Coordinated surveillance of influenza viruses in European pigs: Enhanced Virological and Epidemiological analysis from the European Surveillance Network for Influenza in Pigs (ESNIP3)

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ESNIP3 objectives

- Expand knowledge of epidemiology and evolution of SIVs in Europe
  - Surveillance for influenza in pigs; harmonised
  - Contemporary data available at EU level
- Rapid virus characterisation
- Use of new technologies/improvements linking datasets
  - Antigenic characterisation/mapping
  - Heterogeneity defined; cartography
  - Genetic characterisation
  - Phylogeography
  - Genotypic data
- Provide timely insights to veterinary public health risk
- EU SI Virus database and repository
- Global dissemination of information/exchange
  - Network interaction

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Project consortia

- 25 partners:
  - Veterinary institutes
    - Belgium, UK, The Netherlands, Italy, France, Germany, Denmark, Poland, Spain, Israel, Hungary, Finland, Greece, USA, China
  - Vaccine manufacturers
    - Merial (France), IDT (Germany) & Hipra (Spain)

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WP2 - Summary of the surveillance programmes conducted by partners

Partners	Country	Virological surveillance		Serological surveillance	Who is conducting the surveillance programs ?
		Passive	Active		
P1 - AHVLA	UK	**X**	-	-	VLA (Defra Surveillance program) + Collaboration with Merial
P2 - UGent	Belgium	**X**	-	**X**	UGent + Collaboration with Merial
P3 - Anses	France	**X**	**(X)**	**X**	Anses-Ploufragan (NRL for swine influenza) + Ministry and Vet (national surveillance network) + Collaboration with Merial
P4 - IZLER	Italy	**X**	-	**X**	ISZLER + Diagnosis requests from vets + Collaboration with Merial
P5 - VET-DTU	Denmark	**X**	**(X)**	**X**	VET-DTU + Collaboration with Merial
P6 - NVRI	Poland	**X**	**(X)**	**X**	NVRI (swine diseases department) + Collaboration with Merial
P7 - LCV	Spain	**X**	-	-	Spanish Surveillance program + Collaboration with Merial
P8 - IDT	Germany	**X**	**(X)**	**X**	IDT
P9 - EVIRA	Finland	**X**	-	-	EVIRA
P10 -KVI	Israel	**X**	**(X)**	**X**	KVI
P11 - CAO	Hungary	**X**	-	-	CAO - Diagnosis requests from vets + Collaboration with Merial
P12 - CVI	The Netherlands	**X**	-	**X**	CVI
P13 - UTH	Greece	**X**	**(X)**	**X**	UTH + Collaboration with Merial
P21 - Merial	France/Europe	**X**	-	-	Merial + Collaboration with partners in several European countries
P22 - Hipra	Spain	**X**	-	-	Hipra

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Current status

Numbers of outbreaks: highly variable depending on partners/countries
> *Related to surveillance programs or to regional SI epidemiology ?*

Frequencies of positive cases: highly variable depending on partners/countries
> *Related to surveillance programs or to SI epidemiology or to vet's experience or to diagnostic methods ?*

Nov10/Oct12

Country	Partner	Number of herds investigated[a]	Number of positive cases	Frequency of positive cases (%)
United-Kingdom	P1-AHVLA	332	66	19,87
Belgium	P2-UGhent	107	41	37,96
Netherlands	P2-UGhent			
	P12-CVI	23	13	56,52
France	P3-Anses	417	191	47,9
Italy	P4-IZSLER	1056	216	20,40
Denmark	P5-DTU	513	219	42,69
Poland	P6-NVRI	98	38	38,78
Slovakia	P6-NVRI			
Spain	P7-LCV	10	1	10
	P22-HIPRA	187	36	19,25
Germany	P8-IDT	1178	537	30,2
	P17-FLI	366	154	42,08
	P2-UGhent	1	1	100
Finland	P9-EVIRA	45	1	2,20
Israel	P10-KVI	7	?	?
Hungary	P11-CAO	51	16	31,37
Greece	P13-UTH	22	3	13,6
Total		**4413**	**1533**	**34,74**

Data from preliminary molecular and/or antigenic subtyping (number of viruses detected within each lineage when known) (to be updated after sequencing)

			H1N1			H3N2	H1N2		Other lineages	
Country	Partner	Number of subtyped viruses[b]	Av-like sw H1N1	Reass. sw H1N1 (hu-like HA)	pdm-like sw H1N1	Hu-like reass. sw H3N2	Hu-like reass. sw H1N2[c]	Reass. sw H1N2 (av-like HA)[d]	reass. pdm-like sw HxNx	Other
United-Kingdom	P1-AHVLA	39	2	?	27	0	10	?	?	?
Belgium	P2-UGhent	20	11	?	0	8	1	?	?	0
Netherlands	P2-UGhent	20	10	?	0	5	1	?	?	0
	P12-CVI	10	6	0	0	2	2	0	0	0
France	P3-Anses	185	128	1	5	1	44	6	0	0
Italy	P4-IZSLER	121	57	1	6	24	29	4	0	0
Denmark	P5-DTU	170	44	0	50	0	0	63	10	0
Poland	P6-NVRI	13	11	0	0	1	1	0	0	0
Slovakia	P6-NVRI	1	1	0	0	0	0	0	0	0
Spain	P7-LCV	0	0	0	0	0	0	0	0	0
	P22-HIPRA	19	6	0	0	9	4	0	0	0
Germany	P8-IDT	323	196	2	12	31	58	6	18	0
	P17-FLI	119	77	0	3	10	16	1	12	0
	P2-UGhent	1	0	?	0	0	1	0	?	0
Finland	P9-EVIRA	1	0	0	1	0	0	0	0	0
Israel	P10-KVI	0	?	?	?	?	?	?	?	?
Hungary	P11-CAO	16	11	0	2	2	0	0	1	0
Greece	P13-UTH	3	0	0	0	3	0	0	0	0
Total		**1061**	**560**	**4**	**106**	**96**	**167**	**80**	**41**	0
	Frequency (%) of each lineage		**52,78**	**0,38**	**9,99**	**9,05**	**15,74**	**7,54**	**3,86**	**0**

- 53% belong to enzootic "avian-like swine H1N1" lineage (1979)
- 16% belong to enzootic "human like reassortant swine H1N2" lineage (1994)
- 9% belong to enzootic "human-like reassortant swine H3N2" lineage (1984)
- 8% are reassortants between enzootic SIVs
- 14% are pdm-like viruses or reassortants that have acquired gene(s) from H1N1pdm

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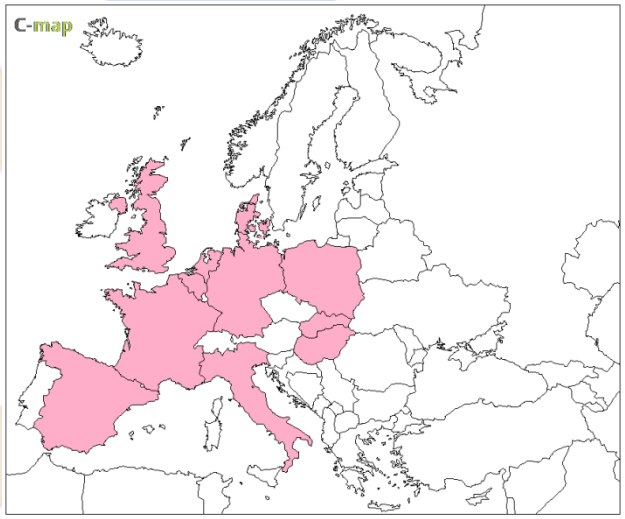
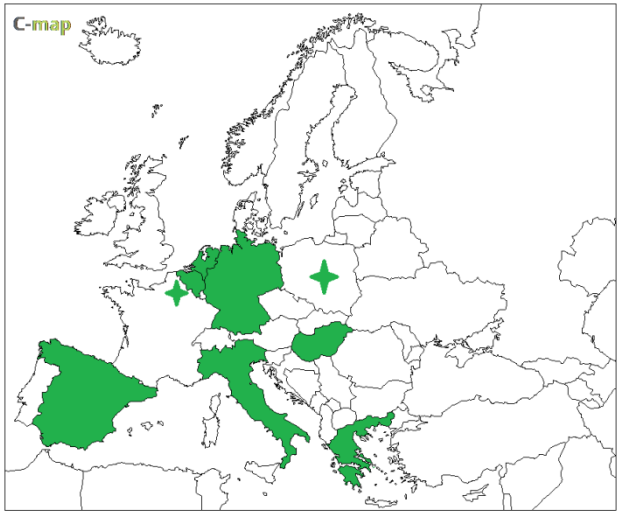
C-map
Finland
Denmark
United Kingdom
Netherlands
Belgium
Germany
Poland
France
Slovakia
Hungary
Italy
Spain
Greece

Regional variation in the epidemiology of SI in Europe (ESNIP3)

H1avN1 (53%)



H3N2 (9%)

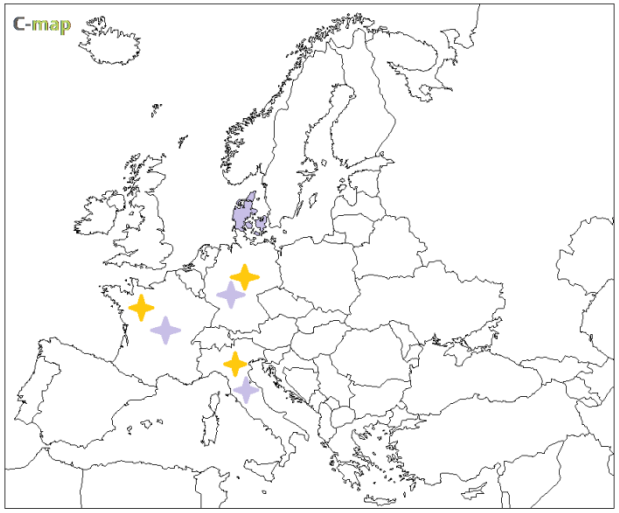


H1huN2 (16%)

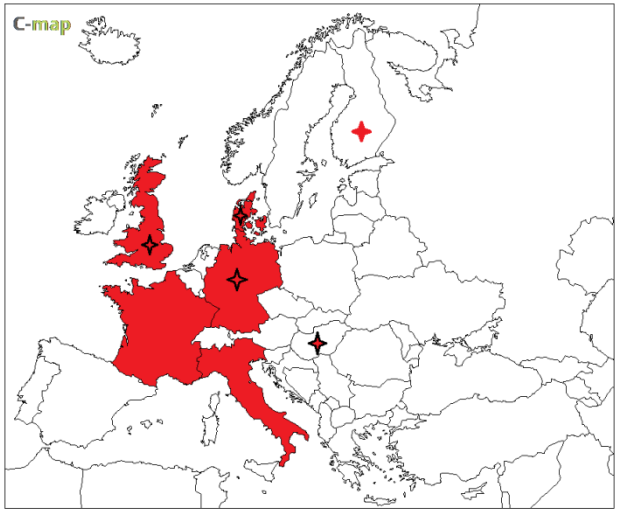
Enzootic lineages

Epizootic lineages
(occasional detections)

rH1huN1 and rH1avN2 (8%)



H1N1pdm and reass. (14%)



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PCR ring trial - conclusions

- Most of the participants were able to detect influenza A virus genome, especially when M-gene as targeted
- NP gene was less frequently used
- Conventional RT-PCR was less sensitive than RRT-PCR

- Specific detection of H3N2v confirmed

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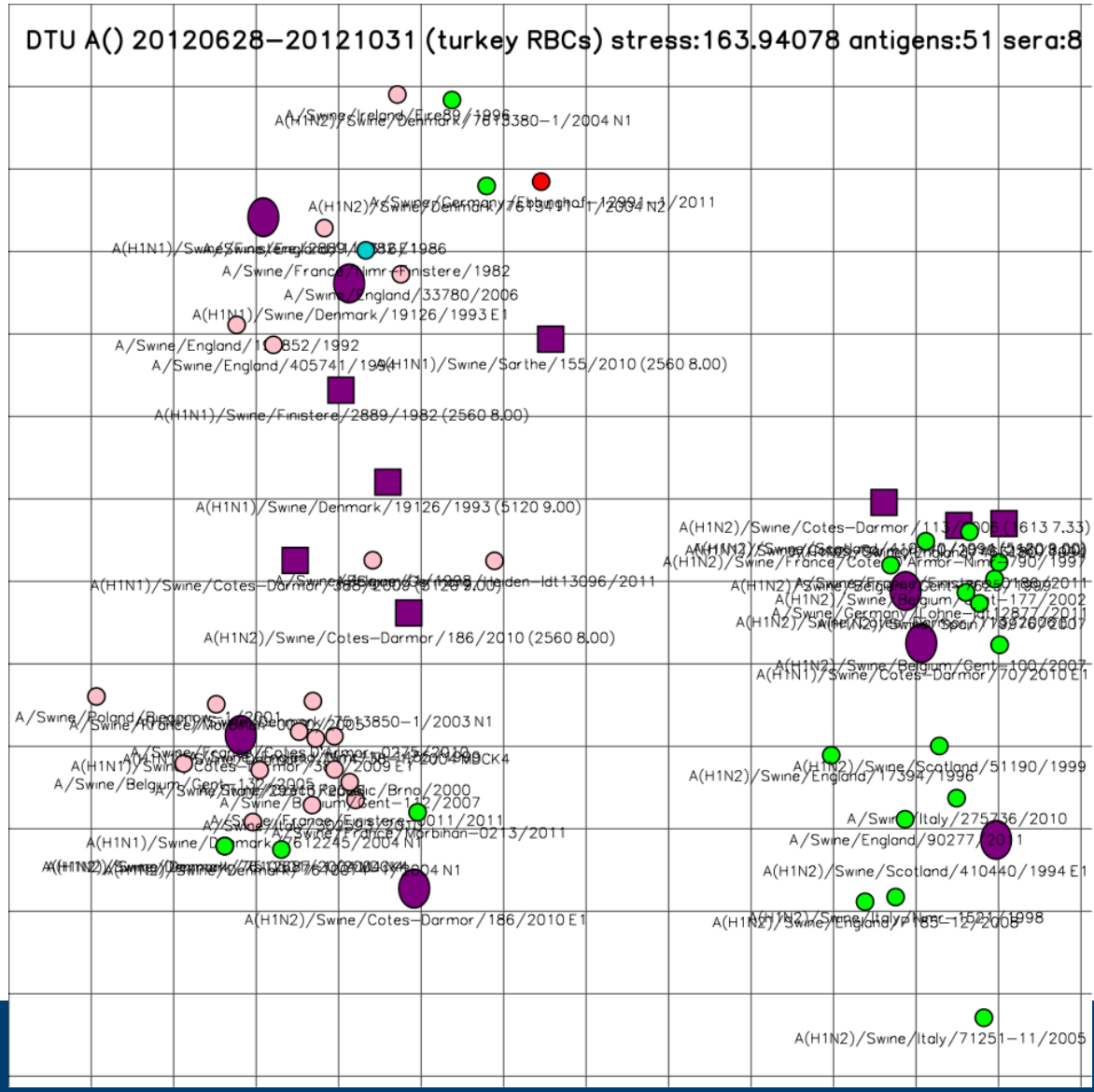
Results

Swine influenza A H1 viruses

51 antigens
8 hyperimmune sera



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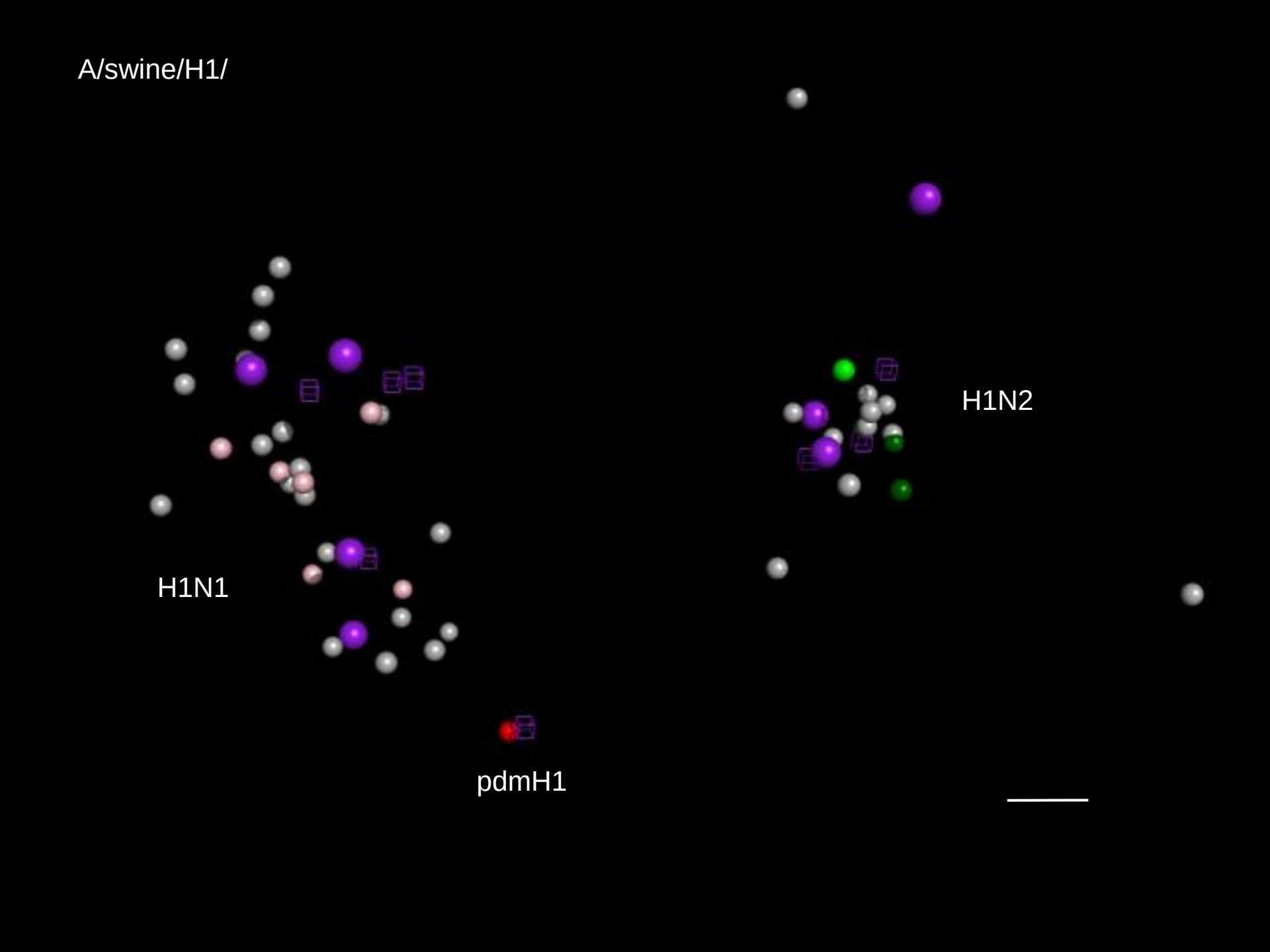
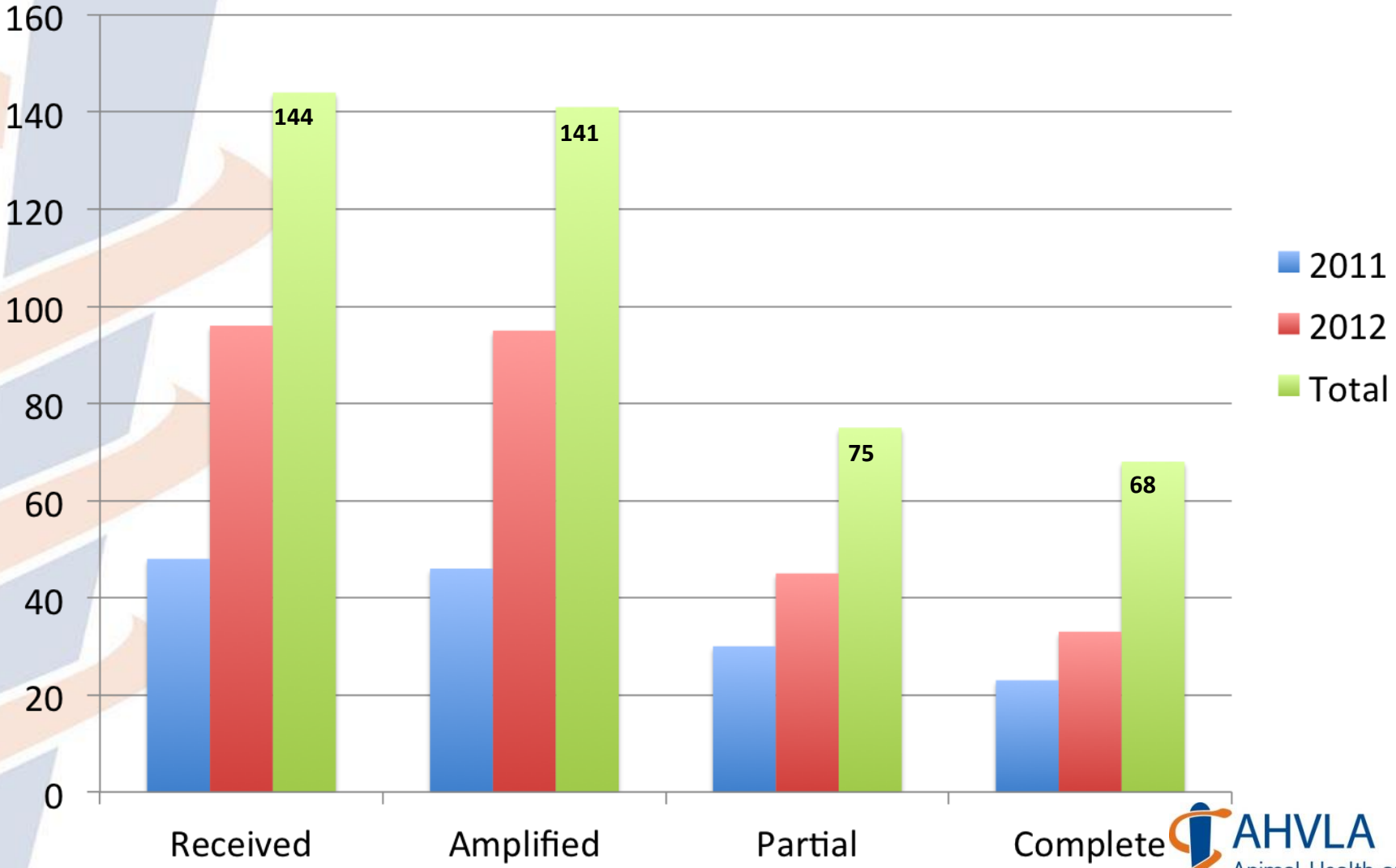

A/swine/H1/
H1N2
H1N1
pdmH1

Statistics: Total samples received



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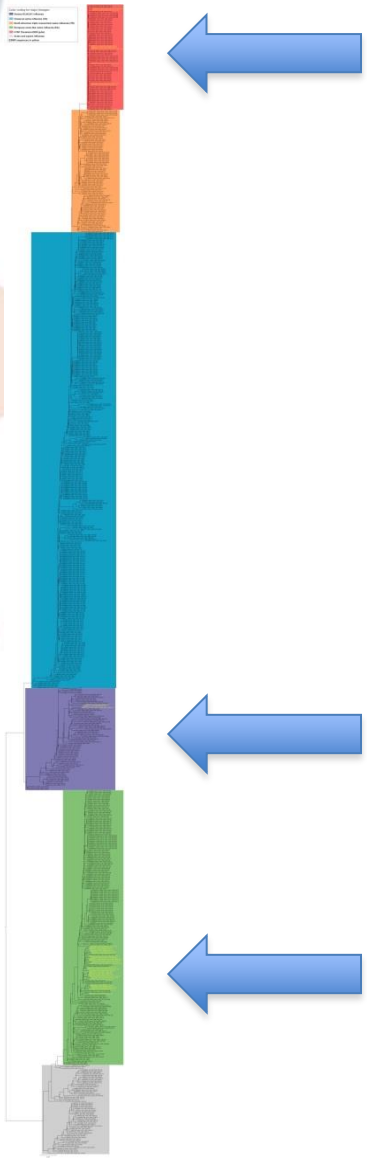
Results: Phylogenetic analysis of H1



Color coding for major lineages:

- Human H3,H2,H1 influenza
- Classical swine influenza (CS)
- North American triple reassortant swine influenza (TR)
- European avian-like swine influenza (EA)
- H1N1 Pandemic/2009 (pdm)
- Avian and equine influenza

ESNIP sequences in yellow

Background data taken from:
TTY Lam *et al.* (2011) J. Virol

Courtesy of TTY Lam, Oxford Zoology Group

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Results: Phylogenetic analysis of MP

Pandemic 2009

Courtesy of TTY Lam, Oxford Zoology Group

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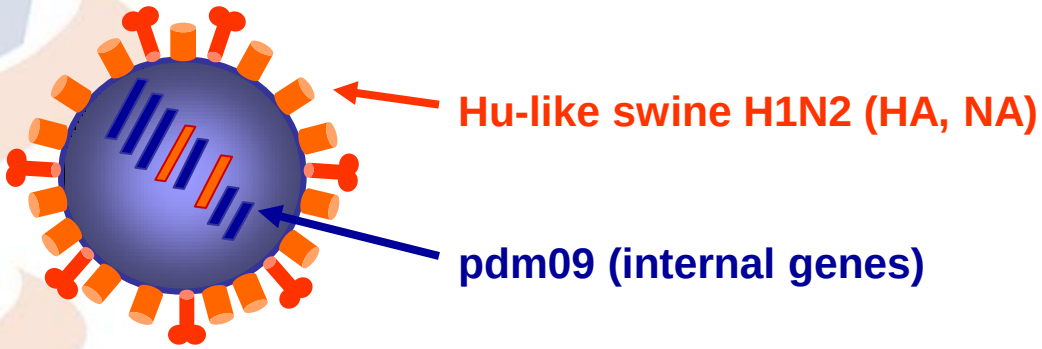
H1N2/pdm09 reassortants in UK swine 2009-2012

- H1N2/pdm09 reassortant virus first isolated in UK in April 2010 (Howard et al., EID 2011)



- Methods: Egg grown virus
  HI tests for subtyping
  RNA extraction and partial gene sequencing (>180bp)
  BLAST analysis

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Genotyping

- 60 full genomes from 11 countries

Genotypic variation in European SIVs

- Avian – like H1N1
  - No reassortment with pdm09
  - France N2 (1 virus!)
- H1N2
  - Majority av-like x human H1 & N2
  - UK viruses all now pdm09 IPG
  - Denmark H1N2 HA av-like
- H3N2
  - All as previous av-like IPG
  - No pdm to date!

- H1pdm09
  - All pdm09 constellation; 1 exception NL N2 from H1N2

my presentation

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Conclusions

- Surveillance approaches harmonised
- Four viruses cocirculating
- Significant regional variation
- Diagnostics fit for purpose
- Preliminary antigenic maps for H1
- Genomic data generated- genotypic evolution including with pdm09

- Data/knowledge exchanged with other networks, official bodies

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ESNIP1

Thanks to EU!

http://www.esnip3.eu

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Coordinator Ian Brown, AHVLA,

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Consortium

Name	No.	Country	Name	No.	Country
AHVLA	1	UK	WTSI	14	UK
UGent	2	Belgium	UCAM	15	UK
ANSES	3	France	UOXF.AT	16	UK
ISZLER	4	Italy	FLI	17	Germany
DTU	5	Denmark	IZSV	18	Italy
NVRI	6	Poland	USDA	19	USA
LCV	7	Spain	HVRI	20	China
IDT	8	Germany	MSS	21	France
EVIRA	9	Finland	HIPRA	22	Spain
KVI	10	Israel	AHT	23	UK
CAO	11	Hungary	AFBI	24	UK
CVI	12	Netherlands			
UTH	13	Greece			

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