

## RAPID COMMUNICATIONS

# Predominance of influenza A(H1N1)pdm09 virus genetic subclade 6B.1 and influenza B/Victoria lineage viruses at the start of the 2015/16 influenza season in Europe

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**Influenza A(H1N1)pdm09 viruses predominated in the European influenza 2015/16 season. Most analysed viruses clustered in a new genetic subclade 6B.1, antigenically similar to the northern hemisphere vaccine component A/California/7/2009. The predominant influenza B lineage was Victoria compared with Yamagata in the previous season. It remains to be evaluated at the end of the season if these changes affected the effectiveness of the vaccine for the 2015/16 season.**

For the current northern hemisphere season, several reports have indicated intense influenza activity [1–5]. We analysed virological surveillance data from 20 European countries to study the genetic and antigenic characteristics of the circulating influenza viruses and compare them with the vaccine viruses and previously circulating strains.

## Virological influenza surveillance in Europe, influenza season 2015/16

Virological influenza surveillance data in the World Health Organization (WHO) European Region are collected on a weekly basis and reported to The European Surveillance System (TESSy), a database hosted by the European Centre for Disease Prevention and Control (ECDC), as previously described [6]. From week 40/2015 to week 4/2016, 49 Member States of the Region reported influenza virus detections to TESSy, including 20 Member States (Belgium, Croatia, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Latvia, Netherlands, Norway, Portugal, Romania, Russia, Slovakia, Slovenia, Spain, Sweden, Switzerland, and

the United Kingdom (UK)) that also reported antigenic or genetic characterisation data.

The antigenic and genetic reporting categories for TESSy are predefined by the WHO Collaborating Centre for Reference and Research on Influenza, London, for each influenza season. For antigenic characterisation, to denote a virus isolate as being like a vaccine or reference virus its haemagglutination inhibition (HI) titre with post-infection ferret antiserum raised against the reference virus should differ by no more than fourfold. For genetic characterisation, the allocation to reporting category is based on the phylogenetic and amino acid sequence analyses of haemagglutinin (HA) gene.

The summary analysis of the data are presented weekly in the Joint ECDC–WHO Regional Office for Europe weekly ‘Flu News Europe’ (<http://flunewseurope.org/>). Data on detections, antigenic and genetic characterisations were extracted on 8 February 2016 for analysis.

Between week 40/2015 and week 4/2016, influenza viruses were detected in 1,879 (19%) of 9,882 sentinel specimens tested in the 20 countries also reporting on virus characterisation. Of these 1,879 specimens, 1,512 (80%) were positive for type A influenza virus and 367 (20%) for type B. Of 1,441 subtyped influenza A viruses, 1,268 (88%) were A(H1N1)pdm09. Of 129 type B viruses with known lineage, 115 (89%) were of the B/Victoria/2/1987 lineage.

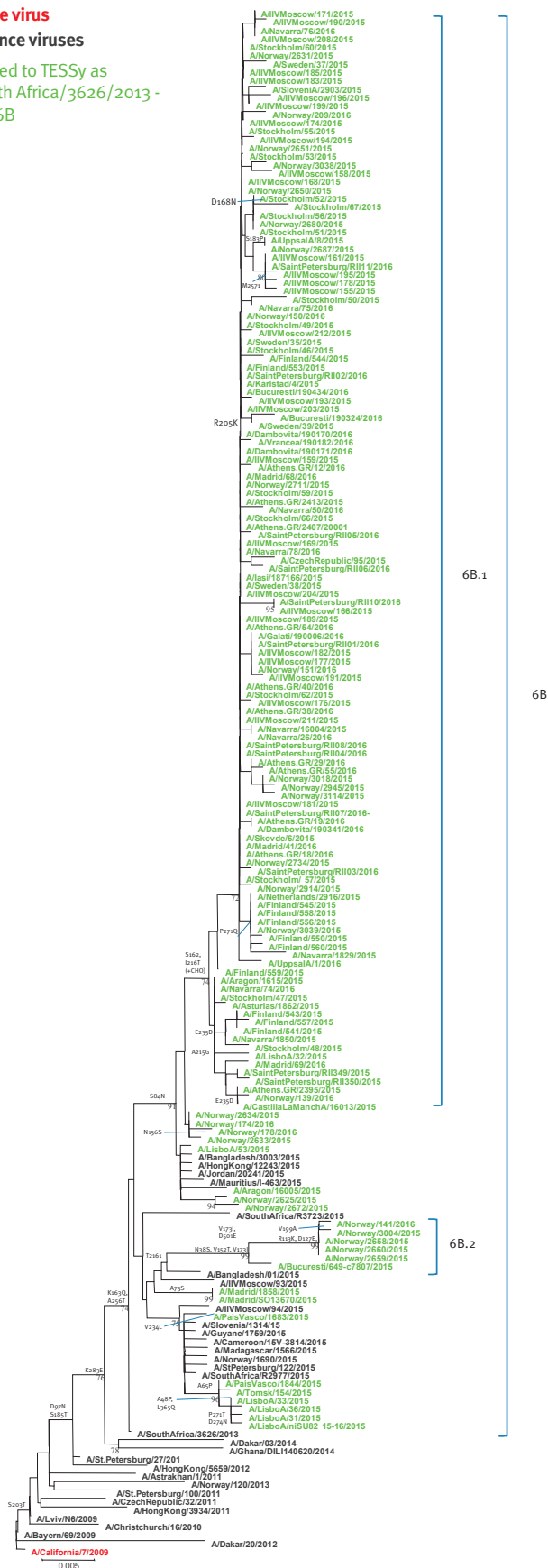
**FIGURE 1**

Phylogenetic analysis of A(H1N1)pdm09 haemagglutinin (HA) nt sequences reported from European countries, between week 40/2015 and 4/2016

**Vaccine virus**

**Reference viruses**

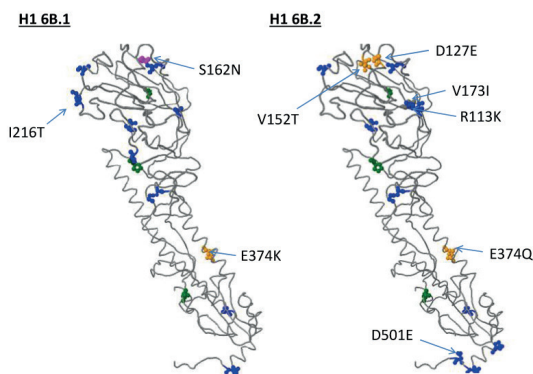
Reported to TESSy as  
A/South Africa/3626/2013 -  
clade 6B



Some sequences obtained in this study were not used to construct the phylogenetic tree because they were identical and redundant. The sequences used for the phylogenetic analysis were moreover only those of suitable length, and encode HA1 amino acids 3–327. These included sequences reported by the Czech Republic, Finland, Greece, Netherlands, Norway, Portugal, Romania, Russia, Slovenia, Spain and Sweden as well as sequences from reference A(H1N1)pdm09 viruses. The tree was constructed with the neighbour-joining method, using Kimura-2 parameter-corrected distances and bootstrapped with 1,000 replicates, Molecular Evolutionary Genetics Analysis (MEGA) software version 5.0.

## FIGURE 2

Protein structure model (FluSurver-JSmol) of the haemagglutinin protein monomer of A(H1N1)pdm09 subclade 6B.1, represented by A/Norway/2650/2015 (left), and subclade 6B.2, represented by A/Norway/2658/2015 (right)



Amino acid differences compared with A/California/07/2009 are indicated in colour. Well-known differences are marked in blue. Common variant marker positions are indicated in green. Amino acid involved in virulence or antigenic drift is marked in orange. Amino acid not previously associated with a specific feature is marked in grey. Amino acid that creates a new potential N-glycosylation site is marked in magenta.

## Virus characterisation

Between weeks 40/2015 and 4/2016, 447 (24%) of 1,879 influenza viruses were attributed to a genetic group by 16 countries (Belgium, Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Netherlands, Norway, Portugal, Romania, Russia, Slovenia, Spain, Sweden and UK), and 429 (23%) were attributed to an antigenic category by also 16 reporting countries (Croatia, Czech Republic, Denmark, Finland, Germany, Greece, Latvia, Netherlands, Portugal, Romania, Russia, Slovakia, Slovenia, Spain, Switzerland and UK) (Table 1).

The majority (68%) of all genetic characterisations were reported from Norway (n=84), Spain (n=66), Germany (n=54), Russia (n=54) and Sweden (n=46). The majority (70%) of antigenic reports were from Russia (n=124), Portugal (n=99) and Germany (n=78). For 150 viruses, reported in strain-based manner, both genetic and antigenic data were available.

All 313 A(H1N1)pdm09 viruses characterised genetically fell in clade 6, subgroup 6B, represented by A/South Africa/3626/2013. Viruses falling in this genetic subgroup, were all attributed to an antigenic category A/California/7/2009 that corresponds to the component included in the 2015/16 northern hemisphere vaccines.

Of the 77 A(H3N2) viruses attributed to a genetic group, 50 (65%) fell into genetic subgroup 3C.2a (represented by A/Hong Kong/4801/2014) that has been shown to be antigenically similar to A/Hong Kong/4801/2014 and also to the current A(H3N2) vaccine virus A/Switzerland/9715293/2013 (Table 1). Twenty-six A(H3N2) viruses fell into the vaccine virus category of 3C.3a subgroup. Viruses in subgroup 3C.3b (represented by A/Stockholm/28/2014) constituted a substantial part (98/401) of the A(H3N2) viruses in Europe in the 2014/15 season [7], but none were yet reported by week 4/2016 (Table 1). Of 20 A(H3N2) viruses attributed to an antigenic category, 14 were A/Switzerland/9715293/2013-like and thus similar to the northern hemisphere 2015/16 vaccine component and six were A/Hong Kong/4801/2014-like, similar to the southern hemisphere 2016 vaccine component and recommendation for northern hemisphere 2016/17 season.

All of the 44 B/Victoria lineage viruses characterised genetically to date fell in the clade 1A, represented by B/Brisbane/60/2008 which is included in quadrivalent vaccines for northern hemisphere 2015/16. The 13 B/Yamagata lineage viruses all genetically resembled B/Phuket/3073/2013 recommended for inclusion in trivalent vaccines for northern hemisphere 2015/16. Thirty influenza B viruses were antigenically characterised, 29 as B/Brisbane/60/2008-like and one as B/Phuket/3073/2013-like.

Analysis of A(H1N1)pdm09 HA gene sequences from 12 countries (Czech Republic, Finland, Greece, Ireland, Netherlands, Norway, Portugal, Romania, Russia, Slovenia, Spain and Sweden) reported to TESSy, with provision of accession numbers in publicly accessible databases, confirmed that all these analysed viruses possessed the signature amino acid variations that define subgroup 6B viruses: D97N, K163Q, S185T, K283E and A256T [7-9]. All 215 analysed sequences, apart from two viruses isolated in Russia, also carried P83S and I321V substitutions in HA1.

The majority of sequences (173 of 215 TESSy-reported viruses) also possessed the amino acid signature of subclade 6B.1 and formed a separate branch in the phylogenetic analysis (Figure 1, Figure 2). The 6B.1 subclade is characterised by the amino acid substitutions S84N (present in a wider subgroup), S162N and I216T [8]. Six viruses carried amino acid substitutions V152T, V173I, D501E (the latter in HA2) characterising 6B.2 subclade. In addition the five most recently sampled of these six 6B.2 viruses all possessed the R113K, D127E and E374Q substitutions (Figure 1).

The highest number of accumulated variations in the known antigenic sites were observed in the antigenic site Ca. All subgroup 6B viruses possessed the K163Q substitution, while the vast majority (173/215; 80%) also possessed the S162N substitution in HA1, resulting in a gain of a potential glycosylation site. Additional

**TABLE 1**Viruses attributed to genetic and antigenic groups<sup>a</sup>, weeks 40/2015–04/2016

| Genetic group  | Number of viruses | Antigenic group  | Number of viruses |
|--|-------------------|--|-------------------|
| A(H1N1)pdm09 A/South Africa/3626/2013 (subgroup 6B) <sup>b</sup> | 313               | A(H1N1)pdm09 A/California/7/2009-like                                    | 379               |
| A(H3N2) A/Hong Kong/4801/2014 (subgroup 3C.2a) <sup>b</sup>      | 50                | A(H3N2) A/Hong Kong/4801/2014-like                                       | 6                 |
| A(H3N2) A/Samara/73/2013 (subgroup 3C.3) <sup>c</sup>            | 1                 | No separate antigenic category; expected to resemble A/Stockholm/28/2014 | –                 |
| A(H3N2) A/Stockholm/28/2014 (subgroup 3C.3b) <sup>c</sup>        | 0                 | A(H3N2) A/ Stockholm/28/2014-like  | 0                 |
| A(H3N2) A/Switzerland/9715293/2013 (subgroup 3C.3a) <sup>b</sup> | 26                | A(H3N2) A/Switzerland/9715293/2013                                       | 14                |
| B/Phuket/3073/2013 (Yamagata lineage clade 3) <sup>b</sup>       | 13                | B/Phuket/3073/2013 (Yamagata lineage) -like                              | 1                 |
| B/Brisbane/60/2008 (Victoria lineage clade 1A) <sup>d</sup>      | 44                | B/Brisbane/60/2008 (Victoria lineage) -like                              | 29                |

The viruses which were genetically characterised are not necessarily the same than the viruses that were antigenically characterised.

<sup>a</sup> Genetic and antigenic groups used for reporting into The European Surveillance System are defined by World Health Organization Collaborating Centre for Reference and Research on Influenza for each influenza season. For antigenic characterisation, to denote a virus isolate as being like a vaccine or reference virus its haemagglutination inhibition (HI) titre with post-infection ferret antiserum raised against the reference virus should differ by no more than fourfold. For genetic characterisation, the allocation to reporting category is based on the phylogenetic and amino acid sequence analyses of haemagglutinin (HA) gene.

<sup>b</sup> These genetic groups contain viruses with antigenic properties similar to the viruses included in the trivalent influenza vaccine for 2015/16.

<sup>c</sup> These genetic groups contain viruses with antigenic properties dissimilar to the viruses included in the trivalent influenza vaccine for 2015/16.

<sup>d</sup> Viruses in this genetic group have antigenic properties similar to those of the vaccine component (B/Brisbane/60/2008) recommended for use in quadrivalent influenza vaccines for 2015/16.

variations observed were S162K, D168N, K170E, R205K, A215G, E235D and a partial A139D. Cb antigenic site variation A73S was observed in four viruses from Spain, one of which also possessed substitution N156K in Sa antigenic site. Another Norwegian virus had a N156S substitution in Sa antigenic site. Notably, all 6B.2 viruses and also two of the 6B viruses not belonging to any of the newly identified subgroups possessed substitutions affecting the loop that consists of amino acid positions 151 to 159 located adjacent to the receptor binding site.

When comparing the A(H1N1)pdm09 strains with the corresponding strain in the current northern hemisphere influenza vaccine, A/California/7/2009, the HA1 sequences (nt 1–981, amino acids 1–327) exhibited nt similarity of 96.8 to 98.0% and deduced amino acid similarity of 95.4 to 96.3%. Viruses within subclade 6B.1 exhibited higher HA nt heterogeneity, with similarities ranging between 98.8 and 100%, while within subclade 6B.2 strains exhibited higher nt similarity, ranging between 99.3 and 100%, as the group consists of fewer sequences and most of them from one region only. The viruses analysed phylogenetically are listed in Table 2.

## Discussion

Continuous surveillance of influenza viruses is essential for detecting emerging new variant strains and providing viruses for vaccine production [10]. In Europe, within the detected A subtypes, influenza A(H1N1)pdm09 predominated during 2010/11, 2012/13 and 2013/14 seasons and concerned 97% [11], 62% [12] and 53% [13] of subtyped influenza viruses respectively, with variation in country-specific proportions. The

A(H1N1)pdm09 vaccine component A/California/7/2009 has not been changed since the 2009 pandemic and the circulating A(H1N1)pdm09 viruses have remained antigenically similar to the virus included in the vaccines throughout the influenza 2009/10 to 2015/16 seasons. However, since 2013, several reports have indicated the emergence of an expanding subgroup of A(H1N1)pdm09 viruses, designated 6B [1,8,9]. This subgroup appeared in 2012/13 and became predominant in 2013/14 [14].

In this study, we observe the further emergence of a subclade within the 6B subgroup, designated 6B.1 [15], which accounted for the majority of the A(H1N1)pdm09 viruses detected across the WHO European Region during the first weeks of the 2015/16 influenza season. In addition, the surveillance data show a change in the predominant B virus lineage from B/Yamagata which predominated in the preceding three seasons in Europe to B/Victoria.

Our data are preliminary for this season and are based on influenza surveillance without detailed reporting of clinical symptoms or vaccination status. Our genetic analysis was only based on the HA gene and does not extend to changes e.g. in genes encoding internal proteins of influenza viruses. The data reported to TESSy do not include antigenic titres and therefore no direct analysis of antigenic properties was possible. However, the antigenic reports rely on national influenza centres' antigenic analysis that the viruses reported as like to vaccine virus were not more than fourfold different in HI titres from the vaccine or reference viruses.

**TABLE 2A**

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country     | Strain name             | Collection date | Originating laboratory   | Submitting laboratory   |
|-----------|-------------|-------------------------|-----------------|--|---|
| EPI685415 | Netherlands | A/Netherlands/2916/2015 | 6/11/2015       | National Institute for Public Health and the Environment (RIVM)                        | National Institute for Public Health and the Environment (RIVM) |
| EPI674853 | Sweden      | A/Stockholm/46/2015     | 9/10/2015       | –  | Swedish Institute for Infectious Disease Control                |
| EPI674745 | Sweden      | A/Stockholm/47/2015     | 22/10/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674753 | Sweden      | A/Stockholm/48/2015     | 24/10/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674841 | Sweden      | A/Karlstad/4/2015       | 25/10/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674777 | Sweden      | A/Stockholm/49/2015     | 7/11/2015       | –  | Swedish Institute for Infectious Disease Control                |
| EPI686820 | Sweden      | A/Skovde/6/2015         | 18/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686772 | Sweden      | A/Stockholm/ 57/2015    | 18/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674785 | Sweden      | A/Stockholm/50/2015     | 11/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674793 | Sweden      | A/Stockholm/51/2015     | 11/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674801 | Sweden      | A/Stockholm/52/2015     | 11/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674847 | Sweden      | A/Stockholm/53/2015     | 12/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674809 | Sweden      | A/Stockholm/55/2015     | 10/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686764 | Sweden      | A/Stockholm/56/2015     | 18/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686799 | Sweden      | A/Stockholm/59/2015     | 19/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686828 | Sweden      | A/Stockholm/60/2015     | 25/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686844 | Sweden      | A/Stockholm/62/2015     | 26/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI687173 | Sweden      | A/Stockholm/66/2015     | 23/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI687199 | Sweden      | A/Stockholm/67/2015     | 21/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI674825 | Sweden      | A/Sweden/35/2015        | 12/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686852 | Sweden      | A/Uppsala/8/2015        | 27/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686892 | Sweden      | A/Sweden/37/2015        | 26/11/2015      | –  | Swedish Institute for Infectious Disease Control                |
| EPI686900 | Sweden      | A/Sweden/38/2015        | 2/12/2015       | –  | Swedish Institute for Infectious Disease Control                |
| EPI686908 | Sweden      | A/Sweden/39/2015        | 2/12/2015       | –  | Swedish Institute for Infectious Disease Control                |
| EPI694343 | Sweden      | A/Uppsala/1/2016        | 11/1/2016       | –  | Swedish Institute for Infectious Disease Control                |
| EPI671518 | Norway      | A/Norway/2625/2015      | 21/10/2015      | Sorlandet Sykehus HF, Dept. of Medical Microbiology                                    | Norwegian Institute of Public Health                            |
| EPI675750 | Norway      | A/Norway/2659/2015      | 3/11/2015       | Drammen Hospital / Vestreviken HF, Department for Medical Microbiology section Drammen | Norwegian Institute of Public Health                            |
| EPI675751 | Norway      | A/Norway/2660/2015      | 3/11/2015       | Drammen Hospital / Vestreviken HF, Department for Medical Microbiology section Drammen | Norwegian Institute of Public Health                            |

ID: identity; SAR: Special Administrative Region; WHO: World Health Organization.

**TABLE 2B**

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country | Strain name           | Collection date | Originating laboratory   | Submitting laboratory                            |
|-----------|---------|-----------------------|-----------------|--|--|
| EPI675754 | Norway  | A/Norway/2672/2015    | 1/11/2015       | Oslo University Hospital, Ullevål Hospital, Dept. of Microbiology                      | Norwegian Institute of Public Health             |
| EPI675756 | Norway  | A/Norway/2680/2015    | 12/11/2015      | Ostfold Hospital - Fredrikstad, Dept. of Microbiology                                  | Norwegian Institute of Public Health             |
| EPI675760 | Norway  | A/Norway/2687/2015    | 13/11/2015      | –  | Norwegian Institute of Public Health             |
| EPI695284 | Norway  | A/Norway/2711/2015    | 18/11/2015      | –  | Norwegian Institute of Public Health             |
| EPI695299 | Norway  | A/Norway/2914/2015    | 14/12/2015      | Sorlandet Sykehus HF, Dept. of Medical Microbiology                                    | Norwegian Institute of Public Health             |
| EPI695310 | Norway  | A/Norway/3004/2015    | 15/12/2015      | Innlandet Hospital Trust, Division Lillehammer, Department for Microbiology            | Norwegian Institute of Public Health             |
| EPI695311 | Norway  | A/Norway/3018/2015    | 26/12/2015      | –  | Norwegian Institute of Public Health             |
| EPI695313 | Norway  | A/Norway/3038/2015    | 26/12/2015      | Aalesund sjukehus  | Norwegian Institute of Public Health             |
| EPI695343 | Norway  | A/Norway/174/2016     | 7/1/2016        | St. Olavs Hospital HF, Dept. of Medical Microbiology                                   | Norwegian Institute of Public Health             |
| EPI695344 | Norway  | A/Norway/178/2016     | 6/1/2016        | Health Forde, Department of Microbiology   | Norwegian Institute of Public Health             |
| EPI695349 | Norway  | A/Norway/209/2016     | 8/1/2016        | Stavanger Universitetssykehus, Avd. for Medisinsk Mikrobiologi                         | Norwegian Institute of Public Health             |
| EPI677648 | Finland | A/Finland/541/2015    | 9/11/2015       | Helsinki University Central Hospital, Laboratory Services (HUSLAB)                     | National Institute for Health and Welfare        |
| EPI677651 | Finland | A/Finland/543/2015    | 19/11/2015      | Helsinki University Central Hospital, Laboratory Services (HUSLAB)                     | National Institute for Health and Welfare        |
| EPI678232 | Finland | A/Finland/544/2015    | 13/11/2015      | Helsinki University Central Hospital, Laboratory Services (HUSLAB)                     | National Institute for Health and Welfare        |
| EPI696158 | Russia  | A/Tomsk/154/2015      | 19/11/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow                       | WHO National Influenza Centre Russian Federation |
| EPI696470 | Russia  | A/IIV-Moscow/211/2015 | 23/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow                       | WHO National Influenza Centre Russian Federation |
| EPI696478 | Russia  | A/IIV-Moscow/212/2015 | 23/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow                       | WHO National Influenza Centre Russian Federation |
| EPI690291 | Spain   | A/Aragon/16005/2015   | 21/12/2015      | Servicio de Microbiología Hospital Miguel Servet                                       | Instituto de Salud Carlos III                    |
| EPI671520 | Norway  | A/Norway/2631/2015    | 26/10/2015      | Sorlandet Sykehus HF, Dept. of Medical Microbiology                                    | Norwegian Institute of Public Health             |
| EPI671521 | Norway  | A/Norway/2633/2015    | 27/10/2015      | Haukeland University Hospital, Dept. of Microbiology                                   | Norwegian Institute of Public Health             |
| EPI671522 | Norway  | A/Norway/2634/2015    | 27/10/2015      | Haukeland University Hospital, Dept. of Microbiology                                   | Norwegian Institute of Public Health             |
| EPI671525 | Norway  | A/Norway/2650/2015    | 3/11/2015       | Ostfold Hospital - Fredrikstad, Dept. of Microbiology                                  | Norwegian Institute of Public Health             |
| EPI675748 | Norway  | A/Norway/2651/2015    | 2/11/2015       | Mikrobiologisk laboratorium, Sykehuset i Vestfold                                      | Norwegian Institute of Public Health             |
| EPI675749 | Norway  | A/Norway/2658/2015    | 4/11/2015       | Drammen Hospital / Vestreviken HF, Department for Medical Microbiology section Drammen | Norwegian Institute of Public Health             |
| EPI695334 | Norway  | A/Norway/139/2016     | 4/1/2016        | Haukeland University Hospital, Dept. of Microbiology                                   | Norwegian Institute of Public Health             |
| EPI695336 | Norway  | A/Norway/141/2016     | 4/1/2016        | Unilabs Telelab, Laboratory for Medical Microbiology                                   | Norwegian Institute of Public Health             |

ID: identity; SAR: Special Administrative Region; WHO: World Health Organization.

TABLE 2C

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country  | Strain name                | Collection date | Originating laboratory   | Submitting laboratory                            |
|-----------|----------|----------------------------|-----------------|--|--|
| EPI695339 | Norway   | A/Norway/150/2016          | 12/1/2016       | Stavanger Universitetssykehus, Avd. for Medisinsk Mikrobiologi                         | Norwegian Institute of Public Health             |
| EPI695340 | Norway   | A/Norway/151/2016          | 12/1/2016       | Stavanger Universitetssykehus, Avd. for Medisinsk Mikrobiologi                         | Norwegian Institute of Public Health             |
| EPI695287 | Norway   | A/Norway/2734/2015         | 13/11/2015      | Innlandet Hospital Trust, Division Lillehammer, Department for Microbiology            | Norwegian Institute of Public Health             |
| EPI695304 | Norway   | A/Norway/2945/2015         | 16/12/2015      | –  | Norwegian Institute of Public Health             |
| EPI695314 | Norway   | A/Norway/3039/2015         | 28/12/2015      | Aalesund sjukehus  | Norwegian Institute of Public Health             |
| EPI695326 | Norway   | A/Norway/3114/2015         | 28/12/2015      | Drammen Hospital / Vestreviken HF, Department for Medical Microbiology section Drammen | Norwegian Institute of Public Health             |
| EPI678234 | Finland  | A/Finland/545/2015         | 19/11/2015      | Helsinki University Central Hospital, Laboratory Services (HUSLAB)                     | National Institute for Health and Welfare        |
| EPI678238 | Finland  | A/Finland/550/2015         | 4/12/2015       | National Institute for Health and Welfare  | National Institute for Health and Welfare        |
| EPI678240 | Finland  | A/Finland/553/2015         | 6/12/2015       | NordLab Oulu   | National Institute for Health and Welfare        |
| EPI693689 | Finland  | A/Finland/556/2015         | 16/12/2015      | National Institute for Health and Welfare  | National Institute for Health and Welfare        |
| EPI687734 | Finland  | A/Finland/557/2015         | 15/12/2015      | National Institute for Health and Welfare  | National Institute for Health and Welfare        |
| EPI693690 | Finland  | A/Finland/558/2015         | 19/12/2015      | National Institute for Health and Welfare  | National Institute for Health and Welfare        |
| EPI693691 | Finland  | A/Finland/559/2015         | 14/12/2015      | National Institute for Health and Welfare  | National Institute for Health and Welfare        |
| EPI693692 | Finland  | A/Finland/560/2015         | 18/12/2015      | National Institute for Health and Welfare  | National Institute for Health and Welfare        |
| EPI674284 | Portugal | A/Lisboa/31/2015           | 19/11/2015      | Instituto Nacional de Saude  | INSA National Institute of Health Portugal       |
| EPI674285 | Portugal | A/Lisboa/32/2015           | 18/11/2015      | Instituto Nacional de Saude  | INSA National Institute of Health Portugal       |
| EPI678690 | Portugal | A/Lisboa/33/2015           | 25/11/2015      | Instituto Nacional de Saude  | INSA National Institute of Health Portugal       |
| EPI678691 | Portugal | A/Lisboa/36/2015           | 2/12/2015       | Instituto Nacional de Saude  | INSA National Institute of Health Portugal       |
| EPI692997 | Portugal | A/Lisboa/53/2015           | 22/12/2015      | Instituto Nacional de Saude  | INSA National Institute of Health Portugal       |
| EPI678693 | Portugal | A/Lisboa/niSU82_15–16/2015 | 2/12/2015       | Instituto Nacional de Saude  | INSA National Institute of Health Portugal       |
| EPI699780 | Greece   | A/Athens.GR/18/2016        | 4/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI699778 | Greece   | A/Athens.GR/19/2016        | 4/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI699774 | Greece   | A/Athens.GR/29/2016        | 7/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI699772 | Greece   | A/Athens.GR/38/2016        | 7/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI699770 | Greece   | A/Athens.GR/40/2016        | 7/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI699766 | Greece   | A/Athens.GR/54/2016        | 8/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI699764 | Greece   | A/Athens.GR/55/2016        | 8/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute                       |
| EPI670326 | Romania  | A/Iasi/187166/2015         | 13/10/2015      | Cantacuzino Institute  | Cantacuzino Institute                            |
| EPI690111 | Romania  | A/Bucuresti/649-c7807/2015 | 22/12/2015      | Cantacuzino Institute  | Cantacuzino Institute                            |
| EPI699023 | Romania  | A/Bucuresti/190460/2016    | 19/1/2016       | Cantacuzino Institute  | Cantacuzino Institute                            |
| EPI696174 | Russia   | A/IIV-Moscow/158/2015      | 12/2015         | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow                       | WHO National Influenza Centre Russian Federation |

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**TABLE 2D**

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country | Strain name                    | Collection date | Originating laboratory  | Submitting laboratory                            |
|-----------|---------|--------------------------------|-----------------|---|--|
| EPI696182 | Russia  | A/IIV-Moscow/159/2015          | 12/2015         | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696198 | Russia  | A/IIV-Moscow/161/2015          | 14/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696246 | Russia  | A/IIV-Moscow/169/2015          | 17/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696270 | Russia  | A/IIV-Moscow/174/2015          | 16/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696278 | Russia  | A/IIV-Moscow/176/2015          | 15/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696286 | Russia  | A/IIV-Moscow/177/2015          | 16/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696326 | Russia  | A/IIV-Moscow/183/2015          | 21/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696382 | Russia  | A/IIV-Moscow/191/2015          | 20/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696414 | Russia  | A/IIV-Moscow/195/2015          | 22/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI687093 | Russia  | A/Saint-Petersburg/RII349/2015 | 25/11/2015      |   | WHO National Influenza Centre Russian Federation |
| EPI696574 | Russia  | A/Saint-Petersburg/RII350/2015 | 30/11/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696486 | Russia  | A/Saint-Petersburg/RII01/2016  | 19/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696494 | Russia  | A/Saint-Petersburg/RII02/2016  | 21/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696502 | Russia  | A/Saint-Petersburg/RII03/2016  | 21/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696510 | Russia  | A/Saint-Petersburg/RII04/2016  | 21/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696166 | Russia  | A/IIV-Moscow/155/2015          | 7/12/2015       | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696518 | Russia  | A/Saint-Petersburg/RII05/2016  | 14/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696526 | Russia  | A/Saint-Petersburg/RII06/2016  | 14/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696534 | Russia  | A/Saint-Petersburg/RII07/2016  | 21/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696542 | Russia  | A/Saint-Petersburg/RII08/2016  | 22/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696558 | Russia  | A/Saint-Petersburg/RII10/2016  | 23/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696566 | Russia  | A/Saint-Petersburg/RII11/2016  | 24/12/2015      | WHO National Influenza Centre Russian Federation                | WHO National Influenza Centre Russian Federation |
| EPI696222 | Russia  | A/IIV-Moscow/166/2015          | 16/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |
| EPI696238 | Russia  | A/IIV-Moscow/168/2015          | 15/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF,Moscow | WHO National Influenza Centre Russian Federation |

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**TABLE 2E**

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country | Strain name           | Collection date | Originating laboratory   | Submitting laboratory                            |
|-----------|---------|-----------------------|-----------------|--|--|
| EPI696254 | Russia  | A/IIV-Moscow/171/2015 | 17/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696294 | Russia  | A/IIV-Moscow/178/2015 | 17/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696318 | Russia  | A/IIV-Moscow/182/2015 | 18/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696334 | Russia  | A/IIV-Moscow/185/2015 | 18/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696366 | Russia  | A/IIV-Moscow/189/2015 | 19/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696374 | Russia  | A/IIV-Moscow/190/2015 | 20/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696398 | Russia  | A/IIV-Moscow/193/2015 | 21/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696406 | Russia  | A/IIV-Moscow/194/2015 | 20/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696422 | Russia  | A/IIV-Moscow/196/2015 | 22/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696430 | Russia  | A/IIV-Moscow/199/2015 | 22/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696446 | Russia  | A/IIV-Moscow/203/2015 | 22/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696454 | Russia  | A/IIV-Moscow/204/2015 | 22/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI696462 | Russia  | A/IIV-Moscow/208/2015 | 23/12/2015      | D.I. Ivanovsky Research Institute of virology MoPH of RF, Moscow | WHO National Influenza Centre Russian Federation |
| EPI686526 | Spain   | A/Madrid/1858/2015    | 22/12/2015      | Servicio de Microbiología Hospital Ramón y Cajal                 | Instituto de Salud Carlos III                    |
| EPI690296 | Spain   | A/Madrid/1859/2015    | 23/12/2015      | Servicio de Microbiología Hospital Ramón y Cajal                 | Instituto de Salud Carlos III                    |
| EPI672780 | Spain   | A/Madrid/SO13656/2015 | 21/10/2015      | Instituto de Salud Carlos III                                    | Instituto de Salud Carlos III                    |
| EPI674599 | Spain   | A/Madrid/SO13670/2015 | 20/10/2015      | Instituto de Salud Carlos III                                    | Instituto de Salud Carlos III                    |
| EPI680490 | Spain   | A/Madrid/SO13763/2015 | 8/12/2015       | Instituto de Salud Carlos III                                    | Instituto de Salud Carlos III                    |
| EPI699957 | Spain   | A/Madrid/41/2016      | 13/1/2016       | Instituto de Salud Carlos III                                    | Instituto de Salud Carlos III                    |
| EPI699959 | Spain   | A/Madrid/68/2016      | 12/1/2016       | Servicio de Microbiología Hospital Ramón y Cajal                 | Instituto de Salud Carlos III                    |
| EPI699960 | Spain   | A/Madrid/69/2016      | 12/1/2016       | Servicio de Microbiología Hospital Ramón y Cajal                 | Instituto de Salud Carlos III                    |
| EPI690298 | Spain   | A/Navarra/16004/2015  | 27/12/2015      | Servicio de Microbiología Complejo Hospitalario de Navarra       | Instituto de Salud Carlos III                    |
| EPI686527 | Spain   | A/Navarra/1829/2015   | 15/12/2015      | Servicio de Microbiología Complejo Hospitalario de Navarra       | Instituto de Salud Carlos III                    |
| EPI686528 | Spain   | A/Navarra/1850/2015   | 17/12/2015      | Servicio de Microbiología Complejo Hospitalario de Navarra       | Instituto de Salud Carlos III                    |

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TABLE 2F

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country        | Strain name                   | Collection date | Originating laboratory   | Submitting laboratory               |
|-----------|----------------|-------------------------------|-----------------|--|-------------------------------------|
| EPI690302 | Spain          | A/Navarra/26/2016             | 3/1/2016        | Servicio de Microbiología Complejo Hospitalario de Navarra           | Instituto de Salud Carlos III       |
| EPI699967 | Spain          | A/Navarra/50/2016             | 11/1/2016       | Servicio de Microbiología Complejo Hospitalario de Navarra           | Instituto de Salud Carlos III       |
| EPI699973 | Spain          | A/Navarra/74/2016             | 14/1/2016       | Servicio de Microbiología Complejo Hospitalario de Navarra           | Instituto de Salud Carlos III       |
| EPI699974 | Spain          | A/Navarra/75/2016             | 12/1/2016       | Servicio de Microbiología Complejo Hospitalario de Navarra           | Instituto de Salud Carlos III       |
| EPI699975 | Spain          | A/Navarra/76/2016             | 14/1/2016       | Servicio de Microbiología Complejo Hospitalario de Navarra           | Instituto de Salud Carlos III       |
| EPI699977 | Spain          | A/Navarra/78/2016             | 14/1/2016       | Servicio de Microbiología Complejo Hospitalario de Navarra           | Instituto de Salud Carlos III       |
| EPI672781 | Spain          | A/PaisVasco/1683/2015         | 21/10/2015      | Servicio de Microbiología Hospital Donostia                          | Instituto de Salud Carlos III       |
| EPI686529 | Spain          | A/PaisVasco/1844/2015         | 15/12/2015      | Servicio de Microbiología Hospital Donostia                          | Instituto de Salud Carlos III       |
| EPI687827 | Slovenia       | A/Slovenia/2903/2015          | 26/10/2015      | Laboratory for Virology, National Institute of Public Health         | Crick Worldwide Influenza Centre    |
| KU558983  | Czech Republic | A/Czech Republic/95/2015      | 1/12/2015       | National Institute of Public Health                                  | National Institute of Public Health |
| EPI699832 | Greece         | A/Athens.GR/2395/2015         | 23/12/2015      | Hellenic Pasteur Institute   | Hellenic Pasteur Institute          |
| EPI699830 | Greece         | A/Athens.GR/2407/2015         | 28/12/2015      | Hellenic Pasteur Institute   | Hellenic Pasteur Institute          |
| EPI699827 | Greece         | A/Athens.GR/2413/2015         | 29/12/2015      | Hellenic Pasteur Institute   | Hellenic Pasteur Institute          |
| EPI699824 | Greece         | A/Athens.GR/12/2016           | 5/1/2016        | Hellenic Pasteur Institute   | Hellenic Pasteur Institute          |
| EPI698911 | Romania        | A/Dambovita/190170/2016       | 18/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI698910 | Romania        | A/Galati/190006/2016          | 8/1/2016        | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI699021 | Romania        | A/Vrancea/190182/2016         | 18/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI699023 | Romania        | A/Bucuresti/190324/2016       | 19/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI699059 | Romania        | A/Bucuresti/190434/2016       | 23/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI698912 | Romania        | A/Dambovita/190171/2016       | 18/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI699024 | Romania        | A/Dambovita/190341/2016       | 21/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI699000 | Romania        | A/Vrancea/190181/2016         | 11/1/2016       | Cantacuzino Institute  | Cantacuzino Institute               |
| EPI672779 | Spain          | A/Aragon/1615/2015            | 29/9/2015       | Servicio de Microbiología Hospital Miguel Servet                     | Instituto de Salud Carlos III       |
| EPI690293 | Spain          | A/Asturias/1862/2015          | 17/12/2015      | Servicio de Microbiología Hospital Central Universitario de Asturias | Instituto de Salud Carlos III       |
| EPI699955 | Spain          | A/Baleares/16036/2015         | 30/12/2015      | Servicio de Microbiología Hospital Universitario Son Espases         | Instituto de Salud Carlos III       |
| EPI699956 | Spain          | A/Baleares/35/2016            | 5/1/2016        | Servicio de Microbiología Hospital Universitario Son Espases         | Instituto de Salud Carlos III       |
| EPI690295 | Spain          | A/CastillaLaMancha/16013/2015 | 30/12/2015      | Instituto de Salud Carlos III  | Instituto de Salud Carlos III       |
| EPI624748 | Russia         | A/St-Petersburg/122/2015      | 26/2/2015       | WHO National Influenza Centre Russian Federation                     | Crick Worldwide Influenza Centre    |
| EPI624673 | Cameroon       | A/Cameroon/15V-3814/2015      | 7/5/2015        | Centre Pasteur du Cameroun   | Crick Worldwide Influenza Centre    |
| EPI624730 | Norway         | A/Norway/1690/2015            | 17/3/2015       | WHO National Influenza Centre  | Crick Worldwide Influenza Centre    |

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TABLE 2G

Details of the A(H1N1)pdm09 sequences retrieved from the Global Initiative on Sharing All Influenza Data (GISAID)'s EpiFlu Database or GenBank, for haemagglutinin-gene-based phylogenetic analysis in this study

| ID        | Country        | Strain name               | Collection date | Originating laboratory  | Submitting laboratory  |
|-----------|----------------|---------------------------|-----------------|---|--|
| EPI630638 | Mauritius      | A/Mauritius/I-463/2015    | 18/5/2015       | Central Health Laboratory   | Crick Worldwide Influenza Centre                                 |
| EPI621835 | Madagascar     | A/Madagascar/1566/2015    | 15/4/2015       | Institut Pasteur de Madagascar  | Crick Worldwide Influenza Centre                                 |
| EPI630634 | Hong Kong SAR  | A/Hong Kong/12243/2015    | 14/6/2015       | Government Virus Unit   | Crick Worldwide Influenza Centre                                 |
| EPI630684 | South Africa   | A/South Africa/R3723/2015 | 29/6/2015       | Sandringham, National Institute for Communicable D  | Crick Worldwide Influenza Centre                                 |
| EPI630676 | South Africa   | A/South Africa/R2977/2015 | 5/6/2015        | Sandringham, National Institute for Communicable D  | Crick Worldwide Influenza Centre                                 |
| EPI630652 | Slovenia       | A/Slovenia/1314/15        | 5/3/2015        | Laboratory for Virology, National Institute of Public Health  | Crick Worldwide Influenza Centre                                 |
| EPI624706 | Russia         | A/IIV-Moscow/94/2015      | 12/3/2015       | Ivanovsky Research Institute of Virology RAMS   | Crick Worldwide Influenza Centre                                 |
| EPI624704 | Russia         | A/IIV-Moscow/93/2015      | 10/3/2015       | Ivanovsky Research Institute of Virology RAMS   | Crick Worldwide Influenza Centre                                 |
| EPI589565 | Jordan         | A/Jordan/20241/2015       | 22/3/2015       | Laboratory Directorate  | Crick Worldwide Influenza Centre                                 |
| EPI253705 | Germany        | A/Bayern/69/2009          | 1/1/2009        | Robert-Koch-Institute   | Robert-Koch-Institute  |
| EPI278607 | New Zealand    | A/Christchurch/16/2010    | 12/7/2010       | Canterbury Health Services  | WHO Collaborating Centre for Reference and Research on Influenza |
| EPI319590 | Russia         | A/Astrakhan/1/2011        | 28/2/2011       | WHO National Influenza Centre Russian Federation  | National Institute for Medical Research                          |
| EPI319527 | Russia         | A/St. Petersburg/27/2011  | 14/2/2011       | WHO National Influenza Centre Russian Federation  | National Institute for Medical Research                          |
| EPI416411 | Norway         | A/Norway/120/2013         | 2/1/2013        | WHO National Influenza Centre   | National Institute for Medical Research                          |
| EPI574439 | Ghana          | A/Ghana/DILL-14-0620/2014 | 7/7/2014        | University of Ghana   | National Institute for Medical Research                          |
| EPI390473 | Hong Kong SAR  | A/Hong Kong/5659/2012     | 21/5/2012       | Government Virus Unit   | National Institute for Medical Research                          |
| EPI326206 | Hong Kong SAR  | A/Hong Kong/3934/2011     | 29/3/2011       | Government Virus Unit   | National Institute for Medical Research                          |
| EPI466626 | South Africa   | A/South Africa/3626/2013  | 6/6/2013        | Sandringham, National Institute for Communicable D  | National Institute for Medical Research                          |
| EPI539472 | Senegal        | A/Dakar/04/2014           | 3/2/2014        | Institut Pasteur de Dakar   | National Institute for Medical Research                          |
| EPI417122 | Senegal        | A/Dakar/20/2012           | 9/12/2012       | Institut Pasteur de Dakar   | National Institute for Medical Research                          |
| EPI319447 | Czech Republic | A/Czech Republic/32/2011  | 18/1/2011       | National Institute of Public Health   | National Institute for Medical Research                          |
| EPI215957 | Ukraine        | A/Lviv/N6/2009            | 27/10/2009      | Ministry of Health of Ukraine   | National Institute for Medical Research                          |
| EPI320141 | Russia         | A/St. Petersburg/100/2011 | 14/3/2011       | Russian Academy of Medical Sciences   | Centers for Disease Control and Prevention                       |
| EPI626148 | Bangladesh     | A/Bangladesh/3003/2015    | 4/5/2015        | Institute of Epidemiology Disease Control and Research (IEDCR) and Bangladesh National Influenza Centre (NIC) | Centers for Disease Control and Prevention                       |
| EPI626140 | Bangladesh     | A/Bangladesh/01/2015      | 10/5/2015       | Institute of Epidemiology Disease Control and Research (IEDCR) and Bangladesh National Influenza Centre (NIC) | Centers for Disease Control and Prevention                       |
| EPI176620 | United States  | A/California/07/2009      | 9/4/2009        | Naval Health Research Center  | Centers for Disease Control and Prevention                       |
| EPI624468 | French Guiana  | A/Guyane/1759/2015        | 9/4/2015        | Institut Pasteur  | Institut Pasteur   |

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The data supporting the predominance of the 6B.1 subclade stem from the subset of 12 European countries that reported virus characterisation data referring to sequences available in publically accessible databases. These countries are well spread across Europe which corroborates the conclusion of widespread 6B.1 subclade circulation. Data from the WHO Collaborating Centres indicate that the new subgroup remains antigenically similar to the vaccine component A/California/7/2009 [1], but some recent A(H1N1)pdm09 viruses within the 6B.1 and 6B.2 subclades reacted poorly with sera from individuals vaccinated with A/California/7/2009-like-strain-containing vaccine [15].

The emergence of a new A(H1N1)pdm09 subclade may eventually affect the susceptibility of the population to the currently circulating A(H1N1)pdm09 viruses, e.g. by viruses drifting closer to become immune escape variants. It is not clear whether the emergence and predominance of subclade 6B.1 has been driven by immune selection or what its impact on vaccine effectiveness may be and this needs assessment e.g. by generating lineage-specific estimation of vaccine effectiveness. Early vaccine effectiveness estimates for A(H1N1)pdm09 this season compared with the previous ones are not significantly different [16] from previous seasons. As to the severity observed this season [1-4], similar observations have been made also in earlier seasons e.g. in 2010/11 in the United Kingdom, which experienced notably severe A(H1N1)pdm09 impact in the first post-pandemic season.

Notably, recent studies have demonstrated that antigenic change in A(H1N1)pdm09 viruses is mainly caused by single amino acid substitutions affecting the loop located adjacent to the receptor binding site [17]; eight of the 215 analysed 2015/16 viruses possessed such substitutions, all six of the viruses in subclade 6B.2 and two in 6B subgroup, that do not belong to any of the newly emerged subclades.

Further enhancement of the antigenicity and virulence of influenza virus has been attributed to shielding of the major antigenic epitopes by alteration of N-linked glycosylation sites [18]. D127E substitution seen in 6B.2 has been associated with antigenic change of other influenza viruses through modelling [17]. The change at position 173 (V173I) also in the 6B.2 subclade of viruses is located in antigenic site Ca1 (position 169–173), and therefore a change here could contribute to antigen drift. It has been proposed that the evolution of A(H1N1)pdm09 will involve the acquisition of additional glycosylations, as for former seasonal A(H1N1) HA [19]. Noteworthy, 80% of the analysed HA sequences have gained a potential glycosylation site S162N. No D222G/E/N substitutions were detected, nor N129D which was recently identified in India in two severe or fatal cases [9]. If the emerging groups continue to diversify from the vaccine component, their antigenic properties may change and the vaccine effectiveness might be reduced. WHO recommended not to

change the vaccine component of A(H1N1)pdm09 for the northern hemisphere 2016/17 season [20].

Early vaccine effectiveness estimates for 2015/16 are not yet available for A(H3N2) and B viruses which have been detected in lower numbers in most countries. The B/Victoria virus component is available only in the quadrivalent vaccines in the northern hemisphere for this season. As the majority of the countries use trivalent vaccines, the lineage switch from B/Yamagata to B/Victoria may contribute to lower vaccine effectiveness against influenza B. For A(H3N2), the current component of influenza vaccines is expected to have improved vaccine effectiveness compared with the two previous seasons [21,22]. In the southern hemisphere, seasonal influenza vaccine has been demonstrated to have an overall effectiveness against A(H3N2) of 36% (95% confidence interval (CI): 11–54) for general practice encounters and 50% (95%-CI: 20–68) for hospitalisations in 2015 [23]. Despite the changes in the genetic makeup of influenza A(H1N1)pdm09 viruses and the predominance of B/Victoria lineage over B/Yamagata lineage, seasonal influenza vaccine remains the single most effective measure to prevent severe outcomes of influenza.

#### Disclaimer

The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

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## Conflict of interest

None declared.

## Authors' contributions

Eeva Broberg: Data extraction, data maintenance, first draft of the manuscript, study design, revisions of the article. Angeliki Melidou: data processing, phylogenetic analysis and text. Katarina Prosenec: data processing, analysis, text. Karoline Bragstad: data processing, amino acid analysis, text. Olav Hungnes: data processing, analysis, text. ECDC and WHO Regional Office for Europe staff: influenza surveillance data maintenance, management and analysis. Country experts: surveillance systems, data collection, data analysis at national level and reporting to TESSy.

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