SHORT REPORT
Estimated cumulative incidence of West Nile virus infection in US adults, 1999–2010

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SUMMARY

West Nile virus (WNV) was first recognized in the USA in 1999. We estimated the cumulative incidence of WNV infection in the USA from 1999 to 2010 using recently derived age- and sex-stratified ratios of infections to WNV neuroinvasive disease (WNND) and the number of WNND cases reported to national surveillance. We estimate that over 3 million persons have been infected with WNV in the USA, with the highest incidence rates in the central plains states. These 3 million infections would have resulted in about 780 000 illnesses. A substantial number of WNV infections and illnesses have occurred during the virus' first decade in the USA.

Key words: Epidemiology, incidence, West Nile virus, zoonoses.

Since the first identification of West Nile virus (WNV) in North America in 1999, the national ArboNET surveillance system has documented that the virus has become endemic throughout most of the USA [1]. Studies conducted in the USA indicate that in persons infected with WNV, about 75% remain asymptomatic, 25% develop West Nile fever (WNF), and <1% develop West Nile neuroinvasive disease (WNND) [2, 3]. Since routine diagnostic testing is not recommended for WNF patients and many of these patients do not seek medical care, WNF cases are considerably underreported. In contrast, WNND reporting to ArboNet is thought to be nearly complete, particularly in older persons and persons with compatible clinical features [4, 5]. From 1999 to 2010, the ArboNET surveillance system recorded 12 823 cases of WNND from 47 states.

Several studies have attempted to estimate the true number of WNV infections in the USA. Seroprevalence surveys conducted to determine cumulative infection incidence have found seroprevalences of WNV IgG antibody ranging from 1·9% to 14% [3, 6, 7]; however, these studies were limited by surveying small geographical areas and relatively few subjects. Cumulative infection incidence has also been estimated by multiplying the total number of reported WNND cases by the estimated proportion of total infections per WNND case. Results from

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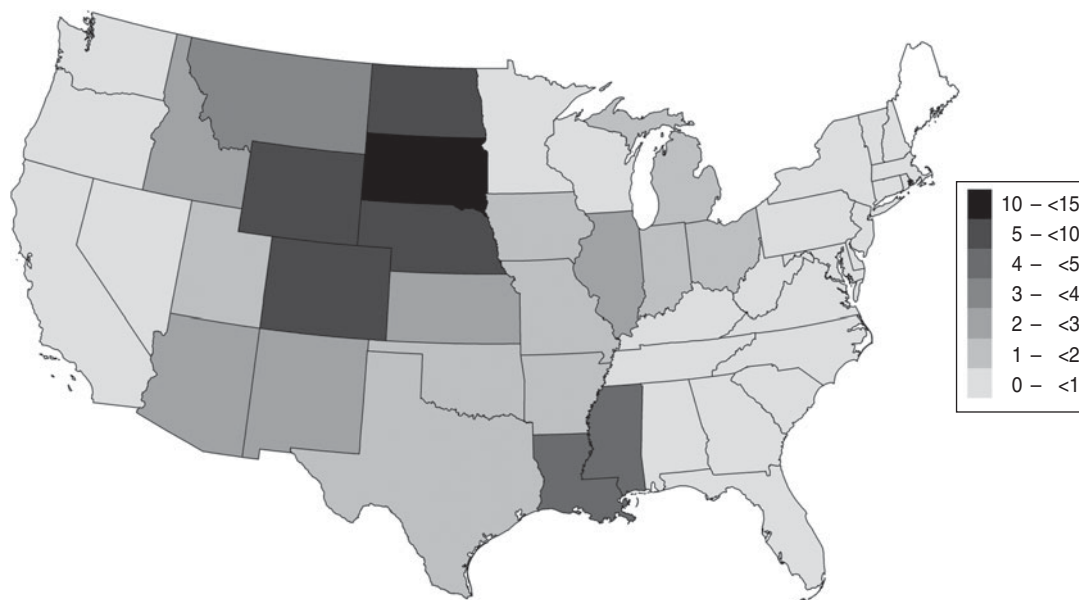
Fig. 1. Estimated cumulative incidence of West Nile virus infection (per cent of population infected) in US adults aged ⩾16 years, 1999–2010.

a seroprevalence survey in New York after the 1999 epidemic suggested that each reported case of WNND resulted from an average of 140 infections [3]. This ratio was later used to estimate a cumulative infection incidence of 1 655 080 up to 2006 in the USA [8]. However, this cumulative incidence estimate was subject to considerable uncertainty given that the 140:1 ratio of infection to WNND was based on a seroprevalence estimate (2·6%) whose confidence limits spanned more than threefold (1·2–4·1%) [3]. In fact, data derived from blood donor screening suggested that there may be as many as 256–353 infections for each reported WNND case [9]. More recently, data from a serosurvey of blood donors and WNND reporting from an entire state indicated that 213–286 infections are necessary to result in a case of WNND [10]. This last study was of sufficient scope to estimate age- and gender-specific infection-to-WNND ratios; however, the ratio in children could not be ascertained since infection data were derived from blood donors. The risk of WNND following infection was estimated as more than 20 times higher in men aged ⩾65 years than women aged 16–24 years, a finding consistent with national WNND surveillance data [8]. Thus, population age and gender structure is an important consideration when computing national WNV infection estimates.

In order to estimate the number of WNV infections in adults in the USA by state to the end of 2010, taking into account the substantial variation in risk in age and gender groups, we multiplied the age- and gender-stratified number of WNND cases with onset up to the end of 2010 (reported through the ArboNET surveillance system) by the recently derived, corresponding estimated infection-to-WNND ratios [10]. Cumulative incidence (percent of population previously infected) was then calculated by dividing these numbers by the corresponding state population (US Census Bureau, 2010). ArboNET was missing age and/or gender data for 79 of the 12 823 WNND cases reported to the end of 2010. For the above calculations, those cases were assigned to the various age and gender strata proportionally based on the cases' state's percentage of WNND cases in each stratum. Variance estimates for the total number of previously infected individuals for each state were also computed by accounting for the stratification by age and gender. The estimated total number of infections (variance estimates) for the whole of USA was computed by summing the state-specific totals (variances), and a Wald 95% confidence interval (CI) was computed using these. Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., USA), Epi Info (CDC, USA), and R version 2.11.1 (www.r-project.org). R was also used to produce the estimated cumulative incidence map (Fig. 1).

State-specific cumulative infection incidence estimates indicated that the central plains states had the highest cumulative incidence, with South Dakota (13·4%), Wyoming (8·2%), North Dakota (7·5%),

Table 1. *Reported cases of West Nile virus (WNV) neuroinvasive disease, estimated number of WNV infections, and estimated cumulative incidence of WNV infection in adults aged ≥ 16 years, by state, 1999–2010, USA*

State	Total WNND cases*	Estimated WNV infections†	Total population‡	Cumulative incidence (%)	95% CI
South Dakota	321	84 920	634 183	13·3	11·9–14·9
Wyoming	142	36 195	443 141	8·2	7·2–9·1
North Dakota	187	40 472	539 946	7·5	6·7–8·03
Nebraska	440	104 677	1 417 810	7·4	6·6–8·2
Colorado	963	235 512	3 937 831	6·0	5·3–6·6
Mississippi	445	100 001	2 299 852	4·4	3·9–4·8
Louisiana	659	150 230	3 544 274	4·2	3·8–4·7
Montana	132	28 785	792 520	3·6	3·2–4·0
Idaho	157	35 426	1 184 858	3·0	2·7–3·3
Arizona	609	134 614	4 944 481	2·7	2·4–3·0
New Mexico	196	43 549	1 600 398	2·7	2·4–3·0
Kansas	206	46 952	2 206 600	2·1	1·9–2·3
Illinois	991	201 223	10 072 849	2·0	1·8–2·2
Michigan	723	144 033	7 832 236	1·8	1·6–2·0
Iowa	176	41 604	2 402 200	1·7	1·5–1·9
Texas	1458	320 993	19 035 255	1·7	1·5–1·9
Utah	113	32 849	1 978 979	1·7	1·5–1·9
Missouri	335	68 182	4 730 501	1·4	1·3–1·6
Oklahoma	197	39 584	2 924 289	1·4	1·2–1·5
Arkansas	135	28 911	2 284 744	1·3	1·1–1·4
District of Columbia	32	6261	512 575	1·2	1·1–1·4
Indiana	263	57 996	5 061 394	1·2	1·0–1·3
Ohio	504	93 903	9 133 831	1·0	0·9–1·2
Minnesota	174	40 424	4 168 319	1·0	0·9–1·1
California	1272	275 083	29 079 048	0·9	0·9–1·0
Nevada	93	17 831	2 109 730	0·8	0·8–0·9
Maryland	135	25 500	4 584 109	0·6	0·5–0·6
Pennsylvania	255	53 402	10 260 299	0·5	0·5–0·6
Alabama	118	19 360	3 781 800	0·5	0·5–0·6
New York	438	74 262	15 588 804	0·5	0·4–0·5
Tennessee	136	22 690	5 022 781	0·4	0·4–0·5
Connecticut	56	11 673	2 859 207	0·4	0·4–0·5
Kentucky	86	13 606	3 432 660	0·4	0·3–0·5
Georgia	124	24 731	7 478 195	0·3	0·3–0·4
Delaware	13	1940	716 853	0·3	0·2–0·3
Wisconsin	69	12 013	4 506 907	0·3	0·2–0·3
New Jersey	100	15 737	6 976 489	0·2	0·2–0·3
Florida	162	32 307	15 283 266	0·2	0·2–0·2
Massachusetts	49	8380	5 303 787	0·2	0·1–0·2
Rhode Island	8	1289	857 232	0·2	0·1–0·2
Virginia	50	7736	6 362 861	0·1	0·1–0·1
South Carolina	17	4290	3 669 965	0·1	0·1–0·1
New Hampshire	3	1116	1 066 277	0·1	0·1–0·1
Oregon	18	3179	3 064 689	0·1	0·1–0·1
North Carolina	28	7791	7 510 570	0·1	0·1–0·1
Washington	29	4850	5 327 767	0·1	0·1–0·1
West Virginia	6	969	1 511 356	0·1	0·1–0·1
Total	12 823	2 757 029	240 037 748	1·1	1·1–1·2

* West Nile neuroinvasive disease (WNND) cases reported to CDC through ArboNET; Alaska, Maine, Vermont and Hawaii reported no cases up to 2010.
† Product of WNND cases by age and gender reported in state and corresponding ratios of WNV infections per WNND case reported by Carson *et al.* [10].
‡ US Census Bureau data for 2010, persons aged ≥ 16 years.

Nebraska (7·4%), and Colorado (6·0%) leading in incidence (Fig. 1, Table 1). An estimated 2 757 029 (95% CI 2 688 327–2 825 730) persons aged ⩾16 years were infected with WNV by the end of 2010 in the USA.

Our study estimated that almost 2·8 million adults in the USA had been infected with WNV by 2010. Estimates obtained from serological surveys of the risk of WNV infection in children compared to adults vary [3, 6]; however, if similar infection rates are assumed in children aged <16 years as in persons aged 16–24 years, the estimated number of infections in all persons in the USA would be closer to 3·2 million. Assuming that about 26% of persons contracting WNV will develop clinical disease by the virus [2], an estimated 780 000 persons in the USA have become ill by the end of 2010. A recent study estimated acute care medical costs of US$46 530 for each case of WNND and US$302 for WNF [11]. Applying these figures to the 12 823 reported cases of WNND and the estimated 780 000 cases of WNF yields an estimate of the total acute care medical cost of about US$832 million.

The reasons for the geographical pattern in WNV infection incidence are probably complex and are not well understood. The extensive acreage of irrigated farmland in the central plains and some western states may explain the high incidences observed in those locations [12–14]. Irrigated farmland provides excellent habitat for *Culex tarsalis*, an efficient vector for WNV transmission [15, 16]. Other factors associated with WNV incidence in other areas include surface water and wetlands [17–19]; avian density, diversity, and abundance [20–22]; and human density, urbanization, and housing [20, 22–24].

Because not all patients with WNND are recognized and reported to ArboNET [4, 5], the actual number of WNND cases was probably higher than the reported number used in our calculations. Thus, the actual number of infections may be higher than that estimated in this study. Although all states use ArboNET's standardized reporting system, completeness of recognition and reporting of cases may vary among states. In addition, uncertainties regarding the age- and gender-specific infection-to-WNND ratios [10] used in our calculations could have resulted in an over- or underestimate of the actual number of infections. Another limitation is that our study spans 12 years, and 2010 census data were used in the extrapolation to derive state-specific and national infection rates; however, our incidence estimates were

similar when using census estimates for 2005 (data not presented).

In conclusion, our data indicate that over 3 million people have become infected with WNV in the USA by the end of 2010, almost twice the number estimated based on prior non-stratified estimates up to 2006 [8]. Since 2003, the US blood supply has been screened for WNV. Had this not been done, the 2·8 million infected adults would have represented a transfusion safety risk during their acute infection since most are asymptomatic or mildly symptomatic. It is important to note that despite the many people infected so far, over 98% of the US population remains at risk of infection, and hence efforts to prevent infection through vector control and personal protection measures remain important. Our findings indicating high infection incidences in people living in central midwestern states stress the particular importance of prevention measures during the summer WNV transmission season in that region.

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DECLARATION OF INTEREST

None.

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