Vaccine: X 9 (2021) 100115

Contents lists available at ScienceDirect

Vaccine: X

journal homepage: www.elsevier.com/locate/jvacx

Co-administration of routine paediatric vaccines in England often deviates from the immunisation schedule

Jorgen Bauwens [a,b,*], Simon de Lusignan [c,d], Julian Sherlock [c], Filipa Ferreira [c], Nino Künzli [a,e], Jan Bonhoeffer [b]

[a] University of Basel, Switzerland
[b] University of Basel Children's Hospital, Switzerland
[c] Nuffield Department of Primary Care Health Sciences, University of Oxford, United Kingdom
[d] Royal College of General Practitioners, United Kingdom
[e] Swiss Tropical and Public Health Institute, Switzerland

ARTICLE INFO

Article history:
Received 27 January 2021
Received in revised form 13 August 2021
Accepted 10 September 2021
Available online 15 September 2021

Keywords:
Children
Co-administration. Immunisation Schedule
Minors
Vaccination
Vaccines

ABSTRACT

Vaccine co-administration can facilitate the introduction of new vaccines in immunisation schedules and improve coverage. We analysed real life data to quantify the extent of routine paediatric vaccine co-administrations as recommended and as never recommended in the immunisation schedule in England, and assessed factors for recommended and never recommended vaccine co-administrations.

Immunisation data for all scheduled routine paediatric vaccines between 2008 and 2018 was obtained from the Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC).

We included 6′257′828 doses administered to 1′005′827 children. Twenty-one percent of vaccines were given separately, 79% were co-administered. Sixty-four percent of vaccines scheduled for co-administration were co-administered as recommended while 15% were administered separately. Among all vaccine co-administrations, 75% happened as recommended in the schedule, 4% were never recommended, while 21% deviated from the schedule. Vaccine co-administration according to the schedule varied greatly between vaccines. Forty-eight percent of English children received at least one of their vaccine co-administrations not as recommended in the immunisation schedule, with 19% of children receiving none of their co-administered vaccines as recommended. Late administration of one or more vaccines increased the odds for deviated co-administrations (OR 1.60) and strongly increased the odds for never recommended co-administrations (OR 5.34). Differences between genders, NHS regions, and IMD quintiles were statistically significant but small.

Suboptimal co-administration rates for routine paediatric vaccines are a missed opportunity and should be optimised by concerted public health action.

Introduction

Vaccine co-administrations can be useful to introduce new vaccines in immunisation schedules and to maximise coverage, including facilitated catching-up for missed doses [1–6]. Co-administration may also improve adherence to immunisation schedules (i.e., timeliness) and minimise physician visits [7]. Thus, it is more cost-effective than giving each vaccine alone [5,8]. In 2018, the NHS paediatric routine immunisation schedule recommended six co-administrations (see Fig. 1) [9]. Immunisation schedules are developed to assure optimal protection against vaccine preventable diseases while minimising potential side effects [10,11]. However, adherence to crowded immunisation schedules may not always be possible and the timing of vaccinations may be shifted for various reasons. This may lead to delays and unscheduled co-administrations. Such unscheduled co-

Abbreviations: DTaP/HepB/IPV/Hib, Diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B, inactivated poliovirus, and *Haemophilus influenzae* type b conjugate vaccine; DTaP/IPV/Hib, Diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus, and *Haemophilus influenzae* type b conjugate vaccine; DTaP/IPV or dTaP/IPV, Diphtheria and tetanus toxoids and acellular pertussis adsorbed, and inactivated poliovirus vaccine; Hib/MenC, Haemophilus influenzae type b conjugate, and bivalent meningococcal conjugate vaccine; HPV, Human papillomavirus vaccine; MenACWY, Quadrivalent meningococcal conjugate vaccine; MenB, Serogroup B meningococcal vaccine; MenC, Serogroup C meningococcal vaccine; MMR, Measles, mumps, and rubella vaccine; PCV, Pneumococcal conjugate vaccine; RV, Rotavirus vaccine; Td/IPV, Tetanus and diphtheria toxoids and inactivated poliovirus vaccine; COVER, Cover of Vaccination Evaluated Rapidly; GP, General Practitioner; IMD, Index of Multiple Deprivation; IQR, Interquartile Range; OR, Odds Ratio; PHE, Public Health England; RCGP, Royal College of General Practitioners; RSC, Research and Surveillance Centre.

* Corresponding author at: University Children's Hospital Basel, Spitalstrasse 33, 4056 Basel, Switzerland.
E-mail address: jorgen.bauwens@unibas.ch (J. Bauwens).

https://doi.org/10.1016/j.jvacx.2021.100115
2590-1362/

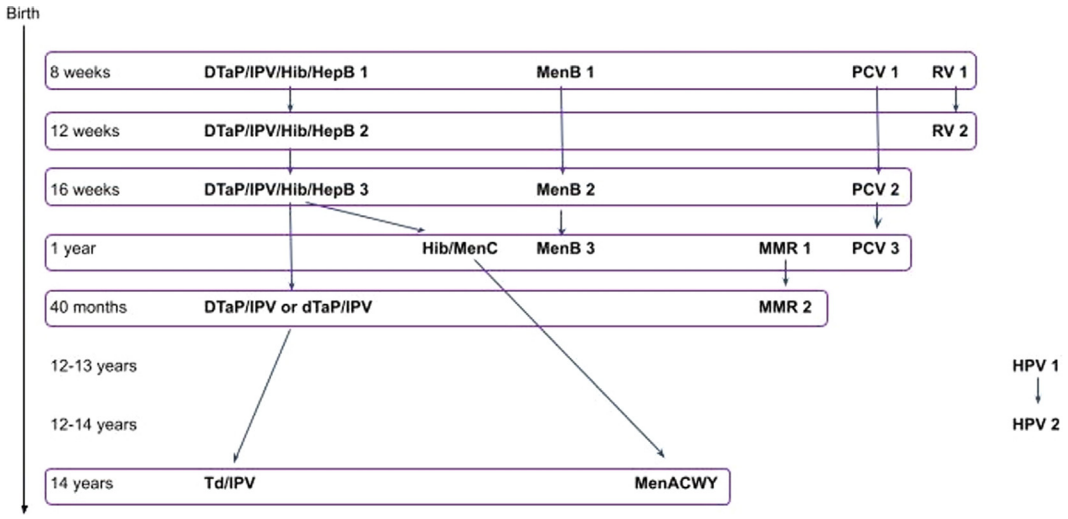

Fig. 1. Co-administrations in the routine paediatric immunisation schedule in 2018. [9]

administrations of vaccines, particularly when off-label, may lead to interference and potentially alter their efficacy and safety profiles [12,13].

Studies investigating vaccine co-administration typically document schedule feasibility [2,3], often to inform programme introduction. Studies assessing adherence to vaccination schedules typically evaluate programme implementation and coverage without much attention to co-administration specifically [14]. We analysed to which extent routine paediatric vaccines in England are co-administered, as recommended in the immunisation schedule as well as never recommended, and assessed potential factors for recommended and never recommended vaccine co-administrations.

Methods

The data and study population were described in detail before [15]. In brief, data was extracted from the Oxford Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC), a national, electronic, primary health care, medical record database, representative for the English population [16,17]. A previous database characterisation study assessed this database and found it fit to provide reliable evidence on vaccination [18]. Calculated vaccine uptake in the RCGP RSC network is similar to national rates published by Public Health England (PHE) [17] while providing access to more granular data than provided by the NHS Cover of Vaccination Evaluated Rapidly (COVER) statistics. We included all children between 0 and 18 years old during the study period from 1 January 2008 to 31 December 2018. Children were excluded from analyses if they were registered in the database after the age for the first scheduled dose of a vaccine. Every child had a unique, anonymised patient identifier. For each child, we also collected the gender, the NHS-region of residence in England, and the postcode-based Index of Multiple Deprivation (IMD) quintiles. Vaccination types, doses, and dates were collected for all routinely scheduled paediatric vaccines by Public Health England between 2008 and 2018: DTaP/IPV/Hib/HepB, DTaP/IPV/Hib, DTaP/IPV, dTaP/IPV, Td/IPV, MMR, PCV, MenB, MenC, MenACWY, Hib/MenC, RV, HPV [9,19–26]. Except for HPV, all these vaccines were scheduled for co-administration. Dose numbers were determined according to the chronological order of vaccinations. Records with a missing patient-ID, vaccination type or date were excluded.

We defined co-administration as having received more than one of the included routine paediatric vaccines on the same day. We distinguished three main categories of co-administration:

1.“Recommended co-administration” for vaccines that were co-administered exactly as recommended in the immunisation schedule;

2.“Deviated co-administration” encompasses vaccine co-administrations that deviate from the actual immunisations schedule. This includes vaccines that are co-administered according to an outdated schedule (“outdated”), vaccines that are co-administered according to the immunisation schedule but not the recommended doses of these vaccines (“shifted doses”), vaccines co-administered according to an outdated schedule and with shifted doses (“outdated and shifted doses”), or co-administrations that lacked at least one of the vaccines scheduled to be co-administered together (“fewer vaccines”).

3.“Never recommended co-administration” for co-administered vaccines that had never been scheduled to be given together.

For each routine paediatric vaccine, the proportion of vaccines co-administered, as well as the amount of vaccines co-administered according to each of the defined categories (i.e. recommended, deviated, never recommended) were calculated. We also identified the ten mostly co-administered vaccines in each of these three categories of co-administration.

We analysed whether recommended, deviated, and never recommended vaccine co-administration differed between the factors gender, NHS region, and IMD quintile, as well as the impact of the timeliness of vaccination, using Pearson’s chi-square test and multivariate logistic regression. We used a significance level of 0.05 to determine whether the co-administration category was independent of any of the potential factors or not. Logistic regression coefficients were transformed to odd ratios to quantify the impact of these factors. Analyses were performed in R [27].

Results

6′257′828 vaccines in 1′005′827 children met our inclusion criteria for analysis. This study population was representative for the entire population in the database [15]. 1′344′659 (21%) routine paediatric vaccines were given separately, while 4′913′169 (79%) were co-administered: 2′277′482 (36%) vaccines were given with a second vaccine; 2′088′153 (33%) were co-administrations of three, and 541′276 (9%) were co-administrations of four vaccines. Of all 5′782′118 vaccines scheduled for co-administration with at

least one other vaccine, 3′689′268 (64%) were co-administered as recommended in the schedule, 1′039′698 (18%) deviated from the schedule and 181′097 (3%) were co-administered as never recommended, while 872′055 (15%) vaccines were administered separately. As shown in Fig. 2, between 84% and 98% of vaccines scheduled in the first year of age were co-administered with at least one other vaccine, except for Hib/MenC (70%) and the ratio of vaccines co-administered decreased for vaccines scheduled later in life (DTaP/IPV or dTaP/IPV, Td/IPV, MenACWY, MMR dose 2). Fig. 2 shows the observed patterns of co-administration for each vaccine and dose: the proportions of each vaccine and dose that were co-administered with other vaccines according to the schedule varied between 87% for DTap/IPV/Hib dose 2 and 17% for both Td/IPV and MenACWY.

We found statistically significant differences for the ratio of vaccines co-administered between genders, NHS regions, and IMD quintiles ($p < 0.05$). Boys received a larger proportion (85%) of their vaccines co-administered than girls (72% including HPV vaccine, 84% excluding HPV vaccine). Co-administration ratios were higher in London, Midlands and East-England (both 80%) while lower in South England (77%) and North England (78%). There was a slight decrease in the proportion of vaccine co-administrations with decreasing area deprivation from 80% in the first to 78% in the fifth quintile.

The most often co-administered vaccines as recommended in the immunisation schedule were DTaP/IPV/Hib + PCV (13.9%), the most often co-administered vaccines that deviated from the schedule were Hib/MenC + MMR + PCV (2.6%), and the most often never recommended co-administered vaccines MMR + Td/IPV (0.6%). The ten most often co-administered vaccines as recommended, deviated, and never recommended in the immunisation schedule are listed in Table 1.

Seventy-five percent of co-administrations happened as recommended in the immunisation schedule. Four percent were never recommended. The remaining 21% deviated from the schedule: 10% percent were co-administered according to an outdated schedule (“outdated”), 7% received fewer vaccines than scheduled, 3% had shifted doses, and 1% of co-administered vaccines concerned an outdated co-administration with shifted doses (“outdated and shifted doses”). Fifty-two percent of children received all their co-administered vaccines as recommended in the immunisation schedule, while 19% of children received none of their co-administered vaccines exactly as listed in the schedule. We found statistically significant associations between receiving co-administrations as recommended in the schedule and the factors gender, NHS regions, and IMD quintiles, as well as the timeliness of vaccinations ($p < 0.05$).

Boys had slightly more co-administrations as recommended (76%) than girls (75%). The proportion of recommended vaccine co-administrations was the highest in North England (78%), 76% in Midlands and East, and South England, while the lowest in London (71%). The ratio of recommended co-administrations was the lowest for areas in the second most deprived quintile (73%) and improved to 78% for areas in the least deprived quintile. We observed 75% recommended co-administrations in the most deprived quintile and 76% in the third and fourth quintiles. The OR for recommended vaccine co-administrations when having received all vaccines on time was 2.46 (95% CI: 2.44–2.48).

Girls were slightly more likely to have neer recommended co-administrations (4%) than boys (3%). The highest proportions of deviated and never recommended co-administrations were observed in London (24% and 5%) and the lowest in North England (19% and 3%). The ratios of deviated and never recommended co-administrations were 20% and 4% in Midlands and East England

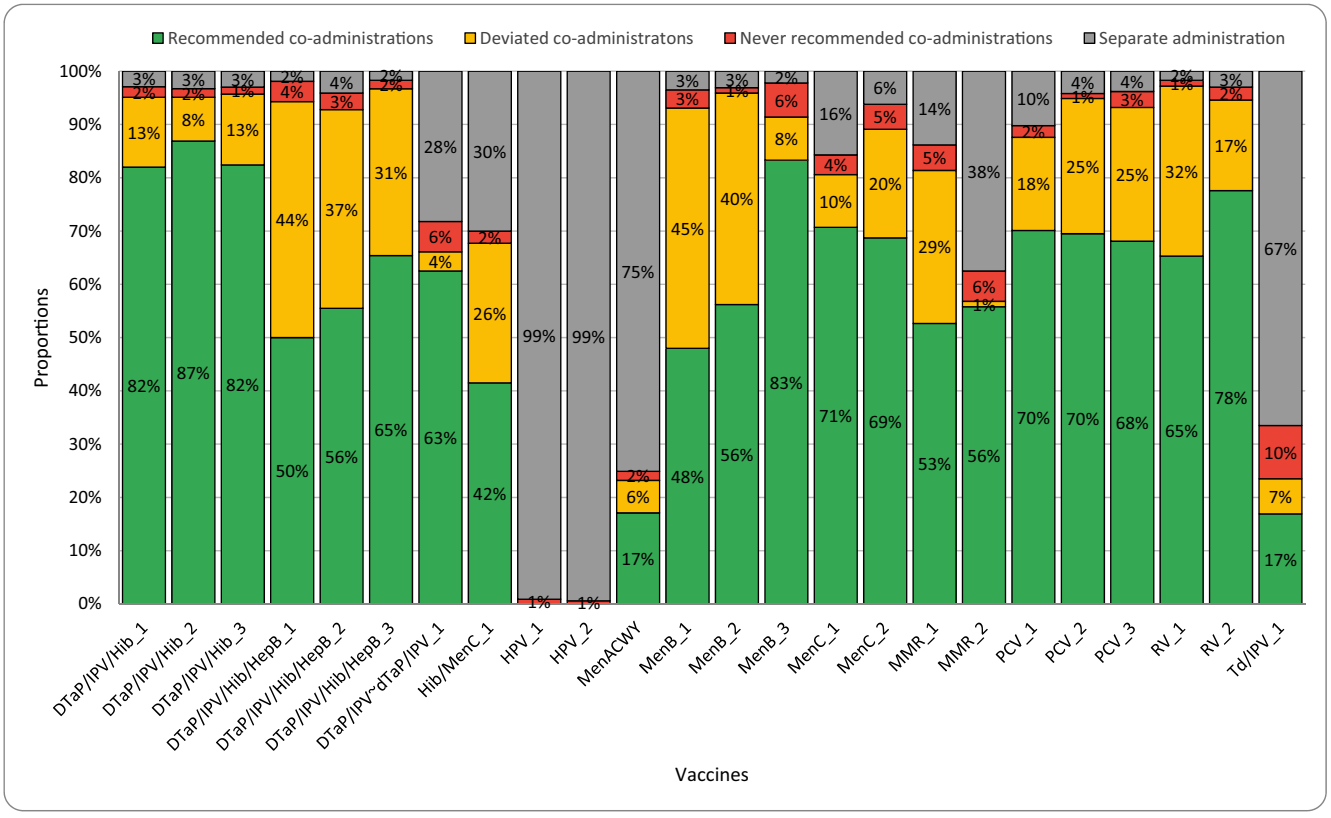

Fig. 2. Proportions of routine paediatric vaccine doses co-administered with at least one other vaccine according to the immunisation schedule, deviated, or off-schedule, or given separately.

Table 1
Vaccines most often co-administered between 2008 and 2018, by category. *Percentages indicate the proportion of each listed co-administration on the total number of vaccine co-administrations (all categories) during the study period.*

Recommended co-administrations[1]	n	%	Scheduled ages[2]
DTaP/IPV/Hib + PCV	274,919	13,9%	8 weeks; 16 weeks
DTaP/IPV or dTaP/IPV + MMR	205,362	10,4%	40 months
DTaP/IPV/Hib + MenC	194,083	9,8%	3 months; 4 months
DTaP/IPV/Hib + MenC + PCV	180,688	9,2%	4 months
Hib/MenC + MMR + PCV	148,218	7,5%	1 year
MMR + PCV	91,134	4,6%	1 year
DTaP/IPV/Hib + MenC + RV	89,332	4,5%	3 months
DTaP/IPV/Hib + PCV + RV	74,704	3,8%	2 months
DTaP/IPV/Hib + MenB + PCV	42,154	2,1%	8 weeks; 16 weeks; 1 year
DTaP/IPV/Hib + RV	40,668	2,1%	8 weeks; 12 weeks
Deviated co-administrations[3]	**n**	**%**	**Scheduled ages**
Hib/MenC + MMR + PCV	52,121	2,6%	1 year
MenC + PCV	43,965	2,2%	4 months
Hib/MenC + MMR	41,995	2,1%	1 year
MMR + PCV	35,025	1,8%	1 year
DTaP/IPV/Hib + MenB + PCV	29,183	1,5%	8 weeks; 16 weeks; 1 year
DTaP/IPV/Hib + MenB + PCV + RV	28,872	1,5%	8 weeks
DTaP/IPV/Hib + PCV	23,602	1,2%	8 weeks; 16 weeks
DTaP/IPV/Hib + MenC	21,005	1,1%	3 months; 4 months
DTaP/IPV/Hib/HepB + MenB + PCV + RV	14,309	0,7%	8 weeks
DTaP/IPV/Hib + MenC + PCV	12,509	0,6%	4 months
Never recommended co-administrations[4]	**n**	**%**	**Scheduled ages[5]**
MMR + Td/IPV	10,927	0,6%	See Fig. 1
MenC + MMR + PCV	8779	0,4%	See Fig. 1
DTaP/IPV/Hib + MMR	7452	0,4%	See Fig. 1
DTaP/IPV or dTaP/IPV + PCV	6800	0,3%	See Fig. 1
MenC + MMR	4922	0,2%	See Fig. 1
DTaP/IPV or dTaP/IPV + Hib/MenC + MMR	2834	0,1%	See Fig. 1
DTaP/IPV/Hib + MenB + MenC + RV	2748	0,1%	See Fig. 1
DTaP/IPV or dTaP/IPV + Hib/MenC	2127	0,1%	See Fig. 1
MenB + MenC + MMR + PCV	1630	0,1%	See Fig. 1
HPV + Td/IPV	1273	0,1%	See Fig. 1

[1] Vaccines co-administered exactly as recommended in the immunisation schedule.
[2] Scheduled ages for co-administering the vaccines according to the most recent immunisation schedule in the study period.
[3] Vaccine co-administrations deviating from the actual immunisations schedule (includes vaccines co-administered according to an outdated schedule, vaccines co-administered according to the immunisation schedule but not the recommended doses of these vaccines, vaccines co-administered according to an outdated schedule but with shifted doses, or co-administrations lacking at least one of the vaccines scheduled to be co-administered together.
[4] Co-administered vaccines that were never scheduled together.
[5] The individual ages for administering each of these vaccines can be found in Fig. 1 for the most recent immunisation schedule in the study period. These vaccines were at no age scheduled for co-administration.

and 21% and 3% in South England. Both ratios of deviated and never recommended co-administrations slightly increased with increasing area deprivation (from 20% to 21% for deviated and from 3% to 4% for never recommended co-administrations. Having received at least one vaccine too late increased the odds for deviated co-administrations (OR 1.60; 95% CI 1.58–1.62) and strongly increased the odds for never recommended co-administrations (OR 5.34; 95% CI 5.19–5.50).

Discussion

Our analysis of real-life GP practice data showed that 15% of routine paediatric vaccines scheduled for co-administration in England were administered separately and that more than one third of the vaccines scheduled for co-administration were not co-administered as recommended in the actual immunisation schedule. Almost half of the English children received at least one of their vaccine co-administrations not as recommended in the immunisation schedule, with almost one in five children receiving none of their co-administered vaccines as listed in the schedule. Overall, three quarters of co-administrations happened completely as recommended in the immunisation schedule, while about one fifth of co-administrations deviated from the actual schedule: either different doses or fewer vaccines were given, or co-administration happened according to an outdated schedule. A small proportion of co-administered paediatric vaccines (4%) was not given in line with any immunisation schedule in England during the study period.

The extent to which vaccines were co-administered as recommended in the schedule varied greatly between vaccines. Particularly vaccines scheduled for co-administration after the first year of life were less co-administered according to the schedule, with DTaP/IPV or dTaP/IPV and MMR dose 2 having more than one third never recommended co-administrations or separate administrations. We found that more than 75% of MenACWY and Td/IPV vaccines administered at GP practices were given separately or co-administered as never has been recommended. However, these findings may not be representative for the entire population because these vaccines are typically offered in schools [28] while our study relied on GP data only. .

To the best of our knowledge, this is the first study describing vaccine co-administration practices to this extent. We retrieved one study from the United States of America reporting that 65% of eligible children received MenC with Tdap co-administered, and 26% of boys and 28% of girls received Tdap with HPV together. [3] Since these vaccines were not scheduled for co-administration in England these numbers do not allow for a direct comparison. Nevertheless, this study also indicates suboptimal co-administration practices. Despite differences between immunisation schedules in different countries, most vaccines included in our study are part of immunisation programmes in a majority of countries globally [29] and the vaccine co-administrations recommended by the NHS are recommended in multiple other countries too [30,31]. Hence, our findings can be relevant for countries with similar immunisation policies.

Timely vaccination was the major factor for recommended co-administrations. Having received at least one vaccine too late significantly decreased the odds for a recommended vaccine co-administration. We previously found that only about three quarters of paediatric vaccines are given on time and almost 20% too late [15]. These findings demonstrate that there is room to improve the timeliness of paediatric vaccinations, and that efforts aiming at this could also improve the ratio of recommended vaccine co-administrations.

Although differences between genders, NHS regions, and IMD quintiles were statistically significant, these differences were generally small. This is in line with our previous study that did not find major differences in vaccination timeliness for these factors. [15] Also other studies found that attitudes towards co-administration were barely influenced by socioeconomic determinants [32–34]. On the other hand, parents prefer fewer vaccines co-administered to avoid adverse events and discomfort [32–34] and co-administrations may provoke fear for an increased risk of adverse reactions and undesired effects among health care staff [35]. This indicates that efforts promoting co-administration should address safety concerns among both parents and health care professionals across regions and communities, independent of deprivation.

Co-administrations categorised as deviated in our study merely indicate that immunisations do not happen as recommended. Co-

administering fewer vaccines or other doses than recommended or co-administering according to an outdated schedule may have a limited impact on the health outcomes of the immunisations. However, never recommended co-administrations may lead to undesired and unknown immunogenicity and safety outcomes of the vaccines co-administered, particularly when co-administration occurs off-label [12,13]. Immunisation schedules, including foreseen vaccine co-administrations, are designed based on known immunogenicity and safety information as listed on vaccine labels, relying on data from clinical trials including specific vaccine co-administrations. Such evidence may not be available for never recommended vaccine co-administrations. Co-administered vaccines may face inter-vaccine interference which can be caused by competition between vaccines, systemic effects provided by one vaccine affecting the performance of another vaccine, and usage related factors such as the age and dosing interval [13]. These interferences may result in a decreased immune response to one or more of the administered strains [13]. Given the complexity of interactions among co-administered vaccines, gathering and analysing vaccine co-administration data is essential to ensure their ongoing effectiveness and safety in immunisation programmes [5]. Since never recommended vaccine co-administrations are rare, real-world evidence on their effectiveness and safety remains scarce and therefore should be avoided.

In addition, suboptimal co-administration rates negatively affect other benefits associated with co-administration, such as vaccination coverage [2,5,6], vaccine acceptance [5], and lower handling costs [5]. Particularly now that coverage for all paediatric vaccines declines in England, with most coverage rates dropping below the targeted 95% [36], strategies promoting co-administration may help raising vaccine coverage.

Including over 6 million vaccinations in children, obtained from real-life data, our study provides a detailed description of vaccine co-administration practices in England. However, data from medical records may be prone to misclassification and heterogeneous as they are recorded by different persons and institutions to document actual medical practice and not for the purpose of this study. Another disadvantage of relying on existing medical records is that analyses are restricted to the available variables captured in the database. [37] Therefore, we could only explore the potential factors as listed above and must rely on other study designs to further investigate factors of deviated or never recommended co-administration in the future. Our data may also be biased for missingness, because the RCGP RCS database only collects data from GP practices. However, this effect may be small, as routine childhood vaccines in England are typically given by GPs. [38]

Suboptimal co-administration rates for routine paediatric vaccines indicate that the potential benefits of co-administration are not fully exploited so far. This is a missed opportunity. Further research is needed to quantify the impact on health outcomes and inefficient use of health care resources due to deviated vaccine co-administrations. This would inform concerted public health action to advise parents' and health care providers' about the benefits of vaccine co-administration and adequately address potential safety concerns.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Tafuri S, Martinelli D, Caputi G, Balducci MT, Germinario C, Prato R. Simultaneous administration of vaccines in immunization protocols: an audit in healthcare workers in the Puglia region of Italy. Hum Vaccin 2009;5 (11):745–7. https://doi.org/10.4161/hv.5.11.9438.

[2] Pellegrino A, Busellu G, Cucchi A, Cavallaro A, Gabutti G. Vaccine co-administration in paediatric age: the experience of the Local Health Unit of Cuneo-1 (Ambito di Cuneo). Italy. Acta Biomed 2010;81:204–9.

[3] Sull M, Eavey J, Papadouka V, Mandell R, Hansen MA, Zucker JR. Adolescent vaccine co-administration and coverage in New York City: 2007–2013. Pediatrics 2014;134(6):e1576–83. https://doi.org/10.1542/peds.2014-1452.

[4] Suarez-Castaneda E, Burnett E, Elas M, Baltrons R, Pezzoli L, Flannery B, et al. Catching-up with pentavalent vaccine: Exploring reasons behind lower rotavirus vaccine coverage in El Salvador. Vaccine 2015;33(48):6865–70. https://doi.org/10.1016/j.vaccine.2015.07.092.

[5] Dolhain J, Janssens W, Dindore V, Mihalyi A. Infant vaccine co-administration: review of 18 years of experience with GSK's hexavalent vaccine co-administered with routine childhood vaccines. Expert Review of Vaccines 2020;19(5):419–43. https://doi.org/10.1080/14760584.2020.1758560.

[6] Centers for Disease Control and Prevention. General Recommendations on Immunization. 2011..

[7] Kosalaraksa P, Mehlsen J, Vesikari T, Forstén A, Helm K, Van Damme P, et al. An open-label, randomized study of a 9-valent human papillomavirus vaccine given concomitantly with diphtheria, tetanus, pertussis and poliomyelitis vaccines to healthy adolescents 11–15 years of age. Pediatr Infect Dis J 2015;34 (6):627–34. https://doi.org/10.1097/INF.0000000000000694.

[8] Gilchrist SAN, Nanni A, Levine O. Benefits and effectiveness of administering pneumococcal polysaccharide vaccine with seasonal influenza vaccine: an approach for policymakers. Am J Public Health 2012;102(4):596–605. https://doi.org/10.2105/AJPH.2011.300512.

[9] NHS. The routine immunisation schedule from Autumn 2018. 2018..

[10] Oleár V, Krištúfková Z, Štefkovičová M. How do we evaluate and manage the many different vaccination schedules in the EU?. CEJPH 2015;23:218–22. https://doi.org/10.21101/cejph.a4170.

[11] Committee on the Assessment of Studies of Health Outcomes Related to the Recommended Childhood Immunization Schedule, Board on Population Health and Public Health Practice, Institute of Medicine. The Childhood Immunization Schedule and Safety: Stakeholder Concerns, Scientific Evidence, and Future Studies. Washington (DC): National Academies Press (US); 2013..

[12] Stockwell MS, Broder K, LaRussa P, Lewis P, Fernandez N, Sharma D, et al. Risk of fever after pediatric trivalent inactivated influenza vaccine and. JAMA Pediatr 2014;168:211–9. https://doi.org/10.1001/jamapediatrics.2013.4469.

[13] Vidor E. The Nature and Consequences of Intra- and Inter-Vaccine Interference. J Comp Pathol 2007;137:S62–6. https://doi.org/10.1016/j.jcpa.2007.04.014.

[14] Gervaix A, Ansaldi F, Brito-Avô A, Azzari C, Knuf M, Martinón-Torres F, et al. Pneumococcal vaccination in Europe: schedule adherence. Clin Ther 2014;36 (5):802–812.e1. https://doi.org/10.1016/j.clinthera.2014.03.001.

[15] Bauwens J, de Lusignan S, Sherlock J, Ferreira F, Künzli N, Bonhoeffer J. Adherence to the paediatric immunisation schedule in England n.d..

[16] University of Surrey. Clinical Informatics and Health Outcomes Research Group. ClinInfEu 2020. https://clininf.eu/ (accessed April 28, 2020)..

[17] Correa A, Hinton W, McGovern A, van Vlymen J, Yonova I, Jones S, et al. Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) sentinel network: a cohort profile. BMJ Open 2016;6(4):e011092. https://doi.org/10.1136/bmjopen-2016-011092.

[18] Sturkenboom M, Braeye T, van der Aa L, Danieli G, Dodd C, Duarte-Salles T, et al. ADVANCE database characterisation and fit for purpose assessment for multi-country studies on the coverage, benefits and risks of pertussis vaccinations. Vaccine 2020;38:B8–B21. https://doi.org/10.1016/j.vaccine.2020.01.100.

[19] NHS. Routine childhood immunisation programme 2008..

[20] Bevan-Jones L, No SY. Nonsense Vaccine Handbook. 2009.

[21] Thomson J. Paediatric Pearls 2011..

[22] NHS. Routine childhood immunisations from September 2012. 2012..

[23] NHS. Routine childhood immunisations from June 2013. 2013..

[24] NHS. Routine childhood immunisations from July 2014. 2014..

[25] NHS. The routine immunisation schedule from summer 2016. 2016..

[26] NHS. The routine immunisation schedule from April 2018. 2018..

[27] R Core Team. R. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2017.

[28] MenACWY vaccine - NHS. NhsUk 2019. https://www.nhs.uk/conditions/vaccinations/men-acwy-vaccine/ (accessed September 22, 2020)..

[29] Peck M, Gacic-Dobo M, Diallo MS, Nedelec Y, Sodha SS, Wallace AS. Global Routine Vaccination Coverage, 2018. MMWR Morb Mortal Wkly Rep 2019;68:937–42. https://doi.org/10.15585/mmwr.mm6842a1.

[30] Doshi P, Stahl-Timmins W, Merino JG, Simpkins C. Visualising childhood vaccination schedules across G8 countries. BMJ 2015;351(nov13 1):h5966. https://doi.org/10.1136/bmj.h5966.

[31] Public Health England. UK and international immunisation schedules comparison tool. GOVUK n.d. https://www.gov.uk/government/publications/uk-and-international-immunisation-schedules-comparison-tool (accessed April 1, 2021)..

[32] Theeten H, Hens N, Aerts M, Vandermeulen C, Roelants M, Hoppenbrouwers K, et al. Common attitudes about concomitant vaccine injections for infants and adolescents in Flanders. Belgium. Vaccine 2009;27(13):1964–9. https://doi.org/10.1016/j.vaccine.2009.01.096.

[33] Kuppermann M, Nease RFJ, Ackerson LM, Black SB, Shinefield HR, Lieu TA. Parents' preferences for outcomes associated with childhood vaccinations. Pediatr Infect Dis J 2000;19:129–33.

[34] Meyerhoff AS, Weniger BG, Jacobs RJ. Economic value to parents of reducing the pain and emotional distress of childhood vaccine injections. Pediatr Infect Dis J 2001;20(Supplement):S57–62.
[35] Wagner A, Kundi M, Zwiauer K, Wiedermann U. Paediatricians require more information before they routinely co-administer the meningococcal B vaccine with routine infant vaccines. Acta Paediatr 2015;104(10):e439–47. https://doi.org/10.1111/apa.13100.
[36] Screening & Immunisations Team (NHS Digital), COVER Team (Public Health England). Childhood Vaccination Coverage Statistics England, 2018-19. NHS Digital; 2019..
[37] Thygesen LC, Ersbøll AK. When the entire population is the sample: strengths and limitations in register-based epidemiology. Eur J Epidemiol 2014;29(8):551–8. https://doi.org/10.1007/s10654-013-9873-0.
[38] NHS vaccinations and when to have them. NHS UK 2019. https://www.nhs.uk/conditions/vaccinations/nhs-vaccinations-and-when-to-have-them/ (accessed May 26, 2020)..