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Vaccination strategies for control of community outbreaks of hepatitis A: A comparison of two outbreaks in England

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ABSTRACT

In August 2015 two community outbreaks of hepatitis A virus (HAV) occurred in sub-urban communities in Northern England. Each was managed by an independent outbreak control team. In outbreak one, mass vaccination was deployed targeting a residential area and two schools, while in outbreak two, vaccination was reserved for household-type contacts of cases. The highest vaccination uptake was achieved in the school settings (82% and 95%). These case studies illustrate the range of approaches that can be used and the factors that influence decision-making in response to a hepatitis A community outbreak. Both outbreaks likely started from importation(s) of HAV by returning travellers and spread through extended social networks and the local community. Vaccination strategies were selected based on hypotheses about transmission pathways, which were informed by evidence from oral fluid (OF) testing of asymptomatic contacts. More evidence about the effectiveness of mass vaccination in community outbreaks of hepatitis A in low endemicity settings is needed. Hepatitis A guidelines should include recommendations for the use of mass vaccination and OF testing in outbreaks.

1. Introduction

Hepatitis A virus (HAV) is a faecal-orally transmitted pathogen which causes acute liver disease. In 2013, HAV was responsible for an estimated 100 million cases worldwide [1]. Clinical presentation is age-dependent: young children often do not have symptoms, while older children and adults usually do. Case fatality ranges from 0.1% in children to 2.1% in adults over 40 [2]. The incubation period is 28 days (15–50) and the infectious period is from two weeks before the onset of symptoms to one week after. Seroprevalence varies widely between countries in accordance with the level of hygiene and sanitation. The UK has very low endemicity, with an incidence of around one case per 100,000 population per year, and high susceptibility, estimated to be over 60% at the age of 30 [3]. Outbreaks occasionally occur in very low endemicity areas if a new source is introduced such as contaminated food [4], or from importation of cases following travel to an endemic country [5].

Safe and effective vaccines against hepatitis A are available for pre-exposure prophylaxis [6]. In England, pre-exposure vaccination is reserved for: groups at high risk of exposure including travellers to endemic areas, men who have sex with men, individuals at occupational risk, people who inject drugs, and people at risk of complications such as those with chronic liver disease [7]. Vaccination for post-exposure prophylaxis is routinely offered to close household-type contacts of cases along with human normal immunoglobulin for persons aged over 60 years and those with chronic liver disease or immunosuppression [8]. Post-exposure prophylaxis is most effective if administered within 14 days of exposure [2,9]. In very low endemicity areas, mass vaccination may be used either in response to a single case, for example where a child is thought to have acquired their infection from asymptomatic school contacts, or as a broader outbreak control measure. A range of mass vaccination strategies to control outbreaks are reported in the literature including: universal community vaccination [10]; targeted vaccination of children [11–16];

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targeted vaccination of risk groups [17]; and targeted vaccination within specific settings [18].

In England there is an established programme of enhanced surveillance. Since 2012, serum samples that test positive for HAV have been routinely submitted to Public Health England's (PHE) Virus Reference Department (VRD) for genotyping. Amplification and sequencing of a 505 base pair region of the VP1/2PA junction is performed using Sanger sequencing and phylogenetic analysis is conducted. A confirmed case is defined as a person that meets the clinical case definition (a person with an acute illness, discrete onset of symptoms and jaundice or elevated serum aminotransferase levels) and is confirmed through IgM and IgG antibodies to hepatitis A or an asymptomatic person with no recent history of immunisation with anti-HAV IgM from oral fluid or serum and an epidemiological link to a confirmed case. Symptomatic cases are excluded from work/school until 7 days post onset of jaundice.

Oral fluid (OF) testing is also available on request from the VRD and is used to identify asymptomatic cases of hepatitis A among close household-type contacts of cases. Diagnosis of recent infection is based on the detection of both anti-HAV IgM and IgG in a sample. Comparing the relative reactivity of anti-HAV IgM and IgG within a sample and between samples taken at the same time can indicate the chronology of infection within a household. Typing of OF-positive cases is not generally possible. OF testing is currently recommended for household contacts of a confirmed acute hepatitis case where the index case is a child (under 16 years) or a member of teaching staff at a school, with no known risk factors for infection [8]. If testing of household-type contacts can demonstrate a source external to the school this may avoid unnecessary intervention in the school. OF testing can be used more widely during outbreaks to determine the extent of transmission. OF testing of asymptomatic contacts has implications for individuals found to be positive as a period of exclusion may be required. For asymptomatic OF-positive cases it is difficult to determine the infectious period as there is no symptom onset date. If the timing of infection cannot be inferred, a pragmatic decision about exclusion has to be made based on the available evidence.

This paper presents experience from two recent UK community outbreaks of hepatitis A. These particular outbreaks were chosen because they were similar in size, timing and geography but different vaccination strategies were used. National guidelines at the time of the outbreaks focussed primarily on the management of single cases of disease with few specific recommendations about the use of vaccine to control community outbreaks [19], therefore vaccination strategies were chosen primarily based on the risk assessment undertaken by the outbreak control team (OCT). The objectives of this paper are: to compare the two outbreaks, explain the vaccination strategies used and identify the factors that influence decision making, in order to inform the development of public health guidance for hepatitis A outbreaks.

2. Outbreak one

A case of hepatitis A infection was notified on 28th August 2015 (week 35) with symptom onset 17th August (week 34) and no travel history or source identified (Fig. 1, Table 1). The three children within the household were screened using OF testing and all three were later found to be positive for hepatitis A IgM indicative of recent infection. Two of these children were school age, however they were diagnosed at the end of the school summer holidays so unlikely acquired their infections in school (neither school was later linked to any other case). The reason for screening the children was to identify possible links to another case of hepatitis A in a nearby resident with onset of symptoms 22nd July (week 30) however this case was found to be a different genotype to the outbreak so is excluded from further discussion. A second adult case was diagnosed two weeks later on 7th September (week 37) (symptom onset 31st August (week 36)). The routine questionnaire did not highlight any contact with case one, however they lived in the same postcode district[1] and had extended household contacts who lived in the same postcode sector[2] (a smaller area than postcode district). These individuals lived in an area of very high deprivation[3] among the 10% most deprived in England.[4] Both cases were confirmed to be genotype (IA), with an identical genetic sequence, suggesting that HAV was circulating within the local community. The cases were interviewed by public health officials and household-type contacts were offered vaccination in line with national guidance [19]. An outbreak control team (OCT) was convened on 10th September 2015 (week 37).

A case was defined as: confirmed hepatitis A (see above definition) with symptom onset from 17th August 2015 in a resident of the affected postcode district, excluding cases with a different genotype and those with travel history to endemic countries during the eight weeks before symptom onset. A household-type contact was defined as a person living in the same household as the case or regularly sharing food or toilet facilities with the case during the infectious period (this would include extended family members who frequently visit the household). During the investigation, oral fluid (OF) testing of asymptomatic household-type contacts was used in some instances to assess the degree of household transmission, gain evidence to support or refute transmission hypotheses and to better understand the overall dynamics of the outbreak.

By week 40, there were 10 confirmed cases (four symptomatic, six asymptomatic OF-positive). The cases were all clustered geographically within two specific areas of the same postcode district. Two asymptomatic siblings, contacts of case two, were found to be positive on OF testing on 11th September indicating recent infection. They both attended the same school (school A). Given the date of their diagnosis just after the end of the school summer holidays, which ran from 21st July (week 30) to 7th September (week 37), they likely acquired their infections during the summer holidays. Estimation of the infectious period is generally based on the symptom onset date, but given that these were asymptomatic infections it is difficult to assess whether they were infectious at the time of returning to school. Review of passive surveillance data found six cases in the two months prior to the notification of the first case, all of which were a different genotype. This was the first identification of genotype IA in this community. The working hypothesis at this time (week 40) was that there had been a recent introduction of this HAV strain into this community and that transmission had occurred during the school summer holidays (Fig. 1), primarily among asymptomatic children who were reported to have extensive contact through outdoor and household play and through informal childcare.

The OCT recommended a community vaccination session for local residents within a small radius of the cases. The target area

[1] The postcode district is made of the postcode area (denoted by one or two letters) plus one or two digits (and sometimes a final letter) and is between two and four characters long. Examples of postcode districts include "W1A", "RH1″, "RH10″ or "SE1P".

[2] The postcode sector is made up of the postcode district, a single space, and a number. It is between four and six characters long (including the single space). Examples of sector postcodes include "SW1W 0″, "PO16 7″, "GU16 7″, or "L1 8″, "CV1 4″.

[3] The Index of Multiple Deprivation (IMD) 2015 is the official measure of relative deprivation for small areas (lower-layer super output areas (LSOAs) contain on average 1,500 residents) in England. The IMD ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area) https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015.

[4] The average index of multiple deprivation (IMD) rank of the five affected LSOAs was 2917/32,844.

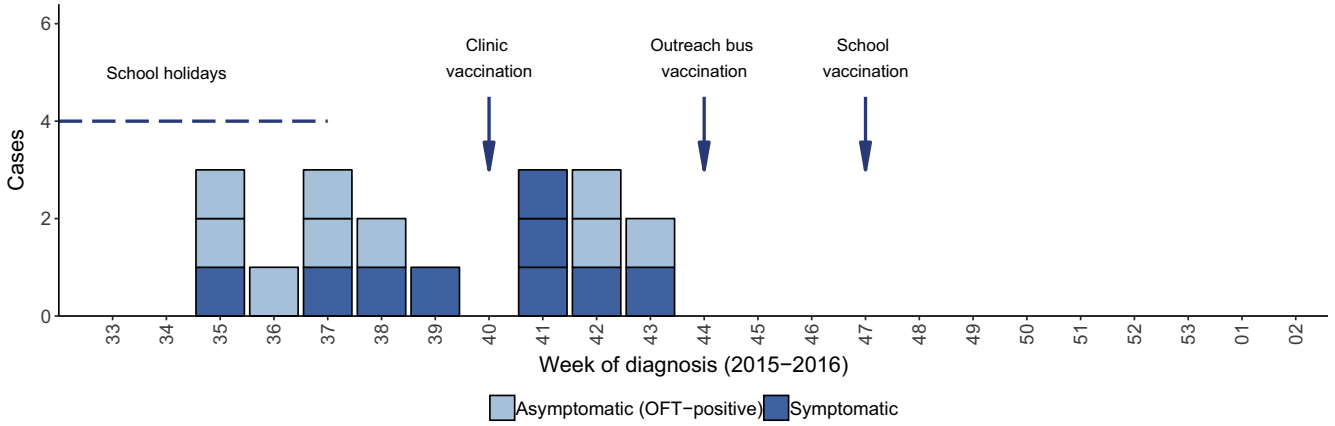

Fig. 1. Outbreak one: Epidemic curve of cases of hepatitis A by week of diagnosis and symptoms.

Table 1
Characteristics of the outbreaks.

		Outbreak one		Outbreak two	
		Symptomatic	Asymptomatic (OFT positive)	Symptomatic	Asymptomatic (OFT positive)
No. cases		9	9 (22 tested)	15	3 (13 tested)
No. cases Genotype IA		8	–	11	–
Age (years)	Minimum	5	1	1	3
	Median	25	8	19	5
	Maximum	32	13	27	10
Age category	Pre-school	0	2	2	1
	Primary school	3	6	4	2
	Secondary school	0	1	0	0
	Adult	6	0	9	0
Sex	Female	6	5	6	1
	Male	3	4	9	2
Hospital admission	Yes	7	0	3	0
	No	2	9	12	3
No. Households affected		10		12	
Geographical distribution[a]		5.0 by 2.2 km		3.0 by 1.9 km	
Average deprivation rank[b]		2917		5234	

[a] Directional distribution (standard deviational ellipse), X by Y.
[b] The Index of Multiple Deprivation (IMD) 2015 is the official measure of relative deprivation for small areas (lower-layer super output areas (LSOAs) contain on average 1,500 residents) in England. The IMD ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area) https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015.

was chosen pragmatically based on proximity to and presumed social interaction with the cases. This area contained approximately 601 residents who were registered with a primary care clinic. The vaccination sessions were arranged at a local primary care clinic over two days in week 40. Vaccine uptake was modest at 28% (171/601) of the registered population, despite extensive promotion by door-knocking and leaflet drops. Local primary care clinics continued to offer vaccination to eligible individuals from week 41 onwards but further vaccine uptake data is unavailable. By the end of week 43 there were a further 8 cases (5 symptomatic, 3 asymptomatic OF positive). To increase coverage, nurses offered vaccination from a mobile clinic (a community-outreach bus) during a single day in week 44. This proved more popular with a further 135 people receiving vaccination. It is not possible to calculate overall uptake as the true population denominator of residents is not known, only those registered with a health centre.

In October (week 43), two primary school clusters were identified. The first cluster (school B) involved two symptomatic cases, with onset on the 2nd (week 40) and 12th (week 42) of October, who lived on the same street as each other and attended the same school in different year groups (one of these was a household contact of a symptomatic adult case). The hypothesis was that transmission occurred either in the school or in the local neighbourhood. The second cluster (school C) involved two asymptomatic OF-positive children both diagnosed on 14th October (week 42) living with a symptomatic adult case, with onset on the 3rd of October (week 40); their questionnaires did not highlight any contact with other cases. The hypothesis was that the two children had acquired asymptomatic infection within the school resulting in a secondary symptomatic case in the household. Given that cases continued to occur despite the community vaccination campaign and there was new evidence of potential transmission in schools the OCT decided to offer vaccination to all pupils and staff within both implicated schools. The rationale was twofold: first, to prevent tertiary cases within the affected schools and second, to quickly reduce the proportion of susceptible children in the local community to prevent further community transmission and spread. Nurses delivered school-based vaccination sessions during week 47, and uptake was high in both schools: 690/730 (95%) and 430/524 (82%) among staff and pupils. There were 10 schools in the area that could have been targeted but no further cases were reported, so wider vaccination was not indicated.

Fig. 1 and Table 1 provide a summary of the outbreak. The outbreak was declared over after no cases occurred within two maximum incubation periods since the last case. There was no evidence

found of an environmental or food source and no cases were found among food handlers. The overall hypothesis was that the outbreak was caused by person-to-person spread, mainly between asymptomatic children in the community setting. There was transmission within households and between households, probably through children playing with their neighbours, or through informal childcare arrangements. Much of the transmission probably took place during the school summer holidays (week 30–36 inclusive), however five cases (including four primary school aged children) probably acquired their infection after schools reopened in September (week 37). The two primary school clusters indicated likely transmission within the schools. It is certainly plausible that there were many undiagnosed asymptomatic cases within the community. The primary case remained unknown but was likely an imported case from travel to an endemic country.

3. Outbreak two

In August 2015 (week 34) public health officials in a neighbouring region to that of outbreak one were notified of a cluster of four cases of hepatitis A among primary school aged children within an extended family network living in a small ethnic community (Fig. 2, Table 1). None of the cases had a history of overseas travel to an endemic country within the incubation period and the source of the infection was unknown. Cases lived in areas of high deprivation:[5] among the 20% most deprived in England.[6] An OCT was convened, and cases were followed up according to national guidelines [19] with vaccination of household-type contacts. All samples were submitted to PHE's VRD for sequencing. A case was defined as: confirmed hepatitis A (see above) with symptom onset from 15th January 2015 in a resident of the affected town, excluding cases with a different genotype and those with travel history to endemic countries during the eight weeks before symptom onset. OF testing of household-type contacts was used early in the outbreak, in order to assess the extent of household transmission, which led to the identification of three cases with evidence of recent infection. On review of public health records, a case of hepatitis A was identified from January 2015 in a child from the same local ethnic community and of a similar age to the initial four cases. There was no typing available, so a link with the current outbreak could not be confirmed, but this raised the possibility that undetected transmission had been on-going among children in this community for several months. At that time, a school source had been suspected so vaccination was offered to classmates and teachers, with high uptake (29/30).

A second extended family network of 11 cases was later identified, which included a resident of the same street as cases from the first network. A further three cases had no apparent links to either network, but shared the outbreak sequence: these were notified in October (week 42), November (week 47) and December (week 51). On several occasions during the outbreak the OCT considered mass vaccination of residents beyond the two family networks but decided against it for several reasons: it was not felt to be sufficiently timely as transmission had plausibly been on-going in this small ethnic community for some months; the majority of cases were linked to two specific family networks which had been managed appropriately, with vaccination offered to a wide range of contacts within or linked to this network; and there was no 'well-defined' community, such as a single institutional context or socio-ethnic group that could be targeted (a consequence of this is was that no logical denominator for measuring uptake was available). The OCT considered applying an arbitrary definition of a target population based on postcodes but decided that this would not represent a well-defined or closed community with a significantly higher likelihood of acquiring or transmitting the infection than other residents not living in these postcodes. This decision was later supported to by the fact that a number of cases not linked to either of the two family networks occurred outside of these postcodes. Though it is not possible to rule out a source of infection for these cases from within the targeted postcodes, the timings of the cases suggest that the proposed mass vaccination would have unlikely prevented them. The OCT felt that the costs of delivering mass vaccination outweighed the potential benefits, and that adding mass vaccination on top of the control measures already in place would not be a proportionate response for the level of public health risk.

There were two asymptomatic OF-positive children identified through contact tracing in October (week 42) who both attended the same school. These two children were from different households but the same extended family network (of the 11 cases described above), which was known to have high levels of interaction, with regular visits to each other's houses and shared childcare arrangements. The OCT concluded that they probably obtained their infection through their extended family network rather than from school, therefore school vaccination was not recommended. Extensive work with schools was undertaken to raise awareness and improve hygiene levels. No further clusters associated with schools were reported during this incident.

Along with recommending post-exposure vaccination for household-type contacts, the OCT worked with local health and social care partners to increase vaccine uptake among people in risk groups already eligible for pre-exposure vaccination, such as those with chronic liver disease [7]. This began in December (week 49) and involved a local media campaign and briefings to local hepatology, genitourinary and drugs and alcohol services. This was not a separate vaccination programme but an effort to increase uptake among those already eligible due to their risk status and thus protect those most at risk of severe disease.

Fig. 2 and Table 1 provide a summary of the outbreak. The outbreak was declared over after no further cases were observed for two maximum incubation periods since the last case. There was no evidence found of an environmental or food source and no cases were found among food handlers. The overall hypothesis was that this outbreak was caused by person-to-person transmission. There was evidence of transmission within household settings and between households through family networks. There was also evidence of wider community transmission with three cases that were not linked to a family network. There was no strong evidence of transmission within schools: the two asymptomatic cases who attended the same primary school were both contacts of cases and from the same close family network therefore they presumably acquired their infections at home. It is plausible that there were many undiagnosed asymptomatic cases within the community and transmission may have been on-going for several months before this outbreak was detected, likely originating from an imported primary case.

4. Results

Table 2 presents a list of factors which can be considered by OCTs to inform the choice of vaccination strategy. These are arranged into those factors that were similar between the two outbreaks described, those that were different, and other factors that

[5] The Index of Multiple Deprivation (IMD) 2015 is the official measure of relative deprivation for small areas (lower-layer super output areas (LSOAs) contain on average 1,500 residents) in England. The IMD ranks every small area in England from 1 (most deprived area) to 32,844 (least deprived area) https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015.

[6] The average index of multiple deprivation (IMD) rank of the nine affected LSOAs was 5234 out of 32,844.

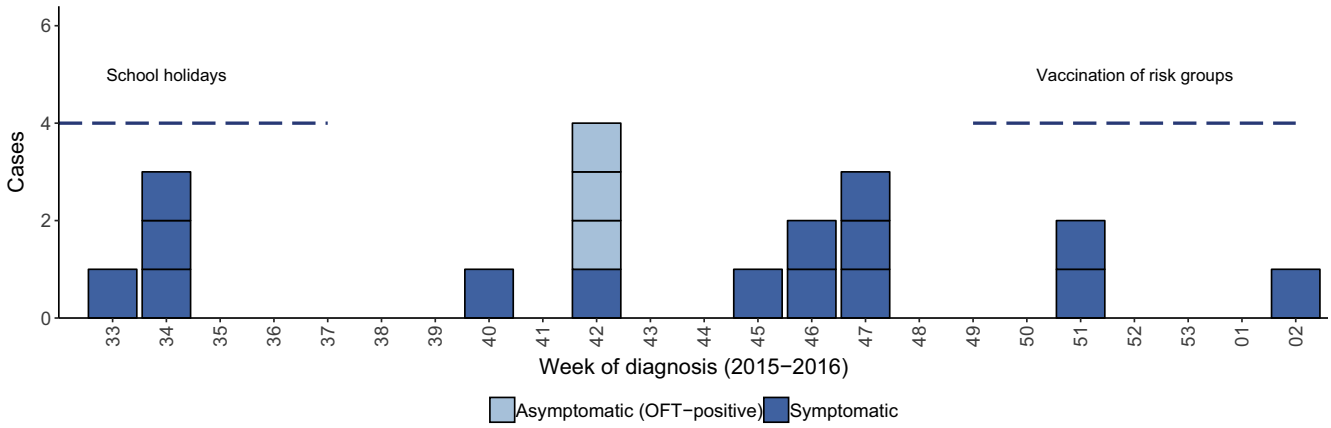

Fig. 2. Outbreak two: Epidemic curve of cases of hepatitis A by week of diagnosis and symptoms.

could be considered. There were many similarities including: the setting, source of infection, level of susceptibility and costs of intervention. Both outbreaks were genotype IA and the sequenced region (a 505 base pair region of the VP1/2PA junction) was identical throughout. No epidemiological links were found between the two outbreaks and they were managed independently. This sequence is relatively common: it was first observed in England in 2013 through PHE's enhanced hepatitis A molecular surveillance programme and has been associated with travel to Romania and Bulgaria. In 2015 and 2016 this sequence was seen in eight cases across England, outside of these two outbreaks, mainly associated with travel to Romania. The two outbreaks may have been linked but there is no evidence of this. It is equally plausible that there were (at least) two separate importations by people returning from Eastern Europe at similar times. The sequencing supports the hypothesis that these outbreaks were due to imported cases from returning travellers. In England, a substantial proportion of reported hepatitis A cases are travel related [5].

Certain differences can be highlighted, which explain the different vaccination strategies. Firstly, regarding the timing of introduction, in outbreak one it was thought that HAV had been recently introduced and there was limited transmission beyond the first cases and their networks and high susceptibility. In outbreak two, the OCT considered that transmission may have already been on-going for some months therefore there may have been more widespread transmission beyond the area of residence of the initial cases and fewer susceptible individuals. This was based on the existence of a case six months earlier in the same ethnic community and of similar age as the initial cases. As genotyping was not done in the historical case a link cannot be proven, and there may have in fact been a separate introduction. Also, it could be argued that if there had been on-going transmission for six months we might have expected at least one case to be notified in this time, though given that many members of this community were born in higher endemicity countries there may be few susceptible adults, meaning transmission can be maintained among children without the occurrence of symptomatic disease. Even in the absence of this historical case the decision not to vaccinate in the community would have likely been the same. Secondly, regarding the hypothesised transmission pathways, in outbreak two, the OCT considered that the main transmission pathways were among extended social contacts in the community and not among local schools or residential areas. In outbreak one the OCT considered that transmission within close residential areas was likely, so took the opportunity to target vaccination to a small residential area. Later the OCT considered transmission within schools was likely so opted to vaccinate implicated schools. This was done both to prevent transmission in those settings and to quickly increase coverage among children as a means of building a buffer of immunity in the community to prevent onward transmission.

5. Discussion

Different vaccination strategies were used as a result of differences in hypothesised transmission pathways, timings, and populations at risk. These were guided by epidemiological and microbiological evidence and knowledge about the local community. Background surveillance data were important in informing the initial hypotheses and choice of control measures.

Where mass vaccination was used, uptake rates differed between settings. Community uptake was modest despite extensive promotional efforts including door-to-door promotion and providing a mobile clinic in a bus. To achieve higher uptake among a community of local residents it would have been necessary to invest further resources over a longer period of time. School vaccination was more successful; experience with other vaccination programmes in schools suggests high uptake is achievable and for school-specific outbreaks this practice is commonplace [20]. In a community outbreak scenario where children are the main source of transmission, vaccinating attendees at an affected school may also be an effective way of gaining control in the community, although several schools may need to be included to provide a sufficient buffer of immunity [19]. The level of uptake required depends on the reproduction rate in that population and the degree of mixing. Estimates from the USA give an R_0 of 1.1–1.5, which may be comparable to UK settings, meaning immunisation coverage of 40% in a susceptible population is likely to interrupt transmission assuming random mixing [8].

Mass vaccination in outbreak one may have shortened the outbreak and offered a public health benefit to the community, but no conclusion can be drawn about this. There is limited evidence of the overall effectiveness and cost effectiveness of mass vaccination to control community outbreaks of hepatitis A in low endemicity settings. In uncontrolled observational studies it is difficult to determine the contribution that mass vaccination makes to the control of the outbreak compared to other control measures such as information campaigns, promoting hand hygiene, and the reduction of susceptible individuals through infection and immunity. There is some ecological evidence of an association between vaccine uptake and number of hepatitis A cases in community outbreaks in the USA [10,12]. Ecological analysis of 268 outbreaks in Catalonia, Spain, found that early administration of immunoglobulin or vaccine was associated with shorter outbreak duration [21]. Interpretation is complicated by variations in seroprevalence

Table 2
Factors influencing choice of vaccine strategy and comparison of outbreaks.

Comparison	Factor	Details
Similarities	Setting (community, institution or mixed)	Both were community outbreaks among similar socioeconomic groups
	Source of infection (food or human)	Both outbreaks were considered to be due to imported cases from returning travellers
	Case definitions	Both OCTs used the same diagnostic criteria and excluded cases with recent travel to endemic areas
	Genotyping and sequencing results	Both outbreaks were genotype IA and the sequenced region (a 505 base pair region of the VP1/2PA junction) was identical throughout
	Spatial distribution of cases (shared residence, institution)	Both covered a similar residential area
	Social networks within the affected and degree of mixing	Both OCTs understood that there was a lot of mixing among local residents through social networks and informal child care arrangements
	Level of susceptibility in the population	There is no reason to expect that there was a difference in baseline susceptibility among these two populations at risk
	Likelihood of onward transmission (levels of hygiene and sanitation)	Both outbreaks involved children under 5 who attended pre-school, but neither outbreak involved food handlers or other risk groups for transmission
	Likelihood of severe disease (age and comorbidities)	Both at-risk populations included adults at risk of severe disease
	Resource implications, logistical implications (staffing, venues, communication) and opportunity cost of any disruption to services	Both OCTs had similar levels of resource and similar logistical challenges
Differences	Hypothesised transmission pathways	In outbreak two, the main transmission pathways were among extended social contacts in the community. In outbreak one transmission within close residential areas and schools was likely
	Timing (since exposure or against predicted course of the outbreak)	In outbreak two, the OCT considered that transmission may have already been on-going for some months therefore there may have been more widespread transmission beyond the area of residence of the initial cases and fewer susceptible individuals
	Whether a well-defined population at risk can be defined and accessed	In outbreak one a well-defined local community and two school populations could be defined
Other factors	Estimated reproduction rate in the population	
	Estimated coverage required to achieve control and whether achievable	
	Population acceptance of immunisation	
	Whether oral fluid testing could be used to test hypotheses	

between settings, differences in timing of vaccination during the course of the outbreak and different dosing regimens (one vs. two doses).

Given resources are limited and costs may be significant, the use of mass vaccination requires careful consideration. Vaccinating young children and preventing asymptomatic infection is only beneficial if it interrupts transmission to older contacts at risk of symptomatic infection. The number needed to vaccinate to prevent a single case of disease may be substantial. Focussing on just household-type contacts, as in outbreak two, has limited impact on the population susceptibility but is much less costly. Any outbreak is an opportunity to promote vaccination among those most at risk who are already eligible for vaccination, such as those with liver disease, and this should always be included in control strategies.

In the absence of a clear evidence base, much hinges on expert judgement. WHO does not provide specific recommendations on the use of vaccine for outbreak control [2,22]. Both outbreaks were managed according to existing national guidelines. Guidelines in use in England at the time of these outbreaks focussed mainly on the management of single cases with few specific recommendations about the use of vaccination in outbreak control, stating that effectiveness "depends on how well the community is defined, the coverage achieved with the intervention and the time elapsed since the exposure to existing cases" [19]. Following the experience from these and other community outbreaks in England, national guidelines were updated. Among the changes was the addition of specific and general criteria for use of OF testing, and a consideration of intervention options in specific outbreak settings including schools, care homes and community settings [8].

6. Limitations

In neither outbreak can we be certain about the hypothesised transmission pathways and while OF testing provides evidence about the extent of transmission it cannot always add information about the timing and direction of transmission. Choice of control strategy is influenced in part by knowledge about the characteristics and behaviours of a particular community, for which generally no 'hard data' are available. It was not possible to confirm a primary source in either outbreak and while we strongly suspect the initial introduction was from a returning traveller, other possibilities such as a food source cannot be definitively ruled out. Existing surveillance data was used early in the outbreaks to assess the extent of pre-existing transmission, but this data is limited by lack of reporting, or when reporting occurs, lack of referral of the isolate for genotyping.

7. Conclusions and recommendations

OCT decisions will always be made on a case by case basis but guidelines help to inform judgements and encourage consistency. The process of guideline development is helpful as it combines research and practical experience and highlights unknowns. Guidelines should where possible include explicit principles and criteria for selection of a vaccination strategy, including the range of factors described above, though they should also be flexible. Hepatitis A vaccine should be promoted among travellers to endemic countries and this should remain part of travel and migrant health strategies and guidelines.

If school mass vaccination is indicated, high uptake can be achieved quickly with the support and cooperation of the school and local healthcare staff. If community mass vaccination is required, accurate denominator data should be sought. Vaccination days in health centres may provide moderate coverage if a high

proportion of people are registered and willing to seek care and the event is well promoted. Use of community outreach and mobile vaccination may increase uptake further, particularly if many people are unregistered. A combination of approaches may be preferable, depending on the local context. Where children are the main source of transmission in a community outbreak, targeting vaccination in schools may quickly provide high coverage among children, which may provide indirect protection to adults at risk [23].

Further research is needed to determine the effectiveness and cost effectiveness of different mass community vaccination strategies. Economic modelling studies can be parameterised based on evidence collected during outbreaks, including attack rates and direct healthcare costs such as vaccines, consumables and nurse time. Attack rates in a variety of settings such as households, schools and nurseries can be assessed using oral fluid testing, which can be done at the same time as vaccination to minimise disruption. Further research is also needed to determine the infectivity and appropriate period of exclusion for asymptomatic OF-positive cases.

Author contributions

All authors contributed to the writing of this manuscript and approved the final version. AS drafted the manuscript as lead writer. MP, WW, SC and MG led the respective outbreak control teams with support from SLN, SM and KB. SLN was in charge of sequencing the isolates.

Conflict of interest

The authors declare no conflicts of interest.

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