



MI Flu Focus

Influenza Surveillance Updates
Bureaus of Epidemiology and Laboratories

Michigan Department
of Community Health



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Current Influenza Activity Levels:

- **Michigan:** Sporadic influenza activity
- **National:** During November 10-16, influenza activity increased slightly in the United States

Updates of Interest:

- **International:** 3 new human cases of MERS-CoV are reported from Saudi Arabia

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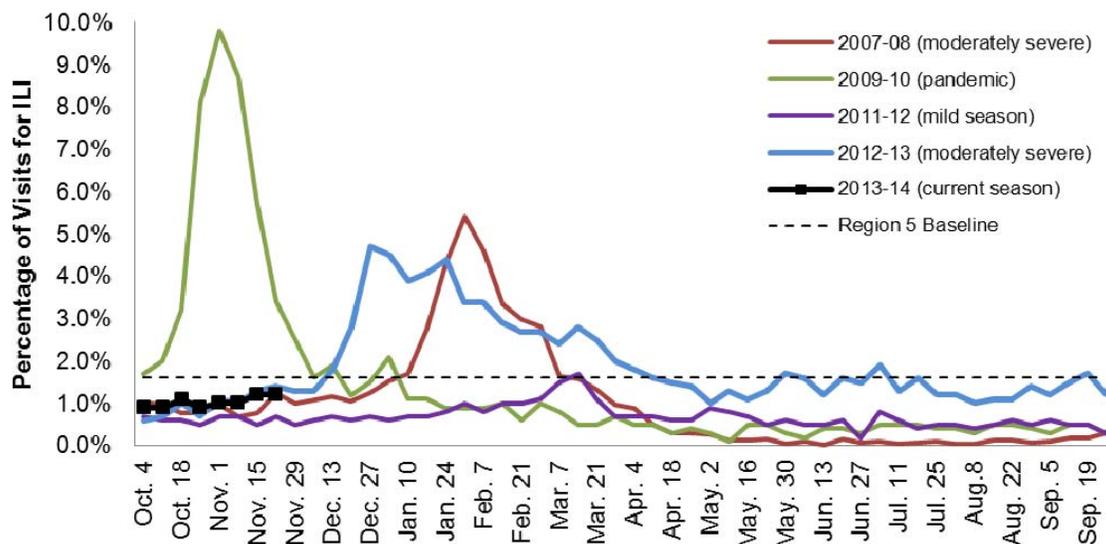
Influenza Surveillance Reports

Michigan Disease Surveillance System (as of November 27): MDSS influenza data for the week ending November 23, 2013 indicated that compared to levels from the previous week, both individual and aggregate reports slightly increased. Both individual and aggregate reports are slightly higher than levels seen during the same time period last year.

Emergency Department Surveillance (as of November 27): Emergency department visits due to both constitutional and respiratory complaints remained steady during the week ending November 23, 2013. Emergency department visits from both constitutional and respiratory complaints were similar to levels during the same time period last year. In the past week, there were 10 constitutional alerts in the C(7) and N(3) Influenza Surveillance Regions and 6 respiratory alerts in the SW(2), C(1) and N(3) Regions.

Sentinel Provider Surveillance (as of November 26): During the week ending November 23, 2013, the proportion of visits due to influenza-like illness (ILI) increased to 1.2% overall; this is below the regional baseline (1.6%). Data were provided by 26 sentinel sites from the following regions: Central (9), North (5), Southeast (10), and Southwest (2). ILI activity increased in one region: C (2.1%), remained the same in one region: SE (0.2%) and decreased in two regions: N (3.7%) and SW (0.7%). Please note: These rates may change as additional reports are received.

Percentage of Visits for Influenza-like Illness (ILI) Reported by the US Outpatient Influenza-like Illness Surveillance Network (ILINet): Michigan, Select Seasons



As part of pandemic influenza surveillance, CDC and MDCH highly encourage year-round participation from all sentinel providers. New practices are encouraged to join the sentinel surveillance program today! Contact Stefanie DeVita at 517-335-3385 or DeVitaS1@michigan.gov for more information.

Hospital Surveillance (as of November 23): The CDC Influenza Hospitalization Surveillance Project provides population-based rates of severe influenza illness through active surveillance and chart review of lab-confirmed cases, starting on October 1, 2013, for Clinton, Eaton, Genesee, and Ingham counties. One new adult case was identified during the past week. As of November 23rd, there have been 4 influenza hospitalizations (2 pediatric, 2 adult) within the catchment area.

The MDCH Influenza Sentinel Hospital Network monitors influenza hospitalizations reported voluntarily by hospitals statewide. 6 hospitals (SE,SW,C,N) reported for the week ending November 23, 2013. Results are listed in the table below.

Age Group	Hospitalizations Reported During Current Week	Total Hospitalizations 2013-14 Season
0-4 years	0	1 (1C)
5-17 years	0	1 (1C)
18-49 years	1 (1SE)	1 (1SE)
50-64 years	1 (1C)	1 (1C)
≥65 years	0	1 (1SE)
Total	2 (1SE,1C)	5 (2SE,3C)

Laboratory Surveillance (as of November 23): During November 17-23, 9 influenza 2009 A/H1N1pdm (7SE,1SW,1C) and 1 influenza A/H3 (1SE) results were reported by MDCH Bureau of Laboratories. For the 2013-14 season (starting Sept. 29, 2013), MDCH has identified 47 positive influenza results:

- Influenza 2009 A/H1N1pdm: 38 (26SE,6SW,6C)
- Influenza A/H3: 5 (5SE)
- Influenza A unsubtypeable: 1 (1SE)
- Influenza B: 3 (1SE,1SW,1C)
- Parainfluenza: 1 (1SE)

13 sentinel labs (SE,SW,C,N) reported for the week ending November 23, 2013. 9 labs (SE,SW,C) reported influenza A activity. 2 labs (SW,C) reported sporadic influenza B activity. 7 labs (SE,SW,C,N) had RSV activity. 4 labs (SE,SW,C) had sporadic parainfluenza activity. 2 labs (SE,SW) had sporadic adenovirus activity. No labs reported hMPV activity. Testing volumes continue to increase at most sites with several approaching moderate to high levels.

Michigan Influenza Antigenic Characterization (as of November 27): For the 2013-14 season, no influenza specimens have been characterized at MDCH BOL.

Michigan Influenza Antiviral Resistance Data (as of November 27): For the 2013-14 season, 7 2009 A/H1N1pdm (7SE) and 1 A/H3 (1SE) influenza specimens have been tested at the MDCH BOL for antiviral resistance. None of the influenza specimens tested have been resistant.

CDC has made recommendations regarding the use of antivirals for treatment and prophylaxis of influenza, which are available at <http://www.cdc.gov/flu/professionals/antivirals/index.htm>.

Influenza-associated Pediatric Mortality (as of November 27): No pediatric influenza-associated influenza mortalities have been reported to MDCH for the 2013-14 season.

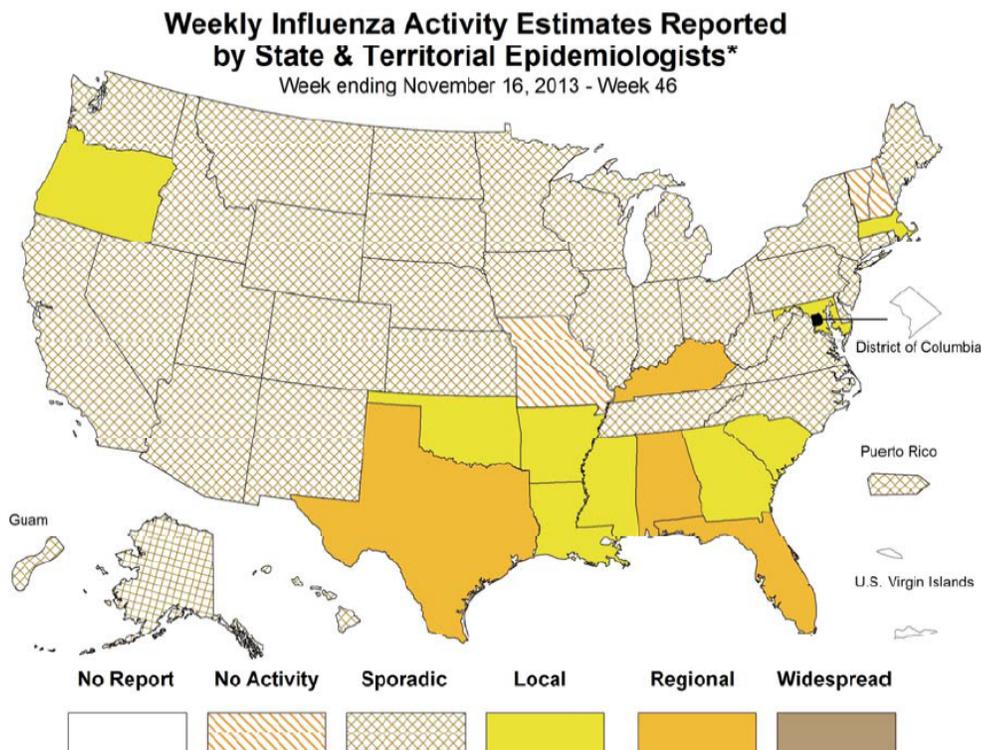
CDC requires reporting of flu-associated pediatric deaths (<18 yrs), including pediatric deaths due to an influenza-like illness with lab confirmation of influenza or any unexplained pediatric death with evidence of an infectious process. Contact MDCH immediately for proper specimen collection. The MDCH protocol is at www.michigan.gov/documents/mdch/ME_pediatric_influenza_guidance_v2_214270_7.pdf.

Influenza Congregate Settings Outbreaks (as of November 27): No respiratory outbreaks have been reported to MDCH during the 2013-14 season.

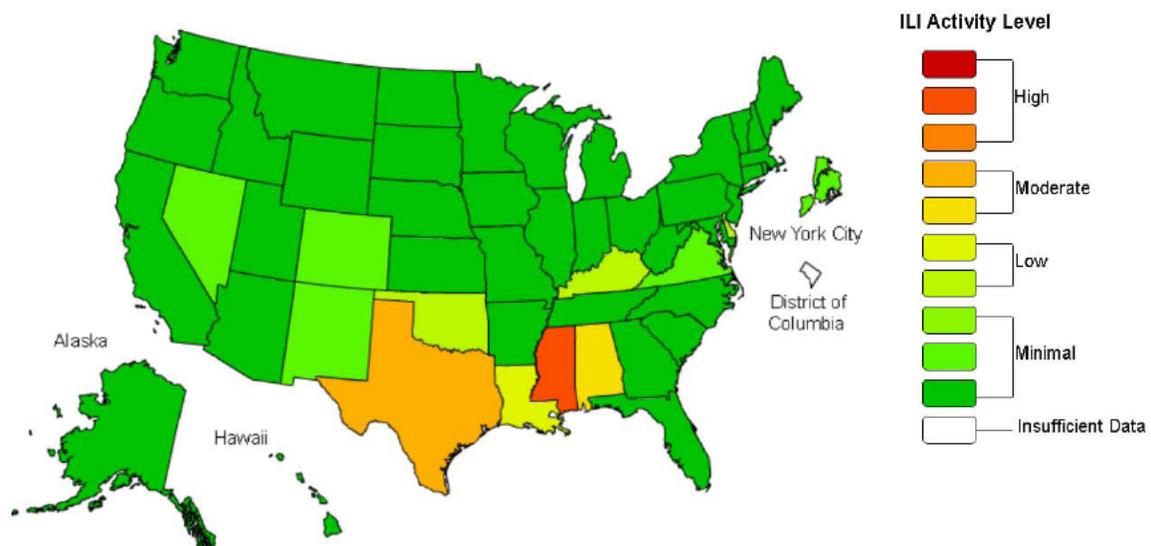
National (CDC [edited], November 22): During week 46 (November 10-16, 2013), influenza activity increased slightly in the United States. Of 4,457 specimens tested and reported by U.S. WHO and NREVSS collaborating laboratories during week 46, 312 (7.0%) were positive for influenza. The proportion of deaths attributed to pneumonia and influenza (P&I) was below the epidemic threshold. No

influenza-associated pediatric deaths were reported. The proportion of outpatient visits for influenza-like illness (ILI) was 1.5%, below the national baseline of 2.0%. One region reported ILI above region-specific baseline levels. One state experienced high ILI activity, two states experienced moderate ILI activity, four states experienced low ILI activity, 43 states and New York City experienced minimal ILI activity and the District of Columbia had insufficient data. The geographic spread of influenza in four states was reported as regional; nine states reported local influenza activity; Puerto Rico, Guam and 34 states reported sporadic influenza activity; three states reported no influenza activity, and the District of Columbia and the U.S. Virgin Islands did not report.

	Week 46
No. of specimens tested	4,457
No. of positive specimens (%)	312 (7.0%)
Positive specimens by type/subtype	
Influenza A	280 (89.7%)
2009 H1N1	118 (42.1%)
H3	14 (5.0%)
Subtyping not performed	148 (52.9%)
Influenza B	32 (10.3%)



**Influenza-Like Illness (ILI) Activity Level Indicator Determined by Data Reported to ILINet
2013-14 Influenza Season Week 46 ending Nov 16, 2013**



This map uses the proportion of outpatient visits to healthcare providers for influenza-like illness to measure the ILI activity level within a state. Therefore, outbreaks occurring in a single city could cause the state to display high activity levels. Data collected in ILINet may disproportionately represent certain populations within a state, and therefore, may not accurately depict the full picture of influenza activity for the whole state. Data displayed on this map are based on data collected in ILINet, whereas the State and Territorial flu activity map are based on reports from state and territorial epidemiologists.

Complete weekly FluView reports are available online at: <http://www.cdc.gov/flu/weekly/>.

International (WHO [edited], November 22): Overall influenza activity in North America increased slightly over the past three weeks, but remained at low levels throughout the region. Countries from the WHO European Region continued to report low levels of influenza activity with only a few countries reporting sporadic influenza detections among samples from sentinel and non-sentinel sources. In northern Asia, influenza activity slightly increased in the north of China and Mongolia. Influenza transmission in southern Asia was low. In Hong Kong Special Administrative Region, China, and in the south of China influenza detections decreased. In South East Asia, influenza activity decreased in Viet Nam, but increased in Cambodia, Lao People's Democratic Republic and Thailand. In this area, co-circulation of influenza A(H1N1)pdm09, influenza A(H3N2) and influenza B virus was reported. In the Caribbean region of Central America and tropical South America, influenza A detections remained at low levels. Respiratory syncytial virus (RSV) continued to predominate in certain countries, but the RSV activity largely remained within expected seasonal levels. The influenza season in the southern hemisphere is largely over.

The entire WHO report is available online at www.who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en/index.html.

MDCH reported SPORADIC INFLUENZA ACTIVITY to CDC for the week ending Nov. 23, 2013.

For additional flu vaccination and education information, the MDCH *FluBytes* newsletter is available at http://www.michigan.gov/mdch/0,1607,7-132-2940_2955_22779_40563-125027--,00.html.

Novel Influenza Activity and Other News

WHO Pandemic Phase: Post-pandemic – Influenza disease activity has returned to levels normally seen for seasonal influenza.

International, MERS-CoV (WHO [edited], November 26): WHO has been informed of an additional three laboratory-confirmed cases of infection with Middle East respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia.

The first patient is a 73-year-old woman with underlying medical conditions from Riyadh who became ill on 12 November 2013, was hospitalized on 14 November 2013 and died on 18 November 2013. The second patient is a 65 year-old man with an underlying medical condition from Jawf region who became ill on 4 November 2013 and was hospitalized on 14 November 2013. The third patient is a 37-year-old man from Riyadh who became ill on 9 November 2013, was hospitalized on 13 November 2013 and died on 18 November 2013. None of the three patients had exposure to animals or contact to a previously laboratory-confirmed case with MERS-CoV.

Globally, from September 2012 to date, WHO has been informed of a total of 160 laboratory-confirmed cases of infection with MERS-CoV, including 68 deaths.

The full report is available online at http://www.who.int/csr/don/2013_11_26/en/index.html.

National, Research (Pediatrics abstract, November 25): Neuraminidase Inhibitors for Critically Ill Children With Influenza. Janice K. Louie, Samuel Yang, Michael C. Samuel, Timothy M. Uyeki, and Robert Schechter. *Pediatrics* 2013-2149; published ahead of print Nov 25 2013, doi:10.1542/peds.2013-2149

OBJECTIVE: Timely treatment with neuraminidase inhibitor (NAI) drugs appears to improve survival in adults hospitalized with influenza. We analyzed California surveillance data to determine whether NAI treatment improves survival in critically ill children with influenza.

METHODS: We analyzed data abstracted from medical records to characterize the outcomes of patients aged 0 to 17 years hospitalized in ICUs with laboratory-confirmed influenza from April 3, 2009, through September 30, 2012.

RESULTS: Seven hundred eighty-four influenza cases aged <18 years hospitalized in ICUs had information on treatment. Ninety percent (532 of 591) of cases during the 2009 H1N1 pandemic (April 3, 2009–August 31, 2010) received NAI treatment compared with 63% (121 of 193) of cases in the postpandemic period (September 1, 2010–September 30, 2012; $P < .0001$). Of 653 cases NAI-treated, 38 (6%) died compared with 11 (8%) of 131 untreated cases (odds ratio = 0.67, 95% confidence interval: 0.34–1.36). In a multivariate model that included receipt of mechanical ventilation and other factors associated with disease severity, the estimated risk of death was reduced in NAI-treated cases (odds ratio 0.36, 95% confidence interval: 0.16–0.83). Treatment within 48 hours of illness onset was significantly associated with survival ($P = .04$). Cases with NAI treatment initiated earlier in illness were less likely to die.

CONCLUSIONS: Prompt treatment with NAIs may improve survival of children critically ill with influenza. Recent decreased frequency of NAI treatment of influenza may be placing untreated critically ill children at an increased risk of death.

The abstract is online at <http://pediatrics.aappublications.org/content/early/2013/11/19/peds.2013-2149>.

International, Research (Lancet abstract, November 22): Efficacy of oseltamivir treatment started within 5 days of symptom onset to reduce influenza illness duration and virus shedding in an urban setting in Bangladesh: a randomised placebo-controlled trial. Fry AM, et al. *Lancet Infect Dis.* 2013 Nov 21. S1473-3099(13)70267-6. [Epub ahead of print]

Background: Influenza causes substantial morbidity and mortality worldwide. Few data exist for the efficacy of neuraminidase inhibitors, which are the only readily available influenza treatment options, especially in low-income settings. We assessed the efficacy of treatment with the neuraminidase inhibitor oseltamivir to reduce patient illness and viral shedding in people with influenza, in whom treatment was started within 5 days of symptom onset, in an urban setting in Bangladesh.

Methods: We undertook a double-blind, randomised, controlled trial between May, 2008, and December, 2010. Patients with a positive rapid influenza test identified by surveillance of households in Kamalapur, Bangladesh were randomly allocated on a 1:1 basis to receive oseltamivir or placebo twice daily for 5 days. Randomisation lists for individuals enrolled less than 48 h and 48 h or longer since illness onset were generated with permuted blocks of variable length between two and eight. Participants and study staff were masked to treatment group. Participants provided nasal wash specimens at enrolment and 2, 4, and 7 days later, and were visited daily to record symptoms. All specimens were tested for influenza with reverse-transcriptase PCR, and if the result was positive, we isolated the virus. The primary endpoints were duration of clinical illness and viral shedding in patients treated less than and more than 48 h since illness onset and the frequency of oseltamivir resistance during treatment. Analyses were intention to treat unless otherwise specified. This trial is registered with ClinicalTrials.gov, number NCT00707941.

Findings: Overall, 1190 people with a median age of 5 years (IQR 2–9) were enrolled: 794 (67%) less than 48 h since symptom onset and 396 (33%) 48 h or longer since symptom onset. 592 participants were assigned to placebo and 598 to oseltamivir. The median duration of symptoms was shorter in the oseltamivir group (3 days, IQR 1–5) than in the placebo group (4 days, 1–6; $p=0.01$). When stratified by timing of treatment initiation, in participants enrolled 48 h or longer since illness onset, the median duration of symptoms was similar in both groups (oseltamivir 3 days [IQR 2–5], placebo 3 days [1–5]; $p=0.04$). The median duration of symptoms was reduced by 1 day in the group given oseltamivir who were enrolled less than 48 h since symptom onset compared with those given placebo, but this difference was not significant. In those with all swab specimens ($n=1134$), oseltamivir significantly reduced virus isolation on days 2 (placebo 374 [66%] vs oseltamivir 321 [56%]; difference 15.2%, 95% CI 9.5–20.8, $p=0.0004$), 4 (241 [43%] vs 174 [30%]; difference 30.2%, 95% CI 24.6–35.8, $p<0.0001$), and 7 (68 [12%] vs 36 [6%]; difference 47.5%, 95% CI 44.2–50.8, $p=0.0009$). In participants enrolled 48 h or longer since illness onset, oseltamivir treatment significantly reduced virus isolation on days 2 and 4, but not day 7. In participants enrolled less than 48 h since illness onset, oseltamivir treatment significantly reduced virus isolation on days 2, 4, and 7. The emergency of resistance to oseltamivir during treatment was rare overall (<1%) and in influenza A H1N1pdm09 viruses (3.9%).

Interpretation: Oseltamivir treatment resulted in a modest reduction in the duration of symptoms and virus shedding in people with uncomplicated influenza infections, even when treatment was started 48 h or longer after illness onset.

The abstract is available online at [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(13\)70267-6/fulltext#article_upsell](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(13)70267-6/fulltext#article_upsell).

International, Research (Science abstract, November 22): Substitutions Near the Receptor Binding Site Determine Major Antigenic Change During Influenza Virus Evolution. Koel B.F., et al. *Science* 22 November 2013: Vol. 342 no. 6161 pp. 976-979. DOI: 10.1126/science.1244730

The molecular basis of antigenic drift was determined for the hemagglutinin (HA) of human influenza A/H3N2 virus. From 1968 to 2003, antigenic change was caused mainly by single amino acid substitutions, which occurred at only seven positions in HA immediately adjacent to the receptor binding site. Most of these substitutions were involved in antigenic change more than once. Equivalent positions were responsible for the recent antigenic changes of influenza B and A/H1N1 viruses. Substitution of a single amino acid at one of these positions substantially changed the virus-specific antibody response in infected ferrets. These findings have potentially far-reaching consequences for understanding the evolutionary mechanisms that govern influenza viruses.

The abstract is available online at <https://www.sciencemag.org/content/342/6161/976.abstract>.

International, Research (PLOS Medicine abstract, November 26): Global Mortality Estimates for the 2009 Influenza Pandemic from the GLaMOR Project: A Modeling Study. Simonsen L., et al. Nov 26 2013. DOI: 10.1371/journal.pmed.1001558

Background: Assessing the mortality impact of the 2009 influenza A H1N1 virus (H1N1pdm09) is essential for optimizing public health responses to future pandemics. The World Health Organization reported 18,631 laboratory-confirmed pandemic deaths, but the total pandemic mortality burden was substantially higher. We estimated the 2009 pandemic mortality burden through statistical modeling of mortality data from multiple countries.

Methods and Findings: We obtained weekly virology and underlying cause-of-death mortality time series for 2005–2009 for 20 countries covering ~35% of the world population. We applied a multivariate linear regression model to estimate pandemic respiratory mortality in each collaborating country. We then used these results plus ten country indicators in a multiple imputation model to project the mortality burden in all world countries. Between 123,000 and 203,000 pandemic respiratory deaths were estimated globally for the last 9 mo of 2009. The majority (62%–85%) were attributed to persons under 65 y of age. We observed a striking regional heterogeneity, with almost 20-fold higher mortality in some countries in the Americas than in Europe. The model attributed 148,000–249,000 respiratory deaths to influenza in an average pre-pandemic season, with only 19% in persons <65 y. Limitations include lack of representation of low-income countries among single-country estimates and an inability to study subsequent pandemic waves (2010–2012).

Conclusions: We estimate that 2009 global pandemic respiratory mortality was ~10-fold higher than the World Health Organization's laboratory-confirmed mortality count. Although the pandemic mortality estimate was similar in magnitude to that of seasonal influenza, a marked shift toward mortality among persons <65 y of age occurred, so that many more life-years were lost. The burden varied greatly among countries, corroborating early reports of far greater pandemic severity in the Americas than in Australia, New Zealand, and Europe. A collaborative network to collect and analyze mortality and hospitalization surveillance data is needed to rapidly establish the severity of future pandemics.

The full manuscript is available at www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001558.

International Poultry and Wild Bird Surveillance (OIE): Reports of avian influenza activity, including summary graphs of avian influenza H5N1 outbreaks in poultry, can be found at the following website: http://www.oie.int/download/AVIAN%20INFLUENZA/A_AI-Asia.htm.

For questions or to be added to the distribution list, please contact Susan Peters at peterss1@michigan.gov

MDCH Contributors

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Table. H5N1 Influenza in Humans – As of October 8, 2013. http://www.who.int/influenza/human_animal_interface/EN_GIP_20131008CumulativeNumberH5N1cases.pdf. Downloaded 10/8/2013. Cumulative lab-confirmed cases reported to WHO. Total cases include deaths.

Country	2003-2009		2010		2011		2012		2013		Total	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Azerbaijan	8	5	0	0	0	0	0	0	0	0	8	5
Bangladesh	1	0	0	0	2	0	3	0	1	1	7	1
Cambodia	9	7	1	1	8	8	3	3	20	11	41	30
China	38	25	2	1	1	1	2	1	2	2	45	30
Djibouti	1	0	0	0	0	0	0	0	0	0	1	0
Egypt	90	27	29	13	39	15	11	5	4	3	173	63
Indonesia	162	134	9	7	12	10	9	9	2	2	194	162
Iraq	3	2	0	0	0	0	0	0	0	0	3	2
Lao PDR	2	2	0	0	0	0	0	0	0	0	2	2
Myanmar	1	0	0	0	0	0	0	0	0	0	1	0
Nigeria	1	1	0	0	0	0	0	0	0	0	1	1
Pakistan	3	1	0	0	0	0	0	0	0	0	3	1
Thailand	25	17	0	0	0	0	0	0	0	0	25	17
Turkey	12	4	0	0	0	0	0	0	0	0	12	4
Vietnam	112	57	7	2	0	0	4	2	2	1	125	62
Total	468	282	48	24	62	34	32	20	31	20	641	380