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Investigating awareness and implementation of adrenaline auto-injectors (AAI) via the 'Spare Pens in Schools' scheme in Wales: a cross-sectional pilot study

Eliana Panayiotou,[1] Athanasios Hassoulas ,[2] David Tuthill ,[3] Elizabeth Miles,[4] Judith Holloway[4]

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[1]Swansea Bay University Hospitals Health Board, Swansea, UK
[2]School of Medicine, Cardiff University College of Biomedical and Life Sciences, Cardiff, UK
[3]Paediatrics, Children's Hospital for Wales, Cardiff, Cardiff, UK
[4]University of Southampton, Southampton, UK

Correspondence to
Dr Eliana Panayiotou; eliana.panayiotou2@wales.nhs.uk

ABSTRACT

Objective To investigate awareness and implementation of the Spare Pens (ie, adrenaline auto-injectors (AAIs)) scheme in primary and secondary schools in two regions in Wales.

Design A cross-sectional pilot study employing a mixed research methods approach was carried out.

Setting and participants State primary and secondary schools within Swansea and Pembrokeshire regional authorities were invited to take part. For geographical context, Swansea is the second largest city in Wales and is situated in the southwest of the country. Pembrokeshire is located in West Wales, with a large rural population outside of its main towns.

Main outcome measures Awareness and implementation of the Spare Pens in Schools scheme. Additionally, compliance with national guidance was measured by administering a questionnaire capturing data on registers, procedures, storage and training in the use of AAIs.

Results 35 schools (30 primary, 5 secondary) participated, with 11% and 6% reporting awareness and implementation of the scheme, respectively. No significant differences in awareness or implementation of the scheme were revealed for school type or region. Secondary schools reportedly stored more AAI devices compared with primary schools. The location of stored AAIs varied by school type, with 46.7% of primary schools storing AAIs in the classroom while 80% of secondary schools stored AAIs in the school office. Procedures for accessing AAI training differed, with 83% of primary schools receiving training by school nurses and 60% of secondary schools accessing training via an allergy team.

Conclusions The overall poor awareness of the Spare Pens in Schools scheme has resulted in a worrying lack of implementation of generic AAI devices. An urgent review of information dissemination regarding the scheme is required.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is no UK-wide data available on awareness and uptake of the Spare Pens in Schools scheme since it became active in 2017. A study conducted in Peterborough showed 45% of schools surveyed were aware of the scheme. No studies have previously assessed uptake and awareness among Welsh schools.

WHAT THIS STUDY ADDS

⇒ This is the first study of its kind in Wales and only the second survey assessing the scheme within the UK. This study has highlighted a lack of awareness of the 'Spare Pens in Schools' scheme among a select sample of schools in Wales. This is likely to be multifactorial with poor dissemination of information and the requirements that schools remain up to date with health-related needs of pupils.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Mandating stock devices may help to address the lack of knowledge around the scheme and help to eliminate unfavourable outcomes for children experiencing anaphylaxis at school. This may be particularly true for children experiencing their first anaphylactic reaction at school. A small change in health policy may have the potential to reduce anaphylaxis fatalities in children in the UK.

INTRODUCTION

Food allergy in children is common and has been increasing in prevalence during recent years.[1–6] Specifically, anaphylaxis is a severe, life-threatening allergic reaction that must be recognised and treated promptly to avoid fatalities.[1 7] First-line immediate treatment is intramuscular-injected adrenaline (epinephrine).[7] Over the last 20 years, admissions to UK hospitals for food anaphylaxis have increased by 5.7% annually, with the greatest increases seen in children.[3] Subsequently, prescriptions for adrenaline auto-injectors (AAIs) have increased by over 300%[3 8] in recent years.

Children with food allergy in the UK are risk-assessed and prescribed AAIs in accordance with guidance published by the British Society of Allergy and Clinical Immunology.[9] Patients prescribed AAIs are advised to carry two devices, ensuring a backup option is available in case the first pen misfires or a second dose of adrenaline is required.[10] As anaphylaxis most commonly occurs at home and is closely followed by the school setting, four devices are usually dispensed (two devices for school, two devices for home/social emergency use).[11] With up to 25% of children experiencing anaphylaxis for the first time while at school, the availability of AAIs in school could be lifesaving.[1 11–17] Anaphylaxis at school mainly occurs in primary school-aged pupils, with nearly all reactions reportedly taking place in the classroom.[1 5 6] Overall, anaphylaxis in children is under-recognised and undertreated.[11 13 18–20] Anaphylaxis-related fatalities have also been reported within the school setting in the UK,[21] further illustrating the importance of a comprehensive policy and set of guidelines to keep children safe.

Schools face several challenges in keeping food-allergic children safe while in their care.[1 17] In 5% of anaphylaxis cases experienced at school, an allergy had not been communicated to staff by parents.[1] Additionally, there are reported failures of parents to supply schools with AAIs when prescribed.[1] Barriers to treatment in school include lack of staff education, staff fears regarding AAI administration/timing, as well as fears of inducing adverse reactions.[6 19 20 22 23] Knowledge gaps in school staff in the identification and treatment of anaphylaxis has been repeatedly reported in the literature, with schools highlighting a greater need for education and training.[6 19 20 23 24]

The UK Department of Health (DoH) published guidelines for schools to advise on procedures for keeping allergic children safe, including recommendations on where and how to appropriately store AAIs and ensuring easy accessibility. For instance, AAIs must be within 5 min of reach from at-risk pupils and must not be stored in locked locations.[21] Staff must be trained in the identification and treatment of anaphylaxis, ensuring annual AAI training is conducted in person and not substituted with online resources.[13 21]

The DoH guidelines additionally outline the 2017 'Spare Pens in Schools' scheme, which resulted in a change to legislation allowing schools to purchase AAIs without prescription.[21 25] These 'spare pens' are stock devices held by schools and are unassigned to named pupils. Stock devices can be used to treat anaphylaxis in any child with known allergies where the patient's own device is; (1) out-of-date, (2) misfires, (3) is not in close vicinity (within 5 min). Spare pens can also be administered to children for whom AAIs have not been prescribed but who have an allergy action plan. Where children with no known allergies experience first-time anaphylaxis at school, emergency services should be contacted, stating access to a spare pen and advice taken from the call handler. Participation in the scheme is voluntary, with purchase costs and pharmacy-handling fees incurred by schools.

Similar stock-AAI schemes operate in the USA, with legislation in 45 states and seven states mandating stock devices.[4 26–28] Emerging data shows that most anaphylactic reactions occurring in schools are treated with stock AAIs.[4 12] In a review of stock-AAI use in Chicago schools, 55% were administered to children with first-time anaphylactic reactions with similar results reported in New York.[4 16] Similarly, 45% of anaphylactic events occurring in schools in Australia are reportedly treated using generic devices.[9 29 30] Where school protocols are in place, AAI administration by staff has been appropriately delivered.[1] Where older children and adolescents are advised to carry their own AAIs, it has been reported that often devices had not been on their persons when they had needed them.[1 31] Recommendations however are that adolescents carry their own AAIs, including while at school.[13 21]

To date, a single survey-based study has been conducted in Peterborough, UK investigating awareness of the scheme, with 11 of 74 regional schools participating.[32] 45% of participating schools reported awareness of the scheme, and 18% opted in. Data on the implementation of the scheme in the UK as a whole, and within the devolved nations specifically, has not been captured.

The current pilot study aimed to investigate awareness and implementation of the 'Spare Pens in Schools' scheme in a sample of Welsh schools, within Swansea and Pembrokeshire local authorities (LA). Accessibility to healthcare varies geographically within Wales, with the study aiming to capture both urban and rural populations in South Wales. Swansea has an established paediatric allergy service, serving the city and surrounding areas for several years. Pembrokeshire, in contrast, is a rural region and does not have a specialist paediatric allergy clinic serving the local population.

METHODS

Participants

All state primary and secondary schools within Swansea and Pembrokeshire LAs were invited to take part. A total of 154 schools were contacted, representing 52 949 pupils. Private (also known as independent) schools were excluded from the study. Open-access contact information for schools was obtained from the Welsh government online.[33] Heads of schools were contacted via email and requested to complete the survey or to forward on to a member of their staff who could provide the necessary information. Approval was therefore provided in all instances by the heads of schools that took part in the study. A follow-up invitation was disseminated via post as well to all schools. Surveys were sent to 77 primary schools, 14 secondary schools and two special schools in Swansea LA. Surveys were administered to 52 primary schools, six secondary schools, two middle schools (pupils aged 3–16 years) and one special school in Pembrokeshire LA.

Patient and public involvement

No patients were involved in this pilot study.

Design and procedure

A mixed research methods approach was implemented. A 21-item questionnaire, along with a cover letter and study information were administered to the respective schools' headteachers.

Completion of the questionnaire was voluntary, and school anonymity was upheld. Demographics in the form of locality, school type and pupil population were captured. Questionnaires were disseminated at the start of the 2021/2022 academic year. The survey remained open for 3 months.

Measures

The primary objective of the study was to investigate awareness and implementation of the scheme. Specifically, the study focused on investigating:

- The frequency of uptake of the scheme in two LAs in Wales.
- Differences in uptake between primary and secondary schools.
- Barriers to implementation of the scheme.

The 21-item questionnaire included 18 close-ended multiple-choice questions and three free-text items. Qualitative items focused on any difficulties and/or barriers not explored in the preceding items. Specific domains explored awareness and uptake of the scheme (including how schools were informed about the scheme), school demographics (ie, school type, location), school allergy procedures, how many AAIs in total schools stored and training in AAI storage and use.

Analysis

Quantitative data were transferred to password-protected files. Data entered into SPSS (V.28) was cross-checked for accuracy prior to analysis. X^2 analysis was performed comparing differences between primary and secondary schools within and between each region. Where assumptions for χ^2 were violated, p values for Fisher's exact test were reported. Qualitative data were analysed using content analysis.

RESULTS

Descriptive results

Of the 154 schools invited to take part in the current study, 35 (22.7%) completed the survey and represented 12 800 pupils in the LAs. Both Welsh-medium (22.9%) and English-medium (77.1%) schools took part. Given that the current pilot study took place in Wales, Welsh-medium schools are defined as schools that deliver teaching in the Welsh language, whereas English-medium schools deliver teaching in English as the primary language of instruction. Most questionnaires (85.7%) were completed by primary schools.

Awareness and implementation of scheme

Awareness of the Spare Pens in Schools scheme was universally poor in both regions with 31 (88.6%) reporting no knowledge of the scheme (table 1). Only 10% of primary schools and 20% of secondary schools reported having heard about/come across the scheme.

AAI school procedures

All participating schools reported maintaining registers of pupils with food allergies and pupils with AAIs. A larger number of pupils prescribed AAIs were reported

Table 1 Spare Pens in Schools scheme

	Swansea LA		Pembrokeshire LA			Comparison, p value	
	Primary school (n=18)	Secondary school (n=4)	Primary school (n=12)	Secondary school (n=1)	Total (n=35)	Primary vs secondary	Swansea vs Pembs
Awareness						0.47	0.99
Yes	2 (11.1)	1 (25)	1 (8.3)	0	4 (11.4)		
No	16 (88.9)	3 (75)	11 (91.7)	1 (100)	31 (88.6)		
Heard about scheme						0.38	0.57
Not aware	16 (88.9)	3 (75)	11 (91.7)	1 (100)	31 (88.6)		
School nurse	1 (5.6)	0	0	0	1 (2.9)		
Allergy team	0	1 (25)	0	0	1 (2.9)		
Charity	0	0	1 (8.3)	0	1 (2.9)		
Other	1 (5.6)	0	0	0	1 (2.9)		
Joined scheme						0.26	0.99
Yes	0	1 (25)	1 (8.3)	0	2 (5.7)		
No	18 (100)	3 (75)	11 (91.7)	1 (100)	33 (94.2)		

Data presented as number of schools (%), p values represent χ^2 or Fisher's exact test with p<0.05 considered as statistically significant.
LA, local authorities; Pembs, Pembrokeshire.

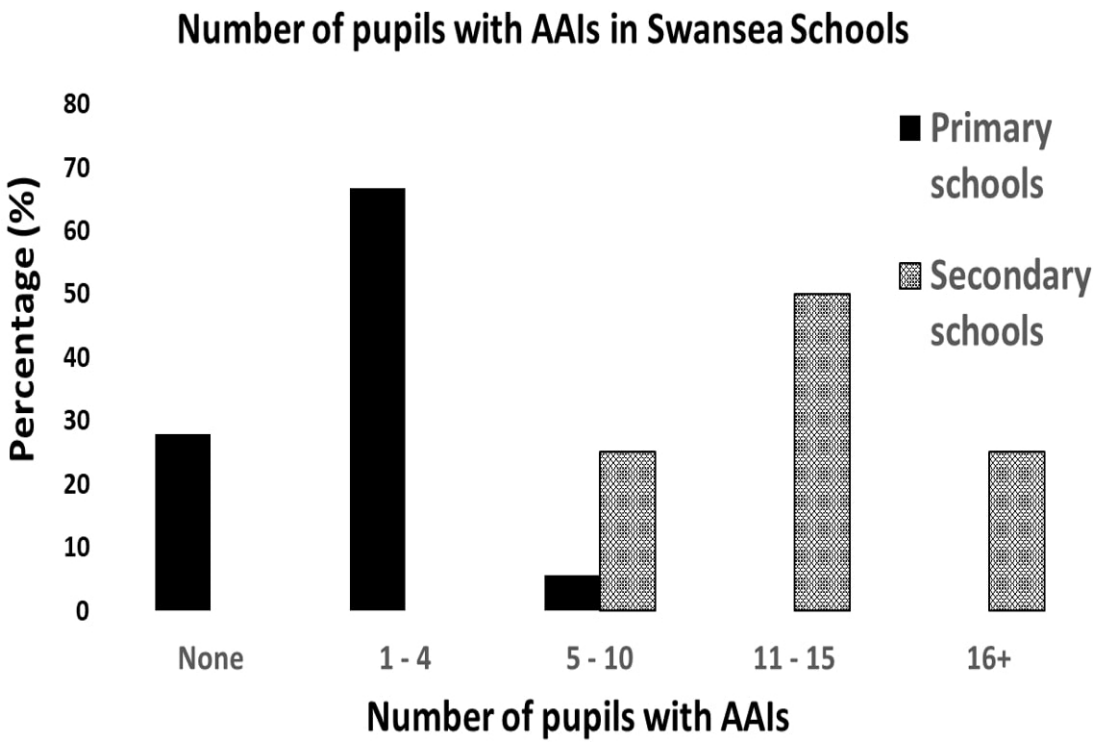

Figure 1

by secondary schools, reflecting larger pupil populations (850–2000 pupils in secondary school vs 22–700 pupils in primary school) (Fisher's exact test, p<0.001). Further analysis showed a significant difference between school type for a number of pupils with AAIs in Swansea (Fisher's exact test, p<0.001) but not for Pembrokeshire (see figure 1). A significant difference was revealed between school type in relation to the number of AAIs stored by schools (Fisher's exact test, p<0.001). All secondary schools stored >11 AAIs, with no difference between regions (figure 2).

Storage locations for AAIs varied (figure 3), with 14 (46.7%) primary schools storing AAIs in the classroom while 4 (80%) secondary schools stored AAIs in the

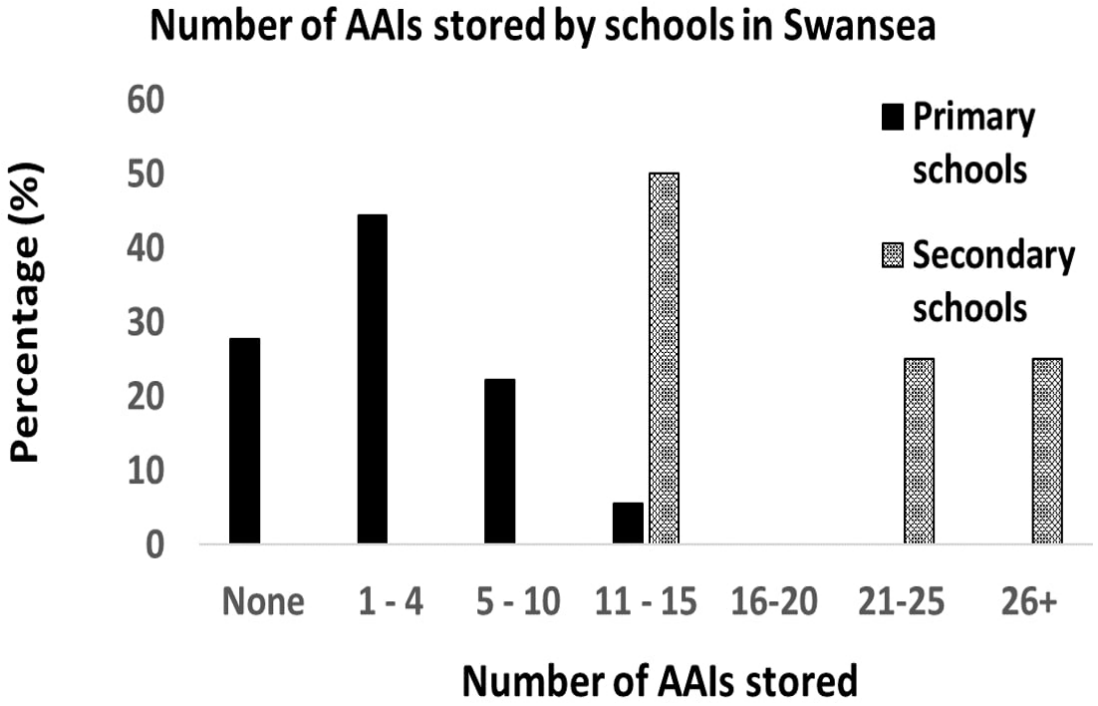

Figure 2 Number of AAIs per school, by percentage of primary and secondary schools surveyed in Swansea. AAI, adrenaline auto-injector.

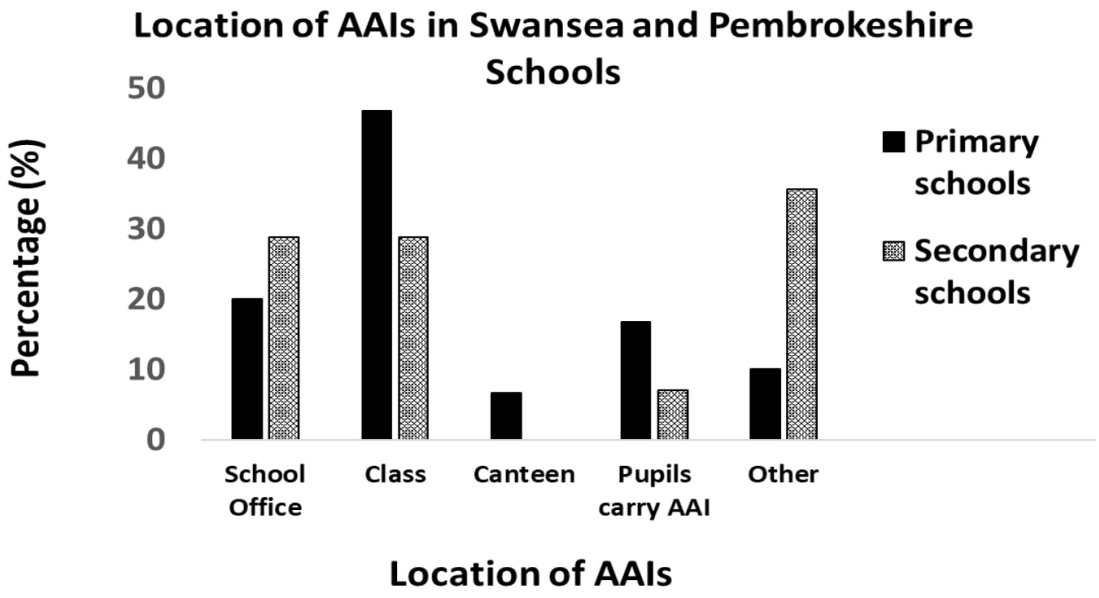

Figure 3 Location of AAIs stored in schools, by percentage of schools surveyed in Swansea and Pembrokeshire. AAI, adrenaline auto-injector.

school office. Other common locations included the medical/first-aid room. There was a statistical difference by school type for the location of stored devices (Fisher's exact test, p<0.001), but no difference between regions.

All schools reported AAIs were within 5 min reach, in line with DoH guidelines. A total of 14 (40%) schools reported storing AAIs in a locked cupboard. Around half of the schools reported storing one AAI device per pupil, contrary to recommendations that pupils should have access to two devices[10] (table 2). No differences were observed between school type or region.

There was no difference in time intervals for checking AAI expiration between school type nor region. 13 (37%) schools reported checking AAIs monthly, with 8 (23%) reportedly conducting checks every 3–12 months. Other schools reported expiry checks to be a parental responsibility.

AAI training

Overall, 74% of schools accessed AAI training through the school nurse. In addition, schools accessed training from the allergy team. A further 14.3% of schools reported a combination of nurse-led and online training for staff (figure 4). There was a statistically significant difference in how training was accessed between primary and secondary schools overall (Fisher's exact test, p<0.05), but no difference between regions (table 2). 16 schools (46%) reported completing training for staff annually.

Content analysis

Key themes from the open-ended items of the questionnaire were identified using content analysis. These items focused on barriers to adopting the scheme, challenges keeping food-allergic children safe and comments on any other areas deemed important. Given the poor awareness of the scheme, no barriers were reported. Schools did however request to learn more about the scheme.

17 schools reported difficulties in keeping food-allergic children safe, giving rise to six themes from responses to this item (figure 5). A widely-reported challenge identified by 12 schools was monitoring the presence of allergens in packed lunches, with reference made specifically to all nuts. Furthermore, four schools emphasised the challenge presented by children sharing food, especially given the lack of parental adherence to school policy on packed lunches.

Three schools reported that parents did not renew expired pens when requested. Additionally, three schools described training-of-staff as a challenge, specifically in relation to new teachers and supply staff. Staff shortages were stated to be an added problem by two schools. One school highlighted that,

> When supply-teachers come into school, it's challenging to ensure all are aware of every matter, not only allergies but other medical conditions which need certain strategies.

Regarding requests for additional information, three themes emerged. The first related to specific training needs of staff and maintaining attainment of competencies. The second made reference to children transitioning to secondary school inappropriately with junior AAI devices. One school requested direct communication between healthcare providers and educators with respect to changes in allergy management:

> …it is surprising how many times parents mention months after a child has been issued with an EpiPen. It is seldom I have any review of allergy action plans and when this changes with age and weight.

Table 2 AAI school demographics and procedures

	Swansea LA		Pembrokeshire LA			Comparison, p value	
	Primary school (n=18)	Secondary school (n=4)	Primary school (n=12)	Secondary school (n=1)	Total (n=35)	Primary vs secondary	Swansea vs Pembs
No. pupils with AAIs						**<0.001**	0.96
None	5 (27.8)	0	2 (16.7)	0	7 (20)		
1–4	12 (66.7)	0	9 (75)	0	21 (60)		
5–10	1 (5.6)	1 (25)	1 (8.3)	0	3 (8.6)		
11–15	0	2 (50)	0	1 (100)	3 (8.6)		
16+	0	1 (25)	0	0	1 (2.9)		
No. AAIs stored by school						**<0.001**	0.39
None	5 (27.8)	0	1 (8.3)	0	6 (17.1)		
1–4	8 (44.4)	0	10 (83.3)	0	18 (51.4)		
5–10	4 (22.2)	0	1 (8.3)	0	5 (14.3)		
11–15	1 (5.6)	2 (50)	0	1 (100)	4 (11.4)		
16–20	0	0	0	0	0		
21–25	0	1 (25)	0	0	1 (2.9)		
>26	0	1 (25)	0	0	1 (2.9)		
No. AAIs per pupil						0.51	0.25
None	1 (5.6)	0	0	0	1 (2.9)		
1	6 (33.3)	1 (25)	9 (75)	0	16 (45.7)		
2	10 (55.6)	3 (75)	3 (25)	1 (100)	17 (48.6)		
>2	1 (5.6)	0	0	0	1 (2.9)		
Location AAIs*	n=23	n=12	n=7	n=2	n=44	**<0.001**	0.22
School office	3 (13)	3 (25)	3 (42.9)	1 (50)	10 (22.7)		
Class	14 (60.9)	4 (33.3)	0	0	18 (40.9)		
Canteen	2 (8.7)	0	0	0	2 (4.5)		
Pupils carry AAI	2 (8.7)	0	3 (42.9)	1 (50)	6 (13.6)		
Other†	2 (8.7)	5 (41.7)	1 (14.3)	0	8 (18.2)		
Locked AAIs							
Yes	5 (27.8)	2 (50)	6 (50)	1 (100)	14 (40)	0.37	0.2
No	13 (72.2)	2 (50)	6 (50)	0	21(60)		
Expiry check						0.74	0.82
Monthly	8 (44.4)	0	4 (33.3)	1 (100)	13 (37.1)		
3 monthly	3 (16.7)	1 (25)	4 (33.3)	0	8 (22.9)		
Annually	4 (22.2)	2 (50)	2 (16.7)	0	8 (22.9)		
Other‡	3 (16.7)	1 (25)	2 (16.7)	0	6 (17.1)		
Access to AAI training						**0.02**	0.51
School nurse	14 (40)	1 (25)	11 (91.7)	0	26 (74.3)		
Allergy team	1 (2.9)	3 (75)	0	0	4 (11.4)		
Nurse and online	3 (8.6)	0	1 (8.3)	1 (100)	5 (14.3)		
AAI training frequency						0.55	
Biannually	2 (11.1)	0	0	1 (100)	3 (8.6)		
Annually	7 (38.9)	2 (50)	7 (58.3)	0	16 (45.7)		0.68
<Annually	8 (44.4)	2 (50)	3 (25)	0	13 (37.1)		
Other	1 (12.5)	0	2 (16.7)	0	3 (8.6)		

Continued

Table 2 Continued

	Swansea LA		Pembrokeshire LA			Comparison, p value	
	Primary school (n=18)	Secondary school (n=4)	Primary school (n=12)	Secondary school (n=1)	Total (n=35)	Primary vs secondary	Swansea vs Pembs

Data presented as number of schools (%), p values represent χ^2 test or Fisher's exact test. P values<0.05 considered statistically significant and displayed in bold.
*AAIs stored in more than one location in some schools.
†Other locations; second AAI stored in a central unlocked location, stored in medical room/first aid room.
‡Other; checked and recorded in electronic diary with alarm set 1 month prior to AAI expiry to remind parents about replacement; parental responsibility, no defined time interval.
§Other; biannually by a specialist but more frequently in the house; when needed with new starters prescribed AAIs.
AAIs, adrenaline auto-injectors; LAs, local authorities; Pembs, Pembrokeshire.

Where schools report additional pressures on staff to deal with all health-related student matters, one school highlighted that:

> At school level, we are expected to be immediate experts in all things, this can be stressful for teachers and teaching assistants.

DISCUSSION

To the authors' knowledge, this is the second study in the UK looking at the uptake and success of the 'Spare Pens for School' scheme, which has been a national initiative since 2017. Our findings highlight poor awareness of the scheme across school types and regions. Overall, only 11.4% of participating schools reported knowledge of the scheme and 5.7% implemented it. This differed from a survey of eleven schools in Peterborough, England, that reported 45% awareness of the scheme, four times that revealed in Swansea and Pembrokeshire.

Additionally, the current study highlights that schools are not meeting several domains of published recommendations. Most notably, staff education and training appear to be lacking, as well as knowledge about appropriate storage and care of AAIs. Only 54.3% of schools were compliant with EAACI (European Academy of Allergy and Clinical Immunology) recommendations for annual anaphylaxis and AAI staff training.[13] Additionally, only 13 schools (37.1%) were compliant with monthly AAI expiration checks. Furthermore, 40% of

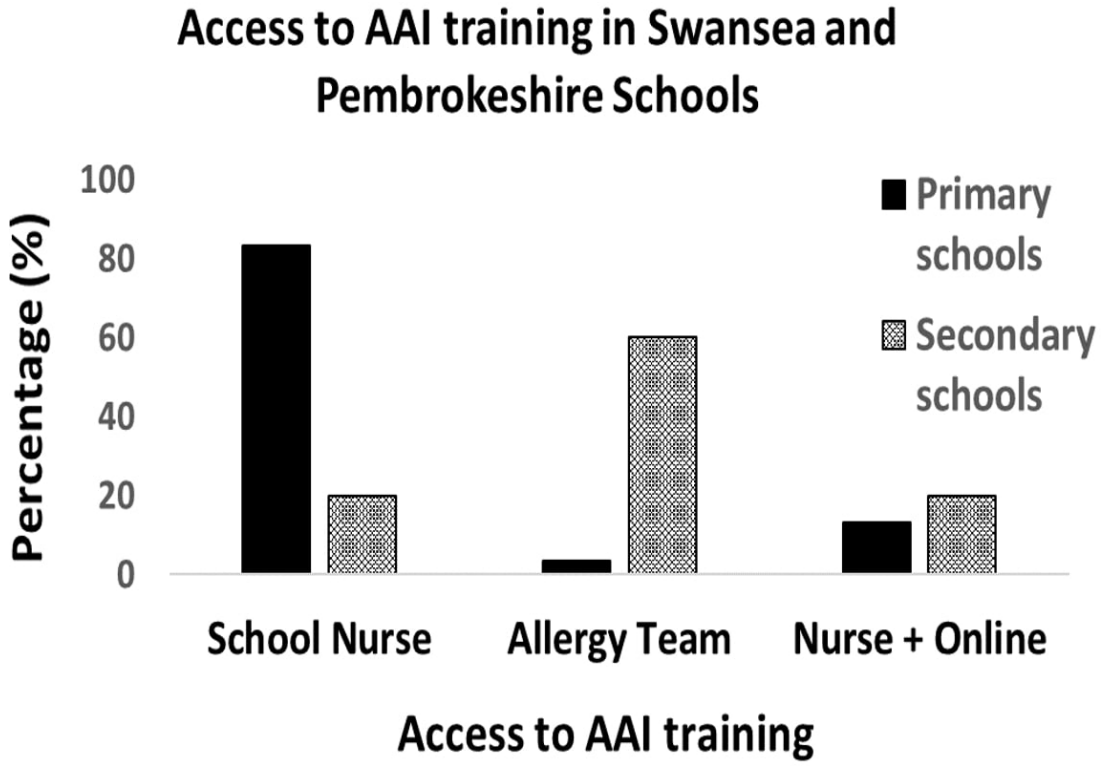

Figure 4 Access to AAI training, by percentage of schools surveyed in Swansea and Pembrokeshire. AAI, adrenaline auto-injector.

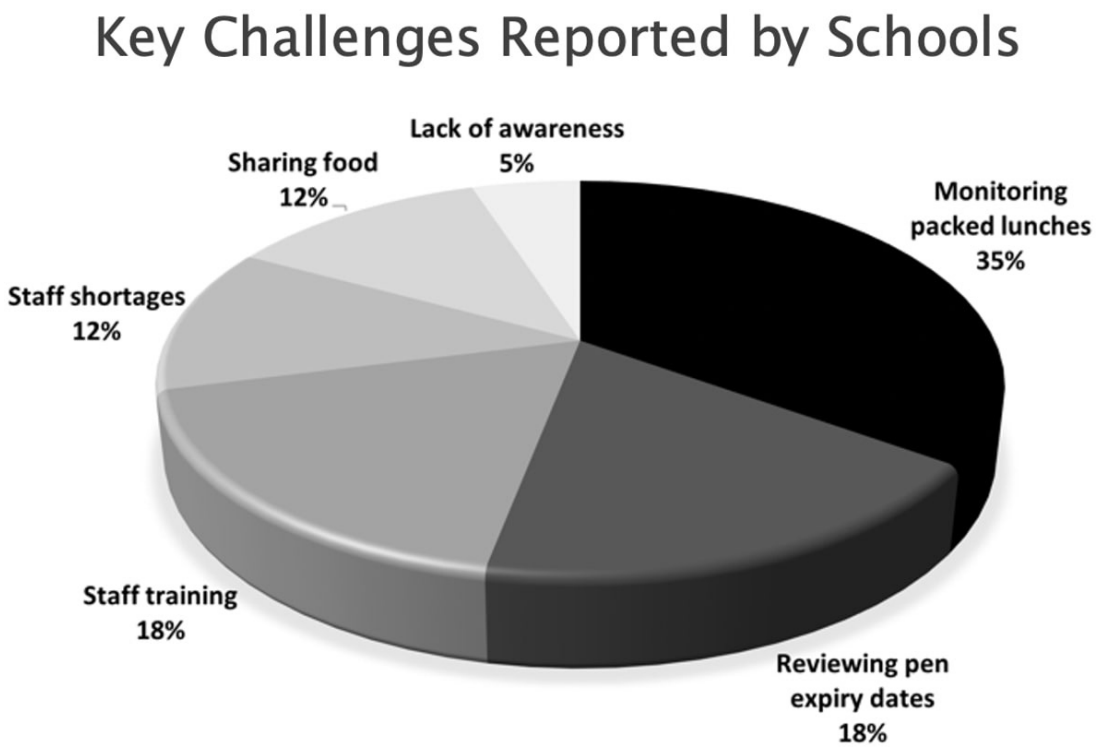

Figure 5 Key challenges reported by schools in keeping food-allergic children safe.

schools reported storing AAIs in a locked location against DoH recommendations. This is notably a problem not unique to the UK, with data from Australia showing that AAIs were stored in a locked location in 37% of schools, against regulations.[23]

With only five secondary schools taking part in the study, compared with 30 primary schools, our results are more representative of primary school AAI procedures. As such, data is required from a larger sample of secondary schools to draw further conclusions in this regard. Despite the small numbers, a larger proportion of secondary school pupils were reportedly prescribed AAIs. The total number of AAIs stored by secondary schools was also significant, with two secondary schools reporting storage in excess of 20 AAIs. Most secondary schools reported storage of AAIs in their school office, with only one secondary school reporting that pupils carry their own AAIs (as is recommended). Managing this volume of AAIs makes the selection of the correct pupil's AAI in an emergency challenging. One-quarter of anaphylactic reactions that take place in schools occur in pupils with no previous known allergies.[12] Without a generic device, schools are not permitted to use a named pupil's AAI to treat another pupil. In these circumstances, schools are required to contact emergency services, leading to a delay in adrenaline administration that could prove fatal. Analysis of AAI administration in the USA and Australia has shown use of stock devices becoming increasingly commonplace.[4 9 12 16 29 30]

As reported in the literature, there are several reasons why a patient's own device may not be available in times of need, including lack of parental communication with schools about allergies, failure of adolescents to carry their own devices and expiration of devices.[1] The literature has reported almost 50% of allergic pupils not bringing AAIs to school.[22] Lack of stock AAIs, therefore leaves schools and pupils vulnerable. A small change in health policy may have the potential to reduce anaphylaxis-related fatalities in children in the UK. Reportedly, 17% of fatal anaphylactic reactions take place on school premises in the UK.[32]

The results of this pilot study indicate a lack of awareness of the scheme is likely to be multifactorial, with poor dissemination of information and the requirement of schools to remain up-to-date with changes in the health needs of pupils being critical factors. This highlights the support schools require, as well as an understanding that teachers are educators and not health professionals. The additional benefit of spare AAIs is accessibility to emergency medication for vulnerable socioeconomic groups.[2] By mandating this, socioeconomic disparity would be eliminated within the school environment. Socioeconomic disparity was not explored in this study, but should be a consideration for future research.

Limitations of the study include a small sample size representing 22.7% of schools in the surveyed regions. Specifically, a limited number of secondary schools took part. The current study excluded private schools and no special schools took part. As such, the data collated may not be truly representative of all regional schools, however, the current pilot does provide a solid foundation on which a subsequent larger-scale study can be conducted. A prior meta-analysis, however, revealed a wide range of survey responses depending on methods

of data collation and setting.[34] In relation specifically to educational settings and faculty/staff recruitment via email, response rates ranged between 6% and 34%. Given that invitations were circulated via email for the current study, the response rate falls within the average of similar studies that were reviewed. As reported by the authors of the meta-analysis, follow-up using either email or postal mail resulted in a slight improvement in response rate, comparable once again with the findings of the current study. Further research is required to draw more detailed and representative national conclusions.

The findings of the current pilot study represent crucial implications for policymakers and key stakeholders in maintaining the health and well-being of children within the education system. Multifaceted planning is required to ensure the safety of food-allergic children at school, which includes mandating stock AAIs. However, this will need to be in addition to structured and standardised staff training.[35]

There is also the potential to introduce sustainable, environmentally-friendly practices as part of a nation-wide policy. AAI devices are manufactured using plastic, housing an encased adrenaline vial. While plastic is resistant to breakage and leaking, it also represents an environmental hazard.[36] With emerging challenges of climate change, the spotlight will soon turn to pharmaceutical disposal and reduction in environmental contaminants and ecotoxicity.[37 38] Although not specific to AAI devices, active pharmaceutical agents have been detected in water supplies and soil.[37] Mandating the Spare Pens in School scheme can therefore take a small step in practicing more sustainable healthcare.

Contributors EP: conceptualisation, methodology, validation, formal analysis, investigation, data curation, writing—original draft. EP is the guarantor and is responsible for the overall content. AH: methodology, formal analysis, data curation, writing—reviewing and editing. DT: methodology, investigation, supervision. EM: conceptualisation, validation, supervision. JH: conceptualisation, methodology, supervision.

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Patient consent for publication Not applicable.

Ethics approval Ethics approval was obtained from the University of Southampton Ethics Committee (ID66689). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Athanasios Hassoulas http://orcid.org/0000-0002-1029-1847
David Tuthill http://orcid.org/0000-0003-0190-0273

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