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Developing a system to estimate the severity of influenza infection in England: findings from a hospital-based surveillance system between 2010/2011 and 2014/2015

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SUMMARY

The UK Severe Influenza Surveillance System (USISS) was established following the 2009 influenza pandemic to monitor severe seasonal influenza. This article describes the severity of influenza observed in five post-2009 pandemic seasons in England. Two key measures were used to assess severity: impact measured through the cumulative incidence of laboratory-confirmed hospitalised influenza and case severity through the proportion of confirmed hospitalised cases admitted into intensive care units (ICU)/high dependency units (HDU). The impact of influenza varied by subtype and age group across the five seasons with the highest crude cumulative hospitalisation incidence for influenza A/H1N1pdm09 cases in 2010/2011 and in 0–4 year olds each season for all-subtypes. Case severity also varied by subtype and season with a higher hospitalisation: ICU ratio for A/H1N1pdm09 and older age groups (older than 45 years). The USISS system provides a tool for measuring severity of influenza each year. Such seasonal surveillance can provide robust baseline estimates to allow for rapid assessment of the severity of seasonal and emerging influenza viruses.

Key words: Influenza, Hospitalisation, Severity.

INTRODUCTION

Prior to the influenza pandemic in 2009, surveillance of severe respiratory infection in the UK resulting in hospitalisation was limited. New hospital-based surveillance systems for influenza were rapidly developed during the pandemic in order to fill this recognised gap [1, 2] and after, the UK, along with a number of other countries, implemented on-going seasonal influenza severe disease surveillance. The intention was that these systems, besides being utilised for seasonal influenza, would also be available during a future pandemic, following guidance from the WHO (World Health Organization) and the European Centre for Disease Prevention and Control (ECDC) [3, 4]. ECDC now coordinate the collection of case-based data on hospitalised severe influenza cases through the EISN (European Influenza Surveillance Network), although the systems employed for the surveillance of hospitalised cases vary significantly across Europe [5]. The UK Severe Influenza Surveillance System (USISS) is a web-based reporting scheme established in 2010 to collect surveillance data on hospitalised laboratory-confirmed influenza cases. It consists of a sentinel network of acute National Health

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Service (NHS) Hospital Trusts in England and aims to describe the epidemiology of severe influenza in time, place and person, to measure case severity and monitor the impact of influenza on the population.

Since the 2009 pandemic, a range of seasonal influenza subtypes have circulated in England. During the 2010/2011 season, the UK experienced a severe first post-pandemic season primarily due to influenza A/H1N1pdm09 mainly in young adults [6]. In contrast, the 2011/2012 season was characterised by low and late influenza activity, predominantly influenza A/H3N2. In 2012/2013 activity rose to higher levels than those seen in the previous season, with activity mainly due to A/H3N2 [7]. In 2013/2014, a season dominated by A/H1N1pdm09 with a higher peak compared with 2012/2013 [8]. In 2014/2015 moderate levels of influenza activity was seen with circulation of a drifted A(H3N2) strain that resulted in significant excess mortality, particularly in the elderly [9].

The severity of seasonal influenza is known to vary by subtype, with influenza B generally affecting younger age groups, influenza A/H3N2 causing severe disease in the elderly [10–12] and the new A/H1N1pdm09 affecting rather younger adults and children. A rapid understanding of the epidemiology of severe influenza each season is important to guide local and national public health planning on an annual basis and provide a baseline for future seasons. Obtaining a rapid assessment of the severity of a new emerging pandemic influenza virus is critical to inform evolving public health interventions. Three key indicators have been identified to measure severity – case severity (the likelihood that an individual who acquires an influenza infection will be hospitalised, be admitted to intensive care or die due to that infection); transmissibility (the likelihood that an infection will spread in the population as measured by parameters such as the household secondary attack rate or indirectly such as the GP (general practice) ILI (influenza-like illness) consultation rate) and population impact, which is a function of the two previous indicators (as measured by indicators such as cumulative hospitalisation incidence and excess mortality).

This paper investigates how the new USISS hospital-based surveillance system can potentially contribute to severity assessment by measuring the case severity and impact of seasonal influenza in the post-pandemic era over five influenza seasons from 2010 to 2015 using two severity measures and explores how this might be utilised for pandemic severity assessment.

METHODS

The USISS sentinel hospital network was initially piloted in the 2010/2011 season and ran in full during the following 2011/2012, 2012/2013, 2013/2014 and 2014/2015 influenza seasons in England.

Method of sampling

NHS Hospital Trusts were recruited using stratified random sampling in order to obtain a representative sample of contributors. A NHS Hospital Trust is an organisation that provides secondary health services within the English NHS. Trusts were stratified according to size (small (<500) and large (>500 beds)), trust type (acute [NHS Acute Trusts manage the hospitals in a particular area in England.] or teaching [Teaching hospitals/trusts are trusts which are affiliated to a medical school and provide clinical education and training to future health professionals.]) and region (there are 10 regions in England). Speciality trusts [Speciality trusts are regional or national centres for more specialised care.] were excluded. Three trusts from each English region (one small acute trust, one large acute trust and one teaching trust) were randomly chosen to participate. In London and the North West, where the population is higher, six trusts, i.e. two of each type were recruited instead of three. Voluntary enrolment of NHS Trusts in each season commenced approximately 1 month prior to the start of the collection (week 40). If a trust chose not to participate, then another was randomly selected from the same group of trusts, i.e. region and size. Trusts that were recruited after week 40 were asked to retrospectively submit their data from week 40 onwards. Trusts who participated in the previous season were asked to re-participate in the scheme the following season.

In total, 23 of 166 (15%) eligible acute hospital trusts from across England were successfully recruited and submitted weekly data during the 2010/2011 season. In the 2011/2012 season, 34 of 148 (23%) trusts were recruited, in 2012/2013, 31 of 143 (22%) trusts, in 2013/2014, 34 of 142 (24%) and in 2014/2015, 32 of 138 (23%) trusts participated. Of the trusts participating in 2010/2011, 13 were re-recruited to participate in 2011/2012, 12 in 2012/2013, 12 in 2013/2014 and 9 in 2014/2015. In each season the representativeness of trusts varied (12 large, 2 teaching and 9 small in 2010/2011; 16 large, 9 teaching and 9 small in 2011/2012, 15 large, 9 teaching and 7 small in 2012/2013, 18

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large, 9 teaching and 7 small in 2013/2014 and 20 large, 8 teaching and 4 small in 2014/2015). A disproportionate number of large trusts were recruited since not all regions had hospitals which met the small trust category. In those cases, trusts with the smallest number of beds within that region were invited to participate.

Case definition

Trusts were asked to undertake respiratory sampling and laboratory investigation for influenza on all suspect influenza cases who presented in hospital with:

(a) Fever ($\geqslant$38 °C) or history of fever in the previous 7 days; and
(b) Two or more of the following symptoms: cough, sore throat, headache, rhinorrhoea, limb or joint pain, vomiting or diarrhoea.

A laboratory-confirmed case was defined as any person who was hospitalised and had laboratory-confirmed influenza A (H1N1pdm09, H3N2 or unknown) or B infection. For the purposes of intensive care units (ICU)/high dependency units (HDU) surveillance, a confirmed case was defined as any person who was admitted to ICU/HDU and had laboratory-confirmed influenza A (H1N1pdm09, H3N2 or unknown) or B infection. These case definitions remained consistent throughout the time period of this study. An HDU provides more extensive care to patients than a normal ward but not to the extent of an ICU.

Data collected

Consultant microbiologists or infection control teams at each participating hospital trust submitted a weekly aggregate report of all laboratory-confirmed cases admitted the previous week, by age group (<1, 1–4, 5–14, 15–44, 45–64 and 65+ year olds) and influenza subtype, at any level of care. In 2011/2012 and 2012/2013, each trust also submitted individual-level data on all cases admitted to ICU/HDU, although only aggregate data was used for this analysis.

Data was collected on cases through a web-based, secure IT (Information technology) platform. Transport-layer encryption is used for this web-tool and trust-based users are only able to access the data within their own hospital trust. The tool is not accessible through standard public internet connections. Data downloaded from the tool are stored on a secure Public Health England (PHE) server protected by a firewall and is only accessible to a minimum number of specific authorised users within the PHE network.

Sampling frame

Data collected between weeks 40 and 20 for the 2011/2012, 2012/2013, 2013/2014 and 2014/2015 seasons were used for this study apart from the 2010/2011 pilot season when data were only collected between weeks 40 and 13. Although the time frames for each period of influenza circulation were not identical in length, they were taken to be equal for the purposes of this study, since a seasonal (or annual) cumulative population risk of hospitalisation was being calculated.

Key indicators examined

Two measures were used to examine severity each season and are described below:
The impact was measured through:

- Risk (cumulative hospitalisation incidence) of hospitalisation was calculated from the number of laboratory-confirmed influenza hospitalisations overall, by age group and by influenza subtype over the season for the acute trust catchment population of all participating NHS Trusts in that corresponding season. The participating trust catchment population estimates were calculated by the ERPHO (Eastern Region Public Health Observatory) derived using Hospital Episode Statistics (HES) data on admissions between 2006/2007 and 2008/2009 and 2009 Office for National Statistics (ONS) mid-year estimates for LSOA (lower super output areas). The proportional flow method was used through which district populations are allocated, pro rata, to a provider based on the proportion of admissions from that district to that provider [13].

The case severity was measured through:

- The proportion of hospitalised-confirmed cases that were reportedly admitted into ICU/HDU, each season stratified by influenza subtype and age group.

Statistical methods

Regression analyses were performed to investigate variation in hospitalisation and ICU/HDU admissions between different subgroups. For each of the analyses the baselines were set as 2011/2012 for year, 15–44 year olds for age group and influenza B for

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influenza subtype. Influenza A unsubtyped results were included as a separate subgroup.
Impact:

- Mixed-effects ordinal logistic regression was used for the analysis where the outcome was the weekly number of hospitalised cases for each trust grouped into three categories (0, 1, 2 or more). Season, age group, influenza subtype and logarithm of the population were the fixed-effect explanatory variables, while week and trust were included by means of a joint random effect. The main model consisted of the random effect, the logarithm of the population and all the two-way interactions between the remaining fixed effects. The P values for the interactions were obtained by means of a χ^2 test on the difference of χ^2 values of the main model and a model without the interaction being tested. Three separate models were then fitted with just one interaction and the other fixed effects as main effects only, with the resulting odds ratios (ORs) of larger counts of hospitalisation and 95% confidence intervals presented in the results section.

Case severity:

- For the analysis of ICU/HDU admissions, the outcome was a binary variable (admitted to ICU or not), no population variable and a mixed-effects logistic regression was used. Season, age group and influenza subtype were the fixed-effect explanatory variables, with reference groups of age group 15–44, influenza B and 2011/2012 respectively, while week and trust were included by means of a joint random effect. Highly non-significant interactions were removed one at a time in a backwards stepwise procedure, with the significance level chosen to be 5%. This analysis was restricted to the 2011/2012 and 2012/2013 seasons.

Laboratory methods

Influenza laboratory confirmation was carried out at a local level by NHS Hospital Trusts. Subtyping either took place locally or at the national PHE Influenza Reference Laboratory.

Ethics

Ethical approval was not sought for this scheme as it is undertaken as part of routine national surveillance under Section 3 of the Health Service (Control of Patient Information) Regulations 2002, Regulation 3 which provides statutory support for disclosure of such data by the NHS, and their processing by PHE, for the purposes of diagnosing communicable diseases and other risks to public health and recognising trends in such diseases and risks.

RESULTS

Impact: descriptive analysis

In 2010/2011, the dominant subtype was influenza A H1N1pdm09 – with 1242 of 1651 total hospitalised cases (75·2% of influenza hospital admissions) due to this subtype, with influenza B co-circulation. The 2011/2012 season was dominated by influenza A (485 of 551 total hospitalised cases, 88·0%) specifically influenza A/H3N2 (196/551, 35·6%) or influenza A not subtyped (281/551, 51·0%). The 2012/2013 season was dominated by influenza B (494/1400, 35·3%) and influenza A/H3N2 (375/1400, 26·5%). The 2013/2014 season was dominated by influenza A/H1N1pdm09 (543/907, 59·9%) and the 2014/2015 season by influenza A/H3N2 (887/1736, 51·1%).

The crude cumulative hospitalisation incidence risk for all influenza types in the 2010/2011 season was 22·0/100 000 in the trust catchment population compared with a cumulative incidence of 4·4/100 000 catchment population in 2011/2012, 12·1/100 000 in 2012/2013, 7·1/100 000 in 2013/2014 and 13·8/100 000 in 2014/2015 (Fig. 1).

By season overall, the age-specific cumulative hospitalisation incidence for all influenza types were highest in the 0–4 year olds each season (65·9/100 000 in 2010/2011, 19·4/100 000 in 2011/2012, 43·5/100 000 in 2012/2013, 23·0/100 000 in 2013/2014 and 30·7/100 000 in 2014/2015). By influenza subtype, the age-specific cumulative hospitalisation incidence for influenza A/H1N1pdm09 were highest in the 0–4 year olds followed by the 15–44 year olds, whereas for influenza A/H3N2 the rates were highest in the 0–4 year olds followed by the 65+ year olds. The median age for all cases in 2010/2011 was 33 years (interquartile range (IQR) 16–51) compared with 27 years in 2011/2012 (IQR 4–60), 33 years in 2012/2013 (IQR 6–58), 34 years in 2013/2014 (IQR 13–55) and 49 years in 2014/2015 (IQR 19–73).

Impact: statistical analysis

All the three two-way interactions were highly significant ($P < 0·001$ in all cases (season–age group,

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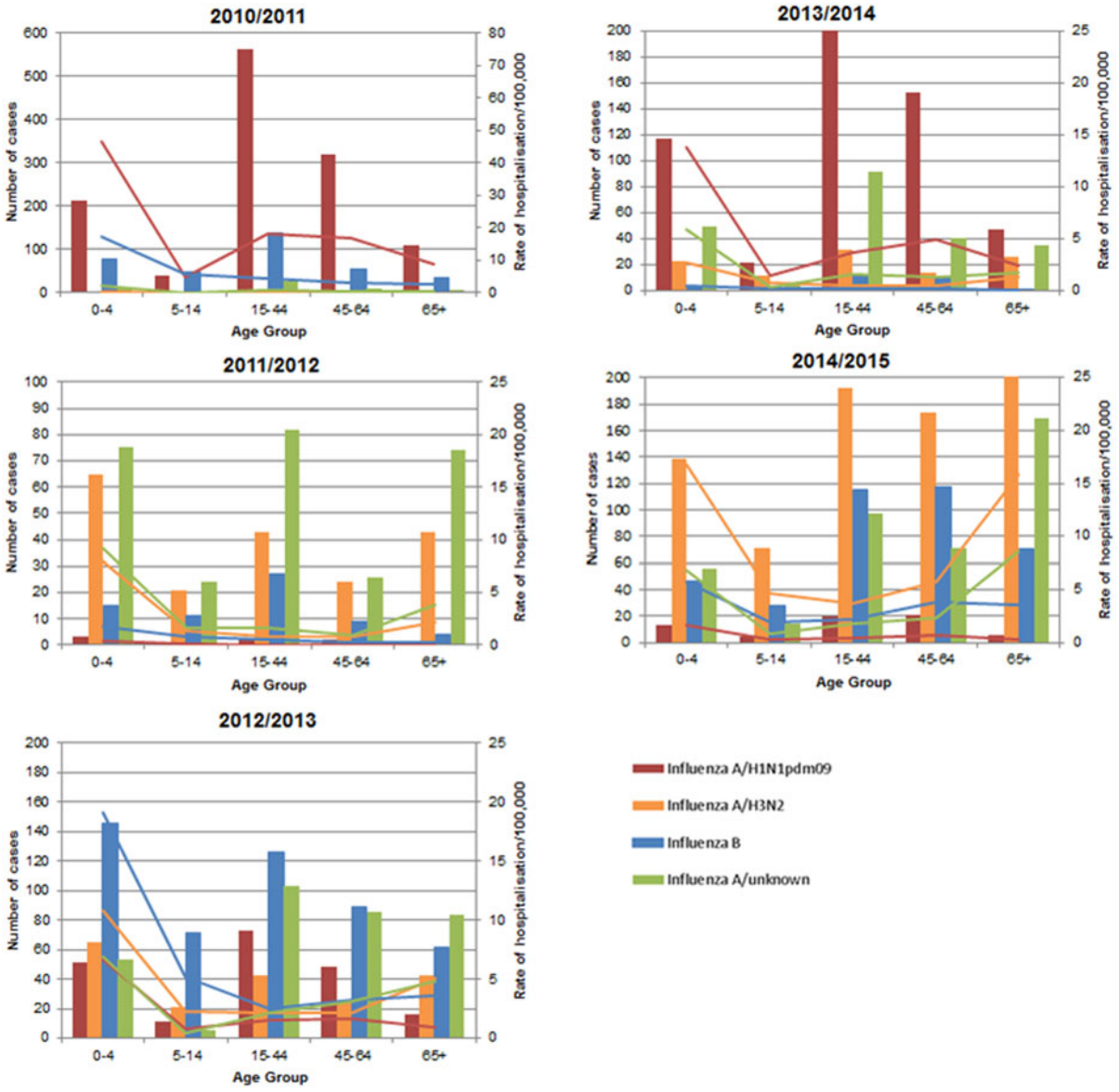

Fig. 1. Cumulative number of hospitalisations in participating trusts by age group and subtype during the 2010/2011–2014/2015 influenza seasons and cumulative hospitalisation incidence per 100 000 catchment population, England. Legend: Bars represent number of hospitalised cases and lines represent rate of hospitalisation per 100 000 catchment population in England.

season–influenza subtype and influenza–subtype-age group)).

By age group, the impact was highest in the under-5 year olds: overall the adjusted ORs of larger counts of hospitalisation were highest in each of the five seasons for 0–4 year olds compared with other age groups (Table 1). The over 65+ year olds were, in three of five seasons, the age group with the second highest OR of hospitalisation. The highest OR of hospitalisation overall by age and season was seen in the 0–4 year olds in the 2010/2011 season (OR 33·7).

The impact by influenza subtype varied across the seasons (Table 2). In 2010/2011 and 2013/2014 the highest OR of hospitalisation by influenza subtype by season were seen in those admitted with influenza A/N1N1pdm09 (OR 47·7 in 2010/2011, 6·9 in 2013/2014) (Table 2). For the remaining seasons, the OR were highest for those admitted with influenza A/unknown in 2011/2012 (OR 3·4), influenza B in 2012/2013 (OR 7·0) and influenza A/H3N2 in 2014/2015 (OR 10·4).

As with season, impact was highest in the 0–4 year old age group regardless of the influenza subtype

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Table 1. *Adjusted ORs of hospitalisation by season and age group*

Age group	OR (95% CI) (2010/2011)	OR (95% CI) (2011/2012)	OR (95% CI) (2012/2013)	OR (95% CI) (2013/2014)	OR (95% CI) (2014/2015)
0–4	33·7 (23·1–49·2)	6·6 (4·6–9·5)	13·8 (9·8–19·3)	7·2 (5·1–10·3)	10·3 (7·2–14·6)
5–14	8·7 (6·0–12·7)	1·5 (1·0–2·2)	2·6 (1·8–3·6)	1·1 (0·7–1·6)	2·7 (1·9–3·7)
15–44	10·2 (7·7–13·3)	1·00	2·7 (2·13–3·48)	2·0 (1·5–2·5)	2·9 (2·3–3·7)
45–64	10·0 (7·4–13·4)	0·9 (0·6–1·2)	3·5 (2·7–4·5)	2·4 (1·8–3·2)	5·1 (3·9–6·6)
65+	6·1 (4·3–8·8)	1·8 (1·3–2·7)	4·6 (3·4–6·2)	2·1 (1·5–3·0)	7·5 (5·7–10·0)

OR, odds ratio; CI, confidence interval.

Table 2. *Adjusted ORs of hospitalisation by season and influenza subtype*

Influenza subtype	OR (95% CI) (2010/2011)	OR (95% CI) (2011/2012)	OR (95% CI) (2012/2013)	OR (95% CI) (2013/2014)	OR (95% CI) (2014/2015)
A/H1N1pdm09	47·7 (35·0–65·1)	0·1 (0·1–0·3)	2·6 (1·9–3·6)	6·9 (5·1–9·2)	1·1 (0·8–1·6)
A/H3N2	0·2 (0·1–0·6)	2·7 (1·9–3·7)	4·5 (3·3–6·1)	1·3 (1·0–1·9)	10·4 (7·7–14·0)
A/unknown	2·2 (1·5–3·4)	3·4 (2·5–4·7)	3·9 (2·9–5·3)	2·7 (2·0–3·7)	4·9 (3·6–6·7)
B	16·7 (12·0–23·0)	1·00	7·0 (5·2–9·3)	0·5 (0·3–0·7)	6·0 (4·4–8·1)

OR, odds ratio; CI, confidence interval.

Table 3. *Adjusted ORs of hospitalisation by influenza subtype and age group*

Age group	OR (95% CI) (A/H1N1pdm09)	OR (95% CI) (A/H3N2)	OR (95% CI) (A/unknown)	OR (95% CI) (B)
0–4	4·5 (3·3–6·1)	3·8 (2·8–5·2)	3·5 (2·6–4·7)	4·1 (3·0–5·5)
5–14	0·7 (0·5–0·9)	1·0 (0·7–1·3)	0·4 (0·3–0·6)	1·4 (1·1–1·8)
15–44	1·3 (1·1–1·6)	0·8 (0·6–0·9)	0·9 (0·8–1·1)	1·00
45–64	1·8 (1·4–2·1)	1·1 (0·9–1·3)	1·0 (0·8–1·2)	1·3 (1·0–1·6)
65+	1·0 (0·7–1·3)	2·1 (1·6–2·6)	1·9 (1·5–2·4)	1·12 (0·9–1·5)

OR, odds ratio; CI, confidence interval.

(Table 3). The odds amongst other age groups after 0–4 year olds however varied with the subtype with influenza A/H1N1pdm09 higher in younger adults, i.e. 15–64 year olds, whereas influenza A/H3N2 and A/unknown was higher in the 65+ year olds and influenza B was higher in school-age children (5–14 year olds) and middle-aged adults (45–64 year olds).

Case severity: descriptive analysis

The proportions of hospitalised cases that were admitted to ICU/HDU are presented in Table 4. In 2010/2011, overall 14·1% (237/1681) of hospitalised cases were admitted to ICU/HDU, 8·3% (46/551) in 2011/2012 and 11·8% (165/1400) in 2012/2013. Case severity varied by influenza subtype and age group. In 2010/2011 the highest proportion of hospitalised cases admitted to ICU/HDU were influenza A/unknown cases, although the numbers were small, followed by A/H1N1pdm09 cases, the main circulating strain that season. Only 46 cases were admitted into ICU/HDU in 2011/2012 with the highest proportion of ICU/HDU admissions being for A/H3N2 and B cases at 11·7% and 10·6%, respectively. In 2012/2013 the highest proportion of ICU/HDU admissions were influenza A/H1N1pdm09 cases (20·6%) and by age group, in those aged 15 years and older.

Case severity: statistical analysis

Neither the season–influenza subtype nor season–age group interaction were significant ($P = 0·5$ and 0·2, respectively). While the age group–influenza subtype was not significant, it was nevertheless retained as it

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Table 4. *Proportion of hospitalised cases admitted to ICU/HDU in participating trusts by age group and influenza subtype*

Season	Age group	Number of influenza A/H1N1pdm09 ICU/HDU cases	Proportion of A/H1N1pdm09 cases admitted to ICU/HDU (%)	Number of Influenza A/H3N2 ICU/ HDU cases	Proportion of A/H3N2 cases admitted to ICU/HDU (%)	Number of influenza B ICU/HDU cases	Proportion of influenza B cases admitted to ICU/HDU (%)	Number of influenza A/unknown ICU/HDU cases	Proportion of A/unknown cases admitted to ICU/HDU (%)	Total number of ICU/ HDU cases	Overall proportion of hospitalised cases admitted to ICU/HDU (%)
2010/2011	0–4	9	4·2	0	0·0	0	0·0	1	10·0	10	3·3
	5–14	3	7·7	0	–	2	4·2	0	0·0	5	5·7
	15–44	103	18·3	0	0·0	5	3·6	6	24·0	114	15·7
	45–64	81	25·4	0	0·0	10	18·2	4	40·0	95	24·7
	65+	10	9·3	0	0·0	3	9·1	0	0·0	13	8·8
	All ages	206	16·6	0	0·0	20	5·7	11	21·2	237	14·4
2011/2012	0–4	0	0·0	5	7·7	0	0·0	75	4·0	8	5·1
	5–14	0	0·0	3	14·3	3	27·3	24	4·2	7	12·3
	15–44	0	0·0	4	9·3	0	0·0	82	7·3	10	6·5
	45–64	1	50·0	1	4·2	4	44·4	26	3·8	7	11·5
	65+	0	–	10	23·3	0	0·0	74	5·4	14	11·6
	All ages	1	12·5	23	11·7	7	10·6	281	5·3	46	8·3
2012/2013	0–4	6	11·8	10	12·0	8	5·5	53	3·8	26	7·8
	5–14	2	18·2	2	6·5	5	7·0	6	0·0	9	7·6
	15–44	17	23·3	10	8·8	7	5·6	103	7·8	42	10·1
	45–64	13	27·1	4	6·6	18	20·2	86	12·8	46	16·2
	65+	3	18·8	14	16·1	14	22·6	84	13·1	42	16·9
	All ages	41	20·6	40	10·7	52	10·5	332	9·6	165	11·8

ICU, intensive care units; HDU, high dependency units.

Table 5. *Adjusted ORs of ICU/HDU admission in 2011/2012 and 2012/2013 by influenza subtype and age group*

Influenza subtype	Age group	ORs	95% CI	*P* value
A/H1N1pdm09	0–4	2·43	0·73–8·09	
	5–14	3·27	0·53–20·36	
	15–44	5·72	2·11–15·52	
	45–64	8·97	3·09–25·99	
	65+	5·49	1·13–26·70	
A/H3N2	0–4	2·16	0·81–5·80	
	5–14	2·00	0·56–7·09	
	15–44	1·78	0·66–4·80	
	45–64	1·12	0·32–3·85	
	65+	4·47	1·73–11·50	
A/unknown	0–4	0·85	0·25–2·93	
	5–14	0·92	0·10–8·50	
	15–44	1·91	0·71–5·15	
	45–64	2·93	1·05–8·15	
	65+	2·72	1·01–7·38	
B	0–4	0·96	0·33–2·85	
	5–14	1·89	0·62–5·80	
	15–44	1·00		0·03
	45–64	5·94	2·30–15·36	
	65+	7·08	2·50–20·01	
Season	2011/2012	1·00		0·9
	2012/2013	1·03	0·68–1·58	

ICU, intensive care units; HDU, high dependency units; ORs, odds ratios; CI, confidence interval.

was close to statistical significance and the likelihood ratio test suggested it significantly improved the fit of the model.

The adjusted odds that a case admitted to hospital with influenza infection will be admitted to ICU/HDU are given in Table 5. Overall the odds of being admitted to ICU/HDU were consistently higher in the older age groups (45 years and above) for each of the subtypes. The highest odds of admission to ICU/HDU overall was in 45–64 year olds admitted with influenza A/H1N1pdm09 (OR 8·97). The odds of admission to ICU/HDU were generally highest following influenza A/H1N1pdm09 infection, followed by influenza A/H3N2 and then influenza B for each age group, except for those >65 years of age, where the highest odds were seen for influenza B (Table 5).

DISCUSSION

The value of USISS sentinel surveillance

The USISS sentinel system has now run successfully for five seasons up until 2014/2015 and has been able to provide measures of the severity of influenza each season on a weekly and end of season basis. Data collected over these seasons has allowed for inter-seasonal comparisons of influenza and has provided a unique opportunity to describe the epidemiology of severe influenza in England in the post-2009 influenza pandemic era.

Estimates of severity

Two measures were used to assess influenza case severity and impact. In this study each provided valuable information by influenza subtype and age group which can have important public health implications and inform healthcare resource allocation.

We clearly show that the case severity, i.e. the proportion of cases admitted to hospital with confirmed influenza infection being admitted to ICU/HDU were consistently higher in the older age groups (45+) for each influenza subtype. Furthermore, the OR of ICU/HDU admission were generally higher for influenza A/H1N1pdm09 cases compared with the other seasonal strains.

However, we also show that the impact, as measured by the cumulative incidence of hospitalisation varied by influenza subtype and age group across the five seasons. By age group, the greatest impact was consistently observed in the paediatric population <5 years of age thus supporting the rationale for the introduction of universal childhood influenza vaccine programme in 2013/2014, which was initially offered to those 2 and 3 years of age to provide direct protection to this group [14]. However, in seasons during which influenza A/H3N2 was the dominant circulating subtype, the impact was also high in the older age groups, confirming that influenza A/H3N2 can cause considerable impact in older age groups. This variation in impact presumably reflects both the underlying immunity profile of the population due to previous exposure to infection and vaccination; the amount of influenza that circulates and the likelihood that a person will develop severe disease following infection (case severity). Thus for influenza A/H1N1pdm09, although the case severity is highest in the elderly, the impact is mainly seen in younger adults and children, due to underlying cross-protective immunity in the elderly [15], which limits the impact in this age group. This age-specific variation in impact of circulating strains can have important local public health consequences with influenza A/H3N2 often resulting in outbreaks in care homes, resulting in

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notable mortality [10, 11, 16, 17], whereas influenza B often results in outbreaks in schools [7]. Rapidly estimating the severity of influenza is very important to determine the morbidity and mortality impact in different segments of the population, to guide anti-viral strategy and vaccination programmes and plan for seasonal epidemics and future pandemics. Such measures of severity have also been suggested as parameters for defining pandemic scenarios [18].

Limitations of the study

There are a number of limitations of this study. Firstly, across all seasons a large proportion of influenza cases with no subtyping information were reported. In 2010/2011 and 2013/2014 due to the predominance of influenza A/H1N1pdm09, it is likely that the majority of these cases were A/H1N1pdm09, and in 2014/2015 to influenza A/H3N2. However, during the other seasons more than one strain circulated.

Inter-seasonal comparisons are limited within this study, particularly for the hospitalisation incidence analysis, since the same trusts did not participate each season and there was a different mix across the recruitment stratum in each season. Under-ascertainment of cases within the system may have occurred, as although guidance on who to test was provided to minimise differential testing and ensure standardisation, trusts may still have applied local testing criteria to hospital admissions. Other studies have shown underdetection to vary by age, site and season and have attempted to correct surveillance data for under-detection [19]. In addition, the trust's target population data used to calculate hospitalisation rates were based on the latest available 2009 ONS data for all years and HES data from 2006/2007 and 2008/2009 and it was assumed that there have not been any major changes with trust populations over this period. However, the availability of these catchments areas allowed for age-specific estimates of hospitalisation rates. While censoring may have occurred during the season, when some severe events resulting from infections to date have yet to occur, this is less likely to be an issue in a retrospective analysis such as this where data was updated throughout the seasons. Real-time monitoring will require statistical adjustment to take into account these reporting delays.

In addition, the higher impact in children may be because children shed more virus and for longer and are therefore more likely to be correctly ascertained as influenza cases, compared with the elderly who shed less and are less likely to fit the case definition as they do not always have fever with influenza [20].

CONCLUSIONS

This study has highlighted the value in using a variety of severity measures to compare between seasons, age groups and influenza subtypes. The study has demonstrated the varying severity of influenza by age and influenza subtype. In particular, we demonstrate the severity of influenza A/H3N2 and the impact of hospitalisations in children. With the start of the introduction of universal paediatric influenza vaccination ultimately for all 2–16 year olds with LAIV (live attenuated influenza vaccine), it will be important to monitor the performance of the vaccine programme in terms of reducing hospitalisations in children and indirectly through reducing transmission in the population, reducing infection across all groups and thus severe disease in adults. This study will provide baseline rates to enable this over the coming seasons.

The USISS system provides a consistent and timely tool for estimating case severity and impact during seasonal influenza epidemics and provides baseline data to evaluate and to guide rapid severity assessment during future influenza pandemics.

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DECLARATION OF INTEREST

None.

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