

The macroepidemiology of influenza vaccination in 56 countries, 1997–2003

The Macroepidemiology of Influenza Vaccination (MIV) Study Group^{1,2}

Received 8 April 2005; received in revised form 9 June 2005; accepted 17 June 2005
Available online 5 July 2005

Abstract

The WHO Global Agenda on Influenza calls for measuring the progress of national influenza vaccination programs. In response, the Macroepidemiology of Influenza Vaccination (MIV) Study Group has gathered information on influenza vaccination in 56 countries. During the period 1997–2003, influenza vaccine distribution increased considerably in almost all countries. In 2003, the countries with the highest levels of vaccination (doses distributed/1000 population) were Canada (344), the Republic of Korea (311), the United States (286) and Japan (230). Most countries recommended influenza vaccination for elderly persons and those with high-risk medical conditions, including immunocompromise. Fewer countries provided public reimbursement for vaccination through national or social health insurance. Higher levels of vaccination were not closely related to higher levels of economic development, but in many instances public reimbursement for vaccination seemed to be associated with greater vaccine use. From 1994 to 2003, the global use of influenza vaccines increased more than two-fold. In 2003, the 56 MIV Study Group countries accounted for approximately 95% of the 292 million doses of influenza vaccine distributed worldwide, and 62% of these doses were distributed within nine vaccine-producing countries in North America, Western Europe, Japan and Australia. However, influenza vaccination was increasing rapidly in many non vaccine-producing countries, and this change has important implications for pandemic vaccination.

© 2005 Elsevier Ltd. All rights reserved.

Keywords: Influenza vaccination; Vaccination recommendations; Vaccination reimbursement

1. Introduction

In the early 1990s, independent investigators in several countries began gathering information on the comparative use of influenza vaccine in their countries. In 1996, the European Scientific Working Group on Influenza (ESWI) assumed responsibility for this project. The work of both groups has led to four publications that have provided the foundation for understanding the macroepidemiology of influenza vaccination throughout the world [1–4].

The term ‘macroepidemiology’ of influenza vaccination refers to the comparative use of influenza vaccine between different countries or regions, states or provinces within coun-

tries. It also describes other features such as vaccination recommendations or policies for vaccination reimbursement. In contrast, the term ‘microepidemiology’ of influenza vaccination refers to the patterns of vaccine use within smaller institutions such as hospitals or between different physician groups. Specific surveys of vaccination coverage can be either ‘macro’ or ‘micro’ depending on the populations studied.

The World Health Organization’s (WHO) Global Agenda on Influenza calls for implementing methods for measuring the progress of national influenza vaccination programs [5]. For many years, influenza vaccination has been a well-established feature of healthcare programs in almost all developed countries. In recent years, however, it has become more common in many rapidly developing countries [4]. A recent report by the Influenza Vaccine Supply (IVS) International Task Force documented the global distribution of influenza vaccine for the period 2000–2003 [6]. Vaccine distribution

¹ See Acknowledgements for a list of the co-authors of this report.

² David S. Fedson, Coordinator, MIV Study Group, 57, chemin du Lavoir, 01630 Sergy Haut France, E-mail address: dfedson@wanadoo.fr.

levels were reported for all six WHO regions, but country-specific information was available for relatively few countries.

Because influenza vaccination is increasing throughout the world, a global rather than regional (i.e., ESWI) process for evaluating vaccine use has become necessary. For this reason, a group of investigators known as the Macroepidemiology of Influenza Vaccination (MIV) Study Group has been recruited. This report summarizes the findings for 56 countries. It documents vaccine distribution for the period 1997–2003 and vaccination recommendations and public reimbursement in 2003.

2. Methods

For 54 of the 56 countries, investigators were recruited to be members of the MIV Study Group. They were drawn from academic institutions or government health departments and laboratories. None was an employee of a vaccine company, although several were contacted at the suggestion of local or regional vaccine company personnel. Each MIV Study Group investigator was sent an e-mail questionnaire that asked for information on the number of doses of influenza vaccine distributed in his or her country for the calendar years 1997–2003. The information was obtained either from national regulatory authorities or from all vaccine companies active in the country. The questionnaire also asked for information on national recommendations for influenza vaccination (2003) and policies for public reimbursement for vaccination by national or social health insurance (2003). For Hong Kong and Israel, no investigators could be recruited, so information on vaccine distribution, recommendations and public reimbursement was obtained from vaccine companies.

For each country, influenza vaccine distribution was expressed as the number of doses distributed/1000 total population each year. Population data were obtained from the U.S. Bureau of the Census [7]. In earlier studies [2–4], vaccine distribution rates were calculated using population data obtained from a 1996 WHO publication [8]. When rates for the 56 countries were calculated for the years 1997–2000 using the two population databases, they differed by 0–2 doses per 1000 population in virtually all instances (data not shown).

For 55 of the 56 countries (excluding Taiwan), economic data on Gross National Income (GNI) per capita, adjusted for purchasing power parity, were obtained from the World Bank [9]. In 2003, the term GNI per capita replaced the earlier term Gross Domestic Product per capita.

3. Results

3.1. Vaccine distribution

The distribution of influenza vaccine in the 56 countries is shown in Table 1. In almost all countries that were using

vaccine in 1997, rates of use had increased by 2003. This is better seen in Fig. 1 in which rates in 1997 and 2003 are compared, ranked from high to low in 2003. With the exception of a few countries, rates of vaccine use in 2003 were considerably higher than they were in 1997. Nonetheless, several countries (Estonia, Israel, the Russian Federation, Argentina, Brazil, Egypt and South Africa) showed higher rates in 2000 than in the years that followed.

3.2. Vaccination recommendations

Table 2 shows recommendations for influenza vaccination in 2003. Also shown are the recommendations issued by WHO in 2000 [10]. Virtually all countries recommended vaccinating elderly people above a certain age, usually 65 years. However, 14 countries had lower age cut-offs and in four (Israel, the Kyrgyz Republic, the United States and the Republic of Korea) the age cut-off was 50 years. Similarly, almost all countries recommended vaccinating people with high-risk medical conditions (cardiopulmonary diseases, diabetes mellitus and renal disease) and most recommended vaccinating those with conditions associated with immunocompromise, including HIV/AIDS. In 33 countries there were recommendations to vaccinate children on long-term aspirin treatment, but only 14 countries recommended vaccinating pregnant women. Among other target groups, 40 countries recommended vaccinating nursing home residents, 43 healthcare workers and 24 household contacts of high-risk individuals.

3.3. Vaccination reimbursement

Many countries provided public reimbursement for vaccination of recommended target groups through either national or social health insurance (Table 2). However, in several countries, public reimbursement was partial, covering some but not all of the target populations. In Western Europe, only Austria and Iceland lacked some form of public reimbursement and Austria had relatively low vaccine distribution rates. In the 20 countries of Central and Eastern Europe, only 7 countries had either full or partial public reimbursement, and 6 of them ranked among the top 9 countries in vaccine distribution in this region (Table 2). Full or partial public reimbursement was common in the Americas, but less so in the Western Pacific. These two regions included the four countries with the highest rates of vaccine distribution (Canada, the Republic of Korea, the United States and Japan; Table 1 and Fig. 1). Interestingly, only Canada provided full public reimbursement (through provincial health insurance programs), whereas the Republic of Korea had no national program for public reimbursement.

The extent of influenza vaccine use in each country did not seem to depend on its level of economic development, as indicated by its GNI per capita (Fig. 2). However, between countries with similar levels of economic development, the availability of public reimbursement often seemed important.

Table 1
Annual number of doses of influenza vaccine distributed/1000 total population

Region/Country	1997	1998	1999	2000	2001	2002	2003
Western Europe							
Austria	77	85	107	118	121	106	127
Belgium	136	162	165	171	184	195	177
Denmark	82	103	107	111	108	113	133
Finland	144	122	114	99	102	145	136
France	158	151	145	163	168	168	171
Germany	104	131	173	180	163	181	210
Greece	62	88	90	110	120	148	165
Iceland	134	173	161	172	174	170	181
Ireland	84	85	86	84	78	136	148
Italy	157	127	138	143	185	170	206
Netherlands	158	158	177	181	182	187	191
Norway	98	94	105	87	89	89	102
Portugal	105	98	125	124	127	129	145
Spain	172	165	167	188	169	203	212
Sweden	73	83	78	92	108	120	127
Switzerland	71	97	123	137	149	154	170
United Kingdom	124	130	138	176	193	186	200
Central and Eastern Europe							
Albania	0	0	0	<1	1	2	2
Bulgaria	22	19	28	34	49	43	46
Croatia	36	42	49	82	92	114	130
Czech Republic	21	35	35	40	49	54	73
Estonia	26	37	42	72	35	33	40
Georgia	0	0	0	1	1	1	2
Hungary	69	97	22	126	136	133	135
Israel	n.d.	n.d.	111	160	143	127	144
Kyrgyz Republic	0	0	0	0	<1	<1	1
Latvia	15	25	27	32	51	56	65
Lithuania	22	40	22	17	37	45	53
Moldova	0	0	2	0	0	0	2
Poland	22	27	42	73	99	88	79
Romania	11	23	24	38	45	50	67
Russian Federation	37	48	70	126	145	136	99
Slovak Republic	32	34	39	59	85	95	98
Slovenia	53	54	67	87	110	92	99
Turkey	7	10	11	15	15	16	19
Ukraine	<1	<1	3	8	17	11	18
Uzbekistan	0	0	0	4	4	2	6
North America							
Canada	160	165	190	390	295	328	344
Mexico	1	1	4	9	15	22	29
United States	281	231	270	249	273	289	286
Central and South America							
Argentina	64	76	80	101	83	82	85
Brazil	4	15	75	81	79	76	87
Chile	62	68	93	118	103	127	126
Costa Rica	n.d.	n.d.	12	14	12	18	49
Uruguay	66	80	94	97	109	106	105
Western Pacific							
Australia	125	160	169	183	192	204	214
Hong Kong SAR	n.d.	n.d.	25	28	31	32	191
Japan	10	22	54	99	137	164	230
New Zealand	108	115	142	171	163	171	173
Republic of Korea	87	87	175	171	231	218	311
Singapore	<3	<3	<3	<3	3	7	90
Taiwan	n.d.	14	30	47	83	113	145
Southeast Asia							
Thailand	<1	<1	<1	1	1	<1	1
Eastern Mediterranean and Africa							
Egypt	1	1	28	20	1	1	1
Jordan	3	3	6	5	9	8	9
South Africa	13	17	40	55	41	34	25

n.d. indicates no data were available.

Table 2
Influenza vaccination recommendations and reimbursement and vaccine distribution in 56 countries in 2003

Countries	Age cut-off (year)	High risk conditions, ≥6 months							Other target groups			Public reimbursement	Vaccine doses/1000
		Cardio-pulmonary diseases	Diabetes mellitus	Renal diseases	Immunologic disorders	HIV/AIDS	Long-term aspirin for children	Pregnant women	Nursing home residents	Healthcare workers	Household contacts		
WHO	–	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	Yes	–	–
Western Europe													
Austria	60	Yes	Yes	Yes	Yes	– ^a	–	–	Yes	Yes	Yes	–	127
Belgium	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	(Yes) ^b	177
Denmark	65	Yes	Yes	–	Yes	–	–	–	Yes	–	–	(Yes)	133
Finland	65	Yes	Yes	Yes	Yes	–	Yes	–	Yes	–	–	Yes	136
France	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	–	Yes	171
Germany	60	Yes	Yes	Yes	Yes	Yes	–	–	Yes	Yes	Yes	Yes	210
Greece	65	Yes	Yes	Yes	Yes	Yes	Yes	–	–	Yes	–	Yes	165
Iceland	60	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	–	181
Ireland	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	–	Yes	148
Italy	65	Yes	Yes	Yes	Yes	–	Yes	–	Yes	Yes	Yes	Yes	206
Netherlands	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	–	–	Yes	191
Norway	65	Yes	–	–	Yes	–	–	–	Yes	Yes	–	(Yes)	102
Portugal	65	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	Yes	Yes	(Yes)	145
Spain	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	Yes	212
Sweden	65	Yes	(Yes)	–	Yes	Yes	–	–	–	–	–	(Yes)	127
Switzerland	65	Yes	Yes	Yes	Yes	Yes	–	–	Yes	Yes	Yes	Yes	170
United Kingdom	65	Yes	Yes	Yes	Yes	Yes	–	–	Yes	Yes	–	Yes	200
Central and Eastern Europe													
Albania	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	2
Bulgaria	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	–	46
Croatia	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	Yes	130
Czech Republic	–	Yes	Yes	Yes	Yes	–	–	–	Yes	Yes	–	Yes	73
Estonia	–	–	–	–	–	–	–	–	–	–	–	–	40
Georgia	–	–	–	–	–	–	–	–	–	Yes	–	–	2
Hungary	60	Yes	Yes	Yes	Yes	–	Yes	–	–	Yes	–	–	135
Israel	50	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	144
Kyrgyz Republic	50	Yes	–	–	Yes	–	Yes	–	–	–	–	–	1
Latvia	60	Yes	Yes	Yes	Yes	Yes	–	–	–	Yes	–	–	65
Lithuania	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	53
Moldova	60	Yes	Yes	Yes	Yes	Yes	Yes	–	–	Yes	–	–	2
Poland	–	Yes	Yes	Yes	Yes	Yes	–	–	Yes	Yes	–	–	79
Romania	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	(Yes)	67
Russian Federation	65	Yes	Yes	Yes	–	–	–	–	Yes	Yes	Yes	–	99
Slovak Republic	65	Yes	Yes	Yes	Yes	–	–	–	Yes	Yes	Yes	Yes	98
Slovenia	65	Yes	Yes	Yes	Yes	Yes	Yes	–	–	–	–	(Yes)	99
Turkey	–	–	–	–	–	–	–	–	–	–	–	–	19
Ukraine	60	–	–	–	–	–	–	–	–	Yes	–	(Yes)	18
Uzbekistan	65	–	–	–	–	–	–	–	Yes	Yes	–	–	6

Table 2 (Continued)

Countries	Age cut-off (year)	High risk conditions, ≥6 months							Other target groups			Public reimbursement	Vaccine doses/1000
		Cardio-pulmonary diseases	Diabetes mellitus	Renal diseases	Immunologic disorders	HIV/AIDS	Long-term aspirin for children	Pregnant women	Nursing home residents	Healthcare workers	Household contacts		
North America													
Canada	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	Yes	344
Mexico	60	–	–	–	–	–	–	–	–	–	–	(Yes)	29
United States	50	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	(Yes)	286
Central and South America													
Argentina	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	(Yes)	85
Brazil	60	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	87
Chile	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	–	(Yes)	126
Costa Rica	65	Yes	Yes	–	Yes	Yes	–	–	–	–	–	–	49
Uruguay	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	–	Yes	105
Western Pacific													
Australia	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	214
Hong Kong SAR	65	Yes	Yes	Yes	Yes	–	Yes	–	Yes	Yes	–	(Yes)	191
Japan	65	Yes	–	Yes	Yes	Yes	–	–	Yes	–	–	(Yes)	230
New Zealand	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	173
Republic of Korea	50	Yes	Yes	Yes	Yes	–	Yes	Yes	Yes	Yes	–	–	311
Singapore	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	90
Taiwan	65	Yes	Yes	Yes	Yes	Yes	Yes	–	Yes	Yes	–	(Yes)	145
Southeast Asia													
Thailand	–	–	–	–	–	–	–	–	–	–	–	–	1
Eastern Mediterranean and Africa													
Egypt	60	Yes	Yes	Yes	–	–	–	–	Yes	Yes	Yes	–	1
Jordan	–	–	–	–	–	–	–	–	–	–	–	–	9
South Africa	65	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	25

^a Indicates no recommendation or no public reimbursement.

^b Indicates public reimbursement for some but not all recommended groups.

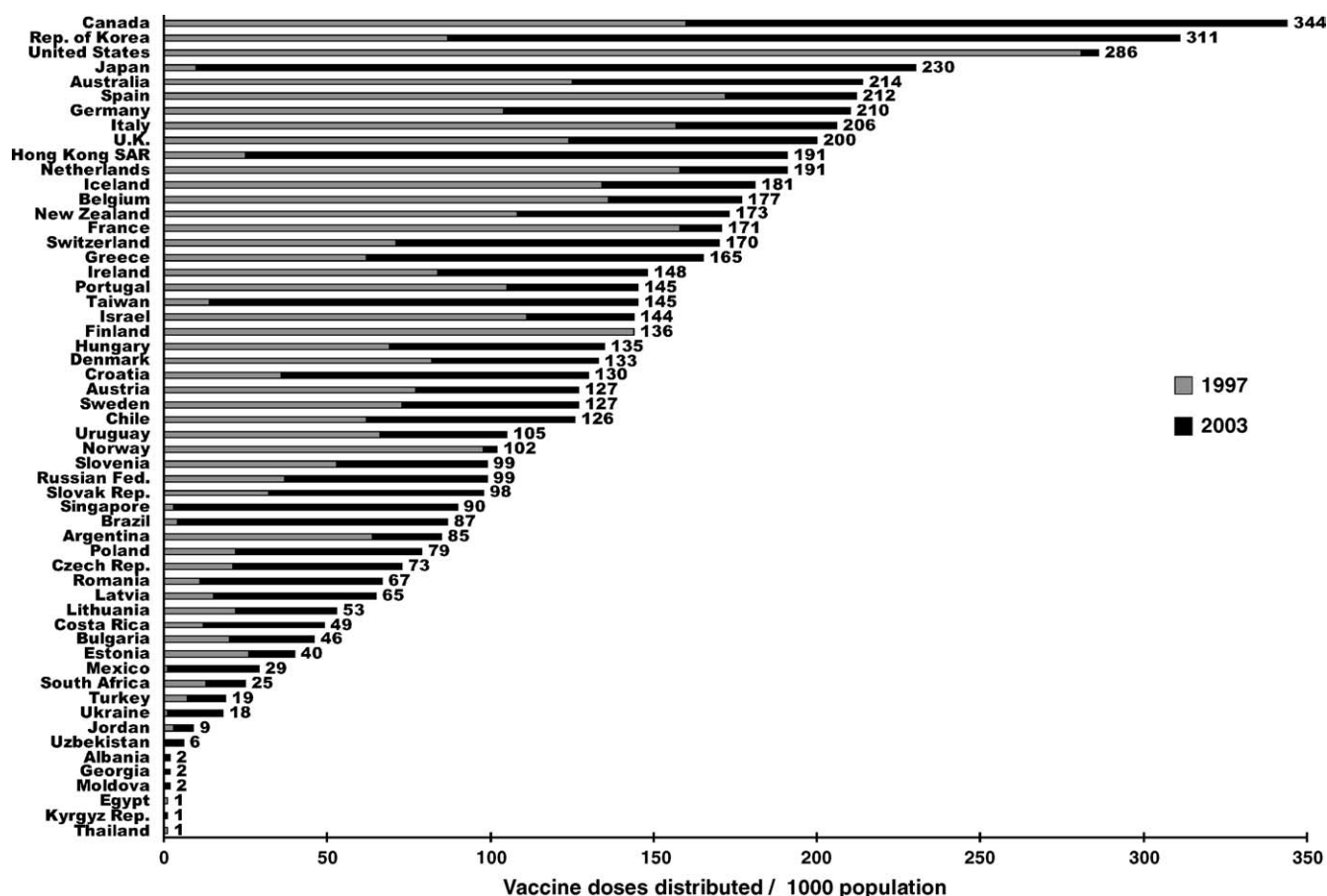


Fig. 1. Influenza vaccine distribution in 56 countries, 1997 and 2003. Rates of vaccine distribution for each country were taken from Table 1.

For example, in 2003 Croatia and Latvia had similar GNIs per capita (\$10,710 and \$10,310, respectively), but the rate of vaccine distribution in Croatia (with public reimbursement) was twice that of Latvia (no public reimbursement). The same could be seen with the Slovak Republic (GNI \$13,420 per capita, public reimbursement) and Estonia (GNI \$12,400 per capita, no public reimbursement).

3.4. The MIV Study Group findings and the global use of influenza vaccine in 2003

Table 3 documents the extent to which the MIV Study Group findings for 2003 captured the global distribution of influenza vaccine as reported by the IVS International Task Force [6]. For individual countries or regions from which data were obtained by both reporting systems (Western Europe, Canada, the United States, Australia, Japan and New Zealand), the numbers of doses reported by MIV Study Group investigators tended to be 0–4% lower than the numbers reported by the IVS International Task Force. Overall, the MIV Study Group documented >95% of the doses of vaccine distributed in Europe and the Americas and almost 90% of the doses distributed in the Western Pacific and Africa. Reports for Southeast Asia and the Eastern Mediterranean

were much less complete, but these two regions accounted for less than 1% of global vaccine distribution as reported by the IVS International Task Force.

Given the slight degree of underreporting by the MIV Study Group (or over-reporting by the IVS International Task Force), the 56 countries represented in the MIV Study Group accounted for approximately 95% of the global distribution of influenza vaccine in 2003. Nine MIV Study Group countries (Australia, Canada, France, Germany, Italy, Japan, the Netherlands, the United Kingdom and the United States) produced >95% of all doses of influenza vaccine distributed worldwide [6]. These nine countries used 182.3 million (62.4%) of the global total of 292 million doses of influenza vaccine reported by the IVS International Task Force [6].

3.5. The global evolution of influenza vaccination, 1994–2003

Information gathered for previous reports [2,3,6] and for this report provided a clear picture of the global evolution of influenza vaccination during the period 1994–2003. During this 10-year period, vaccine distribution increased more than two-fold (Fig. 3). Of the 134.9 million doses distributed in 1994, 74.3 million (55.1%) were distributed in Canada and

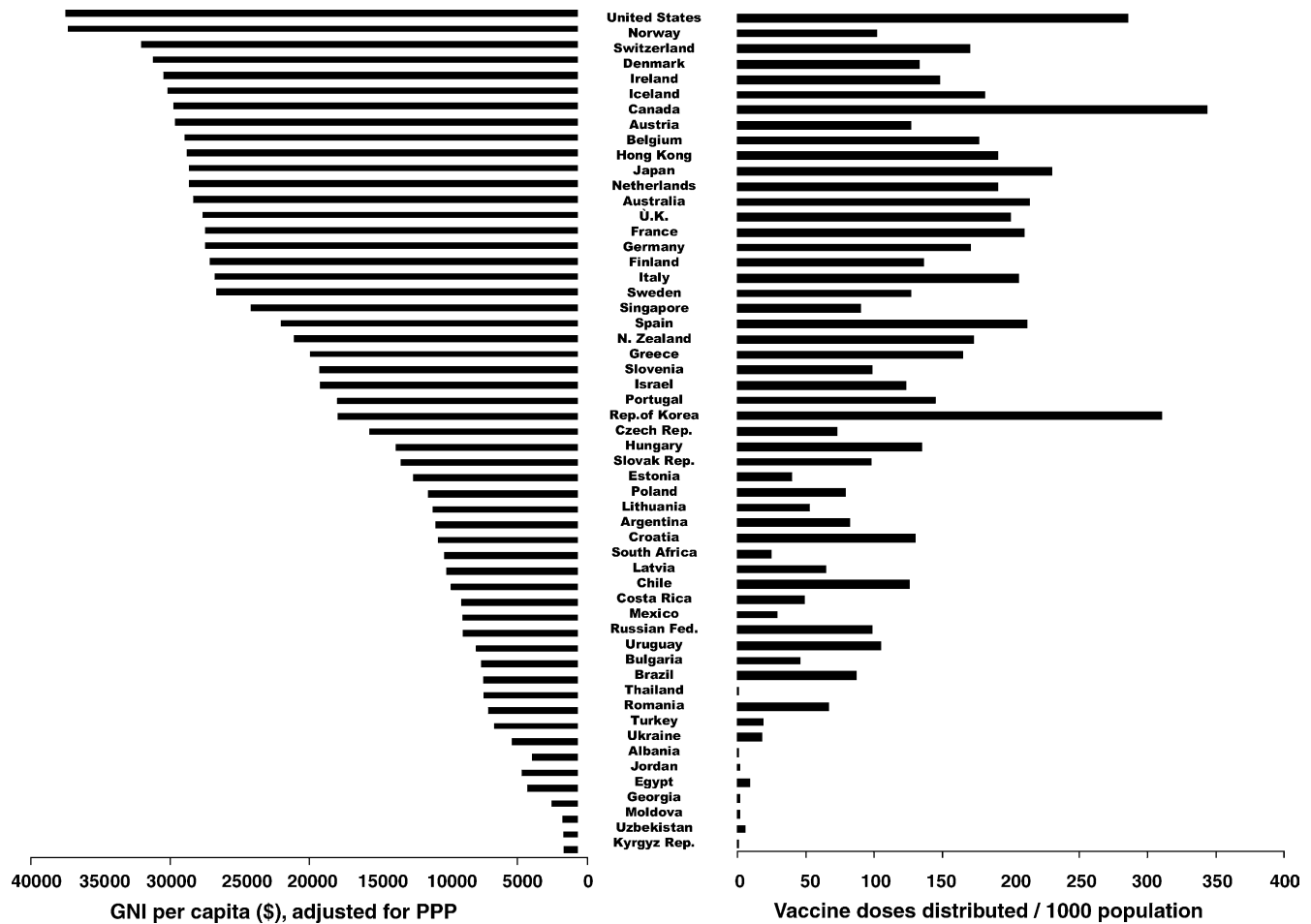


Fig. 2. Economic development and influenza vaccine distribution, 2003. Data on Gross National Income (GNI) per capita, adjusted for purchasing power parity (PPP), were taken from reference 9. Rates of vaccine distribution were taken from Table 1.

Table 3

Documenting the distribution of influenza vaccine in 2003: comparing the findings of the MIV Study Group and the IVS International Task Force

WHO region	Doses of influenza vaccine distributed (000s)		
	MIV Study Group	IVS International Task Force ^a	% documented ^b
Europe	100, 610	102, 891	97.8
Western Europe	74, 236	76, 523	97.0
Central and Eastern Europe	26, 374	26, 368	100.0
Americas	118, 835	123, 578	96.2
Canada	11, 081	11, 100	99.8
United States	83, 061	84, 913	97.8
Mexico, Central and South America	24, 693	27, 565	89.6
Western Pacific	54, 259	61, 189	88.7
Australia	4, 220	4, 357	96.9
Japan	29, 253	29, 253	100.0
New Zealand	683	715	95.6
Other countries	20, 103	26, 864	74.8
Southeast Asia	82	253	32.5
Eastern Mediterranean	139	1540	9.1
Africa	1080	1230	87.8
Total	275, 006	291, 979	94.2

^a Data obtained from reference 6.

^b Percentage of IVS International Task Force doses documented by the MIV Study Group.

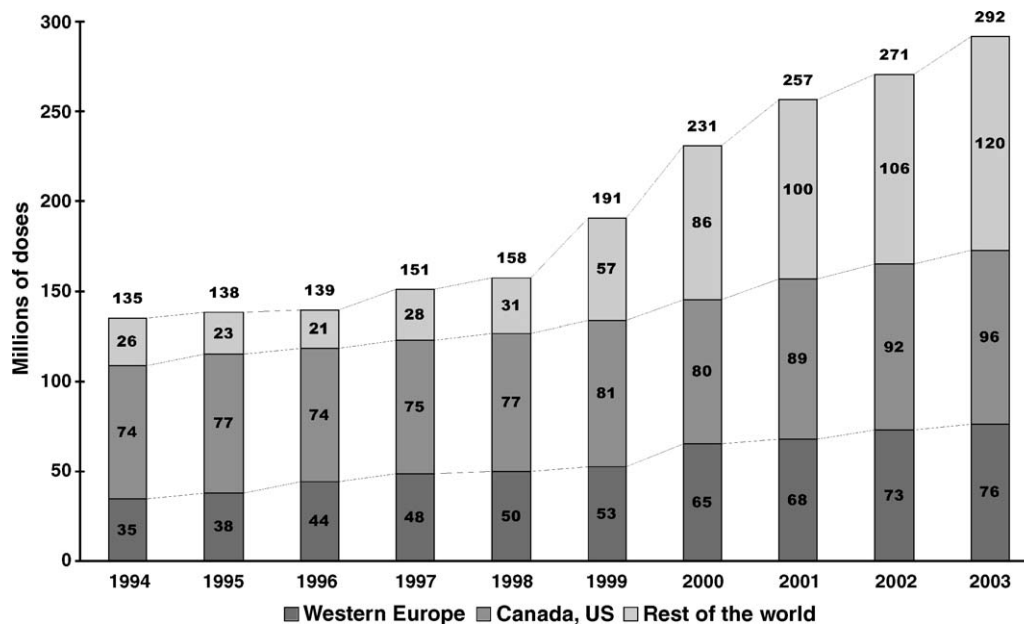


Fig. 3. Global evolution of influenza vaccination, 1994–2003. Data for 1994–1999 were provided by David S. Fedson (unpublished observations). Data for 2000–2004 were taken from [6].

in the United States, 34.6 million (25.6%) in Western Europe and only 26.0 million (19.3%) in the rest of the world (DS Fedson, unpublished observations). Compared with levels in 1994, the increase in vaccine distribution in 2003 (using both MIV Study Group and IVS International Task Force data; see Table 3) was approximately 29% in Canada and the United States, approximately 121% in Western Europe and approximately 360% in the rest of the world. Most of the increase in the rest of the world occurred in the Republic of Korea, Japan and several countries in South America and Central Europe. Of the 292 million doses of vaccine distributed worldwide in 2003, the rest of the world accounted for approximately 41–42% of all doses distributed.

4. Discussion

4.1. Vaccine distribution

The MIV Study Group followed the approach of previous reports [1–4] in using annual rates of influenza vaccine distribution within countries to compare influenza vaccination practices between countries in a given year and to document changing vaccination practices within individual countries over time. Vaccine distribution rates, however, provide no indication of vaccine coverage levels within defined target groups nor can they account for vaccine use in non-targeted populations or vaccine wastage. Nonetheless, despite their imperfections, the annual rates of vaccine distribution provide a clear picture of the international evolution of influenza vaccination.

The most important findings of this survey are that influenza vaccination grew steadily over the past decade and

that this growth was most striking in countries outside North America and Western Europe. By 2003, rates of vaccine use had increased in almost all countries, regardless of the levels of use in 1997 (Fig. 1). Moreover, the increase in vaccination did not seem to depend on a country's level of economic development; many countries with relatively low GNIs per capita had higher levels of vaccine use than were seen in other countries that were more economically developed (Fig. 2). Public reimbursement for vaccination often appeared to be an important contributor to higher levels of vaccine use, but there were frequent exceptions.

4.2. Vaccination recommendations

In 2003, among all 56 MIV Study Group countries, only seven did not recommend influenza vaccination for elderly people above a certain age. Eight countries did not recommend vaccination for persons with cardiopulmonary conditions, 11 excluded those with diabetes mellitus and 13 excluded those with renal diseases. All but ten countries recommended vaccinating people with immunocompromise and in most instances they included patients with HIV/AIDS, a group for whom influenza vaccination has been shown to be safe and well tolerated [11]. Whether patients with HIV/AIDS are at increased risk of influenza-related complications is uncertain; in the United States, rates of influenza-related hospitalizations for AIDS patients were shown to be comparable to those of other high-risk groups and they declined noticeably following the introduction of highly active anti-retroviral therapy [12].

Fewer (33) countries recommended influenza vaccination for children on long-term aspirin treatment. Children with influenza who are treated with aspirin are at increased risk of

developing Reye's syndrome [11,13]. Influenza vaccination was recommended for pregnant women in only 14 countries. In most, it was limited to those in the second and third trimesters, a period when influenza-related hospitalizations for cardiopulmonary conditions, especially asthma, increase [14]. However, serious influenza-related complications in mothers and their newborn infants are unusual [15]. The effectiveness of influenza vaccination in reducing the occurrence of hospitalizations and outpatient visits in pregnant women and their infants has not yet been demonstrated [16], in large measure because the recommendation has not been widely implemented.

Influenza vaccination is effective in reducing influenza-related complications in nursing home residents [11,17], and most countries recommended vaccinating this target group. Recommendations to vaccinate healthcare workers were also common, although vaccination rates in this group are widely regarded as inadequate. Vaccination of household contacts of high-risk individuals was recommended less frequently. The effectiveness of this recommendation has not been well documented, although vaccination of school-age children in Japan reduced winter season mortality, most likely among grandparents living in the same households as their grandchildren [18].

In a few countries, publicly reimbursed influenza vaccination was provided for special groups; for example, younger groups of indigenous people (Australia), poultry workers involved in culling chickens infected with avian influenza virus (Taiwan and Thailand) and pilgrims to the Hajj (Jordan and Thailand).

WHO recommendations for influenza vaccination were issued in 2000 and included almost all of the conditions and target groups shown in Table 2 [10]. The MIV Study Group did not evaluate whether the WHO recommendations had led to the adoption of similar recommendations by any country. However, several countries with very low levels of vaccine distribution in 2003 (≤ 6 doses/1000 population; Albania, Egypt, the Kyrgyz Republic, Moldova, and Uzbekistan) had already adopted most if not all of the WHO recommendations.

In 2003, influenza vaccination was not recommended for healthy children in any of the MIV Study Group countries. However, preliminary reports for 2004 indicate that children 6–23 months in age were added to national recommendations in the United States [11] and in Greece, Mexico, Taiwan and Uruguay (Andreas Constantopoulos, Agustin Lara Esqueda, Shu-Fong Chen and Homero Bagnulo, unpublished observations). A future report will document the extent of childhood vaccination recommendations in all 56 MIV Study Group countries.

4.3. Vaccination reimbursement

Comparing public reimbursement policies between countries was more difficult than comparing vaccination recommendations because reimbursement policies varied widely

and different policies often applied to different regions within the same country. Often, vaccination was recommended for high-risk people of any age, but reimbursement was provided only for those above the age cut-off. Moreover, in some countries influenza vaccine was offered at no charge to high-risk people seen in public clinics, so specific reimbursement for vaccination was not necessary. Nonetheless, public reimbursement policies did not seem to be conditioned by the general level of economic well being within a country. Several countries that offered public reimbursement to most if not all of their high-risk populations had much lower GNIs per capita than other countries with higher GNIs per capita (for example, Croatia vs. Austria).

4.4. The MIV Study Group findings, the global use of influenza vaccine in 2003 and the global evolution of influenza vaccination, 1994–2003

The WHO Global Agenda on Influenza calls for an ongoing evaluation of influenza vaccine use worldwide [5]. Companies that produce influenza vaccines are generally reluctant to report the number of doses they distribute to individual countries because this information is commercially sensitive. However, the IVS International Task Force companies have provided WHO with such information for the six WHO regions. These data, together with data reported by companies in Hungary, Romania and the Russian Federation, indicated that 292 million doses were distributed in 2003 [6]. This total did not include vaccines produced in other countries, particularly China, but nonetheless it probably represented 95–99% of all doses distributed worldwide. Thus the data in the WHO report provide a denominator against which the MIV Study Group findings can be measured.

In 2003, the 56 MIV Study Group countries accounted for approximately 95% of the 292 million doses of influenza vaccine distributed throughout the world. Of these doses, 62% were distributed within nine major vaccine-producing countries that together accounted for only 11.8% of the world's population [7]. If three additional vaccine-producing countries (Hungary, Romania and the Russian Federation) are included, these 12 vaccine-producing countries accounted for 14.7% of the world's population. Vaccine companies located in seven of these countries (Australia, Canada, Hungary, Japan, Romania, the Russian Federation and the United States) exported very few doses of vaccine to other countries. Thus, almost all doses distributed to countries without vaccine companies were produced by companies located in five Western European countries. Many of the 'have not' countries are economically highly developed. Considered together, the 'have not' countries account for 85% of the world's population.

The more than two-fold increase in influenza vaccination worldwide over the 1994–2003 period reflects greater understanding of the burden of influenza disease and the effectiveness of influenza vaccination [11,19], especially in countries that previously have not used the vaccine [20–23].

Also important has been experience with SARS and concern that a new pandemic virus might emerge out of the H5N1 avian influenza outbreaks in Southeast Asia [24,25]. The global use of influenza vaccine will almost certainly continue to increase, and this means that an increasing portion of the vaccine distributed each year will be used in countries that do not produce it. This changing pattern in the distribution of influenza vaccine will have important implications for the next pandemic, for it suggests that 'have not' countries will expect but find it difficult to obtain adequate supplies of pandemic vaccines [26,27].

Acknowledgements

This report represents the collective efforts of the MIV Study Group investigators and each should be considered a co-author. The report was prepared by David S. Fedson, Coordinator of the MIV Study Group, and G.A. (Ted) van Essen. The members of the MIV Study Group are: *Western Europe*: Austria, Michael Kunze; Belgium, Rene Snacken; Denmark, Ann E. Ottosen; Finland, Olli Ruuskanen; France, Jean-Marie Cohen; Germany, Peter Wutzler; Greece, Andreas Constantopoulos; Iceland, Thorolfur Gudnason; Ireland, Lisa Domegan; Italy, Isabella Donatelli; Netherlands, G.A. (Ted) van Essen; Norway, Lars Haaheim; Portugal, Helena Rebelo de Andrade; Spain, Magda Campins and Agustin Portela; Sweden, Ake Ortqvist; Switzerland, Reto Hagmann; United Kingdom, Jane Leese and Jonathan Nguyen-Van-Tam. *Central and Eastern Europe*: Albania, Miriam Xibinaku; Bulgaria, Mira Kojouharova; Croatia, Ira Gjenero-Margan; Czech Republic, Bela Tumova and Eva Vitkova; Estonia, Natalia Kerbo; Georgia, Levan Baramidze; Hungary, Zsuzsanna Molnar; Kyrgyz Republic, Kalia Kasymbekova; Latvia, Inga Velicko and K. Velga; Lithuania, Arvydas Ambrozaitis; Moldova, Peter G. Scoferts; Poland, Lidia Brydak; Romania, Viorel Alexandrescu and Emilia Lupulescu; Russian Federation, Larisa Rudenko; Slovak Republic, Zuzana Kristufkova; Slovenia, Maja Socan; Turkey, Selim Badur; Ukraine, Anna V. Moiseeva; Uzbekistan, Dilorom Tursunova. *North America*: Canada, Theresa Tam; Mexico, Augstin Lara Esqueda; United States, Dennis O'Mara. *Central and South America*: Argentina, Vilma Savy; Brazil, Joao Toniolo-Neto; Chile, Leonardo Maggi; Costa Rica, Maritza Morena Singler; Uruguay, Homero Bagnulo. *Eastern Mediterranean and Africa*: Egypt, Mostafa Orkhan; Jordan, Ali Muhaidat; South Africa, Barry D. Schoub. *Western Pacific*: Australia, Alan Hampson; Japan, Kosaku Uchida; New Zealand, Lance Jennings; Republic of Korea, Park Seung Cheul; Singapore, Ai Ee Ling; Taiwan, Shu-Fong Chen. *Southeast Asia*: Thailand, Piyani Tharmphornpilas. Jonathan Nguyen-Van Tam is at the Health Protection Agency in the UK, but previously worked for the vaccine company Aventis Pasteur MSD.

The MIV Study Group is especially grateful for guidance provided by Cesar Mascrenas and Clemens Vlasich. Oth-

ers who provided important assistance are Guenaelle Angier, Sabine Arnoux, Gyorgy Berencsi, Christian Courtois, Florian Dashi, Hugo Dibarboure, Marja Esveld, Peter Falus, Simone Fiaccavento, Eduardo Forleo, Sandra Garcia, Philippe Ghem, Anne-Marie Graffin, Julian Jerez, Carol Joseph, Helle Konradsen, Nada Kostopoulou, Tamer Pehlivan, Guillaume Reny, Mark Simmerman, Benoit Soubeyrand and Stanka Vidmar.

The MIV Study Group welcomes comments and criticism of this report, especially of the findings reported in Table 2. The group is interested in recruiting new investigators in other countries. Anyone interested should write to the Coordinator (dfedson@wanadoo.fr).

References

- [1] Fedson DS, Leese J, Hannoun C, Sprenger MJ, Hampson AW, Bro-Jorgensen K, et al. Influenza vaccination in 18 developed countries, 1980–1992. *Vaccine* 1995;13:623–7.
- [2] Fedson DS, Hirota Y, Shin HK, Cambillard PE, Kiely J, Ambrosch F, et al. Influenza vaccination in 22 developed countries: an update to 1995. *Vaccine* 1997;15:1506–11.
- [3] Ambrosch F, Fedson DS. Influenza vaccination in 29 countries. An update to 1997. *Pharmacoeconomics* 1999;16(Suppl. 1):47–54.
- [4] van Essen GA, Palache AM, Forleo E, Fedson DS. Influenza vaccination in 2000: recommendations and vaccine use in 50 developed and rapidly developing countries. *Vaccine* 2003;21:1780–5.
- [5] World Health Organization. Adoption of the global agenda on influenza. Part II. *Wkly Epidemiol Rec* 2002;77:179–82.
- [6] World Health Organization. Global distribution of influenza vaccines, 2000–2003. *Wkly Epidemiol Rec* 2004;79:366–7.
- [7] U.S. Bureau of the Census. IDB Summary Demographic Data, updated July 17, 2003. (<http://www.census.gov/ipc/www/idbsum.html>).
- [8] World Health Organization. Demographic data for health situation assessment and projections—1996. Geneva: World Health Organization, Division of Health Situation and Trend Assessment, 1996. Table 1, pp. 1–7.
- [9] World Bank. World Development Indicators database, September 2004. (<http://www.worldbank.org/data/quickreference/quickref.html>).
- [10] World Health Organization. Influenza vaccines: recommendations for the use of inactivated influenza vaccines and other preventive measures. *Wkly Epidemiol Rec* 2000;75:281–8.
- [11] Centers for Disease Control and Prevention. Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morbid Mortal Wkly Rep* 2004;53(RR06):1–40.
- [12] Neuzil KM, Coffey CS, Mitchel Jr EF, Griffin MR. Cardiopulmonary hospitalizations during influenza season in adults and adolescents with advanced HIV infections. *J Acquir Immune Defic Syndr* 2003;34:304–7.
- [13] Belay ED, Bresee JS, Holman RC, Khan AS, Shahriari A, Schonberger LB. Reye's syndrome in the United States from 1981 through 1999. *N Engl J Med* 1999;340:1377–82.
- [14] Neuzil KM, Reed GQW, Mitchell EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol* 1998;148:1094–102.
- [15] Hartert TV, Neuzil KM, Shintani AK, Mitchell Jr EF, Snowden MS, Wood LB, et al. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. *Am J Obstet Gynecol* 2003;189:1705–12.

- [16] Black SB, Shinefield HR, France EK, Fireman BH, Platt ST, Shay D, et al. Effectiveness of influenza vaccine during pregnancy in preventing hospitalizations and outpatient visits for respiratory illness in pregnant women and their infants. *Am J Perinatol* 2004;21:333–9.
- [17] Monto AS, Hornbuckle K, Ohmit SE. Influenza vaccine effectiveness among elderly nursing home residents: a cohort study. *Am J Epidemiol* 2001;154:155–60.
- [18] Reichert TA, Sugaya N, Fedson DS, Glezen WP, Simonsen L, Tashiro M. The Japanese experience with vaccinating schoolchildren against influenza. *N Engl J Med* 2001;344:889–96.
- [19] Nicholson KG, Wood JM, Zambon M. Influenza. *Lancet* 2003;362:1733–45.
- [20] Narukawa M, Minezaki K, Okubo M, Kario K. Impact of an influenza pandemic (sic) on the mortality of congestive heart failure in older Japanese: the 1998 Japanese influenza pandemic. *J Am Geriatr Soc* 2001;49:689–90.
- [21] Yap FHY, Ho P-L, Lam K-F, Chan PKS, Cheng Y-H, Peiris JMS. Excess hospital admissions for pneumonia, chronic obstructive pulmonary disease, and heart failure during influenza seasons in Hong Kong. *J Med Virol* 2004;73:617–23.
- [22] Chen Y-H, Liou S-H, Chou C-C, Su W-L, Loh C-H, Lin S-H. Influenza and pneumococcal vaccination of the elderly in Taiwan. *Vaccine* 2004;2806–11.
- [23] Simmerman JM, Thawatsupha P, Kingnate D, Fukuda K, Chaising A, Dowell SF. Influenza in Thailand: a case study for middle income countries. *Vaccine* 2004;23:182–7.
- [24] Webby RJ, Webster RG. Are we ready for pandemic influenza? *Science* 2003;302:1519–22.
- [25] Ungchusak K, Auewarakul P, Dowell SR, Kitphati R, Auwanit W, Puthavathana P, et al. Probable person-to-person transmission of avian influenza A (H5N1). *N Engl J Med* 2005;352:333–40.
- [26] Fedson DS. Pandemic influenza and the global vaccine supply. *Clin Infect Dis* 2003;36:1552–61.
- [27] Fedson DS. Preparing for pandemic vaccination: an international policy agenda for vaccine development. *J Public Health Policy* 2005;26:4–29.