附录三：纳入研究的基线特征表

问题 1：预防儿童流感，四价流感疫苗（quadrivalent influenza vaccine，QIV）是否优于三价流感疫苗（trivalent influenza vaccines，TIV）？

表 1 随机对照研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	对照组
Domachowske 2013	Czech Republic, France, Germany,Philippines, and USA	I: 915; TIV-Vic: 912; TIV-Yam: 911	Children were aged 3 to 17 years and were in stable health.	Inactivated quadrivalent influenza vaccine (QIV); GlaxoSmithKline Vaccines in Dresden, Germany. The QIV candidate contained influenza A/H1N1 (A/California/7/2009) and A/H3N2 (A/Victoria/210/2009) and B/Brisbane/60/2008 (B/Victoria lineage). The QIV candidate contained influenza A/H1N1 (A/California/7/2009) and A/H3N2 (A/Victoria/210/2009) and B/Brisbane/60/2008 (B/Victoria lineage). The inactivated split virion vaccines were thimerosal-free, contained 15 µg of each hemagglutinin antigen	Trivalent influenza vaccines (TIVs) [Fluarix™]; GlaxoSmithKline Vaccines in Dresden, Germany. The TIV scontained the same influenza Astrainsas the QIV candidate, and eithe rB/Brisbane/60/2008 (B/Victorialineage) [Fluarix™] or B/Bris-bane/3/2007(B/Yamagatalineage). The inactivated split virion vaccines were thimerosal-free, contained 15 µg of each hemagglutinin antigen.
Langley 2013	Canada, USA, Mexico, Spain, and China (Taiwan)	I: 932; TIV-Vic: 929; TIV-Yam: 932	Children were in stable health, between 3-17 years of age, and not pregnant if female.	Inactivated quadrivalent influenza vaccine candidate (QIV): GlaxoSmithKline Vaccines (Quebec City, Canada); The QIV contained 60 µg of HA: 15 µg of the same 2 influenza A strains as the TIVs, as well as 15 µg of each of the B lineage strains.	Trivalent inactivated influenza vaccine (TIV)-Victoria (Vic) and TIV-Yamagata (Yam), GlaxoSmithKline Vaccines (Dresden, Germany). TIVVic contained 15 µg of B/Brisbane/60/2008, and TIV-Yam contained 15 µg of B/Brisbane/3/2007; 15 µg each of hemagglutinin antigen (HA) from each of A/H1N1 (A/California/7/2009) and A/H3N2 (A/Victoria/210/2009).
Greenberg 2014	USA	I: 2902; Licensed TIV: 736; Investigational TIV: 725	Children had to be 6 months to < 9 years of age and generally in good health.	Quadrivalent influenza vaccines (QIVs). A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (B Victoria lineage) and B/Florida/04/2006 (B Yamagata lineage) strains.	A licensed 2010-2011 formulation of TIV (Fluzone, Sanofi Pasteur, Swiftwater, PA) contained B/Brisbane/60/2008 and an investigational TIV contained B/Florida/04/2006. Contained B/Brisbane/60/2008 and an investigational TIV contained B/Florida/04/2006. Each TIV contained the same A/H1N1 and A/H3N2 strains as QIV.
Weber 2014	Mexico	I: 95; C: 97	Children aged 18-47 months who had received 2 doses of TIV in a study during the previous season.	(Fluarix™ Quadrivalent): GlaxoSmithKline (GSK) Biologicals (Dresden, Germany). The QIV were inactivated split virion vaccines containing 15 µg hemagglutinin antigen (HA) of each vaccine strain recommended by WHO for the 2009-2010 influenza season in the Northern Hemisphere: A/Brisbane/59/2007 (H1N1), A/Uruguay/716/07 (H3N2) and B/Brisbane/60/2008 (B/Victoria lineage) or B/Brisbane/3/2007(B/Yamagata lineage).	TIV; Fluarix™: GlaxoSmithKline (GSK) Biologicals (Dresden, Germany) TIV containing 15 µg HA each of A/Brisbane/59/2007 (H1N1), A/Uruguay/716/07 (H3N2) and B/Brisbane/3/2007 (B/Yamagata lineage).
Carlos 2015	Philippines and Australia	I: 329; C: 55	Children 9-17 years old who had not been previously vaccinated against influenza with a	Inactivated quadrivalent influenza vaccine (IIV4) . Inactivated, split-virion preparations containing 15g hemagglutinin per strain in a total volume of 0.5 mL. IIV4lot 1 (batch S4361), lot 2 (batch S4362), and lot 3	The licensed IIV3 (batch H0290) was the 2011/2012 Northern Hemisphere formulation of Vaxigrip® (Sanofi Pasteur, Marcy-l' Etoile, France), Contained the A/California/07/2009

			2012 Southern Hemisphere formulation or a 2011-2012 Northern Hemisphere formulation in the previous 6 months.	(batch S4363) contained the A/California/07/2009 (H1N1), A/Victoria/210/2009(H3N2), and B/Brisbane/60/2008 (Victoria lineage) strains (which were among those recommended for the 2011/2012 Northern Hemisphere and the 2012 Southern Hemisphere formulations), and the B/Florida/04/2006 strain (Yamagata lineage).	(H1N1), A/Victoria/210/2009(H3N2), and B/Brisbane/60/2008 (Victoria lineage) strains.
Hartvickson 2015	USA	I: 1159; TIV1c: 593; TIV2c: 581	Healthy children aged 4-18 years.	Cell-derived quadrivalent influenza vaccine (QIVc). Each 0.5-ml dose of the investigational QIVc contained purified viral hemagglutinin (HA) antigens, approx. 15 mg of HA for each of the four influenza strains recommended by the WHO for the 2013/14 influenza vaccine composition for the Northern Hemisphere season: A/Brisbane/10/2010 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012, and B/Brisbane/60/2008.	Trivalent influenza vaccines (TIV1c/TIV2c). The comparator TIVc vaccines administered (TIV1c and TIV2c) consisted of approximately 0.5 ml, which included purified viral HA from each of the three influenza strains A/Brisbane/10/2010 (H1N1), A/Texas/50/2012 NYMC X-223A (H3N2), and B/Massachusetts/02/2012 (B1) in TIV1c, recommended by the WHO for inclusion in the trivalent vaccine composition for the 2013/2014 influenza season, and A/Brisbane/10/2010 (H1N1), A/Texas/50/2012 NYMC X-223A (H3N2), and B/Brisbane/60/2008 (B2) in TIV2c.
Langley 2015	Canada, Dominican Republic, and Honduras	I: 299; C: 302	Children were in stable health and between 6 and 35 months of age at the time of the first vaccination.	Inactivated quadrivalent influenza vaccine: (QIV GlaxoSmithKline Vaccines, Sainte-Foy, Quebec, Canada. The QIV contained 15 µg of hemagglutinin (HA) from 4 strains recommended for the 2012-2013 season: A/California/7/2009(H1N1) pdm09, A/Victoria/361/2011(H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Hubei-Wujiagang/158/2009 (Yamagata lineage).	Trivalent control vaccine (TIV): GlaxoSmithKline Vaccines, Dresden, Germany. The TIV contained the same H1N1, H3N2, and B Yamagata components but no B Victoria lineage component
Wang 2015	USA	I: 158; C: 156	Healthy children 6-35 months of age and those with chronic illness who were not acutely ill.	The investigational QIV (GSK Vaccines, dba ID Biomedical Corporation, Sainte-Foy, Quebec, Canada). Contained 15 µg HA of each of 4 strains (A/California/7/2009 [A/H1N1], A/Texas/50/2012 [A/H3N2], B/Brisbane/60/2008 [B/Victoria], and B/Massachusetts/2/2012 [B/Yamagata]), in a 0.5 mL dose.	The licensed comparator TIV (Sanofi Pasteur, Swiftwater, PA). Contained 7.5 µg of each of the same A/H1N1, A/H3N2, and B Yamagata strains in a 0.25 mL dose.
Pepin 2016	Poland, Finland, Mexico and China (Taiwan)	I: 863; IIV3-1: 175; IIV3-2: 169	Healthy children 3 to 8 y of age	Quadrivalent Influenza Vaccine (split-virion, inactivated). IIV4 contained the 4 Northern Hemisphere 2013/2014 influenza strains recommended by the World Health Organization and the European Union: A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (B Victoria lineage), and B/Massachusetts/02/2012 (B Yamagata lineage)	IIV3-1: Vaxigrip® Sanofi Pasteur, Lyon, Franc; IIV3-2: An investigational formulation of IIV3 containing. IIV3-1: A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (B Victoria lineage); IIV3-2: A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/02/2012 (B Yamagata lineage)
Lee 2017	South Korean	I: 422; C:106	The present trial included healthy children and young adults aged ≥ 6 months to < 19 years.	GC3110A, a quadrivalent split-virion influenza vaccine: Green Cross Corporation (Yongin & Hwasun, Korea). Each 0.5 mL dose of the vaccine contained 15 µg of each of the four purified hemagglutinin antigens (60 µg total):	GC Flu pre-filled syringes,Green Cross Corporation (Yongin & Hwasun, Korea). A 0.5 mL dose of the vaccine contained 15 µg of each of the three purified hemagglutinin antigens (45 µg total):

				A/California/7/2009 (H1N1), A/Switzerland/9715293/2013 (H3N2), B/Phuket/3073/2013, and B/Brisbane/60/2008.	A/California/7/2009 (H1N1), A/Switzerland/9715293/2013 (H3N2), and B/Phuket/3073/2013.
Wang 2017	China	I:916; TIV-Yam: 458; TIV-Vic: 458	Healthy children aged 3-17 years old.	The experimental QIVs were developed by Jiangsu GDK Biotechnology Co., Ltd.. Each dose contained 60 μg of hemagglutinin antigen (HA) in total, 15μg of HA per strain (A/California/7/2009, A/Switzerland/9715293/2013, B/Brisbane/60/2008 and B/Phuket/3073/2013).	Positive controls were manufactured by Changsheng Biology Science & Technology Co. Ltd., Changchun, China. Each dose contained 15μg of each HA of two influenza A strains (A/California/7/2009, A/Switzerland/9715293/2013) and one influenza B strain (B/Brisbane/60/2008 for TIV-Victoria [Vic] or B/Phuket/3073/2013 for TIV-Yamagata [Yam]).
Pepin 2018	Latin America, Europe, and Africa	I: 2721; IIV3-1: 183; IIV3-2: 186	Healthy children aged 6-35 months who had not been previously vaccinated and aged < 24 -months had to be born at full term (≧ 37 weeks) or with a birth weight ≧ 2.5 kg.	Quadrivalent Influenza Vaccine (split-virion, inactivated). All vaccines were thimerosal-free, inactivated, split-virion, and contained 15 lg of HA from each strain per 0.5-ml dose. IIV4 formulation 1: SH 2014 and NH 2014/2015 , A/California/7/2009, A/Texas/50/2012, B/Brisbane/60/2008, B/Massachusetts/02/2012; IIV4 formulation 2: SH 2015 and NH 2015/2016, A/California/7/2009, A/South Australia/55/2014, B/Brisbane/60/2008, B/Phuket/3073/2013	Trivalent Influenza Vaccine (split-virion, inactivated; TIV1). All vaccines were thimerosal-free, inactivated, split-virion, and contained 15 lg of HA from each strain per 0.5-ml dose. IIV3-1: NH 2014/2015, A/California/7/2009, A/Texas/50/2012, B/Brisbane/60/2008; IIV3-2: NH 2014/2015, A/California/7/2009 A/Texas/50/2012, B/Massachusetts/02/2012
Eun 2019	South Korean	I: 366; C: 88	Healthy children 6 months to 18 years old who had not been previously vaccinated against influenza in the previous 6 months.	NBP607-QIV Lot no.: quadrivalent, inactivated subunit influenza vaccine; a novel cIIV4, CT3DS201; SK Bioscience (Seongnam, Republic of Korea). 0.5mL Madin-Darby canine kidney (MDCK) cell culture-derived quadrivalent, inactivated subunit influenza vaccine loaded into prefilled syringes containing 15 μg of hemagglutinin per strain. virus strains: A/Christchurch/16/2010 (H1N1)-like virus, A/Texas/50/2012 (H3N2)-like virus, B/Massachusetts/2/2012 (Yamagata lineage)-like virus and B/Brisbane/60/2008 (Victoria lineage)-like virus	AgrippalS1, Lot no.: trivalent influenza vaccine, 148402 and 147001, respectively, Novartis Vaccine and Diagnostics Srl, Siena, Italy). A/Christchurch/16/2010 (H1N1)-like virus, A/Texas/50/2012 (H3N2)-like virus only 1 B strain (B/Massachusetts/2/2012(Yamagata lineage)-like virus or B/Brisbane/60/2008(Victoria lineage)-like virus) was a 0.25mL or 0.5mL commercial egg-derived trivalent, provided in prefilled syringes containing 7.5 μg or 15 μg of hemagglutinin
Lee 2019	South Korean	I: 81; C: 43	Healthy children aged 6-35 months who had not been previously vaccinated for the current influenza season (2016-2017).	Madin-Darby Canine Kidney cell culture-derived quadrivalent inactivated subunit influenza vaccine (SKYCellflu4®; SK Chemicals, Seongnam, Korea). A full dose QIV contained 15 μg hemagglutinin per strain. The 2016-2017 TIV included A/California/7/2009 (H1N1) pdm09, A/Hong Kong/4801/2014 (H3N2), and B/Brisbane/60/2008 (B/Victoria lineage) and the QIV included additionally B/Phuket/3073/2013 (B/Yamagata lineage), in accordance with the WHO recommendation for the composition of the northern hemisphere 2016-2017 influenza vaccine.	Trivalent inactivated subunit influenza vaccine (SK influenza trivaccine®; SK Chemicals). A half dose (0.25 mL) of TIV was administered to the enrollees, both of which were loaded into pre-filled syringes. A full dose QIV contained 15 μg hemagglutinin per strain, and a half dose TIV contained 7.5 μg hemagglutinin per strain. The 2016-2017 TIV included A/California/7/2009 (H1N1) pdm09, A/Hong Kong/4801/2014 (H3N2), and B/Brisbane/60/2008 (B/Victoria lineage).

Vesikar 2019	Estonia, Finland, Germany, Hungary, Lithuania, and Poland	I: 402; TIV(Vic): 404; TIV(Yam): 394	Children and adolescents 3-17 years of age on the day of vaccination who were in stable health.	Inactivated subunit quadrivalent influenza vaccine (QIV): Abbott Biologicals B.V.. For all vaccines, the active drug substance contained 15mg of hemagglutinin for each of the three (TIV) or four (QIV) virus strains recommended for the northern hemisphere 2016/2017 season (World Health Organization (WHO), 2016).	Trivalent influenza vaccine (TIV): Abbott Biologicals B.V. For all vaccines, the active drug substance contained 15mg of hemagglutinin for each of the three (TIV) or four (QIV) virus strains recommended for the northern hemisphere 2016/2017 season (World Health Organization (WHO), 2016).
Hu 2020	China	I: 1160; TIV-Vic: 580; TIV-Yam: 580	Children aged 6–35 months, full term delivered, and with a birth weight over 2500 g.	Quadrivalent influenza vaccines (QIVs): Sinovac (Beijing) Biotech Co., Ltd. QIV contained A/Michigan/45/2015 (H1N1), A/Hong Kong/4801/2014 (H3N2), B/Brisbane/60/2008 (B Victoria lineage) and B/Phuket/3073/2013 (B/Yamagata lineage) four viral strains.	Trivalent influenza vaccine: Sinovac (Beijing) Biotech Co., Ltd. TIV-Vic and TIV-Yam contained the unique strain B/Victoria or B/Yamagata, in addition to the shared strains A/H1N1 and A/H3N2. TIVs containing BV or BY strains were both licensed in China.
Choi 2021	South Korean	I: 160; C:39	Healthy children aged 6-35 months had to be born full-term (≧ 37 weeks).	GC3110A GC Pharma (Yongin, Korea). An egg-grown, split-virion, inactivated QIV, One singledose vial of 0.5 mL contained 15 lg of each of the four purifiedhemagglutinin antigens (60 lg total): A/Singapore/GP1908/2015(H1N1), A/Hong Kong/4801/2014 (H3N2), B/Phuket/3073/2013(Yamagata lineage), B/Brisbane/60/2008 (Victoria lineage)	GC FLU Prefilled Syringe GC Pharma (Yongin, Korea). Syringe, is an egg-grown, split-virion, inactivated TIV. One single-dose vial of 0.25 mL contained 15ug of eachof the following purified hemagglutinin antigens (45 lg total): A/Singapore/GP1908/2015 (H1N1), A/Hong Kong/4801/2014(H3N2), B/Brisbane/60/2008 (Victoria lineage).
Liu 2022	China	I: 2211; C: 1087	Healthy individuals aged ≥6 months.	Participants received either 0.25 mL or 0.5 mL dose of Shz QIV (2019/20 northern hemisphere influenza season containing, respectively, 7.5 μg or 15 μg HA each of A/Brisbane/02/2018, IVR-190, A/Kansas/14/2017, NYMC X-327, B/Maryland/15/ 2016, NYMC BX-69A, and B/Phuket/3073/2013-like strain).	Shz TIV (2019/20 northern hemisphere influenza season containing, respectively, 7.5 μg or 15 μg HA each of A/ Brisbane/02/2018, IVR-190 and A/Kansas/14/2017, NYMC X-327, and either B/Maryland/15/2016, NYMC BX-69A, or B/Phuket/3073/2013-like strain). Randomization was per formed by the sponsor using an interactive response technology system.
唐 2023	China	I: 960; BY：959; BV: 958	6-35 月龄的健康婴儿	四价流感病毒裂解疫苗：华兰生物疫苗股份有限公司. H1N1 型(A/Michigan/45/2015/H1N1pdm09-like virus)、H3N2 型 (A/Singapore/INFIMH-16-0019/2016/H3N2-like virus)、 BY 型(B/Phuket/3073/2013-like virus/Yamagata/16/88 lin-eage、Yamagata)和 BV 型 (B/Colorado/06/2017/-like virus /Victoria/2/87 lineage，Victoria)流感病毒血凝素各 7.5 μg。	BV 三价流感疫苗或 BY 三价流感疫苗：华兰生物疫苗股份有限公司. BY 三价流感疫苗： H1N1 型 (A/Michigan/45/2015/H1N1pdm09-like virus)、H3N2 型 (A/Singapore/INFIMH-16-0019/2016/H3N2-like virus)、 BY 型(B/Phuket/3073/2013-like virus/Yamagata/16/88 lin-eage， Yamagata)流感病毒血凝素各 7. 5 μg； BV 三价流感疫苗 H1N1 型 (A/Michigan/45/2015/H1N1pdm09-like virus)、H3N2 型 (A/Singapore/INFIMH-16-0019/2016/H3N2-like

					virus)、BV 型(B/Colorado/06/2017/-like virus /Victoria/2/87 lineage，Victoria)流感病毒血凝素各 7.5 μg。
Block 2012	USA	I: 1085; C: 723	Children 2-8 years of age	Ann Arbor strain live attenuated influenza vaccine (Q/LAIV)： MedImmune LLC(Louisiana, CA United States). Contained 107.0±0.5 fluorescent focus units of each viral strain.Four cold-adapted, temperature-sensitive, attenuated influenza strains were included in Q/LAIV: A/H1N1 (A/South Dakota/6/2007), A/H3N2 (A/Uruguay/716/2007), B/Victoria (B/ Malaysia/2506/2004) and B/Yamagata (B/Florida/4/2006).	Trivalent vaccines (T/LAIV). Contained 107.0±0.5 fluorescent focus units of each viral strain.Four cold-adapted, temperature-sensitive, attenuated influenza strains were included in Q/LAIV: A/H1N1 (A/South Dakota/6/2007), A/H3N2 (A/Uruguay/716/2007), B/Victoria (B/ Malaysia/2506/2004) or B/Yamagata (B/Florida/4/2006).
Mallory 2019	USA	LAIV4 2015-2016: 66; LAIV4 2017-2018: 67; C: 67	Children were included in the study if they: were aged 24-48months at the time of screening; were healthy by medical history and physical examination or had a stable underlying chronic medical condition for which hospitalization was not required in the previous year.	LAIV4 2017–2018 (LAIV4A/Slovenia [Vaccine lot number: JF2224; Manufacturer: MedImmune, LLC]) or LAIV4 2015–2016 (LAIV4A/Bolivia [Vaccine lot number: JC2196; Manufacturer: MedImmune, LLC]). A/H1N1 (A/Bolivia/559/2013), A/H3N2 (A/Switzerland/9715293/2013), and B/Phuket/3073/2013 (B/Yamagata-lineage) or A/H1N1 (A/Bolivia/559/2013), A/H3N2 (A/Switzerland/9715293/2013), B/Phuket/3073/2013 (B/Yamagata-lineage), and B/Brisbane/60/2008 (B/Victoria-lineage).	Trivalent LAIV (LAIV3) 2015–2016 (LAIV3A/Bolivia [Vaccine lot number: JC2195; Manufacturer: MedImmune, LLC]) (a formulation developed as a comparator for this study). A/H1N1 (A/Bolivia/559/2013), A/H3N2 (A/Switzerland/9715293/2013), B/Phuket/3073/2013 (B/Yamagata-lineage), and B/Brisbane/60/2008 (B/Victoria-lineage).

BY, B/Yamagata; BV, B/Victoria; C, control; I, intervention; LAIV4, Quadrivalent live attenuated influenza vaccine; TIV, Trivalent influenza vaccines.

表 2 队列研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	对照组
Nohynek 2016	Finland	I: 8086; C: 4297	Two-year-old children, the birth cohort of 2013, during the influenza season 2015/16, defined as lasting from week 40 (28 September 2015) to week 20 (22 May 2016).	The quadrivalent LAIV vaccine: live attenuated influenza vaccine.	TIV: trivalent inactivated influenza vaccine.
Stockwell 2016	USA	I: 98; C: 211	24- to 59-month-olds during the 2013-2014 season.	IIV4: quadrivalent inactivated influenza vaccine.	IIV3: trivalent inactivated influenza vaccine.
Shasha 2019	Israel	Season 1 (2015-2016): I: 49726; C: 100792; Season 2 (2017-2018): I: 121741; C: 46555	Adults and children aged 3 years and older.	QIV: quadrivalent influenza vaccine. Fluarix tetra®, GSK.	TIV: trivalent vaccine. Influvac®, Abbott Laboratories, Vaxigrip®, Sanofi Pasteur, or Agrippal®, Seqirus vaccines.

C, control; I, intervention.

问题 2. 预防儿童流感，接种减毒活流感疫苗（live-attenuated influenza vaccine，LAIV）是否优于灭活流感疫苗（inactivated influenza vaccine，IIV）

表 3 随机对照研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	干预组接种方式	对照组	对照组接种方式
Ashkenazi 2006	9 European countries (Belgium, Czech Republic, Finland, Germany, Italy, Poland, Spain, Switzerland, and the United Kingdom) and Israel	I: 1050; C: 1035	Children 6 to 71 months of age with a history of recurrent RTIs were eligible for enrollment	Cold-adapted influenza vaccine, trivalent (CAIV-T): Wyeth Pharmaceuticals (Marietta, PA). Approximately 107 fluorescent focus units of 3 influenza reassortant virus strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens of the A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2), and B/Hong Kong/330/01 influenza strains.	Intranasal administration (0.1 mL into each nostril).	Trivalent inactivated influenza vaccine (TIV): Aventis Pasteur (Lyon, France). Antigens identical to or antigenically representative of the WHO recommendations for the 2002-2003 influenza season, specifically the HAandNAantigensoftheA/Moscow/10/99(H3N2)-likestrain (A/Panama/2007/99), A/New Caledonia/20/99 (H1N1)-like strain (A/New Caledonia/20/99), and B/Hong Kong/330/2001-like strain (B/Shangdong/7/97)	TIV was administered by intramuscular injection according to the manufacturer's dosing instructions.Children aged 6 to < 36months received 0.25mL perdose (7.5 ug of each HA), whereas children 36 to < 72 months of age received 0.5 mL per dose (15 ug of each HA).
Belshe 2007	16 countries: the United States (49% of subjects), 12 countries in Europe and the Middle East (45% of subjects), and 3 countries in Asia (6% of subjects)	I: 4179; C: 4173	Children 6 to 59 months of age	Live Attenuated Vaccine: MedImmune. This vaccine consisted of three cold-adapted reassortant influenza viruses grown in specific pathogen-free chicken eggs. Each dose of vaccine contained approximately 10 7 fluorescence focus assay units of each of the three strains of the 2004-2005 influenza season, as recommended by the Food and Drug Administration (A/New Caledonia/20/99 [H1N1], A/Wyoming/3/2003 [an A/Fujian/411/2002 (H3N2)-like virus] and B/Jilin/20/2003 [a B/Shanghai/361/2002-like virus]).	They were administered intranasally, also received a concurrent injection of intramuscular saline. A total of 0.2 ml of vaccine was administered (0.1 ml into each nostril with the use of an intranasal-spray device).	Inactivated Vaccine: Aventis Pasteur Recommended 2004-2005 influenza strains (A/New Caledonia/20/99 [H1N1], A/Wyoming/3/2003 [an A/Fujian/411/2002 (H3N2)-like virus], and B/Jiangsu/10/2003 [a B/Shanghai/361/2002-like virus]), and the vaccine was administered by intramuscular injection, according to the manufacturer's dosing instructions.	They were administered intramuscularly, also received a concurrent intranasal mist of saline. Children 6 to 35 months of age received 0.25 ml of intramuscular inactivated vaccine, and those 36 to 59 months of age received 0.5 ml of intramuscular inactivated vaccine.

Levin 2008 [Weinberg 2010]	USA	I: 122; C: 121	HIV-infected children and adolescents (≥5 to <18 years of age) on a stable highly active antiretroviral therapy (HAART) regimen for ≥16 weeks.	Live attenuated influenza vaccine (LAIV): MedImmune The strains represented in the vaccines were those recommended by the U.S. Public Health Service (USPHS) for the 2004/2005 season: A/New Caledonia/20/99 (H1N1); A/Wyoming/3/2003 (H3N2) [an A/Fujian/411/2002-like virus]; and B/Jilin/20/2003 (LAIV) or B/Jiangsu/10/2003 (TIV); both are B/Shanghai/361/2002-like viruses.	Arm A (LAIV) received the frozen formulation of Influenza Virus Vaccine Live, Intranasal (FluMist ® MedImmune) 0.5mL (0.25mL per nostril)	Trivalent inactivated influenza vaccine (TIV): Aventis Pasteur, Inc. The strains represented in the vaccines were those recommended by the U.S. Public Health Service (USPHS) for the 2004/2005 season: A/New Caledonia/20/99 (H1N1); A/Wyoming/3/2003 (H3N2) [an A/Fujian/411/2002-like virus]; and B/Jilin/20/2003 (LAIV) or B/Jiangsu/10/2003 (TIV); both are B/Shanghai/361/2002-like viruses.	Arm B (TIV) received Influenza Viral Vaccine, Intramuscular (Fluzone ®: Aventis Pasteur, Inc.) 0.5mL in the deltoid muscle region.
Krishnan 2021	India	I: 1015; C: 1010	Children 2-10 years of age residing in six villages in Ballabgarh Block, Haryana State, northern India	Trivalent live attenuated influenza vaccine (LAIV): the Serum Institute of India (SII, Pune, India) Year 1: vaccines included influenza A/California/7/2009 (A(H1N1)pdm09-like), A/Switzerland/9715293/2013 (A(H3N2)-like), and influenza B/Phuket/3073/2013 -Yamagata-like viruses; Year 2: vaccines included influenza A/California/7/2009(H1N1)pdm09-like, influenza A/Hong Kong/4801/2014 (A(H3N2)-like), and influenza B/Brisbane/ 60/2008 -Victoria-like viruses	One 0.5ml dose equally divided and administered into both nostrils	Trivalent inactivated influenza vaccine (IIV): Sanofi Pasteurrovidet (India) Year 1: vaccines included influenza A/California/7/2009 (A(H1N1) pdm09-like), A/Switzerland/9715293/2013 (A(H3N2)-like), and influenza B/Phuket/3073/2013 -Yamagata-like viruses; Year 2: vaccines included influenza A/California/7/2009(H1N1) pdm 09-like, influenza A/Hong Kong/4801/2014 (A(H3N2)-like), and influenza B/Brisbane/ 60/2008 -Victoria-like viruses	In addition to the second dose requirement in Year 1, dose volume varied by age: children aged <3 years received 0.25 ml IIV and children 3 years and older received 0.5 ml of IIV intramuscularly.
Sokolow 2022	USA	I: 79; C: 72	Children with asthma, aged 5 to 17 years.	Quadrivalent live attenuated influenza vaccine (LAIV4): FluMist uadrivalent, AstraZeneca	A single intranasal dose of LAIV4	Quadrivalent inactivated influenza vaccine (IIV4): Fluzone Quadrivalent Vaccine, SanofiPasteur	An intramuscular injection of IIV4
Williams 2023	USA	I: 68; C: 67	Children/adolescents 4-17 years of age.	Live-attenuated influenza vaccine (LAIV4): AstraZeneca	One metered spray in each nostril	Cell-cultured inactivated influenza vaccine (ccIIV4): AstraZeneca	NR

C, control; I, intervention; RTIs, respiratory tract infections.

表 4 观察性研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	对照组
Buchan 2018	Canada	10169	Children aged 2 to 17 years who received medical attention and were tested for influenza during the 2012-2013 to 2015-2016 influenza seasons in Alberta.	Live attenuated influenza vaccine (LAIV)	Inactivated influenza vaccine (IIV)
Chung 2019	US	17173	Patients aged 2 to 17 years presenting to outpatient settings (including emergency departments) with acute respiratory infection with fever and/or cough.	Quadrivalent live attenuated vaccine (LAIV4)	Inactivated influenza vaccine (IIV)

问题 3：在流感流行季，是否推荐儿童接种流感疫苗?

表 5 纳入研究的基线特征表

研究 ID	研究类型	国家	样本量	人群特征	干预组	对照组
Flannery 2017	Case-control study	US	NR	Children aged 6 months through 17 years.	Inactivated influenza vaccine.	No intervention.
Jefferson 2018	Cochrane Review	USA, Western Europe, Russia, and Bangladesh.	> 200,000	Healthy children under 16 years.	Influenza vaccines.	Placebo or no intervention.
Kalligeros 2020	Systematic review and meta-analysis	Asia, Australasia, New Zealand, Europ, North America, South America, global (with data from 13 sites around the world).	NR	Children.	Influenza vaccines.	NA
Chung 2020	Test-negative case-control study	US	7533	Children aged 6 months to 8 years with an acute respiratory tract illness with cough who presented for outpatient care within 7 days of illness onset were included.	Inactivated influenza vaccine.	No intervention.
Boddington 2021	Systematic review and meta-analysis	UK	NR	Participants were 17 years old or less and influenza infection was laboratory-confirmed.	Influenza vaccines.	NA
Ferdinands 2021	A narrative review	US, Australia, Spain, North Carolina, Mexico, Quebec, China (Hong Kong), Arkansas, Japan, France, Argentina, Michigan, Illinois, Canada, New Zealand, Marshfield, Columbus, OH.	NA	Community-dwelling adults and children 6 months of age with laboratory-confirmed influenza Illness.	Inactivated influenza vaccine.	Non-influenza vaccination, placebo, or no vaccination.
Nolan 2021	Randomized clinicaled trial	Eight countries.	4514	Children and adolescents 2 to less than 18 years of age.	Cell-culture-derived quadrivalent inactivated	Meningococcal ACWY.

					influenza vaccine (IIV4c)	
Olson 2022	Test-negative design	US	291	Children aged <18 years admitted to the intensive care unit with acute respiratory infection across 17 hospitals.	Inactivated influenza vaccine.	No intervention.

NA, not applicable; NR, not reported.

问题 4. 有明确流感密接接触史的儿童，是否推荐暴露后抗病毒药物预防 ？

表 6 随机对照研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	干预组治疗方式	对照组	对照组治疗方式
Welliver 2001	North America and Europe	I: 209 C: 206	Family with a minimum of 2 and a maximum of 8 contacts withn 48 hours of symtom onset (minimum cough and coryza) in a primary (index) case (IC). Children <12 years were excluded from the contacts.	Oseltamivir	75mg daily for 7 days	Placebo	75mg daily for 7 days
Handen 2004	USA	I: 410; C: 402	Contacts aged≥1 year.	Oseltamivir	Began oseltamivir prophylaxis within 48 h of the first onset of influenza like symptoms in the index case(s). The age-adjusted dose was the same as that used for treatment but was given once daily for 10 days.	No treatment	NA
Ikematsu 2020	Japan	I: 374 C: 375	Eligible participants were household contacts who were well (defined as no influenza symptoms and an axillary temperature of <37.0°C) and had lived in the same household as the index patient for at least 48 hours before enrollment.	Baloxavir	Baloxavir 20-mg tablets, 2% granules, was orally administered to participants as a single dose on Day 1.	Placebo	Placebo was orally administered to participants as a single dose on Day 1.

C, control; I, intervention; NA, Not Applicable.

表 7 观察性研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	干预组治疗方式	对照组
Shinjoh 2012	Japan	I: 63; C: 17	We defined contacts as patients who came into contact with index cases of influenza (from a day before the index case devel oped fever >38°C) by any of the following means: • Direct contact, such as playing with or speaking with the index case without wearing a surgical mask Close contact, such as being admitted in the same room as the index case.	Oseltamivir	2mg/kg/dose; 75mg maximum dose; once daily.	No treatment
Ishiguro 2016	Japan	I: 212; C: 15	Inpatients who had been in close contact with the index cases were defined as individuals who had shared a room with an index case within 48 h of illness onset.	Oseltamivir	Oseltamivir 75 mg once daily for adults or 2 mg/kg (maximum of 75 mg) once daily for children for three days.	No treatment

C, control; I, intervention; NA, Not Applicable.

问题 5：对于无并发症、无重症高危因素、无需住院的流感儿童，在发病 48 h 内是否常规推荐抗病毒药物治疗？

表 8 奥司他韦-随机对照研究的基线特征表

研究 ID	国家	样本量	人群特征	干预组	干预组治疗方式	对照组	对照组治疗方式
Whitley 2001	US; Canada	I: 217; C: 235	Infected children between the ages of 1 and 2 years,presenting within 48 h of illness onset and having an oral/otic temperature ≥ 100°F (37.8°C) and at least one respiratory symptom (cough or coryza).	Oseltamivir	Children were randomized to receive either placebo or liquid oseltamivir at 2 mg/kg/dose (to a maximum of 100 mg/dose) twice daily for 10 doses and were stratified for the presence of otitis media at enrollment.	Placebo	Children were randomized to receive either placebo or liquid oseltamivir at 2 mg/kg/dose (to a maximum of 100 mg/dose) twice daily for 10 doses and were stratified for the presence of otitis media at enrollment.
Johnston 2005	UK; The northern and southern hemispheres.	I: 84; C: 95	Subjects 6-12 years of age, with asthma severe enough to require regular medical follow-up monitoring or hospital care, were enrolled if they met the following criteria: presented with influenza symptoms recorded temperature of ≥38.7°C plus 1 respiratory symptom (cough or coryza), presented within 48 hours after symptom onset and were able to perform the pulmonary function tests.	Oseltamivir	Patients were randomized to receive either oseltamivir (2 mg/kg) or placebo, twice daily, as orally administered syrup (6 mg/mL); The first dose of the study drug was administered at the clinic, and the date (and time) at which it was administered was designated day 1. Study day 2 began at 12 midnight of the same calendar day.	Placebo	Patients were randomized to receive either oseltamivir (2 mg/kg) or placebo, twice daily, as orally administered syrup (6 mg/mL); The first dose of the study drug was administered at the clinic, and the date (and time) at which it was administered was designated day 1. Study day 2 began at 12 midnight of the same calendar day.
Heinonen 2010	Finland	I: 37; C: 61	Children 1-3 years of age with laboratory-confirmed influenza had for <24 hours a fever (oral, rectal, or axillary temperature ≥38.0 ℃) and ≥1 sign or symptom of respiratory infection (cough, rhinitis, or sore throat) or a positive rapid influenza test result.	Oseltamivir	The study drugs were administered twice daily for 5 days (total of 10 doses). The dosage of oseltamivir was 30 mg twice daily for children weighing ≤15.0 kg and 45 mg twice daily for children weighing 15.1-23.0 kg.	Placebo	The study drugs were administered twice daily for 5 days (total of 10 doses). The dosage of oseltamivir was 30 mg twice daily for children weighing ≤15.0 kg and 45 mg twice daily for children weighing 15.1-23.0 kg.

何 2017	China	I: 42; C: 31	1-12 岁流感检测阳性患儿，发烧≥38.5℃并伴有呼吸道症状，持续时间≤48 小时.	愈酚伪麻口服溶液+磷酸奥司他韦颗粒剂	试验组给予基础治疗加上磷酸奥司他韦颗粒剂(宜昌长江药业有限公司)；按体重-剂量表进行磷酸奥司他韦颗粒剂给药,每天 2 次,给药间隔约 12 h,连续给药 5 天,愈酚伪麻口服溶液按照药品说明书给药同样连续给药 5 天。	愈酚伪麻口服溶液	对照组给予愈酚伪麻口服溶液(上海强生制药有限公司)作为基础治疗；愈酚伪麻口服溶液按照药品说明书给药同样连续给药 5 天。
蔡 2020	China	I: 50; C: 50	流行性感冒患儿，精神状况、意识状况佳.	磷酸奥司他韦颗粒	给予观察组磷酸奥司他韦颗粒（宜昌东阳光长江药业股份有限公司，国药准字 H20080763）治疗，体质量≤ 15 kg，每日 2 次，每次 30 mg；15 ~ 23 kg，每日 2 次，每次 45 mg；23 ~ 40 kg，每日 2 次，每次 60 mg，两组患儿均连续治疗 5 天。	普通中药制剂	给予对照组常规治疗，让患儿口服普通中药制剂，通过清热解毒缓解临床症状。

C, control; I, intervention.

表 9 玛巴洛沙韦-随机对照研究的基线特征

研究 ID	国家	样本量	人群特征	干预组	干预组治疗方式	对照组	对照组治疗方式
Portsmouth 2020	Japan;USA	I: 63 C: 27	Eligible patients were outpatients aged ≥12 and ≤19 years with suspected influenza A or influenza B virus infection who were considered at high risk of developing influenzaassociated complications.	Baloxavir	A single dose of baloxavir (40 or 80 mg depending on body weight) on day 1 only	Placebo	Matching placebo on day 1 only.
Ison 2020	Japan, South Korea, the Philippines, Taiwan, the USA, Europe (Belgium, Bulgaria, Germany, Spain, the UK, Hungary, Latvia, Poland, and Romania), and areas in the southern hemisphere (Australia, New Zealand, and South Africa)	I-1: 13; I-2: 17 C: 12	Eligible patients were outpatients aged < 18 years with suspected influenza A or influenza B virus infection who were considered at high risk of developing influenzaassociated complications.	Baloxavir; Oseltamivir	Patients in the baloxavir group received a single oral dose of baloxavir at baseline (40 mg for patients weighing <80 kg and 80 mg for those weighing ≥80 kg).	Placebo	Patients in the placebo group received a single oral dose of baloxavir-matched placebo at baseline.

C, control; I, intervention.

表 10 奥司他韦对比玛巴洛沙韦-随机对照研究的基线特征

研究 ID	国家	样本量	人群特征	干预组	干预组治疗方式	对照组	对照组治疗方式
Baker 2020	USA; South America;Europe	I: 117; C: 59	Children 1–<12 years of age with influenza (who were otherwise healthy) during the 2018/2019 Northern Hemisphere influenza season	Baloxavir	A single dose of oral baloxavir on day 1 (2mg/kg for those weighing <20kg and a single dose of 40mg for those weighing ≥20 kg).	Oseltamivir	Oral oseltamivir twice daily according to prescribing information (30mg for patients weighing ≤15 kg, 45mg for >15–≤23kg, 60mg for >23–≤40 kg, and 75mg for >40 kg) on days 1-5.
Wagatsuma 2022	Japan	I: 100; C: 59	Otherwise healthy patients <19 years who presented to the outpatient clinic within 48 h of the onset of influenza-like symptoms, such as the sudden onset of fever, sore throat, cough, sneezing, or general malaise.	Baloxavir	A single oral dose as follows: patients aged 12–18 years received a dose of 40 mg; children aged <12 years received 10 mg if weighing 10-20 kg, 20 mg if weighing 20-40 kg, or 40 mg if weighing >40 kg as a single oral administration.	Oseltamivir	Oseltamivir was administered orally for 5 days, 2 × 75 mg/day for patients weighing ≥37.5 kg, and 2 mg/kg/day for those weighing <37.5 kg.

C, control; I, intervention.

表 11 补充研究的基线特征

研究 ID	研究类型	国家	样本量	人群特征	干预组	干预组治疗方式	对照组	对照组治疗方式
Saito 2020	Prospective observational study	Japan	154	Healthy patients younger than 19 years old who presented at outpatient clinics within 48 h of influenza-like-symptom onset, such as fever, sore throat, coughing, sneezing, or general fatigue were eligible.	Oseltamivir	Oseltamivir was administered orally for 5 days, 2 × 75 mg/day for patients weighing ≥ 37.5 kg and 2 mg/kg/day for those weighing < 37.5 kg.	Baloxavir	Patients aged 12-18 years received a dosage of 40 mg, children aged less than 12 years received a dosage of 10 mg for those weighing 10-20 kg, 20 mg for those weighing 20-40 kg or 40 mg for those weighing more than 40 kg.
Kakuya 2022	Prospective observational study	Japan	235	Influenza-infected patients (3-18 years of age).	Oseltamivir	NR	Baloxavir	NR
Wagatsuma 2022	Observational study	Japan	159	Healthy patients <19 years who presented to the outpatient clinic within 48 h of the onset of influenza-like symptoms, such as the sudden onset of fever, sore throat, cough, sneezing, or general malaise.	Oseltamivir	Oseltamivir was administered orally for 5 days, 2 × 75 mg/day for patients weighing ≥37.5 kg, and 2 mg/kg/day for those weighing <37.5 kg.	Baloxavir	Patients aged 12-18 years received a dose of 40 mg; children aged <12 years received 10 mg if weighing 10-20 kg, 20 mg if weighing 20-40 kg, or 40 mg if eighing >40 kg as a single oral administration.
Nezu 2023	Retrospective observational study	Japan	1410	Pediatric patients aged 006 years. All patients received either baloxavir or oseltamivir within 48 h of disease onset, indicating the presence of fever.	Oseltamivir	Oral oseltamivir twice daily for 5 days (3 mg/kg for those aged 2 weeks to 12 months and 2 mg/kg for those aged 1-6 years on days 1-5).	Baloxavir	A single dose of oral baloxavir on day 1 (10 mg for those weighing 10-20 kg and 20 mg for those weighing 20-40 kg).
Sun 2024	Observational	Japan	1461	Clinicians informed	Oseltamivir	75 mg twice daily, 5 days (body weight >	Baloxavir;	Baloxavir: 80 mg single dose (>12

	study			children and their caregivers about the study after healthy patients <19 years old tested positive for influenza A or B virus using a rapid diagnostic test (RDT) kit.		37.5 kg). 2 mg/kg twice daily, 5 days (maximum 150 mg/day) (body weight < 37.5 kg).	Zanamivir	years old body, weight >80 kg) b. 40 mg single dose (>12 years old, body weight <80 kg) c. 40 mg single dose (<12 years old, body weight ≥80 kg)a d. 20 mg single dose (<12 years old, body weight ≥20 to <40 kg) e. 10 mg single dose (<12 years old, body weight ≥10 to <20 kg). Zanamivir: 10 mg twice daily, 5 days (> 5 years old).
Shobugawa 2012	Observational study	Japan	681	Patients with influenza-like-illness (ILI).	Oseltamivir	Oseltamivir was prescribed to be taken orally twice daily for 5 days (150 mg per day for adults and for children who weighed ≥ 37.5 kg, and 4 mg/kg for chil dren who weighed <37.5 kg.	Zanamivir	Zanamivir inhalation was prescribed to be used twice daily for 5 days (20 mg per day for adults and for children C5 years old).
Hikita 2012	Observational study	Japan	223	Patients under the age of 18 years diagnosed with influenza.	Oseltamivir	Oral oseltamivir was prescribed twice per day in divided dosages for 5 days (4 mg/kg/day, maximum of 150 mg/day).	Peramivir	Peramivir was administered intrave nously as a single dose of 10 mg/kg/dose (maximum 300 mg/dose) over a period of 15 min.
Takemoto 2013	Observational study	Japan	191	The enrolment of patients presenting with influenza took place within 48 h of onset if they had not been treated elsewhere and did not have any other medical conditions.	Oseltamivir	Oseltamivir was administered orally for 5 days (2 × 150 mg/day for adults and children weighing >37.5 kg and 4 mg/kg/day for children <37.5 kg).	Peramivir	Peramivir was intravenously infused once over a period of 15–30 min to infected adults at a dose of 300 mg, and to children at 10 mg/kg as outpatients.
Sugaya 2014	Observational study	Japan	59	All of the patients included in this study arrived at one of our hospitals with a fever >38°C within 48 h after the onset of the	Oseltamivir	Oseltamivir was prescribed in eight-based unit doses to be administered in divided doses twice daily for 5 days.	Peramivir	Peramivir is administered to children as a single 10 mg/kg intravenous dose infused over 15 min (upper limit, 600 mg) on the first day of treatment.

				fever.				
Hirotsu 2018	Randomized clinicaled trial	Japan	123	Patients aged 4-12 years with influenza A virus infection.	Oseltamivir	OV was mixed in a suspension and administered orally twice daily at a dose of 2 mg/kg per administration (66.7 mg/kg as a dry syrup). In children weighing 37.5 kg or more, OV capsules of 75 mg each were administered orally twice a day for 5 days.	Peramivir	PV was intravenously infused at a dose of 10 mg/kg (600 mg in patients whose body weight was 60 kg or more) over more than 15 min once and a repeated dose (treated for >1 day) was administered in accordance with persisting symptoms in pediatric patients.
Ishiguro 2018	Prospective observational study	Japan	1207	Outpatients aged 0 months to 18 years who had an axillary temperature of 37.5 C or higher were diagnosed as having influenza virus infection based on results obtained by a rapid antigen test.	Oseltamivir	Oseltamivir was administered at 2 mg/kg/dose (to a maximum of 75 mg/dose) twice daily for 5 days.	Peramivir	Peramivir was administered intravenously at 10 mg/kg once daily (to a maximum of 600 mg/dose).
Nakazawa 2020	Prospective postmarketing surveillance (PMS)	Japan	3000	Contracted patients at each hospital/clinic and the overall target number.	Baloxavir	Patients were administered a single oral dose of baloxavir on Day 1 and were observed for 7 days. As specified in the package insert, adults and children ≥12 years (adolescents) received 40 mg baloxavir (2×20 mg tablets) if their body weight was <80 kg and 80 mg baloxavir (4×20 mg tablets) if their body weight was ≥80 kg. Children <12 years received 40 mg baloxavir (2×20 mg tablets) if their body weight was≥40 kg, 20 mg baloxavir (1×20 mg tablet) if their body weight was≥20 kg and <40 kg, and ≥10 mg baloxavir (1×10 mg tablet) if their body weight was ≥10 kg and <20 kg. One child who weighed<10 kg received 10 mg baloxavir.		

C, control; I, intervention; NR, not reported.

问题 6：确诊流感的儿童在发病 48 h 后，是否推荐使用抗病毒药物？

表 12 纳入研究的基线特征

研究 ID	研究类型	国家	样本量	人群特征	干预组	干预组治疗方式	对照组
Louie 2013	Observational study	US	784	Patients aged 0 to 17 years hospitalized in ICUs with laboratory-confirmed influenza.	NAI treatment	NR	No treatment
Muthuri 2014	Systematic review and meta-analysis	UK	29234	Patients (all ages) admitted to hospital worldwide with laboratory confi rmed or clinically diagnosed pandemic infl uenza A H1N1pdm09 virus infection.	NAI treatment	NR	No treatment
Dawood 2016	Randomized controlled trial; NCT01690637	Panama; El Salvador	I: 19; C: 11	Children had to be aged≤9 years and hospitalized < 7days after symptom onset with symptoms meeting a modified version of the World Health Organization criteria for severe acute respiratory infection (cough or sore throat plus age-specific tachypnea). And 30 (4%) had laboratory-confirmed influenza.	Oseltamivir	Randomized children received active drug every 12 h for 10 doses. The first dose was given within 2 h of enrollment. For children aged 0-11 months, study drug was dosed at 3 mg/kg/dose. For children aged ≥12 months, study drug was dosed based on standard unit dosing: 30 mg/dose for children ≤15 kg, 45 mg for children >15-23 kg, 60 mg for children >23-40 kg, and 75 mg for children >40 kg. Oseltamivir was prepared according to package insert guidelines for emergency compounding of an oral suspension from 75 mg TAMIFLU® capsules modified to yield a concentration of 15mg/5 mL.	Placebo

C, control; I, intervention; NAI, neuraminidase inhibitor treatment; NR, not reported.

问题 8：对于病情进行性加重、重症流感患儿，是否推荐不同机制抗病毒药物联合或者序贯治疗？

表 13 纳入研究的基线特征

研究 ID	研究类型	国家	样本量	人群特征	干预组	干预组治疗方式	对照组
Kawaguchi 2018	Randomized controlled trial	Japan	18	Japanese healthy adult male subjects aged from 20 to 59 years with a body weight of≥50 kg and body mass index of 18.5–25.0 kg/m2 .	Co-administration	Co-administration of baloxavir marboxil at 40 mg and oseltamivir at 75 mg simultaneously on day 1 in the fasted state, followed by repeated twice-daily administration of oseltamivir at 75 mg until day 5 after each meal.	Baloxavir marboxil alone
Kumar 2022	Randomized controlled trial	25 countries	366	Patients aged 12 years or older who were hospitalised with laboratory-confirmed influenza (by RT-PCR or a rapid test) and had a National Early Warning Score 2 (NEWS2) of 4 or greater.	Baloxavir plus NAI	The standard-of-care NAI (oseltamivir, zanamivir, or peramivir) was given according to local clinical practice, with the choice of NAI made at the discretion of the treating physician. Baloxavir was administered enterally at 40 mg (for 40 kg to <80 kg bodyweight) or 80 mg (for ≥80 kg bodyweight) on day 1 and day 4, with an additional dose on day 7 if no clinical improvement had occurred at day 5.	Placebo plus NAI

C, control; I, intervention; NAI, neuraminidase inhibitor treatment; NR, not reported.