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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

GUIDANCE

PRIORITY RISK GROUPS FOR INFLUENZA VACCINATION

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Priority risk groups for influenza vaccination

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SUMMARY

At the request of the European Commission, ECDC has conducted a scientific public health review concerning influenza risk groups* and other groups that are offered immunisation against seasonal influenza in Europe. The specific objectives of this study were:

- to describe the risk groups recommended for immunisation in the EU/EEA countries, along with details of other groups for which immunisation is offered;
- to summarise the supporting evidence for the risk groups that are recommended for vaccination;
- to suggest a prioritisation of risk groups in the EU, based on transparent criteria;
- to broadly estimate the number of people in EU countries in priority risk groups; and
- to identify areas for further work, including research and development.

The descriptions of the influenza risk groups and the other groups to whom immunisation is currently offered came from a survey conducted in 2008 by the VENICE project working in conjunction with ECDC. According to the criteria developed by ECDC/VENICE, risk groups should be well-defined groups shown to be more likely to develop severe disease than others. In addition, there should be published evidence that their risk of becoming infected was reduced by immunisation. On the first criterion, the work was hampered by the fact that currently no routine surveillance is conducted in Europe for severe influenza-associated morbidity and mortality. Occupational health criteria (primarily immunising health workers) without demonstrated benefit to patients were noted but given a lower weight — with the exception of one group of workers, those caring for elderly people in residential settings where there is good evidence of this protecting patients. Finally, the degree of consensus among EU countries was noted.

The analysis of literature indicates that there are two risk groups where routine annual immunisation with seasonal influenza vaccine is justifiable on scientific and public health grounds in Europe. These are:

- older age groups, usually 65 years and older; and
- people with chronic medical conditions, particularly diseases in the following categories:
  - chronic respiratory diseases;
  - chronic cardiovascular diseases;
  - chronic metabolic disorders;
  - chronic renal and hepatic diseases;
  - persons with deficient immunity (congenital or acquired);
  - young people taking long-term salicylate therapy; and
  - persons with conditions which compromise respiratory function.

These are also the only risk groups for which there is consensus across European Union countries. The exact age definition of the elderly age group is somewhat arbitrary (above 64

* Influenza risk groups are here defined as groups of people who are more likely to experience severe disease if infected and who are also known to benefit from vaccination by reducing the risk of infection.

years, above 59 years, etc.) and a few countries already depart from the over-64-years criterion, depending on national circumstances and analyses.

Some good arguments exist for offering immunisation to two other risk groups: pregnant women and children (variously defined as 'below age two' or 'below age five'). However, for both groups there is only limited information available in Europe, both on risk and on effectiveness, and there is as of yet no European consensus. Data are insufficient for these two groups to be identified as risk groups at the EU level. As more information and data become available, these groups will have to be re-evaluated. It is especially important that data on the impact of immunisation in these groups are collected so that a consensus can be reached after further evaluations.

There are also groups for which immunisation is often offered but that are not in risk groups and for which there is no strong public health case. For example, there is considerable EU consensus that all health-care workers with patient contact should be immunised for occupational health reasons (protecting the workers). There is strong trial-based evidence that immunising those caring for elderly people in residential homes indirectly benefits the patients, protecting them against severe outcomes of influenza infection. However, it is notable that most health workers in Europe decline such offers of immunisation. There is no good evidence of benefits from offering immunisation to people sharing households with people in the two main risks groups.

Broad estimates are made as to the numbers and percentages of people who belong to the two main risk groups in EU countries. This study applied one method that suggested that EU countries currently need to immunise about 25% of their populations every year as they belong to at least one of the two major risk groups. Other national estimates have come up with similar percentages. The national range is from 19% to 28%, depending on the percentage of elderly people in the population in each country. The EU total is estimated to be around 125 million people, split two-thirds (around 84 million people who are 65 years or over) to one-third (around 41 million younger persons with chronic illness). These figures will rise inexorably over time because of aging populations and the success of modern medicine in permitting people with chronic illness to live longer productive lives.

This study recommends a number of priorities for European development and research:

- surveillance development: routine surveillance for severe manifestations of influenza in Europe (hospitalisations and death);
- routine monitoring of the effectiveness of influenza vaccination, especially in reducing the risk of severe disease and death from influenza;
- estimation of the burden of disease from influenza in pregnant women and children, and evaluation of the impact of immunising pregnant women and children of all ages in Europe;
- further investigations to demonstrate whether or not immunisation of health-care staff and household members reduces risk in vulnerable people in the two main risk groups;
- development of projects for stronger promotion of influenza immunisation among health-care workers, both for their own benefit and for that of their patients;
- specific investigations as to whether or not there are higher levels of risk of severe disease from influenza infection in HIV-infected persons in Europe and similar studies for other more common conditions such as mild asthma;

- health impact and health economic studies concerning influenza immunisation, e.g. on persons above the threshold age for immunisation, acknowledging that different countries need to set their own age thresholds;
- investigation of the impact of across-the-board immunisations to determine any indirect benefit from reducing overall levels of transmission.

1. BACKGROUND

This study follows a request from the European Commission to ECDC to provide scientific public health information and advice concerning risk groups for immunisation in Europe. ECDC conducted this study as module within a series of projects on seasonal influenza vaccination in Europe[*]. The output from this project — the ECDC Seasonal Influenza Immunisation Project (SIIP) — which ECDC and various partners (see Acknowledgements) are undertaking in 2008, will eventually result in a portfolio of publications — the SIIP Portfolio:

- a scientific and public health opinion on risk groups (this paper);
- country-specific details (EU and EEA) of immunisation policies and performance (uptake) and recent trends in vaccine use (a package of papers[†]);
- a review of ways of measuring vaccine effectiveness and of published information on effectiveness;
- an estimate of the likely impact of increasing use of immunisation on the burden of disease in the risk groups.

The current document concerns influenza immunisation risk groups. It also gathers information on other groups that are offered immunisation. This document should be considered in the larger context of the portfolio as a whole. It is an interim paper as new evidence will continue to accumulate, but this document constitutes the final version for 2008. It has undergone an ECDC internal review and a review by members of the ECDC's Advisory Forum and, through them a number of national authorities.

2. RISK GROUPS

The immunisation strategy for human seasonal influenza is aimed at protecting vulnerable individuals[‡]. Most people are considered susceptible to human seasonal and pandemic influenza virus infection, and there are various estimates of the numbers that are infected each year [1–4]. However, some are more likely to develop disease and perhaps die as a result of their infection, and ever since the first influenza vaccines were developed, the main approach has been to immunise certain 'risk groups' and other groups (for definitions see Section 4) rather than whole populations. A second reason for this strategy is the need for

[*] Throughout the document the term Europe refers to the countries in the European Union (EU) and European Economic Area (EEA).

[†] There are three documents: a detailed output from the VENICE project, a review of recent trends for selected EU countries by the Universities of Zurich and Basel, and a review of recent trends in vaccine distribution by the European Vaccine Manufacturers.

[‡] Other immunisation strategies are practised for other infections such as the 'herd immunity' approach for polio and measles where the approach is to achieve high rates of population coverage with a vaccine that gives good protection against infection not just disease. As a consequence, transmission of the virus is greatly reduced to the point where remaining susceptible individuals are much less likely to encounter the virus (measles), or the infection is actually eradicated or eliminated. This is not yet possible for influenza, but it may be possible in the future with improved vaccines and attempts at achieving population-level vaccine coverage.

influenza vaccination to be given annually, which introduces an unusual degree of expense and logistical consideration into vaccine production and delivery [5].

3. PURPOSE AND OBJECTIVES OF THIS PAPER

The purpose of this paper is to provide scientific public health information and advice concerning seasonal influenza vaccination, the risk and other groups for which vaccination could be offered in Europe. The specific objectives are:

- to describe the risk groups recommended for immunisation in the EU/EEA countries;
- to identify, describe and define further groups to whom immunisation is offered without actually belonging to a risk group;
- to summarise the evidence supporting immunisation for risk groups;
- to suggest a prioritisation of risk groups for the EU, based on transparent criteria;
- to broadly estimate the number of people in EU countries belonging to prioritised risk groups;
- to identify areas for further work.

4. WHAT IS MEANT BY RISK GROUPS?

While preparing this study, the ECDC team realised that the term 'risk groups' was used in a variety of meanings (see Appendix 1). To meet the above purposes and objectives, this paper employs an ad hoc definition of 'influenza vaccination risk groups', namely 'persons at higher than average risk of adverse outcomes should they be infected with seasonal influenza for whom vaccinating with seasonal influenza vaccination is considered effective on the basis of reducing the risk of specified adverse outcomes' (Definition E in Appendix 1). It is important to note that two factors are combine here:

- being at higher risk of ill health and death from influenza than the population as a whole; and
- evidence of influenza vaccination in reducing that risk.

Risk groups versus those who are offered immunisation

There is an important distinction between:

- the risk groups — those that are at higher risk of adverse outcomes from seasonal influenza (defined as above); and
- those that are offered or recommended for influenza vaccination without necessarily being at higher risk.

For example, groups like health-care workers that are not at a higher risk of adverse outcomes are offered vaccination in some Member States (see Appendix 2 and Section 6).

5. LIMITATIONS OF THE EVIDENCE

Although there are a number of published studies on risk groups and vaccination effectiveness (see Appendix 3), only a few of these are based on data from the European countries. While evidence was considered from other countries, especially on the identification and definition of risks groups and the effectiveness of vaccination, the lack of data on burden of severe disease due to influenza in Europe, notably in children and pregnant women, makes it difficult at this stage to recommend immunisation for these groups. While there is good laboratory surveillance and surveillance of individuals presenting to primary care services with influenza in Europe — conducted by the European Influenza Surveillance System (EISS) and the Member States' national influenza centres in cooperation with WHO's Global Influenza Surveillance Network (GISN) — there are no routine European surveillance systems recording persons with severe adverse outcomes due to influenza, i.e. hospitalisation and/or death as a consequence of severe acute respiratory infection (SARI). Similarly, there is no routine evaluation of influenza vaccine effectiveness in Europe. Therefore, objectively determining which groups are at risk of severe disease from influenza in Europe and which of these groups would gain most from immunisation is not as straightforward an exercise as it could be. This is especially pertinent when dealing with influenza, a disease whose characteristics often change from year to year. These changes can affect the severity of the disease and the effectiveness of vaccination [5]. Another factor that potentially limits the quality of this study is related to conditions with smaller numbers of patients. For these conditions, epidemiological studies objectively determining which groups are at a higher risk of severe disease (and whether immunisation reduces this risk) are difficult if not impossible to conduct. For this exact reason, science-based definitions need to be based on broad-brush categories — such as 'people with chronic respiratory diseases' — rather than long lists of conditions that are used as distinctive criteria.

6. DETERMINING RISK GROUPS IN EUROPE

A survey conducted by the VENICE Project[**] for ECDC as part of this study found a variety of risk groups and other groups recommended for seasonal vaccination by European states (see Appendix 2). However, these groups can be condensed down to a short list (Table 1).

[**] Vaccine European New Integrated Collaboration Effort (VENICE) Project; http://venice.cineca.org/

Table 1. Risk groups and other groups recommended for influenza vaccination in European countries (Source: VENICE survey 2008).

Risk groups

Demographic and patient groups:

1. Older age group, usually 65 years and older[††]
2. Persons with chronic medical conditions[‡‡*]
3. Pregnant women
4. Children (below age 2 or below age 5)

Other groups recommended for immunisation

Health occupational groups:

5. Persons living with persons at higher risk
6. Health care and other care workers[§§]

Other occupational groups

7. Essential services, usually first responders but also groups like military members and airline pilots
8. Veterinarians and poultry workers

In one country (Austria) it is common policy to recommend immunisation to groups outside of the ones listed above, namely all healthy working adults. There is also considerable anecdotal evidence suggesting that some employers in other EU countries offer or recommend immunisation to employees.

The VENICE survey also found that there were a number of other small groups where immunisation was recommended in the different EU/EEA Member States (see Appendix 2).

[††] These are the only two groups recommended for influenza vaccination by the WHO.

[‡‡] Some Member States recommend vaccination for all persons living in group conditions (e.g. living in homes for the elderly or homes for the disabled) and having a chronic medical condition or being elderly, which effectively combines Groups 1 and 2. Also see Appendix 2.

[§§] There are several sub-categories: hospital workers, persons in long-term care facilities, persons in out-patient clinics.

Group 1: The elderly

(See Appendix 2 for details.) The group of elderly people (usually defined as 65 years and above) is considered by all EU-27 countries as an influenza vaccination risk group and has been targeted as a priority for vaccination. Almost all EU Member States have age-based policies, mostly for people aged 65 and older and cite various evidence for this (usually including those references listed in Appendix 3 for Group 1). It is important to note that although there is an EU consensus, a number of Member States — especially those that joined the Union more recently — so far accomplished considerably less than what is recommended by the WHO.

Group 2: Persons with chronic medical conditions

(See Appendix 2 for details.) All EU-27 countries seem to have recognised a number of broad categories such as chronic cardiovascular diseases, respiratory diseases (including moderate or severe asthma) and haematological or metabolic disorders (including diabetes mellitus) as diseases which place individuals at a higher risk of severe outcome if infected with influenza. Consequently, vaccination of people afflicted with these conditions was recommended. Renal and liver diseases, immunologic disorders and HIV are also considered as high-risk conditions by many EU Member States. A few states try to list all individual conditions but most countries describe broad, inclusive groupings and leave decisions regarding individual patients to physician judgement. Children and adolescents on long-term salicylate (aspirin) therapy for certain chronic conditions are a rather small group and are recommended to receive annual influenza immunisation since they are considered more likely to develop Reye Syndrome [14] if falling ill from flu.

7. CRITERIA FOR IDENTIFYING RISK GROUPS AND OTHER GROUPS TO BE OFFERED VACCINATION

After evaluating available literature and national and international recommendations, the ECDC team identified a number of implicit criteria for identifying risk groups:

a. Evidence that the group is at increased risk of adverse outcome (severe illness or death) from influenza infection *and* additional evidence that immunisation reduces this risk, or, alternatively, evidence of the effectiveness of vaccination in this group documented by the presence of serological markers of immunity. (This applies to Groups 1 to 4 in Table 1.)
b. Alternatively, evidence that immunisation of one group reduces the incidence rate of influenza in another group. (Groups 5 and 6.)
c. It has been suggested that some groups should be immunised because they may be at a higher risk of acquiring influenza through their occupation or because they are performing especially essential roles (Groups 6 and 7).
d. There are economic criteria in terms of lost time for production, delivering social care, study time, etc. [6, 9].
e. Since the emergence of avian influenza A (H5N1), a few countries have recommended that veterinarians or people working with poultry should be immunised against human

seasonal influenza on the grounds that this would reduce the risk of becoming dually infected. This also reduces the risk of the common influenza virus recombining with the H5N1 virus to form a pandemic strain.

The team that prepared this paper considers items a) and b) as strong criteria with regard to public health. As to immunising personnel in care settings for patient benefit, very little published evidence can be found that supports immunisation of this particular target group. However, there is at least one well-conducted community trial and one supportive trial demonstrating benefits to patients when care workers in homes for the elderly were immunised [10,11]. For other patient groups, the immunisation of direct care personnel may be beneficial, but there is no clear evidence of patient benefit, especially in Europe. Criterion b), while sound in itself, does not apply to EU countries, with the exception of the specific group mentioned above (see 'Section 14. Areas for further work'). Criterion c) concerns occupational health considerations since the individuals (healthy working adults) should not be at a higher risk of suffering an adverse outcome when infected than the general population. Such a criterion is still important — though less than a) and b) — and in the event of a severe seasonal epidemic or a pandemic, retaining essential staff at work, especially health-care staff, will be a major public health issue. Criterion d) is important but not yet a relevant part of the decision-making process in most European countries. Criterion e) does not seem very substantial (see Table 3 and Notes). Therefore, criteria a) will be the most frequently cited criterion when advising the European Commission.

An important additional public health issue in the European context is the process of consensus building, i.e. the need to develop a consensus on risk groups in the Member States, rather than simply announcing a finalised list of risk groups.

In the light of above arguments, ECDC recommends the following criteria when advising on risk groups.

Table 2. Proposed European criteria for selecting influenza immunisation risk groups and other groups recommended to be immunised (in order of priority).

1. Evidence that the group is at increased risk of adverse outcome (severe illness or death) from influenza infection combined with further evidence that immunisation actually reduces this risk. A less stringent criterion would be merely evidence that vaccination induces serological immunity.
2. Evidence that immunisation of one group (health-care workers, household contacts) reduces incidence of influenza in another risk group.
3. Groups are at higher risk of acquiring influenza through their occupation.
4. Persons that are performing especially essential roles.

8. WHAT ARE THE RATIONALES AND EVIDENCE FOR EACH GROUP?

In Table 3 (below), the available data for the eight groups listed in Table 1 is contrasted with the criteria listed in Table 2, with regard to rationale and evidence. The rationale is not always made explicit in published recommendations, and the following table of rationales and evidence is derived from multiple sources. Details of the evidence appears in Appendix 3, with separate tabulations for each of the major groups.

Table 3a. Rationale and evidence for each risk group; with ECDC comments.

Group	Rationale to vaccinate	Increased risk of severe outcome of infection?	Vaccine shown to reduce that risk?	EU consensus?	ECDC comment
Patient groups					
1. Older age groups, usually 65 years and older	This group is at higher risk of severe influenza-associated morbidity and mortality than younger people, and vaccination has moderate effectiveness in reducing that risk.	Yes	Yes	Yes	Recommended by WHO, with a specific target [12].
2. Persons with chronic medical conditions	This group is at higher risk of severe influenza-associated morbidity and mortality than healthy persons, and vaccination seems to be effective in reducing that risk.	Yes	Somewhat	Yes, with some variations in detail, particularly on who belongs to specific risk groups.	Recommended by WHO, but no target.[12]
3. Pregnant women	This group is at higher risk of severe outcome than non-pregnant women, and it is presumed that vaccination will reduce that risk. Also, immunisation of pregnant women will provide some passive protection to the newborn child.	Some evidence but not from EU.	No	No	
4. Children	This group is considered by some to be at higher risk in Europe and its presumed that vaccination will reduce that risk [7][***]	Some evidence but not from EU [7].	Some not in EU	No [7]	

[***] An ad hoc ECDC panel meeting in 2006 concluded that there was insufficient data available to recommend routine immunisation for children in Europe. http://ecdc.europa.eu/documents/pdf/Flu_vacc_18_Jan.pdf

Table 3b. Rationale and evidence for other groups that were offered immunisation; with ECDC comments.

Group	Rationale				ECDC comment on evidence
		Increased risk of severe outcome of infection?	**Vaccine shown to reduce that risk?**	**EU consensus?**	
Occupational groups					
5. Persons living with persons at higher risk	To reduce the risk of infection posed by household members/direct care personnel to people at higher risk of severe disease.	No	No	No	Evidence is weak. Little or no evidence of risk reduction.
6. Health-care workers and other care workers	Three possible reasons: • reduce risk of illness in staff (staff protection); • reduce loss of staff time (economic and health service function); • reduce risk to those being cared for by staff These three reasons do not suggest that care workers are at higher risk of a severe outcome.	No	No	Yes, though it was noted there is poor uptake in the staff.	Immunisation of care staff is shown to benefit the elderly in care homes; staff protection [10,11].
7. Essential service workers	To avoid work-loss due to illness (adverse effect on the economy and the public-health sector).	No	No	No	May be a sufficient reason for immunisation, assuming that during a severe seasonal epidemic or a pandemic a functioning public-health sector is essential.
8. Veterinarians and those working with poultry	To reduce the (low) risk of a person being dually infected with a human seasonal virus and an avian influenza virus, thus creating	No	No	No	See Section 9.8.

	a risk of the common influenza virus recombining with the avian influenza virus. Particularly relevant in reference to H5N1.				

9. FURTHER COMMENTS ON EVIDENCE

(See also Appendix 3 for references.)

Risk groups

Two notable areas of uncertainty can be identified: age threshold and children. What is the cut-off age for elderly versus non-elderly patients; and which position do EU countries take in regard to children (see Section 9.4)?

9.1 Older age groups

Most commonly, the older age group is defined as persons who are 65 years and older; in many countries, this age group is routinely offered immunisation. But there are exceptions. Some countries have adopted policies for immunising persons at no or a lower age threshold, i.e. Austria (all age-groups); and Germany and Poland (60 years and older). Ireland and the Netherlands [8] are reviewing their age-threshold policies, with the intent to officially lower the age-limit. An industry-sponsored analysis recommended to lower the cut-off age to 50 years [9]. At present, there is insufficient evidence to support such policy changes across Europe. No EU-level debate has been initiated on this topic, and an EU consensus remains unlikely. Keeping in mind that the age structure varies significantly across EU countries, it is quite reasonable to have different age limits in different countries, particularly when considering the relative costs and benefits and the fact that such vaccination policies fall within national responsibilities. Current data and a wide consensus suggest that keeping a threshold of '65 years and older' is a reasonable minimum recommendation for policy decisions.

9.2 Persons with chronic medical conditions[†††]

Some national public-health authorities produce lists of medical and physical conditions for which immunisation is recommended. Others have taken the more pragmatic approach of defining broad categories, e.g. merely mentioning 'all metabolic conditions', rather than specifically mentioning *Addison's disease, childhood diabetes, late-onset diabetes, phenylketonuria*, etc. [8, 13]. This approach is preferable for two reasons:

a. When it comes to rare conditions, case numbers are always too low to allow research; consequently, there can only be presumed evidence of increased risk, and even less

[†††] Some Member States recommend vaccination for all persons living in group conditions (e.g. living in homes for the elderly and homes for the disabled) and having a chronic medical condition or being elderly, which effectively combines Groups 1 and 2. See Appendix 2.

evidence of the effectiveness of vaccination. There can be more evidence for broad groups of conditions as listed in Appendix 3.

b. There are always rare conditions that are not included on lists, and its much easier for busy clinicians to remember or look up a simple list like the one shown in Table 4, supplemented by a list of available evidence (Appendix 3).

When using this broad-brush approach, one of the key questions is whether or not to include mild but chronic conditions that show neither demonstrable evidence of increased risk nor benefit from immunisation. Examples for such chronic conditions are persons with

- asymptomatic HIV infection,
- chronic respiratory disease due to isolated mild asthma (not resulting in hospitalisation over the last five years); and
- chronic cardiovascular disease due to isolated mild hypertension.

Table 4. Suggested chronic medical conditions by groups. (See Appendix 3 for a listing of published evidence.)

Group	**Examples**	**Suggested significant exclusions**
Chronic respiratory diseases	Chronic obstructive airways disease; Severe asthma; Lung cancer.	Children and adults with mild asthma[*].
Chronic cardiovascular diseases	Congestive cardiac failure.	Isolated hypertension controlled by medication.
Metabolic disorders	Early- and late-onset diabetes mellitus.	-
Chronic renal and hepatic diseases	Chronic renal failure; chronic hepatitis and cirrhosis.	Isolated recurrent urinary tract infections.
Other persons with deficient immunity, either congenital or acquired (including HIV infection)[†]	Congenital constitutional immune deficiencies; persons receiving immunosuppressive chemotherapy.	-
All other persons with difficulties in overcoming respiratory infections[‡]	Persons with physical abnormalities affecting respiratory function.	Isolated learning difficulties; isolated psychiatric disorders.

[*] The definitions of asthma have changed over time. Contemporary diagnostic trends tend to widen the definition of asthma, and many more people are being considered to suffer from asthma, or asthmatic tendencies, than in the past. ECDC sees no evidence that persons with only mild intermittent asthma (not hospitalised in the recent past [five years], only occasional use of an inhaler) are at any increased risk from influenza compared to persons who do not display asthmatic tendencies. Conversely, there is good evidence that persons who have asthma and are frequently hospitalised because of asthma do indeed benefit from immunisation. As always, medical judgements have to be made on an individual basis.

[†] The evidence that this group is at an increased risk of severe influenza disease is inconclusive (plus there is insufficient research in Europe). There is equally little evidence that the risk is reduced by immunisation.

[‡] Though the evidence is not strong it does seem reasonable to immunise the more severely handicapped as more severe conditions are frequently associated with a degree of deficient immunity and increased vulnerability to

Other conditions	People 16 years and under taking aspirin (salicylates) continuously [14][*].	

9.3 Pregnant women

Nine European countries currently recommend immunisation of pregnant women (see Appendix 2). There seem to be few data available on whether or not these recommendations are followed.

9.4 Children

In 2007, an ECDC panel noted that European data were insufficient to evaluate the immunisation status of children [7]. The VENICE survey found that six European countries recommend immunising children under two years of age (see Appendix 2), with Finland providing the most evidence-based approach for the immunisation of infants (See Appendix 3). Waiting for evaluation data from the Finnish initiative as well as reviewing data from other countries seems advisable.

Other groups recommended for immunisation: Health occupational groups (See Appendix 2)

9.5 Persons living with persons at higher risk for influenza complications

Immunisation of persons who share a household with people who are at a higher risk for influenza complications is recommended in only a few countries but there is little evidence of its effectiveness internationally and none in Europe. Perceived effectiveness could be solely on theoretical grounds.

9.6 Health care and other care workers[†]

Immunisation of health care and other care workers is recommended in more EU countries than for persons living with persons at higher risk (see Section 8, group 5). Apart from staff caring for the elderly in care homes [10,11] there is little evidence internationally (and none in Europe) that such immunisation is effective in protecting patients, though it could be effective on theoretical grounds. When European coverage is measured in these groups, the proportion of those accepting immunisation is consistently under 50%.[‡]

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to respiratory infections (e.g. Down's syndrome and paraplegia following trauma). Conversely, minor congenital or acquired handicaps (strabismus or loss of a limb) would not be a sufficient reason to recommend immunisation.

[*] This small group is often cited since young people (under age 16) who take aspirin are at risk of developing a potentially lethal liver failure called Reye's syndrome. It was suggested that persons with influenza are especially at risk. The usual way of preventing this is to ban the use of aspirin or other salicylates in children. However, there are few young people who have to use aspirin on a regular basis (e.g. those with juvenile arthritis) and guidelines or physicians often recommended annual routine influenza immunisation for this target group.

[†] Sub-categories: hospital workers, persons in long-term care facilities, persons in out-patient clinics.

[‡] Data from VENICE survey 2008.

Other occupational groups (See Appendix 2)

9.7 Essential workers

A few countries recommend immunisation for this group, e.g. for first responders, military personnel and airline pilots.

9.8 Veterinarians and those working with poultry

There are hardly any cases internationally of veterinarians or poultry workers becoming infected with A/H5N1. In Europe, there are no cases on record. Infections have occurred in families with domestic poultry, but no veterinarians or poultry workers were infected. If anyone should be protected it should be families that raise poultry. Interestingly, immunisation for families with poultry is not currently recommended by WHO Headquarters, which offers comprehensive advice on staff protection.

10. WORLD HEALTH ASSEMBLY POSITION

A resolution approved during the fifty-sixth World Health Assembly 'urges the countries […] to establish and implement strategies to increase vaccination coverage of all people at high risk, including the elderly and persons with underlying diseases' [12]. The document does not specify the age of the elderly and list underlying diseases. More specific information on the composition of the high risk groups can be found on the World Health Organization's website.[15]

- the elderly; and
- people with weakened immune systems and those with underlying chronic diseases where influenza often leads to severe pneumonia and other serious illness due to pre-existing chronic diseases [15].

The formal WHO immunisation coverage target (75% by the year 2010) only applies to the elderly [12]. Since all EU countries are WHO members and there is no record of any country objecting to the WHO's influenza immunisation guidelines, all EU countries have de facto agreed to both the immunisation of these two risk groups and the immunisation coverage target for the elderly.

11. POSITION IN COUNTRIES OUTSIDE THE EU: USA

The position of the United States [16] on this topic is often of particular interest to other countries. The current U.S. (2008–09) recommendations call for the immunisation of people at high risk for complications from the flu, including

- children and young people aged six months until their eighteenth birthday;
- pregnant women;
- people 50 years of age and older;
- people of any age with certain chronic medical conditions; and

- people who live in nursing homes and other long-term care facilities.

Also recommended for flu vaccination are people who live with or care for those at high risk for complications from flu, including:

- household contacts of persons at high risk for complications from the flu (see above);
- household contacts and out-of-home caregivers of children less than six months of age (the children themselves are too young to be vaccinated); and
- health care workers.

In addition, there are other groups included in the U.S. guidance such as those travelling to areas where influenza is circulating outside of the Northern hemisphere influenza season. In 2006, U.S. guidelines and recommendations called for 73% of the U.S. population to be immunised (that percentage is now higher with , but only an estimated 32% were actually immunised, including 64% of the population aged 65 years and above[*].

12. RISK GROUPS: ESTIMATES OF NUMBERS

Broad estimates of the numbers in the major risk groups are required for determining the numbers of vaccine doses and the likely impact of immunisation. ECDC estimated these numbers for the two major risk groups: those 65 years and older and those with chronic diseases. Estimating numbers is a simple process when it comes to the older population; reliable population statistics and projections are easily available. Estimates of the number of people with chronic conditions are more difficult to find. Estimates are not generally included in the regular releases of statistical data, and there is always the danger of double or treble counting, particularly for the elderly where an increasing percentage also suffers from chronic diseases that become more prevalent with age. Double or treble counting is also a problem when it comes to the chronically ill where single-condition surveys (e.g. the prevalence of diabetes in the community) can potentially lead to multiple counts if a single person is afflicted by two or more conditions (e.g. diabetes and cardiovascular disease).

The approach we have chosen uses primary care data provided by Fleming and Eliot [17]; their survey used age-specific primary care estimates from one country (the United Kingdom), measuring the proportion of the population suffering from chronic diseases. ECDC adapted this approach for its own calculations. Since the UK data were age specific, estimates could be applied to other EU countries by making adjustments for the different age-structures of countries. An additional advantage of the UK survey was that it drew on the opinions of primary care doctors who, on a case-to-case basis, decided whether a person's illness was a significant enough reason for immunisation. Doctors would opt, for example, to exclude isolated mild asthma and well controlled isolated mild hypertension.

Based on these calculations, about 25% of the EU-27 population belongs to one or both of the two major risk groups. In individual countries, between 19% an 28% of the population belong to one or both risk groups (see Appendix 4). The total is estimated at around 124 million people, with two thirds (around 81 million) falling into the 65 years or older bracket

[*] United States Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/flu/professionals/vaccination/pdf/targetpopchart.pdf

and one third (around 43 million) constituting the second major risk group (chronic illness in younger persons). Estimates of the proportion of the population from other country-specific surveys came up with similar values (see Appendix 4). These numbers will inevitably rise over time because of aging populations and the success of modern medicine in permitting people with chronic illness to live productive lives.

13. CONCLUSIONS

The above analysis — backed by European and international data — shows that there are two groups where routine annual immunisation with the current seasonal influenza vaccine is highly recommended for both scientific and public health reasons. These are:

1. persons in the older age group, usually 65 years and older; and
2. persons with chronic medical conditions.

The latter are defined as people with diseases in the broad categories shown in Table 4):. For reasons explained earlier (see Section 9.3), it is preferable to use broad inclusive categories with some notable exclusions (Table 4, page 14) rather than attempt to define long lists of single conditions which inevitably will miss important individual conditions.

These are also the only two groups where there is consensus in all European countries. It is also commonly agreed that the definition of the elderly age group is somewhat arbitrary, and countries may have good reasons to use 60 or even 50 years as a cut-off to define the elderly age group.

In addition to persons in Group 1, there is strong data supporting the immunisation of personnel providing care in residential homes for older people and the infirm in order to protect their patients.

There are two other groups where there are some good arguments for offering immunisation: pregnant women and children (variously defined as aged 6 to 24 months or 6 months to five years). The argument for the immunisation of pregnant women is complex because there is some evidence of increased risk for pregnant women, and immunisation could, directly and indirectly, protect the newborn. In both cases there is only limited evidence of increased risk in Europe and even less evidence from countries where immunisation is routinely offered to pregnant women. As of yet, there is no European consensus in this area, but it is important to note that a growing number of countries are conducting research in this area, so the data situation is likely to improve. Based on these new data, informed decisions should be possible in the not-so-distant future.

Protecting the physical well-being of employees can be another reason to routinely offer influenza vaccination. In the case of health-care workers, health economic arguments might play an additional role, namely ensuring uninterrupted health services during an epidemic. With the exception of care home staff there is no strong evidence that the immunisation of staff benefits patients although when reasoning from first principles some benefits are to be expected [10, 11]. Based on these assumed benefits, some countries might opt to

recommend vaccination for all health-care workers but evidence is still too sparse to unequivocally support such policies.

Similarly, there is no evidence that vaccinating persons who share households with people in the two main risks groups reduces the risk, but when reasoning from first principles this should be the case. Again, some countries might chose to recommend vaccination for persons sharing households with members of the two high-risk groups, but there is not yet the evidence to unreservedly support such policies.

14. AREAS FOR FURTHER WORK

There are clear priorities for research and development:

- Surveillance development, i.e. routine surveillance for severe manifestations of influenza in Europe (hospitalisations and death).
- Routine monitoring of the effectiveness of influenza vaccination, especially in respect to reducing the risk of severe disease and death from influenza.
- Evaluation of the impact of immunising pregnant women and children of all ages in Europe and the protective effect of immunisation in these groups
- Investigations to assess if immunisation of health-care staff and household members reduces the risk to vulnerable people in the two main risk groups when compared to elderly patients in care homes.
- Development of projects for stronger promotion of influenza immunisation among health-care workers both for their own sake and as role models for their patients.
- Specific investigations if HIV-infected persons in Europe are at higher risk of severe disease from influenza infection, and similar studies for other more common conditions such as mild asthma.
- Health economic studies, e.g. on the age threshold for immunisation in the elderly, focusing on the need for country-specific differences and guidelines.
- Investigation of the impact in countries or settings where the entire population is vaccinated in order to determine any indirect benefits from reducing overall levels of transmission.

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APPENDIX 1. DEFINING 'RISK GROUPS' AND 'GROUPS FOR WHICH IMMUNISATION IS RECOMMENDED'

Working from first principles, the term 'risk groups' can have several meanings in the context of influenza and influenza vaccination.

A. Persons at higher risk than average for acquiring influenza. This is a function of those who are more likely to be susceptible (non-immune) and at the same time are more likely to encounter infection. It is worthwhile noting that this group varies from year to year with the predominating strain and was different during all pandemics in the 20th century.

B . Persons at a higher than average risk of transmitting influenza. Similar to definition A but not identical to it, since B also includes the likelihood of infectious persons meeting persons susceptible to infection, e.g. an sick child in a classroom might be considered to be in a higher risk group than a person who isolates himself because he feels unwell.

C. Persons at higher risk of having an adverse outcome (severe disease or death) when becoming infected. This is what is commonly understood when referring to 'risk groups for influenza'. This definition usually includes the elderly and those with chronic illnesses, and can sometimes include pregnant women and very young children. See Appendix 2 for more information on the European perspective.

D. Persons who, if infected with influenza, are more likely to transmit the disease to others who will then develop severe disease. This is a combination of B and C and is often part of the rationale behind immunising health-care workers or nursing-home staff.

E. Persons who are at higher-than-average risk of adverse outcome if infected with seasonal influenza and whose risk of specified adverse outcomes is considered to be reduced by influenza vaccination. This group is usually described by the phrase 'risk groups for influenza vaccination'. Unlike definitions C or D, this definition has to take into account whether the vaccine is effective in the target group and then consider economic issues in a cost-benefit analysis. This approach reveals important differences between countries, e.g. when comparing the European and the U.S. positions on childhood vaccination. The WHO position on influenza vaccination is relatively straightforward, but focuses on the elderly and those with chronic debilitating diseases. See http://www.who.int/immunization/wer8033influenza_August2005_position_paper.pdf for details.

Other groups for which immunisation is recommended

There are other large and important groups to whom immunisation is sometimes recommended for reasons apart from their being more likely to suffer from severe infection and disease. These include:

F. To protect those who are in risk groups and who may suffer if the subject group becomes infected (e.g. health-care workers and families of vulnerable individuals).

G. To protect those who are occupationally exposed (e.g. health-care workers).

H. To protect essential functions by avoiding that all people who are able to perform certain tasks or functions become infected.

APPENDIX 2. RISK GROUPS IN EUROPE (BY COUNTRY)

(Source: VENICE survey 2008.)

Age group	Countries[†††††]	Total
6 months – 12 months	Austria, Estonia, Finland, Latvia, Slovakia, Slovenia	6
> 1 year – 2 years	Austria, Estonia, Finland, Latvia, Slovakia, Slovenia	6
> 2 years – 5 years	Austria, Estonia, Slovakia	3
> 5 years – 18 years	Austria	1
> 18 – 49 years	Austria	1
≥ 50 years	Austria, Poland	2
≥ 65 years	Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom	26
Chronically ill persons (different definitions)	Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Germany, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom	28
Pregnant women	Austria, Belgium, Cyprus, Denmark, Estonia, Italy, Portugal, Slovakia, Spain	9

Occupational setting or group	Countries		
	Recommended	**No recommendation**	**Recommended against**
Hospital staff	Austria, Belgium, Bulgaria, Cyprus, Estonia, Germany, Greece, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, United Kingdom, France	Czech Republic, Hungary. (No data available for Denmark, Finland, Sweden.)	Nil
Staff at long-term care facilities (nursing homes and other chronic-care facilities)	Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, United Kingdom	Latvia	Nil
Residents of long-term care facilities (nursing homes and other chronic-care	Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Germany, Estonia, France, Greece, Hungary, Iceland,	Denmark, Latvia	Nil

[†††††] Austria is the only country in Europe that recommends vaccinating the entire population.

facilities)	Ireland, Italy, Lithuania, Luxembourg, Netherlands, Norway, Portugal, Romania, Slovakia, Slovenia, Spain, United Kingdom		
Household contacts of persons for whom vaccination is recommended	Austria, Belgium, Bulgaria, Cyprus, Denmark, Estonia, Ireland, Italy, Lithuania, Luxembourg, Norway, Portugal, Romania, Slovakia, Spain	Czech Republic, Germany, Greece, France, Hungary, Iceland, Latvia, Slovenia, United Kingdom. (No data available for Netherlands.)	Nil
Out-patient care clinics/practices staff	Austria, Belgium, Bulgaria, Cyprus, Estonia, Germany, Greece, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, France	Czech Republic, Hungary, United Kingdom	Nil
Essential services (police, firemen, etc.)	Austria, Bulgaria, Estonia, Italy, Luxembourg, Poland, Romania, Spain,	Belgium, Cyprus, Czech Republic, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Norway, Slovakia, Slovenia, United Kingdom, France. (No data available for Netherlands.)	Portugal
Military	Austria, Bulgaria, Estonia, Germany, Italy, Luxembourg, Romania, Slovakia, Poland	Belgium, Cyprus, Czech Republic, Greece, Hungary, Iceland, Ireland Latvia, Lithuania, Norway, Portugal, Slovenia, France, United Kingdom. (No data available for Netherlands.)	Spain
Veterinary services	Austria, Cyprus, Ireland, Italy, Luxembourg, Slovakia, Slovenia, Spain, Poland	Belgium, Bulgaria, Czech Republic, Estonia, Germany, Greece, Hungary, Iceland, Latvia, Lithuania, Norway, Portugal, Romania, United Kingdom, France. (No data available for Netherlands.)	
Poultry industry	Austria, Cyprus, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Slovakia, Slovenia, Spain, United Kingdom	Belgium, Bulgaria, Czech Republic, Estonia, Iceland, Latvia, Lithuania, Norway, Poland, Portugal, Romania. (No data available for France, Netherlands.)	
None	Denmark, Finland, Sweden		

Other groups recommended for vaccination:

Bulgaria: transport workers.

Denmark: chronically ill persons < 65 years, following medical assessment; persons who took early retirement.

France: airline crews; ships' crews; tour guides.

Germany: generally recommended for people working in public institutions or settings with frequent interpersonal contacts (including essential services); influenza vaccination is also recommended for persons in the health-care sector or in homes for the elderly who could infect unvaccinated risk patients; persons travelling.

Hungary: workers in poultry farms with more than 1 000 birds; workers involved in culling poultry infected with H5N1 avian influenza; persons who may have had contact with infected birds; health-care workers.

Luxembourg: children < 2 years who attend day-care centres; teachers.

Poland: trade workers; transport workers.

Portugal: professionals involved in culling avian-influenza infected poultry and their household contacts; persons providing day care for children.

Romania: persons involved in medical or social care for patients at home.

Spain: risk-group travellers to the southern hemisphere from April to September; travellers to avian influenza risk areas that expect contact with birds.

APPENDIX 3. PUBLISHED EVIDENCE FOR RISK GROUPS

Target population (Risk group)	Risk of severe disease (yes/no/unknown)	Estimated ranges (Odds/RR/comparison of incidences)	References
Age (individuals aged 65 years and older) (Group 1)	Yes	Mortality increased risk OR 2.7. RR 2.18. Influenza vaccine reduced the mortality by 59% in the vaccinated group compared to the control group. Vaccination associated with reduction in the incidence of hospitalization/death 48% (95% CI, 42-52) in year 1 and 31% (95% CI, 26-37) in year 2.	[18, 19] [18-22] [23]
Chronic illness (Group 2)			
Chronic respiratory diseases	Yes	Vaccination was 76% effective in prevention of influenza related to acute respiratory infection in adults. Children with asthma were overall at a higher risk of severe influenza disease, but this was not apparent in cases of mild or moderate asthma.	[24-26]
Chronic cardiovascular disease	Yes	2.7-4.95 times higher risk of acute myocardial infarction shortly after an acute respiratory infection (not necessarily influenza).	[27-30], [24]
Metabolic disorders (including diabetes mellitus)	Yes	Double risk of influenza complications, increased death rates by 5-15 % during influenza epidemics, increased death rates due to pneumonia and influenza.	[31-34] [29]
Chronic renal and hepatic diseases	Yes/limited evidence	Excess mortality in patients on dialysis. Increased incidence of respiratory infections in patients with chronic kidney disease.	[35, 36]
Persons with immune deficiencies	Yes	Higher incidence of complications among organ recipients, high risk of complications in patients with haematological conditions.	[33, 37-39]
HIV	Unknown	Probably high incidence of disease but no evidence of more severe disease than healthy population.	[40-42] [14]
Young people taking salicylates long term	Unknown	Theoretical risk of developing severe disease (Reye syndrome) among people under age 20 taking salicylates.	[14]
Other groups			
Pregnant women (Group 3)	Yes/limited evidence	• Excess hospital admissions rates in second third trimester 6.32 and 10.5/10.000 woman month. • Excess rate of medical visits 48.1/1000 visits.	[43-48]
Pregnant women with risk factors (Group 3)	Yes/limited evidence	• Respiratory illness OR 3.2 CI (3-3.5) when compared with healthy pregnant women. • Influenza-attributable rate of hospital admission increasing with trimester: 3.9 (−6.4 to 14.2), 6.7 (−4.1 to 17.5), and 35.6 (21.1 to 50·1) respectively/per 10 000 woman months –	[43]
Children (Group 4)	Yes/limited evidence for Europe	Excess hospitalisation, medical visits and antibiotic prescriptions in <2 years.	[49-55]

APPENDIX 4. COUNTRY-SPECIFIC ESTIMATES OF THE POPULATION IN THE TWO MAJOR RISK GROUPS FOR EUROPEAN UNION COUNTRIES

(Note: Numbers have been rounded to the nearest thousand; column totals will not necessarily add up to 100%.)

	Population aged 65 or over (Eurostat data; date of extraction: 11 Feb 2008; average population by sex and five-year age groups, 2006)		**Population under 65 with one or more risk morbidities (based on methodology by Fleming and Eliot, 2006 [17])**		**Total pop. at risk**	
Country	**million**	**%**	**million**	**%**	**million**	**%**
Austria	1,403,000	16.9%	689,000	8.3%	2,091,000	25.2%
Belgium	1,810,000	17.1%	879,000	8.3%	2,689,000	25.4%
Bulgaria	1,325,000	17.3%	637,000	8.3%	1,962,000	25.6%
Cyprus	96,000	12.3%	65,000	8.3%	160,000	20.6%
Czech Republic	1,482,000	14.4%	853,000	8.3%	2,336,000	22.7%
Denmark	835,000	15.3%	452,000	8.3%	1,287,000	23.6%
Estonia	229,000	17.1%	111,000	8.3%	340,000	25.4%
Finland	869,000	16.5%	437,000	8.3%	1,306,000	24.8%
France	10,277,000	16.2%	5,262,000	8.3%	15,539,000	24.5%
Germany	16,299,000	19.8%	6,832,000	8.3%	23,131,000	28.1%
Greece	2,074,000	18.6%	927,000	8.3%	3,001,000	26.9%
Hungary	1,605,000	15.9%	835,000	8.3%	2,441,000	24.2%
Ireland	478,000	11.1%	358,000	8.3%	836,000	19.4%
Italy	11,772,000	19.9%	4,907,000	8.3%	16,681,000	28.2%
Latvia	389,000	17.1%	189,000	8.3%	579,000	25.4%
Lithuania	527,000	15.6%	280,000	8.3%	808,000	23.9%
Luxembourg	67,000	14.0%	40,000	8.3%	106,000	22.3%
Malta	56,000	13.8%	34,000	8.3%	91,000	22.1%
Netherlands	2,368,000	14.5%	1,358,000	8.3%	3,726,000	22.8%
Poland	5,116,000	13.4%	3,164,000	8.3%	8,280,000	21.7%
Portugal	1,828,000	17.3%	879,000	8.3%	2,708,000	25.6%
Romania	3,204,000	14.9%	1,789,000	8.3%	4,993,000	23.2%
Slovakia	640,000	11.9%	447,000	8.3%	1,087,000	20.2%
Slovenia	320,000	15.9%	166,000	8.3%	486,000	24.2%
Spain	7,407,000	16.7%	3,691,000	8.3%	11,098,000	25.0%
Sweden	1,581,000	17.4%	756,000	8.3%	2,338,000	25.7%
United Kingdom	9,752,000	16.0%	5.051,000	8.3%	14,802,000	24.3%
Total EU 27	**83,813,000**	**16.9%**	**41,095,000**	**8.3%**	**124,909,000**	**25.2%**

Note: Ryan et al. (2006) [9] estimate 123.5 million people 'at risk' (about 25.3%).

Other sources of information show similar estimates for specific countries:

Belgium

According to the Belgian Health Interview Survey (HIS) conducted in 2004, the estimated number of people belonging to a risk group due to suffering from a chronic disease is 30.2%, which amounts to 3 143 178 people (total population in Belgium: 10 421 137).

In absolute numbers, the population of 65 years or older is 1 789 812 individuals (2004), and the population between 15 and 64 years with chronic health problems is estimated at 1 353 366 individuals. People with more than one chronic disease are not counted twice.

Chronic conditions taken into consideration:

- asthma in the past year;
- chronic bronchitis, other chronic lung disease in the past year;
- serious heart disease or heart attack in the past year;
- hypertension in the past year;
- serious renal disease (not kidney stones) in the past year;
- diabetes in the past year; and
- stroke (and consequences) in the past year.

France

The estimated number of older people in France (65 or older) in 2007 was 9 100 000 (14.4%). The number of people who have used the social security system because of chronic illness is estimated at 7,700,000 (13.6%) in 2006 (Caisse nationale de l'Assurance Maladie, 2007). The percentage of persons in risk groups is about 28.0% of the total population.

ECDC estimates that about 20 to 30% of the EU population belong to at least one of the two main risk groups (the elderly and those with chronic diseases).

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