TIV	No vaccination	Cost-saving (savings of USD 0.34 per vaccinated child)	Cost-saving (savings of USD 1.20 to USD 21.28 per vaccinated child)
Dayan *et al.* (2001)[22]	Vaccination of high-risk children between six months and 15 years	No vaccination	Not stated	Cost-saving (savings of USD 10.04 per vaccinated child)
Esposito *et al.* (2006)[23]	Vaccination of healthy children between two to five years	No vaccination	Not stated	Cost-saving (savings of EUR 131.43 per vaccinated child); BCR 1.29
Fitzner *et al.* (2001)[24]	Vaccination of children between one and 15 years	No vaccination	Not stated	ICER: HD 1,078 per prevented case of ILI
Giglio *et al.* (2012)[25]	Vaccination of children between six and 23 months	No vaccination	ICER: EUR 1,759/QALY	Not stated
	Vaccination of children between six and 36 months	No vaccination	ICER: USD 1,103/QALY	Not stated
	Vaccination of children between six months and five years	No vaccination	ICER: USD 717/QALY	Not stated
Hall and Katz (2005)[26]	Vaccination of high-risk children between six and 23 months	No vaccination	Cost-saving (prevention of 18 hospitalisations requires 3,738 high-risk children to be vaccinated)	Not stated
	Vaccination of children between six and 23 months	No vaccination	CBR: 11.4	Not stated
	Vaccination of healthy and high-risk children between six and 23 months	No vaccination	Cost-neutral	Not stated

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
Hibbert *et al.* (2007)[27]	Vaccination of children between six and 36 months with LAIV	No vaccination	Not stated	Cost-saving (savings of USD 5.47 per vaccinated child in the first season and USD 144.44 per vaccinated child in the second season)
Lee *et al.* (2012)[28]	Vaccination of children between two and 18 years with a universal vaccination providing five years protection	Vaccination of children between two and 18 years with the annual standard vaccination	Not stated	Depending on scenario, the result varies between cost-saving, USD 31,987 to 806,958 per QALY (ICERs) and dominates through the annual standard vaccination
	Vaccination of children between two and 18 years with a universal vaccination providing ten years protection	Vaccination of children between two and 18 years with the annual standard vaccination	Not stated	Depending on scenario, the result varies between cost-saving, USD 1,285 to 380,364 per QALY (ICERs) and dominates through the annual standard vaccination
Luce *et al.* (2001)[29]	Vaccination of children with LAIV as part of an individual-based vaccination programme	No vaccination	ICER: USD 19.10 per day lost with febrile ILI	ICER: USD 29.67 per lost day with febrile ILI
	Vaccination of children with LAIV as part of an groupbased vaccination programme	No vaccination	ICER: USD 19.10 per day lost with febrile ILI	Cost-saving
Luce *et al.* (2008)[46]	Vaccination of children between 24 and 59 months with LAIV	Vaccination of children between 24 and 59 months with TIV	Not stated	Cost-saving (savings of USD 45.80 per vaccinated child, LAIV in comparison to TIV)
Marchetti *et al.* (2007)[30]	Vaccination of children between six and 24 months	Only vaccination of high-risk children	ICER: EUR 10,000/QALY	Cost-saving
	Vaccination of children between six and 60 months	Only vaccination of high-risk children	ICER: EUR 13,333/QALY	Cost-saving

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
Meltzer *et al.* (2005)[31]	Vaccination of children between six and 23 months, six and 59 months and five and 14 years	No vaccination	Not stated	Vaccination of cohorts with 100% at-risk children always result in median cost-savings. For cohorts with 10% of at-risk children, the threshold value for vaccination is a median of USD 45 to 58.
Navas *et al.* (2007)[32]	Vaccination of children between three and 14 years	No vaccination	ICER: EUR 5.80 per prevented febrile respiratory episode; EUR 18.26/QALY	Cost-saving; BCR: 1.80
Newall *et al.* (2013)[33]	Vaccination of children between five and 17 years	5% vaccination coverage for children between six months and 17 years	ICER: AUD 3,500/QALY	Cost-saving
Pitman *et al.* (2013)[34]	Vaccination of children between two and four years with TIV	Only vaccination of high-risk children	Dominated by vaccination of children between two and four years with LAIV	Not stated
	Vaccination of children between two and four years with LAIV	Only vaccination of high-risk children	Cost-saving	Not stated
	Vaccination of children between two and ten years with TIV	Vaccination of children between two and four years with LAIV	Dominated by vaccination of children between two and ten years with LAIV	Not stated
	Vaccination of children between two and ten years with LAIV	Vaccination of children between two and four years with LAIV	ICER: GBP 506/QALY	Not stated
	Vaccination of children between two and 18 years with TIV	Vaccination of children between two and ten years with LAIV	Dominated by vaccination of children between two and 18 years with LAIV	Not stated
	Vaccination of children between two and 18 years with LAIV	Vaccination of children between two and ten years with LAIV	ICER: GBP 298/QALY	Not stated
Prosser *et al.* (2006)[35]	Vaccination of healthy children between 24 and 23 months with TIV	No vaccination	Not stated	ICER: USD 12,000/QALY
	Vaccination of healthy children aged two years with TIV	No vaccination	Not stated	ICER: USD 18,000/QALY

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
	Vaccination of healthy children between three and four years with TIV	No vaccination	Not stated	ICER: USD 28,000/QALY
	Vaccination of healthy children between five and eleven years with TIV	No vaccination	Not stated	ICER: USD 79,000/QALY
	Vaccination of healthy children between twelve and 17 years with TIV	No vaccination	Not stated	ICER: USD 119,000/QALY
	Vaccination of high-risk children between six and 23 months with TIV	No vaccination	Not stated	Cost-saving
	Vaccination of healthy children aged two years with TIV	No vaccination	Not stated	Cost-saving
	Vaccination of high-risk children between three and four years with TIV	No vaccination	Not stated	ICER: USD 1,000/QALY
	Vaccination of high-risk children between three and eleven years with TIV	No vaccination	Not stated	ICER: USD 7,000/QALY
	Vaccination of high-risk children between twelve and 17 months with TIV	No vaccination	Not stated	ICER: USD 10,000/QALY
	Vaccination of healthy children between six and 23 months with LAIV	No vaccination	Not stated	ICER: USD 9,000/QALY
	Vaccination of healthy children aged two years with LAIV	No vaccination	Not stated	ICER: USD 15,000/QALY
	Vaccination of healthy children between three and four years with LAIV	No vaccination	Not stated	ICER: USD 25,000/QALY

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
	Vaccination of healthy children between five and eleven years with LAIV	No vaccination	Not stated	ICER: USD 72,000/QALY
	Vaccination of healthy children between twelve and 17 years with LAIV	No vaccination	Not stated	ICER: USD 109,000/QALY
Prosser *et al.* (2010)[47]	Vaccination of healthy children between 24 and 23 months with TIV	No vaccination	Not stated	ICER: USD 21,000/QALY
	Vaccination of healthy children aged two years with TIV	No vaccination	Not stated	ICER: USD 25,000/QALY
	Vaccination of healthy children between three and four years with TIV	No vaccination	Not stated	ICER: USD 37,000/QALY
	Vaccination of healthy children between six and 23 months with LAIV	No vaccination	Not stated	ICER: USD 18,000 -20,000/QALY
	Vaccination of healthy children aged two years with LAIV	No vaccination	Not stated	ICER: USD 21,000 -23,000/QALY
	Vaccination of healthy children between three and four years with LAIV	No vaccination	Not stated	ICER: USD 32,000 -33,000/QALY
Salleras *et al.* (2009)[36]	Vaccination of children between three and 14 years	No vaccination	Not stated	Family perspective; cost-saving; BCR: 2.15
Salo *et al.* (2006)[37]	Vaccination of children between six months and under three years	No vaccination	Cost-saving	Cost-saving
	Vaccination of healthy children between three and under five years	No vaccination	Cost-saving	Cost-saving

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
	Vaccination of healthy children between five and under seven years	No vaccination	Cost-saving	Cost-saving
	Vaccination of children between seven and 13 years	No vaccination	Cost-saving	Cost-saving
Schmier *et al.* (2008)[38]	Vaccination of children as part of a school vaccination programme	No school vaccination programme	Not stated	Cost-saving (savings of USD 171.96 per household)
Skowronski *et al.* (2006)[39]	Vaccination of children between six and 23 months (two vaccination doses for 100% of cohort in the first year)	No vaccination	ICER: CAD 127/prevented influenza infection in children; CAD 12,694 /prevented hospitalisation; CAD 863,856 /LYG	ICER: CAD 151/prevented influenza infection in children; CAD 15,099 / prevented hospitalisation; CAD 1,027,143 /LYG
	Vaccination of children between six and 23 months (two vaccination doses for 1/3 of cohort in the subsequent years)	No vaccination	ICER: CAD 66/prevented influenza infection in children; CAD 6,603 /prevented hospitalisation; CAD 449,040 /LYG	ICER: CAD 25/prevented influenza infection in children; CAD 2,507 /prevented hospitalisation; CAD 170,710 /LYG
Tarride *et al.* (2012)[40]	Vaccination of children between two and five years with LAIV	Vaccination of children between two and five years with TIV	Cost-saving	Cost-saving
	Vaccination of children between six and nine years with LAIV	Vaccination of children between six and nine years with TIV	Cost-saving	Cost-saving
	Vaccination of children between ten and 17 years with LAIV	Vaccination of children between ten and 17 years with TIV	Cost-saving	Cost-saving
	Vaccination of children between two and 17 years with LAIV	Vaccination of children between two and 17 years with TIV	Cost-saving	Cost-saving
Turner *et al.* (2003)[41]	Vaccination of children of up to twelve years	No vaccination	ICER: GBP 5,024 /QALY (stochastic model); GBP 6,053/QALY (deterministic model)	Not stated
Weycker *et al.* (2005)[42]	Vaccination of children between six months and 18 years	5% vaccination coverage for children between six months and 18 years	Cost-saving (savings of USD 35-89 per vaccinated child without vaccination costs)	Cost-saving (savings of USD 174 to 443 per vaccinated child without vaccination costs)

Publication	Vaccine strategy	Comparison strategy	Results from the payer perspective	Results from a societal perspective
Yoo *et al.* (2013)[43]	Vaccination of children as part of a school vaccination programme	No school vaccination programme	ICER: USD 92.50 per vaccinated pupil (without the assumption of indirect protective effects)	Cost-saving for the assumption of protective effects
BCR= benefit-cost ratio; CBR= cost-benefit ratio ; ICER= incremental cost-effectiveness ratio; ILI= influenza-like infection; LAIV= live-attenuated influenza vaccine; QALY= quality-adjusted life year; TIV= trivalent inactivated influenza vaccine				

Ethical, social and legal publications taken into consideration

As part of the HTA, seven publications were identified (Flood *et al.* (2010)[8]; Flood *et al.* (2011a)[10]; Flood *et al.* (2011b)[9]; Schuller *et al.* (2013)[13]; Shim *et al.* (2012)[14]; Penfold *et al.* (2011)[12]; King *et al.* (2006)[11]) that deal with the ethical, social or legal aspects of general influenza vaccination of children and adolescents or especially with LAIV. Of these identified publications, three deal with the acceptance of influenza vaccinations, one article describes the influence of physicians on the probability of vaccination, a further publication analyses the influence of altruism on the decision for vaccination, one publication analyses the influence of financial factors and cost reimbursements on vaccination coverage and the final article analyses the influence of influenza vaccinations of children and adolescents on absence from school. Because of the very different study designs, it does not seem sensible to present the studies in tabular form.