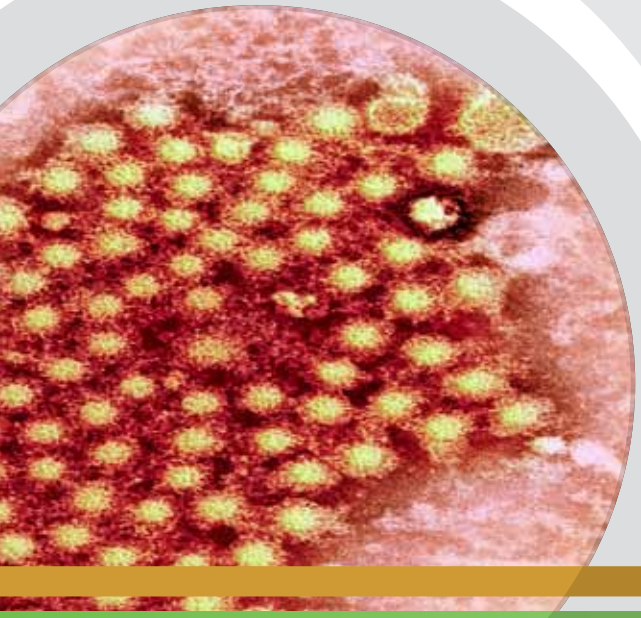

TECHNICAL REPORT

Hepatitis A virus in the EU/EEA, 1975–2014

A systematic review of seroprevalence and incidence comprising European surveillance data and national vaccination recommendations

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ECDC TECHNICAL REPORT

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Abbreviations

EU/EEA	European Union/European Economic Area
EFSA	European Food Saftey Authority
HA	Hepatitis A
HAV	Hepatitis A virus
MSM	Men who have sex with men
TESSy	The European Surveillance System
WHO	World Heath Organization

Summary

Emerging risk factors linked to increasing travel and food importation from both inside and outside the European Union/European Economic Area (EU/EEA) pose new risks of exposure to Hepatitis A virus (HAV). Hepatitis A (HA) epidemiology varies largely across the globe. Areas of high, intermediate, low and very low endemicity are defined[1] in order to identify and inform different prevention strategies, one of which is vaccination. A systematic review of the literature published from 1975 to 2014 was conducted in order to describe HAV seroprevalence and incidence of HA in the EU/EEA countries. We reviewed seroprevalenceand incidence data and HAV vaccination policies in the EU/EEA to support decisions on prevention strategies.

In addition, data from The European Surveillance System (TESSy) were used to complement the available knowledge on incidence of HA. Two hundred and thirty-eight articles were selected for data extraction, of which 228 reported seroprevalence data from 28 EU/EEA Member States (no data available for Hungary, Latvia and Liechtenstein). HAV seroprevalence in EU/EEA countries ranged between intermediate and very low, with most countries (24) falling in the very low endemicity category, based on the World Health Organization (WHO) HAV seroprevalence endemicity categories. Annual notification rates of HA reported through TESSy during the period 2006–2013 suggest incidence ranging from intermediate to very low.

Among the 30 countries providing this information[2], 14 reported very low incidence and two intermediate incidence. The susceptibility to infection among adults ranged between low and very high, with three Member States falling in the low susceptibility category, and five in the very high susceptibility category, with a marked geographical gradient. Based on this descriptive assessment, the HA seroprevalence presents a high degree of temporal and spatial variability across the EU/EEA. There is an overall decreasing trend over time in all countries and an important geographical gradient increasing from northern to central, southern and eastern EU/EEA.

Our analysis shows that susceptibility to HAV among adults (extrapolated from the seroprevalence estimates) is a more specific indicator of HA endemicity level in the EU/EEA than seroprevalence, as it includes historical developments of the disease epidemiology and may more appropriately describe the potential risk for HA outbreaks. Differences in methodology, representativeness and time of conduct of the studies, as well as potential vaccine coverage not captured by our data review should be taken into account. This evidence is of high relevance and can contribute to the design of appropriate hepatitis A control strategies, including vaccination.

[1] The definitions for very low, low, intermediate and high endemicity are taken from the following World Health Organization position paper - WHO position paper on hepatitis A vaccines – June 2012. Available here: http://www.who.int/wer/2012/wer8728_29.pdf

[2] no data available for Liechteistein

1. Objective and background

Objective

The objective of this systematic review is to present HAV seroprevalence and HA incidence in EU/EEA countries from 1975 to 2014 in order to assess HAV endemicity and overall population susceptibility.

Background

Hepatitis A is caused by the hepatitis A virus (HAV), transmited most often through the faecal-oral route, either by person-to-person contact or by consumption of contaminated food or water. Sexual transmission among men who have sex with men and parenteral transmission through infected syringes or, rarely, blood components has been documented as well [1,2].

Average incubation period is 28–30 days ranging from 15 to 50 days. Patients are infectious two weeks after infection and may continue to be infectious for one week or more after symptoms have ended [2].

Up to 90% of HAV infection in children under six years of age is not accompanied by symptoms or jaundice. Cases with jaundice, more common in adults, present also general symptoms such as fever, loss of appetite, nausea and vomiting which may last for several weeks. About 15% of patients have prolonged or relapsing symptoms over a 6–9 month period. No specific treatment is available [2]. As any other form of acute hepatitis, hepatitis A may cause liver failure and death, even though such events are rare and occur more frequently in people older than 50 years or in those with underlying chronic liver diseases [2].

All susceptible people can get hepatitis A infection, but in low endemicity areas there are groups at higher risk. These include those travelling to countries where hepatitis A is common, men who have sexual contact with other men or individuals who use illegal drugs [3-7].

Hepatitis A occurs worldwide. The World Health Organization (WHO) estimates the level of endemicity based on the HAV seroprevalence that varies widely between countries. In high endemicity situations where HAV is widely circulating, most children are infected before the age of 10 and outbreaks are rarely reported as most children have asymptomatic infections and the majority of adults are immune. In areas of intermediate endemicity a larger proportion of children are not infected early in life, leading to higher susceptibility in older age groups and recurrent large outbreaks. Finally, in areas of low to very low endemicity all age groups are highly susceptible to HAV infection and outbreaks can occur when the virus is introduced into the community [8].

Transmission can be reduced by improving sanitation, promoting hygiene in food production and handling, and vaccination [9]. A safe and effective vaccine is available. WHO recommends no vaccination in high endemicity areas, universal vaccination in intermediate endemicity areas and at-risk group vaccination in low and very low endemicity areas [8].

HA remains highly endemic worldwide. Global travel and contaminated food present opportunities for introduction of infection to non-immune populations in the EU [7,10-15]

Despite important differences at national level, average HAV notification rates in the EU have decreased from 14.0 cases per 100 000 population in 1997 to 2.6 cases per 100 000 population in 2010 [16,17]. This most likely reflects improved living conditions, as HAV seroprevalence rates are strongly correlated with socioeconomic status and access to clean water and sanitation [2].

The highest notification rates in the EU are reported among children under 15 years of age. There is a marked seasonal pattern with a peak of reported cases in autumn, which may reflect increased rates of infection during travel to endemic countries over summer [18]. In the absence of vaccination, the low incidence in the EU population can result in a high proportion of susceptible individuals. If the infection is introduced, there is a risk that susceptible adolescents and young adults will be infected [19].

Food-borne transmission of HAV has been implicated in several outbreaks in recent years. Between 2007 and 2011, the European Food Safety Authority (EFSA) and ECDC reported 11 HA outbreaks [20-24]. On the other hand, reported incidence suggests sustained HAV circulation in several EU/EEA countries [18].

In light of the outbreaks occurring in the EU/EEA, and the changes in the epidemiology of HA with a shift to infection in older age groups, an assessment of the epidemiological situation in the EU/EEA is of interest to understand the situation and define better preventive strategies, including potential vaccine recommendations. This report is in line with previous guidance produced by ECDC to 'consider to study the real scale of the epidemic' and to 'develop technical guidelines on hepatitis A outbreak response including e.g. vaccination strategies' [25].

A systematic review of literature was conducted to gather data on seroprevalence and incidence of HAV. The systematic review is a method to collect, critically appraise and summarise the best available evidence, in a transparent and systematic way using generally accepted evidence-based principles. Data on EU/EEA notifications of HA from The European Surveillance System (TESSy) were used to complement the findings from the systematic review.

2. Review methods

Research questions

1. What is the prevalence of anti-HAV antibodies in the general population of EU/EEA countries from 1975 to 2014?

Target population: general population (subgroups have been excluded in a subsequent step); children under 1 year of age were not included because of waning immunity conferred by maternal antibodies;

Outcome: HAV seroprevalence assessed via presence of anti-HAV antibodies (IgG and IgM) in serum samples (saliva excluded);

Study design(s): The most appropriate epidemiological research studies for estimating population exposure and risk are those that measure the seroprevalence rate, which indicates both the proportion of the population that has had past exposure to hepatitis A virus and the remaining proportion that is at risk of infection. Therefore, the primary focus of this review of the literature has been on seroprevalence studies.

2. What is the reported incidence of HA in the general population of EU/EEA countries from 1975 to 2014?

Target population: general population (subgroups have been excluded in a subsequent step)

Outcome: HAV incidence

Study design(s): observational studies, including analysis of routine surveillance data. Outbreak investigations have been excluded.

Search strategy

HAV seroprevalence and incidence search methodology

Original research articles were retrieved to identify the best evidence available from PubMed, Embase and Scopus bibliographic databases on 15 October 2014.

The search strategies combined the concepts of hepatitis A virus with seroprevalence. Controlled vocabulary (i.e. MeSH and Emtree terms) and natural vocabulary (i.e. keywords) were used for representing the concepts in the search strategies. Articles published in all languages from 1 January 1975 to 30 June 2014 were included. To reduce the risk of excluding studies relevant to our question, the geographical concept was avoided in the search strings due to the multiplicity of place names.

Further searches were submitted in Cochrane Library but have not yielded relevant results.

Search strategies are available in Annex 1. The results of this search were transferred to an Endnote library and duplicate articles removed manually.

Grey literature and manual search

The literature search was complemented by manually searching references of the included articles, and by browsing the bibliographies of manuals using the Google search engine. Additionally, personal communications from authors or other colleagues about relevant articles or grey literature were considered. The ECDC website was also used to search for relevant reports and/or information.

National health institutes' or ministries' of health webpages were searched for relevant seroprevalence or incidence data.

Lastly, the EU/EEA Member State ECDC focal points for food- and water-borne and for vaccine preventable diseases, and scientific expert panel members (see Annex 2) were also consulted. The list of retrieved references and the HAV vaccination recommendations were shared for review, comment and validation between October and November 2014. Out of the 30 EU/EEA Member States invited in the consultation, three did not send any feedback.

Literature selection

First selection step: title and abstract.

The Endnote library was exported to an Excel file for review. Articles were split into two groups in alphabetical order. In parallel, two reviewers reviewed the first half and the other two reviewers the second half. A set of inclusion and exclusion criteria were defined before starting the selection and used by the reviewers to assess the articles (see tables 2.1–2.4 below). Articles were classified according to these criteria using dropdown menus created in the Excel sheet. Disagreements were resolved by consultation with one reviewer from the other team.

Table 2.1. Rationale for article inclusion

Inclusion criteria
Report Hepatitis A seroprevalence and/or incidence rate in humans
Report data from the general population and/or special groups[3] in one or more EU/EEA Memebr States
Report data from one or more EU/EEA Member States and/or any of their region/district
Have been published within and report data for the period January 1975–June 2014
Be an original research article, review paper or abstract

Table 2.2. Rationale for article exclusion

Exclusion code	Exclusion criteria
1	Non EU/EEA
2	Non HAV
3	Non seroprevalence/incidence study
4	Non general population
5	Other (e.g. environmental studies, animal studies)

Table 2.3. Article exclusion or inclusion classification

Exclusion/inclusion	Explanation
Y	Yes – included
N	No – excluded (see table 2.4)
P	Potential inclusion – flagged for discussion
I	Interesting – relevant information on the disease but not for inclusion in the review

If more than one exclusion criterion was applicable, articles were classified according to one criterion only, and in priority order as by the list provided (Table 2.2).

The European Outermost regions (i.e. Guadeloupe, French Guyana, Martinique and La Réunion, the Canary Islands, the Azores and Madeira) as well as the European overseas countries and territories (associated to Denmark, France, the Netherlands and the United Kingdom) have been excluded.

Review articles were included and original articles were searched and included if additional information was deemed necessary. Articles in all EU/EEA languages were included.

The articles marked as 'P' were reviewed and discussed by the two reviewers in each team and subsequently marked for inclusion ('Y') or exclusion ('N').

Articles falling in exclusion category 4 (non-general population) have been excluded. However, in order to keep track of them for further analysis outside the scope of this review, a dropdown menu was filled in to classify the groups at risk. Articles dealing with non-general populations but including a control group were included (only data from the control group was extracted).

[3] Special groups to be included are military recruits not yet deployed to the field and blood donors (no distinction between first time and returning blood donors).

Table 2.4. Article classification for articles excluded by exclusion code 4:

Exclusion category	Explanation
HIV	HIV positive patients
Liver disease	Acute or chronic liver disease patients
Haemophiliacs	Haemophiliacs, recipients of blood products and/or transplanted organs
HCW	Healthcare workers (including institutionalised patients' carers)
Institution	Institutionalised patients and prisoners
Sewage	Sewage workers
Travel	Travellers to areas of high endemicity
MSM	Men who have sex with men
PWID	People Who Inject Drugs
Homeless	Homeless people
Teacher	Teachers and other school staff members
Hospital	Hospital patients were excluded if having any liver condition or if admitted to a gastro or infectious diseases ward N.B. hospital patients were included if the sampling approach aimed at being representative of the whole hospital or if sampling was done from the emergency room only.
Minorities	Ethnic minorities NB estimates from the total population (i.e. including minorities) were included in the analysis as deemed representative of the general population of a certain country.
Migrants	Migrants/refugees/asylum seekers and their children NB estimates from the total population (i.e. including migrants) were included in the analysis as deemed representative of the general population of a certain country.
Adoption	Household members and other close contacts of adopted children newly arrived from high endemicity countries
Contacts	Close contacts of hepatitis A cases

Second selection step: full article

The articles selected for full text screening were divided into batches according to language and screened by a total of five reviewers working on different batches and covering the following languages: English, French, Italian, Spanish and Portuguese. Additional support was sought for translating articles in foreign languages such as: Bulgarian, Croatian, Czech, Danish, German, Greek, Hungarian, Polish, Romanian, Russian, Serbian, Slovak and Swedish. Articles were classified as included or excluded following the above mentioned criteria (Table 2.1, 2.2, 2.4).

Critical appraisal of the literature and data extraction

Data extraction and management

Two Excel databases were created to extract i) seroprevalence and ii) incidence data, using pre-defined sets of metadata (see below). The unit of extraction was defined as a 'study'. Each study provided seroprevalence or incidence data for a specific population group in a defined timeframe and/or geographical area. Each article selected for inclusion covered one or more studies.

Seroprevalence database: The following variables were extracted from each study reporting seroprevalence data: Endnote reference number, study ID, country/ies, region/city, urban/rural, study timeframe (period of sampling), study design and/or data source, random sampling (yes/no), case definition. In order to collect age-specific seroprevalence data, the following variables were collected: age group interval (starting and ending age), study population, sample size, seroprevalence (percentage of anti-HAV seropositives, %), weighted/standardised seroprevalence as provided by the study.

Age stratified seroprevalence data were included in the database according to the following criteria: only age bands wide a maximum of 10 years were allowed for individuals under 25; age bands wide a maximum of 20 years for individuals over 25; age bands wide a maximum of 15 years for intervals including 25 years of age (e.g. 18 to 30 was included); those age bands without a lower or an upper limit were excluded (e.g. 60+ age group).

Incidence database: The following variables were extracted from each study reporting incidence data: Endnote reference number, reference, country or countries, region/city, urban/rural, study timeframe (period/year of sampling). In order to collect incidence data the following variables were collected: age group interval (starting and ending age), study population, incidence per 100 000, weighted/standardised incidence.

Gender-stratified incidence and seroprevalence data were excluded.In addition, un-weighted data were preferred to weighted data, if both reported, and; data from the general population (and not on particular group) were preferably included as compared to data from specific population groups (e.g. non-migrant population versus general population including migrants).

When the study sampling timeframe spread over more than one year, we defined the timeframe as the interval middle-year, approximating toward the higher integer (e.g. sampling timeframe 1986–1989, mid-year defined as 1988).

Quality assessment of the studies

We took a simplified approach to assess the quality of the studies due to their heterogeneity and the extremely long period of the review. This does not imply an algorithm for the inclusion of the studies. For the same reason we decided not to perform a metaanalysis of these data. The quality assessment has only visual implications for the display of the data.

Each study included in the analysis was evaluated for its quality on the basis of two dimensions: sample size and sampling approach. The quality score was then captured in the seroprevalence database as an additional variable (quality score).

One point was attributed to the studies if sample size was 500 individuals or more, and one point if sampling was done through random selection. The quality score was obtained as the sum of the points scored by each study: 0 (low quality), 1 (medium quality), 2 (high quality).

Additional source: surveillance data reported to the European Surveillance System

The European Surveillance System (TESSy) is a highly flexible metadata-driven system for collection, validation, cleaning, analysis and dissemination of data. All EU Member States and EEA countries report their available data on communicable diseases to the system, including hepatitis A[4]. The European Surveillance System became functional in 2006.

In order to complement the literature search on incidence, hepatitis A data reported to TESSy were extracted and included in the analysis. The reported incidence data are available for all EU/EEA Member States for the period 2006–2013 with the exception of Croatia that joined the EU in 2013, and Liechtenstein not reporting information on hepatitis A to TESSy.

Data analysis and display

Data analysis

Seroprevalence

We described the included studies reporting seroprevalence data by quality score, sampling time and country.

We identified three time-frame intervals, namely 1975–1989, 1990–1999 and 2000–2014, according to year of sampling. We analysed the distribution of seroprevalence estimates in each defined time period by age and by country.

Given the substantial data variability, the extent of the available evidence among the different countries and the variety in study methodologies and literature available, results should be interpreted with caution. All the analyses are descriptive; the purpose is to summarise the available information from the different sources. The analyses included description of trends by countries.

Incidence

Reported incidence data came from: peer-reviewed articles, national notification registries (national health institute websites, national reports), and TESSy. Data analysis was based on a source prioritisation approach. TESSy data were prioritised for the period 2006–2013; national notification data were prioritised for the period before 2006, and for the period 2006–2013 for those countries not reporting to TESSy; data extracted from peer-reviewed articles were used when any of the above mentioned sources of information were not available.

[4] Decision No 2119/98/EC

Data exploration and graphics

The graphics were created using the statistical software R [26] and the packages ggplot2 [27], RColorBrewer [28] and plyr [29].

Seroprevalence

Each study is described by four dimensions:

- sampling timeframe: the year in which the study was performed (not the publication date) (colour)
- quality score: from 0 to 2 (See paragraph 0) (thickness)
- study-specific age intervals (from minimum to maximum) (x-axis)
- age-specific seroprevalence estimates (y-axis)

Age groups are plotted by a horizontal segment that begin at the minimum age and end at the maximum age. The vertical level gives the estimated level of seroprevalence for that age interval.

All the age intervals (i.e. horizontal segments) of the same study are connected by a thin line. Two vertical dotted lines mark the two age thresholds at 15 and 30 years as per WHO criteria for endemicity classification [8].

A synthetic representation of the seroprevalence profiles was provided drawing a curve of best fit on the scatter plots. A generalised logistic regression function was used to best fit to the points representing the mean estimates of the seroprevalence for each age group. Excel software was used to calculate the parameters used in the model.

Incidence

Each set of information on reported incidence from included studies or additional sources (e.g. TESSy) is displayed by

- Year of notification/sampling (x-axis)
- Reported incidence (y-axis)

Different data are shown either with lines (if values for more than one year are available) or with points (if values for only one year are available). TESSy data are always represented by a bright green line.

Two horizontal green lines mark the two thresholds at 2 and 20 cases per 100 000 population [30].

Presentation of results

Results are presented by country by mean of country profiles. Each country profile contains some brief country background information. Age-specific seroprevalence estimates and reported incidence overtime are presented and synthetised in a summary assessment.

Country background

The country background includes a set of information that can put in context the information retrieved on seroprevalence and incidence. This information has been sourced as follows:

- Total population as of January 2013: source: Eurostat http://epp.eurostat.ec.europa.eu/tgm/table.do?tab=table&language=en&pcode=tps00001&tableSelection=1&footnotes=yes&labeling=labels&plugin=1
- Human development index (2013): source: health for all database http://www.euro.who.int/en/data-and-evidence/databases/european-health-for-all-database-hfa-db
- HAV vaccine policy recommendations: source: internal ECDC survey to the Member States conducted in 2013 and Member State consultation and validation from October toNovember 2014.
- Seroprevalence studies by quality score: number of studies included per country according to their quality.
- Seroprevalence study timeframe: timeframe from the first year with data available to the last by country.

Hepatitis A country assessment

The results of the systematic review on seroprevalence and incidence data are presented and analysed in a country specific approach. The country endemicity profile has been developed against a framework of three indicators as described below. A summary assessment based on these three indicators is provided per each country with available data.

Seroprevalence assessment

Seroprevalence data are presented per country report in a 'Country X_Figure 1' divided into two panels.

- Panel (a) provides a historical perspective on the changes in seroprevalence and distributions of studies over time by presenting the data over the three consecutive periods 1975–1989, 1990-1999 and 2000–2014.
- Panel (b) provides an overall view over the entire time-period, thus helping the appreciation of the changes over time.

Seroprevalence is categorised based on WHO criteria [8]for the sake of comparability:

Table 2.5. Seroprevalence assessment: classification criteria

Classification	Assessment criteria: HAV seroprevalence
Very low	<50% by age 30 years
Low	≥50% by age 30 years, with <50% by age 15
Intermediate	≥50% by age 15 years, with <90% by age 10 years
High	≥90% by age 15 years

The seroprevalence assessment is provided for the periods 1975–1989, 1990–1999 and 2000–2013 based on available data. The assessment provides the seroprevalence-based appraisal at the most recent period, unless differently specified.

In order to assess the size of the EU/EEA population classified under each category for each of the three periods, Eurostat data was used. The year 1980 population was used for 1975–1989; 1990 for 1990–1999; and 2000 for 2000–2014.

Incidence assessment

Incidence was assessed based on reported incidence data over the period 2006–2013. The assessment was based on the threshold of 20 cases per 100 000 according to US CDC recommendations on vaccination strategy [30]. Incidence data are presented in 'Country X_Figure 2' as reported rate per 100 000.

Table 2.6. Incidence assessment: classification criteria

Classification	Assessment criteria: HAV incidence rate
Very low	<2 cases/100 000
Low	between 2 and 19 cases/100 000
Intermediate	between 20 and 199 cases/100 000
High	≥200 cases/100 000

Countries are classified as having a very low incidence profile if incidence was consistently below the threshold of 2 cases per 100 000 over the period 2006–2013; and similarly for the low and intermediate incidence thresholds.

Susceptibility to HAV in adults

The third indicator, HAV susceptibility in adults (≥30 years), aims at providing an estimate of the current proportion of adult susceptible individuals in the population. It combines seroprevalence estimates at 30 years and 50 years in the period 2000–2014, as described in the table below. Countries with discordant assessments at 30 and 50 years were classified according to the lower level of susceptibility to HAV infection. For those countries with no seroprevalence estimates for the period 2000-2014, extrapolations were made based on available seroprevalence and incidence data. Countries were classified in four groups: adults with very high, high, moderate and low susceptibility to HAV infection.

Table 2.7. Susceptibility in adults: classification criteria

Classification – susceptibility to HAV infection at 30 years	Assessment criteria:	Classification – susceptibility to HAV infection at 50 years	Assessment criteria:
Very high	>70%	Very high	>50%
High	50–70%	Very high	>50%
Moderate	30–50%	High	30–50%
Low	<30%	Moderate/low	<30%

3. Results of the systematic literature review

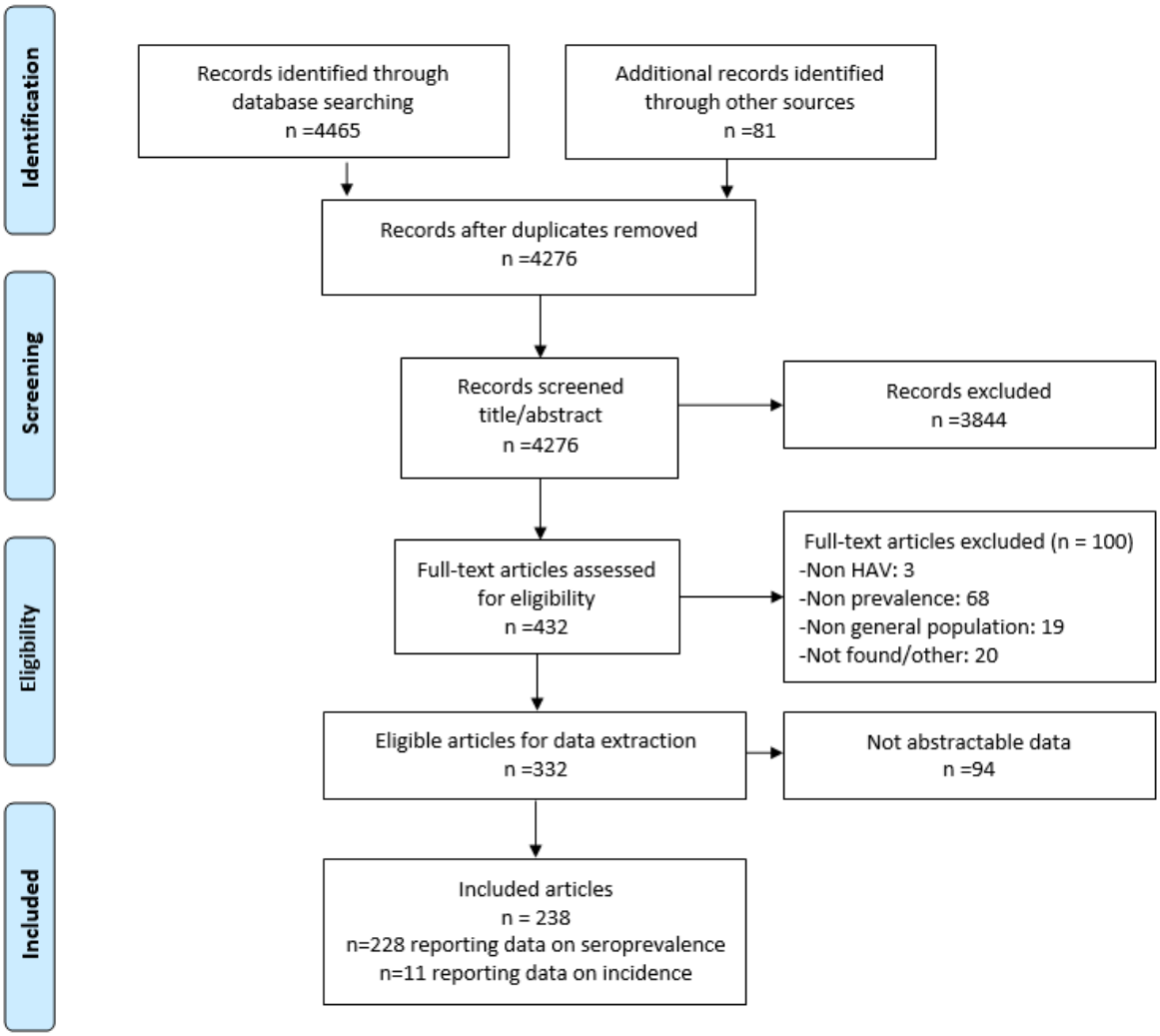
Overall results and flowchart

The results of the literature search are presented in Figure 1. After eliminating duplicates, a total of 4 195 articles were transferred to the Endnote library. An additional 81 articles were retrieved through grey literature search.

After the first round of title/abstract screening, 432 articles were selected for full text screening. Of these, three could not be retrieved. Then, 332 articles of the remaining 428 were selected for data extraction. During this latter phase 94 articles were discarded as data did not comply with the criteria for data extraction detailed above.

A total of 228 articles reporting seroprevalence data on 27 EU/EEA Member States, and 11 articles reporting incidence were included. No data were available for Liechtenstein.

Figure 3.1. Flowchart of literature selection (based on Prisma 2009 Flow Diagram www.prisma-statement.org)



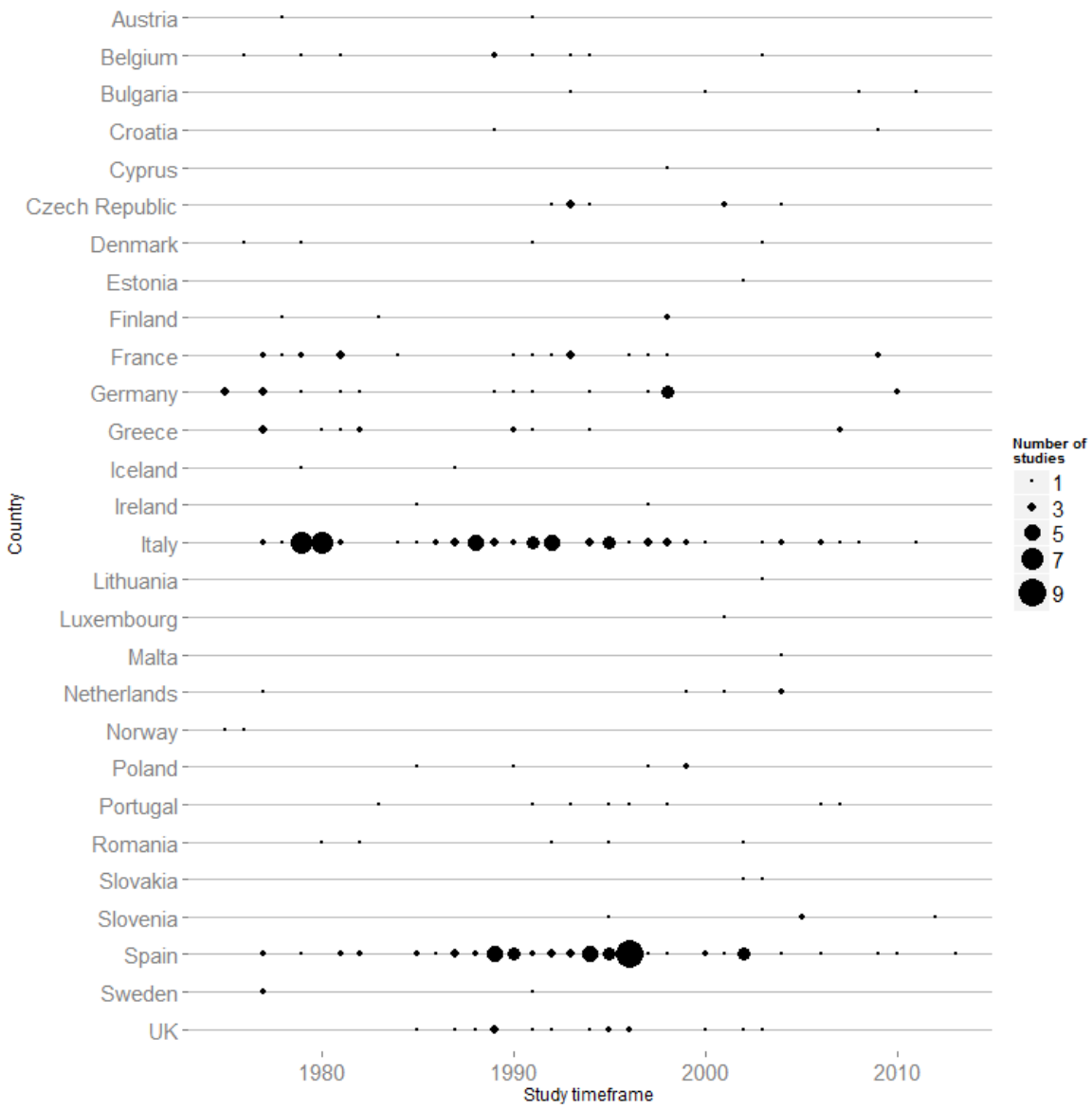
Seroprevalence data

The 228 articles from the systematic literature review for which data were extracted reported 279 studies with a specific timeframe and/or geographical area (Table 7). The 279 studies contributed 1 315 age-specific estimates (median estimates per study: 4; range 1–32). Seroprevalence estimates were related to all EU/EEA countries, except Hungary, Latvia and Liechtenstein for which it was not possible to retrieve any extractable data in the literature. The median number of studies per country was four, ranging from 1– to 70. Date of sampling ranged from 1975 to 2013.

Table 3.1. Distribution of seroprevalence studies, number of estimates, studies timeframe and studies quality score by country

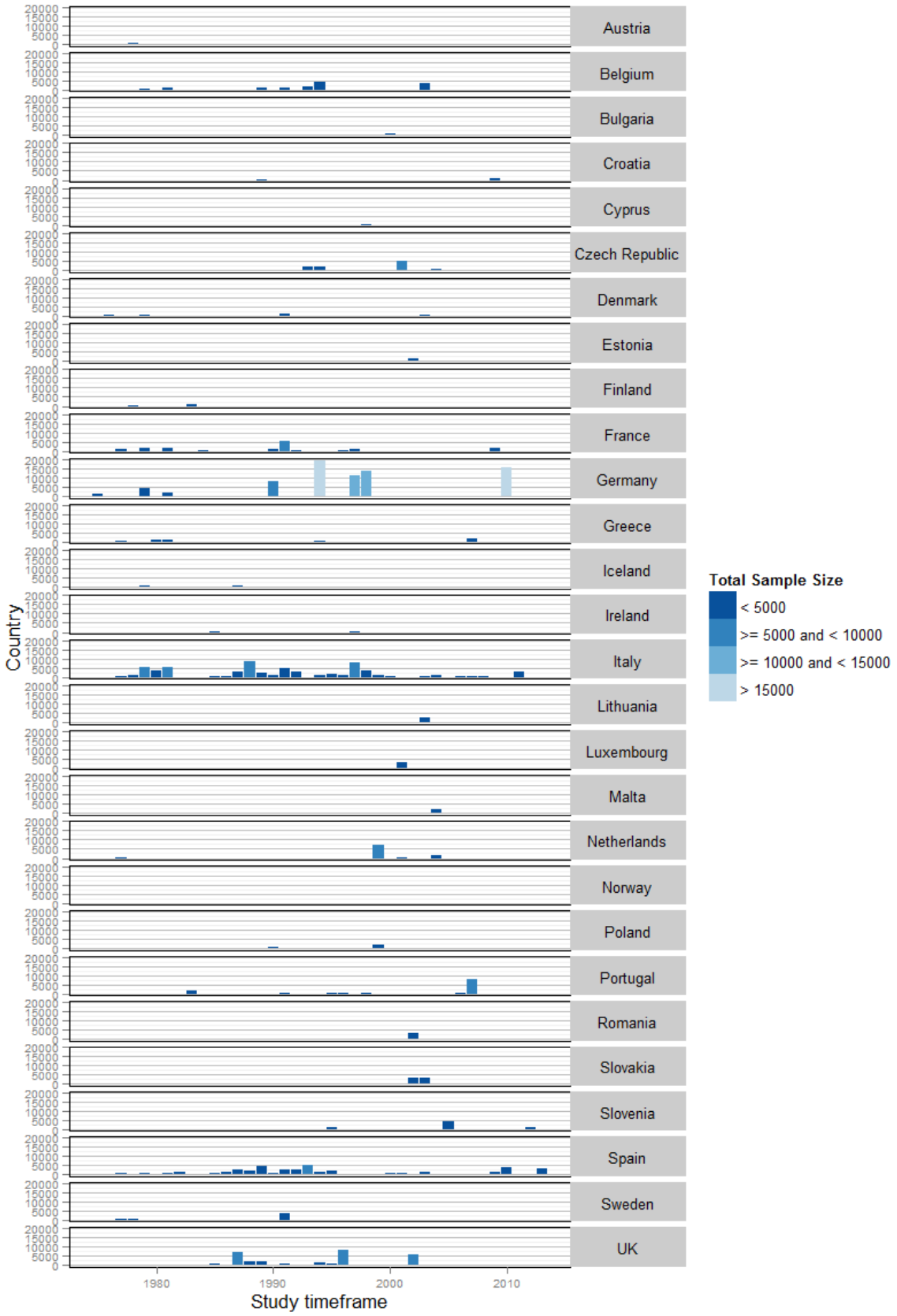
Country	Studies	Estimates	First year	Last year	Quality score 0	Quality score 1	Quality score 2
Austria	2	7	1978	1991	1	1	0
Belgium	9	51	1976	2003	1	6	2
Bulgaria	4	13	1993	2011	2	2	0
Croatia	2	14	1989	2009	1	1	0
Cyprus	1	2	1998	1998	0	1	0
Czech Republic	8	64	1992	2004	1	5	2
Denmark	4	19	1976	2003	1	2	1
Estonia	1	7	2002	2002	0	1	0
Finland	4	18	1978	1998	1	1	2
France	20	77	1977	2009	6	12	2
Germany	20	111	1975	2010	8	5	7
Greece	13	27	1977	2007	9	4	0
Iceland	2	10	1979	1987	1	1	0
Ireland	2	5	1985	1997	2	0	0
Italy	70	312	1977	2011	23	41	6
Lithuania	1	3	2003	2003	0	0	1
Luxembourg	1	22	2001	2001	0	1	0
Malta	1	6	2004	2004	0	0	1
Netherlands	5	14	1977	2007	0	3	2
Norway	2	7	1975	1976	2	0	0
Poland	5	25	1985	1999	3	2	0
Portugal	8	40	1983	2007	3	3	2
Romania	5	20	1980	2002	4	0	1
Slovakia	2	15	2002	2003	0	0	2
Slovenia	4	23	1995	2012	0	4	0
Spain	64	308	1977	2013	26	23	15
Sweden	3	10	1977	1991	0	2	1
UK	16	85	1985	2003	5	6	5
EU/EEA	279	1315	1975	2013	100	127	52

Figure 3.2. Distribution of selected articles over the study period by year of sampling (1975–2013).



The distribution of the sample size of selected articles per year and country is displayed in Figure 3.3 below. If more than one sample was taken in the same year for a country, the samples of the different studies were summed up. Note: this graph gives absolute numbers of total sample size and not relative to population size of the country.

Figure 3.3. Distribution of selected articles' sample size over the study period 1975–2014 (sampling years 1975-2013), by year of sampling.



Incidence data

A total of 11 articles reporting data on HAV incidence were retrieved as part of the systematic literature review. They corresponded to 23 studies with a specific timeframe and/or geographical area. The 23 studies contributed 203 year-specific estimates (median estimates per study: 12; range 1– to 23) and were related to 18 EU/EEA countries (median studies per country: 1; range from 1 to 2). Year of sampling ranges from 1975–5 to 2013.

In addition, national notifications were retrieved for 14 countries contributing to 283 estimates (median number of estimates per national notification source: 19.5; range 4 to 39).

Data from TESSY were extracted for the period 2006–2013 (2006–2012 for Italy) for all EU/EEA countries except Croatia and Liechtenstein.

As previously described, incidence data were included in the analysis based on a source prioritisation algorithm. The included data and their sources are described in details in Table 3.2.

Table 3.2. Distribution of incidence estimates from TESSy, national public health institutes and studies extracted from the literature by country

Country	Estimates from TESSy	Estimates from national reporting	Studies extracted	Study estimates	First year	Last year
Austria	8	0	2	13	1990	2013
Belgium	8	13	1	4	1990	2013
Bulgaria	8	23	0	0	1984	2013
Croatia	0	39	0	0	1975	2013
Cyprus	8	0	0	0	2006	2013
Czech Republic	8	8	2	31	1975	2013
Denmark	8	0	2	17	1980	2013
Estonia	8	7	2	23	1985	2013
Finland	8	0	0	0	2006	2013
France	8	0	1	3	1992	2013
Germany	8	0	1	12	1990	2013
Greece	8	0	1	12	1990	2013
Hungary	8	0	1	12	1990	2013
Iceland	8	0	1	1	1984	2013
Ireland	8	0	0	0	2006	2013
Italy	7	22	0	0	1985	2012
Latvia	8	32	0	0	1999	2013
Lithuania	8	32	0	0	1975	2013
Luxembourg	8	0	1	12	1990	2013
Malta	8	0	1	12	1990	2013
Netherlands	8	0	2	24	1990	2013
Norway	8	32	0	0	1989	2013
Poland	8	8	1	8	1990	2013
Portugal	8	0	0	0	2006	2013
Romania	8	15	1	2	1990	2013
Slovakia	8	31	0	0	2006	2013
Slovenia	8	0	1	12	1990	2013
Spain	8	0	1	1	2006	2013
Sweden	8	4	1	4	1986	2013
UK	8	17	0	0	1990	2013
EU/EEA	231	283	23	203	1975	2013

4. HAV endemicity patterns in the EU/EEA

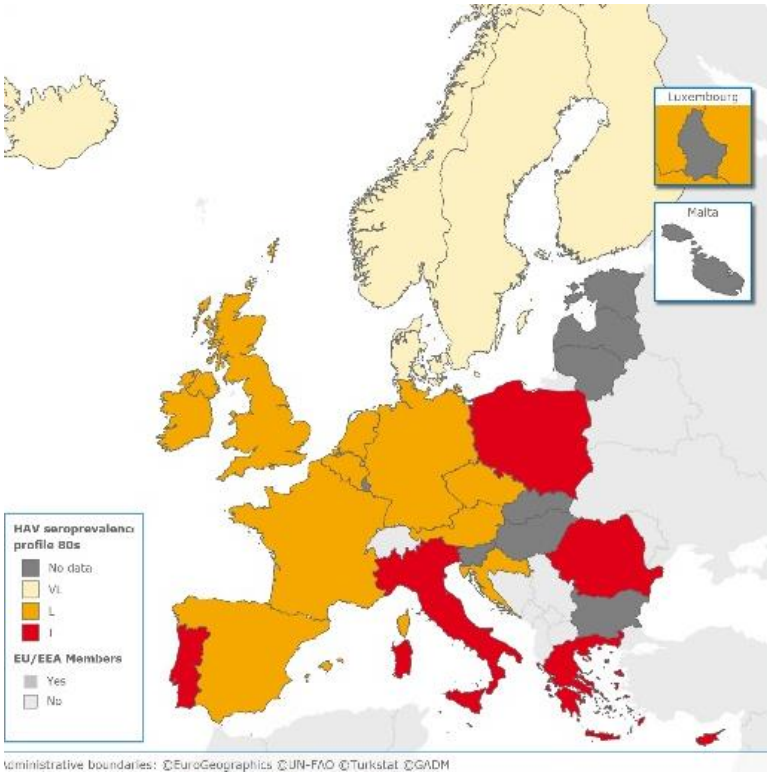
HAV seroprevalence in the EU/EEA

The geographic distribution of the seroprevalence profiles according to the criteria stated in Table 2.5 in the methods section, are represented in Figure 5.1 below, by time period of data collection (1975–1989, 1990–1999 and 2000–2014). Data on seroprevalence by calendar period were available from 23, 24 and 28 countries, respectively.

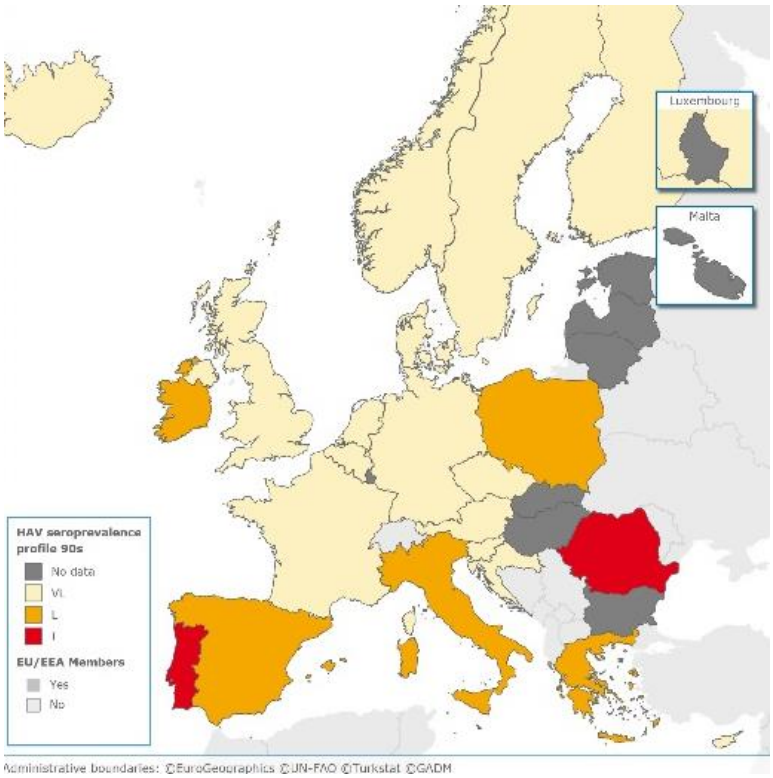
Five countries had a very low seroprevalence profile for the period 1975–1989 (Fig 4.1, panel 1), 15 for the 1990–1999 period (Fig 4.1, panel 2) and 24 for the most recent period studied (Fig 4.3). On the other hand, six countries were at intermediate level for the first period, two in 1990–2000 and in the latest period only one country has been classified as intermediate.

Figure 4.1. Geographical distribution of the HAV seroprevalence profiles in the EU/EEA in three periods, 1975-2013

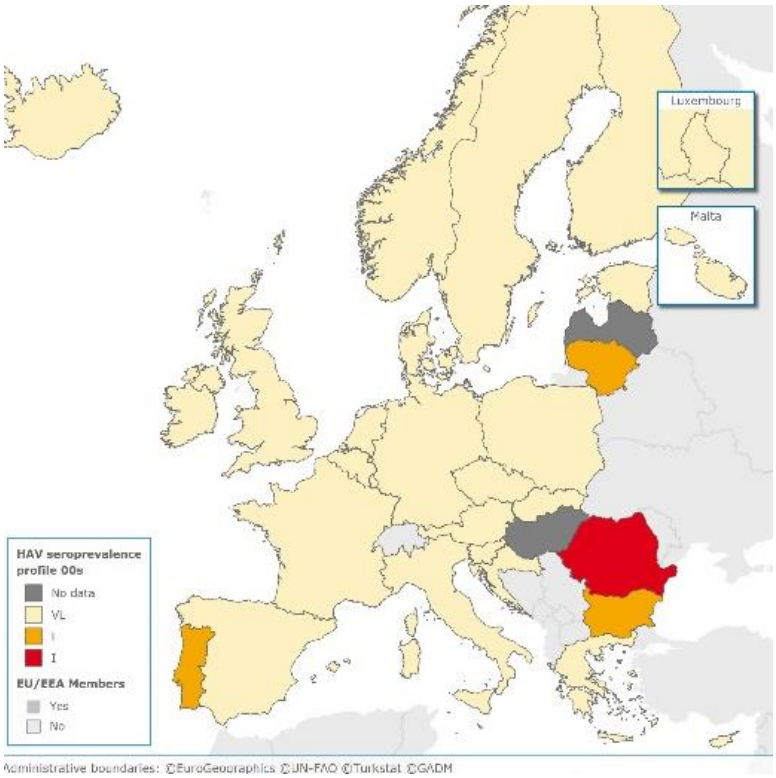
Studies with sampling year from 1975–1989



Studies with sampling year from 1990–1999



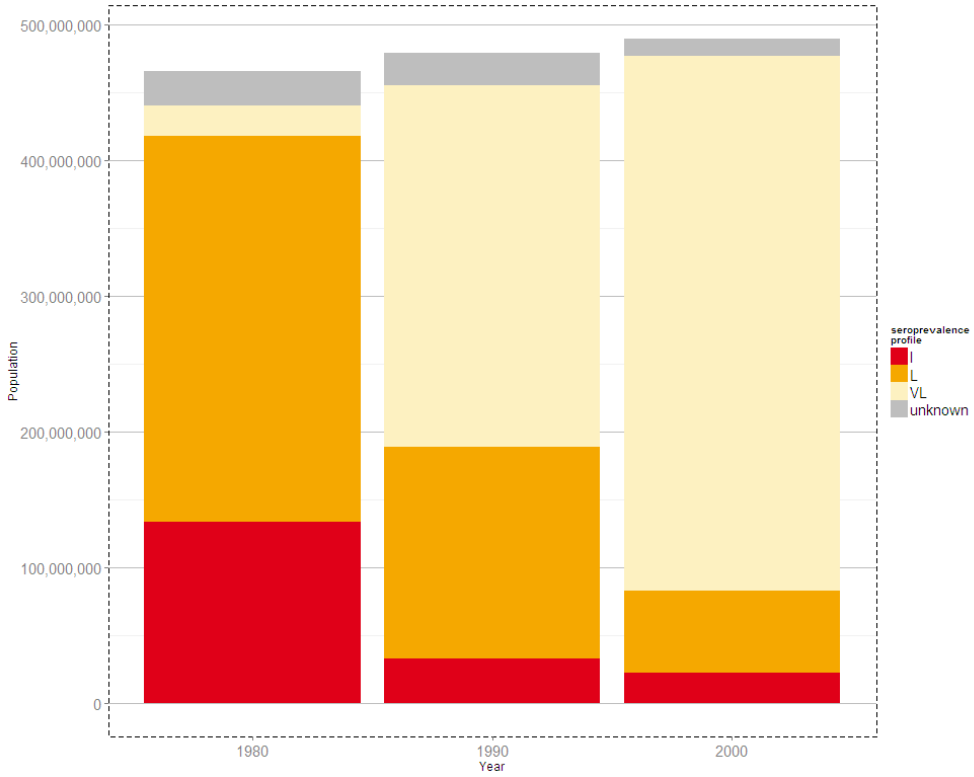
Studies with sampling year from 2000–2013



VL=very low, L=low, I=intermediate

Figure 4.2 and Table 4.1 provide an estimate of the size of the EU/EEA population for each seroepidemiological profile for the three periods. For the period 1975-1990, around 5% of the EU/EEA population was living in areas of very low endemicity (5 EU/EEA countries), whereas nowadays this percentage is around 80% (24 EU/EEA countries).

Figure 4.2. Size of the EU population for each seroepidemiological profile



I= intermediate, L=low, VL=very low

The first bar includes seroprevalence data from 1975–1989 and EU/EEA population data from Eurostat as of 1980; the second bar includes data from 1990–1999 and population as of 1990, and the third bar includes data from 2000–2013 and population as of 2000. The French population used is that of metropolitan France.

Table 4.1. Population[1] in EU/EEA countries according to their seroprevalence profile[2] and year

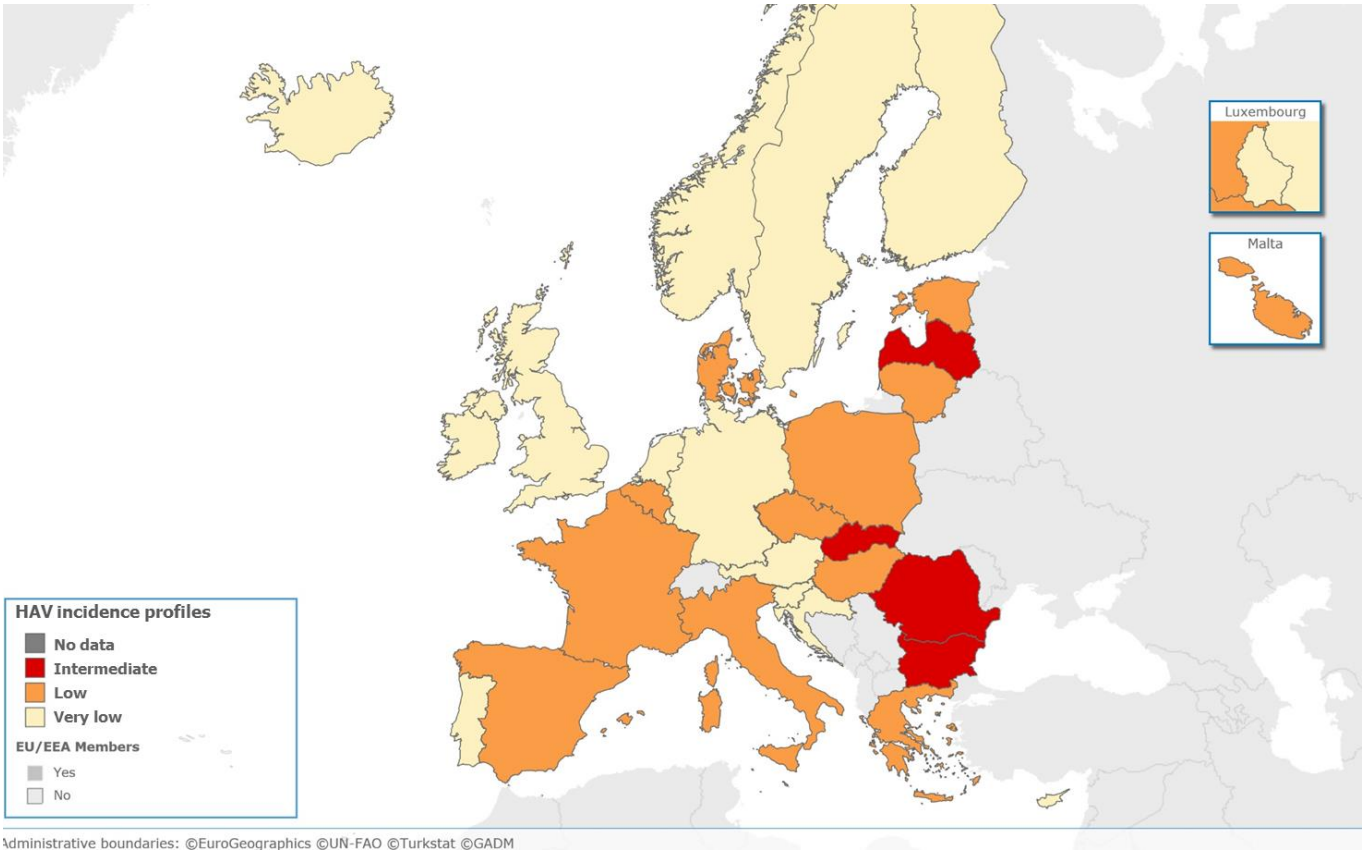
Year	Population of intermediate seroprevalence countries		Population of low seroprevalence countries		Population of very low seroprevalence countries		Population of unknown seroprevalence countries	
	n	%	n	%	n	%	N	%
1980	133 738 138	28.7	284 082 424	61	22 502 299	4.8	25 629 685	5.5
1990	33 207 390	6.9	155 954 230	32.5	266 159 399	55.5	24 326 663	5.1
2000	22 455 485	4.6	60 215 275	12.3	394 754 781	80.6	12 603 359	2.6

Data from Eurostat. [2] In 1980 countries were classified using seroprevalence data from 1975-1989, in 1990 data from 1990 to 1999 and in 2000 from 2000 to 2014. French population used is that of metropolitan France.

HAV incidence in the EU/EEA

Based on TESSy data for the period 2006–2013, and according to the criteria stated in Table 2.6 in the 'Methods' section, the EU/EEA countries display three different incidence profiles. Out of the 30 countries for which incidence data were available, 14 were classified as 'very low'; 12 were classified as 'low' and characterised by a reported incidence oscillating around (eight countries) or above (four countries) 2 cases per 100 000 population; and four were classified as 'intermediate' and characterised by a reported incidence oscillating around two countries or above 20 cases per 100 000 population. The geographical distribution of the different profiles is represented in Figure 4.3 below.

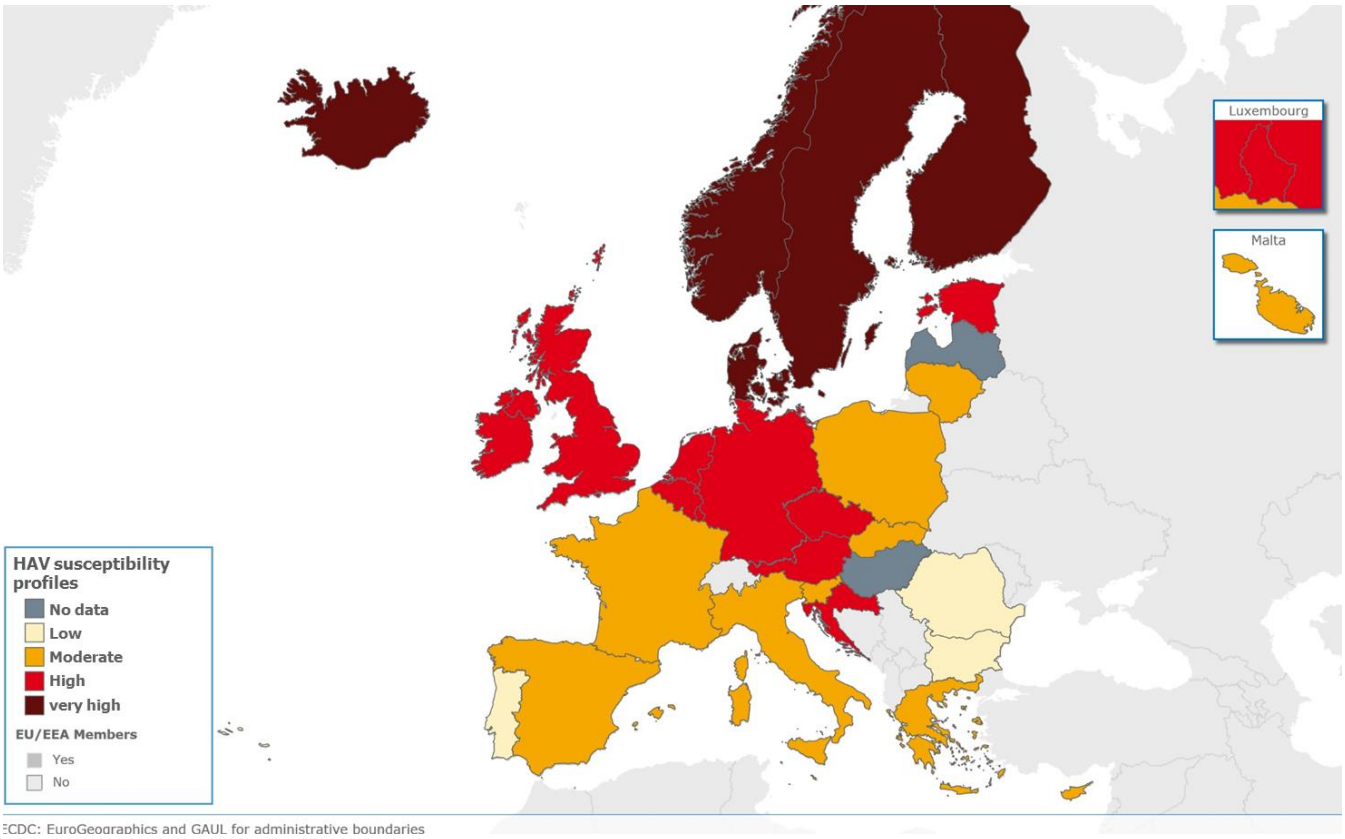
Figure 4.3. Geographical distribution of the reported HAV incidence profiles, EU/EEA 2006–2013



HAV susceptibility in adults in the EU/EEA

Using the criteria discussed in the 'Methods' section (see Table 2.7), the EU/EEA countries belong to one of four different susceptibility-in-adults profiles, extrapolated from the seroprevalence estimates. Out of the 28 countries for which seroprevalence data in adults were available, three were classified as having 'low' susceptibility among adults (Romania, Bulgaria, Portugal), ten as 'moderate' (Spain, Malta, Lithuania, France, Italy, Poland, Cyprus, Slovakia, Greece, Slovenia), ten as 'high' (Croatia, the Netherlands, Ireland, Czech Republic, UK, Germany, Luxembourg, Belgium, Austria and Estonia) and five as 'very high' (Norway, Sweden, Iceland, Finland and Denmark). The geographical distribution of the different profiles is represented in Figure 5.4 below.

Figure 4.4. Geographical distribution of the HAV susceptibility profiles, EU/EEA, 2000–2014.



According to this classification, and considering country population size, we estimate that at the present time, 25 958 327 EU/EEA citizen live in countries with very high susceptibility profiles to HAV infection; 202 048 685 live in countries with a high susceptibility profile; 233 421 161 in countries with a moderate susptibility profile; and 37 791 915 in countries at overall low susceptibility to HAV infection, based on the evidence collected from the seroprevalence estimates reported in this study (Figure 4.4).

HAV seroprevalence according to current susceptibility profiles

We present the seroprevalence data for all EU/EEA countries grouped according to their susceptibility profiles (see previous section) over the three pre-defined time periods spanning the whole study time horizon from 1975 to 2014 (Figure 4.4). The four groups show a similar pattern of decreasing seroprevalence over time, illustrated by the shifting of the seroprevalence curve from the upper left corner of the plot area towards centre/right corner.

A synthetic representation of the seroprevalence profiles as a curve of best fit explained on the point on seroprevalence on page 8, is shown in Figure 4.5. The shape of the seroprevalence curves also changes over time and across groups, evolving from a concave curve (low susceptibility group, 1975–1989) to a sigmoid-shaped curve (moderate susceptibility group, 1990-1999) and to a convex curve (very high susceptibility group, all periods).

These changes in the curves appear to correlate with different levels of transmission and the median age of HAV infection in the population, i.e. high transmission in younger ages is represented by the concave curve; very low transmission in all age groups is represented by a convex curve.

Figure 4.5. Overall age-specific HAV seroprevalence in the EU/EEA by susceptibility profile (low, moderate, high and very high) and time period, 1975–2014.

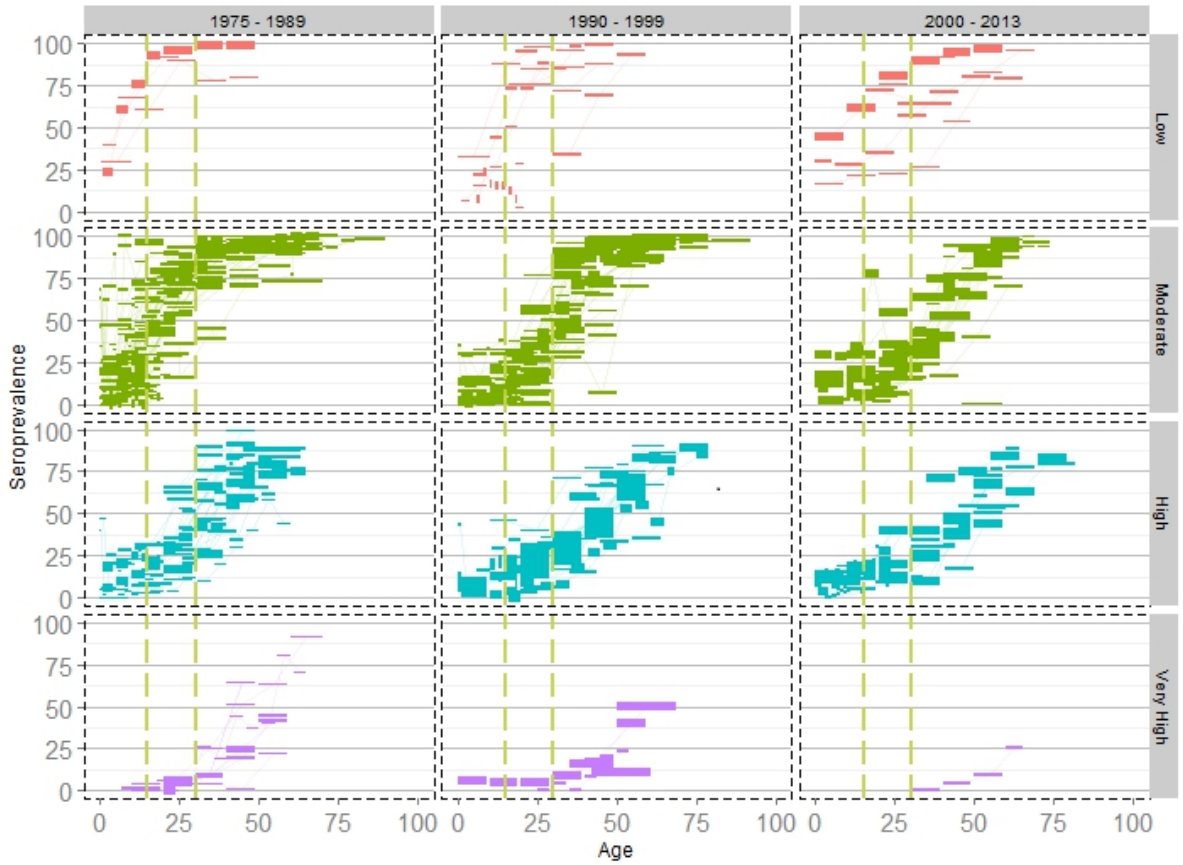
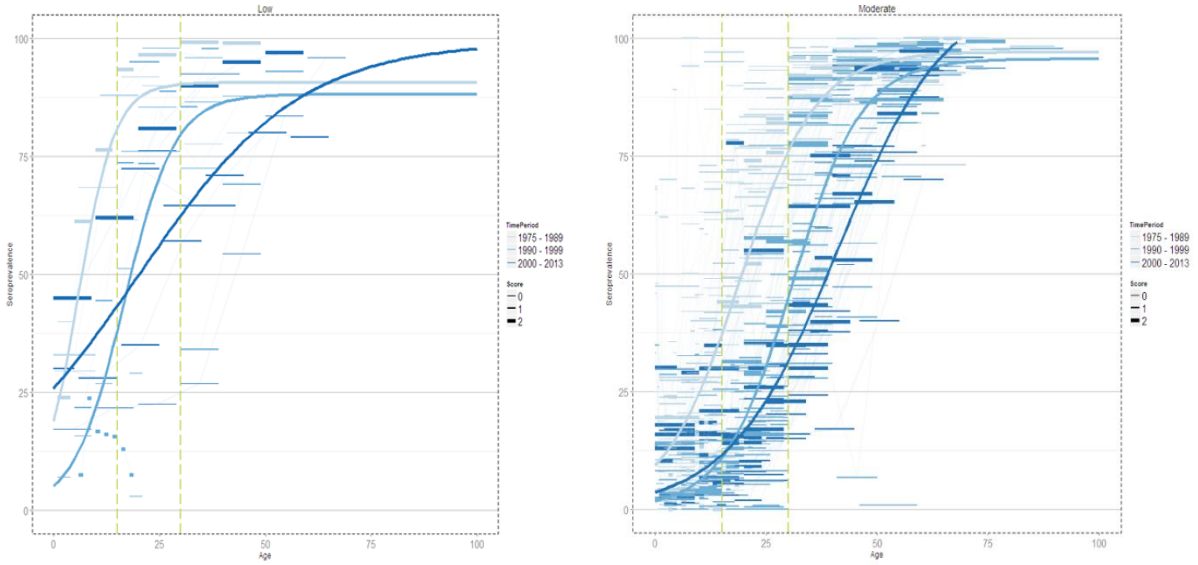
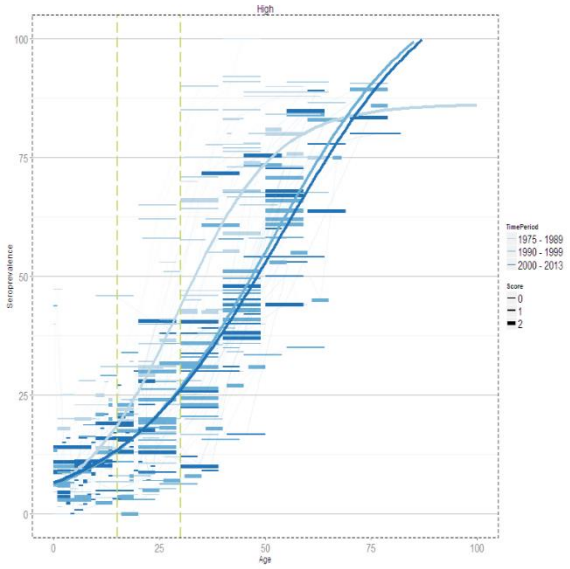
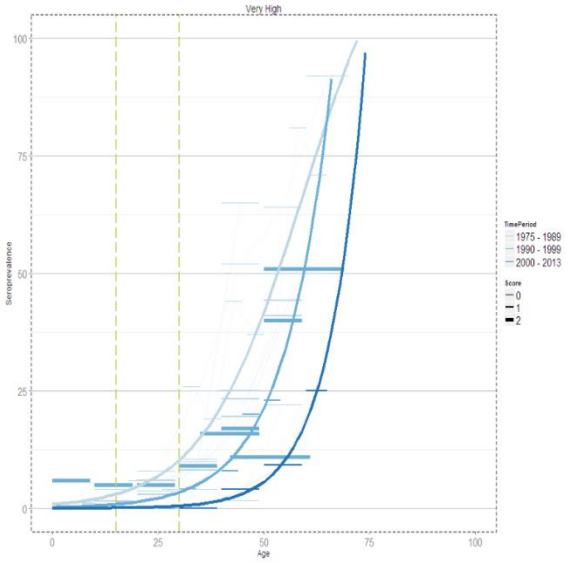


Figure 4.6. Age-specific HAV seroprevalence in the EU/EEA by susceptibility profile (low, moderate, high and very high) and time period (19751989, 1990–1999, 2000–2014)




High
Seroprevalence
Age
TimePeriod
1975 - 1989
1990 - 1999
2000 - 2013
Score
0
1
2


Very High
Seroprevalence
Age
TimePeriod
1975 - 1989
1990 - 1999
2000 - 2013
Score
0
1
2

5. Conclusions

The review of HA endemicity suggests a high degree of temporal and spatial variability across the EU/EEA. The endemicity of HA has changed in the EU/EEA over the past four decades, showing a decreasing trend in both seroprevalence and reported incidence data. HA endemicity has an important geographical gradient. Nordic countries consistently show a lower level of endemicity over time as compared to central, southern and eastern EU/EEA countries.

All countries presented a decreasing trend over time although available seroprevalence data reveal a wide range of variability across the region. . The decreasing trend is probably due to several concurrent factors such as improved hygiene, sanitation, socio-economic conditions and increased availability of vaccines and food-safety measures [2]. Twenty four EU/EEA countries are classified as having a very low seroprevalence profile according to WHO criteria [8], which are based on seroprevalence estimates at 15 and 30 years of age.

However, when taking into consideration the susceptibility profiles, our analysis shows a less homogeneous picture in Europe. According to the susceptibility profiles, and assuming that the most recent protection through vaccination is not reflected, a substantial part of the EU/EEA population may be considered susceptible for HAV infection. The susceptibility indicator is influenced by historical developments of the epidemiology of HAV as reflected by the level of seroprevalence in the birth cohorts 1930–1980, allowing for a higher level of detail and discrimination between countries within the EU/EEA.

Showing susceptibility rather than seroprevalence might indicate more effectively where the morbidity and mortality may be higher, since the risk increases with increasing age. Additionally, the ability to better discriminate the size of the population at risk plays an important role in an aging European population where HAV infection is associated with increasing movement of people and goods. Moreover, these profiles could be used to warn susceptible travellers visiting areas with different HA profiles to be vaccinated before travel [31].

The reported incidence of HA has been steadily decreasing in all EU/EEA countries over the past decades [17,18]. Incidence profiles between 2006 and 2013 were analysed in more detail thanks to the comparability between the data reported to TESSy. Incidence profiles of EU/EEA countries are consistent with the seroprevalence and susceptibility profiles, with few exceptions. These few differences are presumably the consequence of the different sensitivity of the different national surveillance systems or of representativeness and quality of national seroprevalence studies. Fourteen EU/EEA countries are classified as having a very low incidence profile and 12 countries a low one, indicating a minimal level of local virus circulation in these countries. On the other hand, the seroprevalence estimates show evidence that HA is still endemic in a few EU/EEA countries.

Reviewing the vaccination strategies in place in the EU/EEA, most countries follow WHO recommendations [8] for low/very low seroprevalence countries to vaccinate groups at increased risk for infection. There is a high level of heterogeneity in the definition and selection of risk groups, as well as in the financial coverage of the different vaccination interventions, as shown in the country profiles. Few countries/regions in the EU/EEA at low/very low level of seroprevalence recommend or provide universal vaccination; Greece, Catalonia region in Spain and Puglia in Italy provide universal vaccination, whereas in Poland, the Czech Republic and Cyprus, it is recommended but not funded. All countries have risk group vaccination recommendations. Outside the EU/EEA, the US and Israel provide universal childhood vaccination. According to WHO [8], countries at intermediate level of seroprevalence should implement universal vaccination.

There are a number of limitations to the methods and the data analysed in this study. Firstly, the publications retrieved and selected for inclusion in the review may not be fully representative of the epidemiological situation in EU/EEA countries. This may be due to search limitations, e.g. as alternative databases such as Global Health (CAB), Popline and Web of Knowledge (Web of Science) have not been searched or due to publication bias. Historical factors may also have impacted the search, and in particular difficulty in retrieving information from former Soviet Union countries such as the Baltic countries, may have resulted in a potential geographical bias. National representativeness of the data may be sub-optimal as many published studies were carried out at the local level (e.g. focusing on major cities, districts or regions within a country) or focused only on certain time periods.

Variations of HAV seroprevalence levels within countries are known, and published studies may over-represent areas at higher or lower endemicity depending on overarching objectives and local research interest. In addition, at least 15% of the included studies sampled blood donors. Blood donors may not represent the general adult population for various reasons. Certain groups are excluded from blood donation, including pregnant women, people presenting with some chronic illnesses, e.g. blood-borne infections or risk factors for their acquisition. Blood donors' socio-demographic characteristics may also vary amongst countries depending on blood donation performed on a voluntary or reimbursed basis. However, we believe that this should have a limited overall impact on HAV seroprevalence and incidence. Also, data from blood donors were included in the review and analysis without discriminating between first-time and returning blood donors.

Only observational studies were included in this review, and study grading was quite crude, based only on sample size and sampling design (random/non random sampling). No sample size cut-off was applied. Information on sample collection and testing strategy was not extracted, nor analysed. Different sample collection methods (e.g. serum, plasma, blood spot) may lead to different sensitivity and specificity of the estimates. Likewise, different diagnostic methods may affect comparability of the results, even more so if we consider the developments in laboratory HAV diagnosis since 1975 [32].

Preference for incidence data collected through TESSy over other sources was granted on the basis of the higher level of standardisation attributed to the EU-wide surveillance system (e.g. EU case definition, common meta-dataset). Nevertheless, comparability of incidence data across countries is hampered by underlying differences in the national surveillance system and associated underestimation (under-ascertainment and under-reporting) fraction.

The framework for the assessment of country seroprevalence was adopted from WHO [8] to ensure comparability and coherence with already published evidence. In contrast, susceptibility and incidence profile assessment frameworks were developed ad hoc based on available evidence, as to our knowledge there are no similar approaches published in the literature.

Finally, the impact of vaccination coverage on population seroprevalence has not been taken into account, unless captured by seroprevalence studies. This may be an important factor affecting the validity of the seroprevalence data for those countries where no seroprevalence study was conducted in the recent years, i.e. after licensing of HAV vaccines in the second half of the 1990. This is the case of Sweden, a country for which no recent seroprevalence data are available, but with reported high HAV vaccination coverage among travellers (79% of the travellers immunised against HA in 2007) [33] and other high risk groups. In general, lack of robust and widespread data on HAV vaccine coverage at national and EU-level hampers a more accurate assessment of current seroprevalence in the EU/EEA population.

Knowledge gaps

This study has highlighted some important knowledge gaps that should be addressed in order to assess with a higher level of accuracy the current epidemiological situation of HAV infections in the EU/EEA.

Overall, surveillance systems are able to catch only a fraction of the cases in the community, and data on HA incidence may only show the tip of the iceberg. Several steps must be ascertained for a case to be detected by laboratory-based surveillance: the ill person must seek medical care, a stool sample must be taken and tested for, the pathogen must be detected and the laboratory and physician must report to the health authorities.

HAV reporting from all EU/EEA countries through TESSy has reached a considerable level of standardisation. Nevertheless, a detailed analysis to assess the quality and comparability of the data would be needed. This would serve the purpose of understanding how the interplay of national healthcare and surveillance system features affect the underestimation of HAV cases in the population and, in turn, comparability across the whole region. Such an assessment would also constitute a solid basis for further strengthening the current surveillance system.

Presently in the EU/EEA, there is little detailed and up-to-date data available on coverage of HAV vaccination and vaccine-induced protection among the general population and/or risk groups. Some countries have very few or no studies performed after 1996 (when the vaccine was licensed) that could capture vaccine-induced protection; on the other hand, the interpretation of seroprevalence data would be more challenging in these studies. This information gap impacts the assessment of vaccine effectiveness, the currently susceptible population to HAV infection as well as HAV time trends. Furthermore, efforts in implementing seroprevalence surveys and setting up vaccination registries will help in closing this gap at national and supranational level.

Finally, data from HAV molecular surveillance may improve the understanding and the control of HAV transmission patterns and outbreaks within the EU. This has been shown by the experience through HAVNET, a global network of scientists working in HA reference laboratories which share molecular and epidemiological data on HA[34]. Furthermore, increased and more complete information on virus genetic characterisation and comparison within EU/EEA countries would shed more light on the impact of local virus circulation and importation on the occurrence of HAV cases [35].

ECDC will continue working together with Expert Panel members and the EU Member States to address these knowledge gaps.

Key message

In conclusion, this study provides a comprehensive picture of HAV infection epidemiology in the EU/EEA over time and across the region. It demonstrates that the HAV circulation has been decreasing steadily over the past four decades in the EU/EEA as a whole, although with important differences at national and sub-regional level, and that a progressively growing part of the EU/EEA population has become susceptible to HAV infection. This study proposes susceptibility among adults as a more specific indicator of the HAV epidemiological situation in the EU/EEA. Moreover, the high level of susceptibility of the population, together with the evidence of areas of local HAV circulation in the EU/EEA, support the need to reconsider the overall prevention strategy. The study also identifies important knowledge gaps that should be addressed, alongside the evidence base collected in this report, when designing specific prevention and control measures to further decrease HAV circulation in the EU/EEA.

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Annex 1. Country profiles

Austria

Population (January 2013):	8 451 860
Human development index (2013):	0.881
HAV vaccine recommendations:	HAV vaccination is recommended for children over 2 years of age and adults, particularly if the following indicators apply: • 1. children entering institutions • 2. adults at occupational increased risk of exposure • 3. persons with chronic liver disease • 4. contacts of HAV patients or HAV shedders • 5. tourists, occupational travellers, diplomatic service and development assistance in endemic areas. HAV vaccination is not publicly funded.
Seroprevalence studies by quality score:	score 0:1 study score 1:1 study score 2: 0 studies
Seroprevalence studies timeframe:	1978–1991

A study in 1978 estimated HAV seroprevalence in those under 30 years of age to be over 50%, while one in 1991 estimated that HAV seroprevalence in this age group was 7%. Therefore, it is likely that Austria transitioned from a low to a very low HAV endemicity during the 1980s (Austria_Figure 1).

Austria_Table 1. Hepatitis A endemicity level by time period

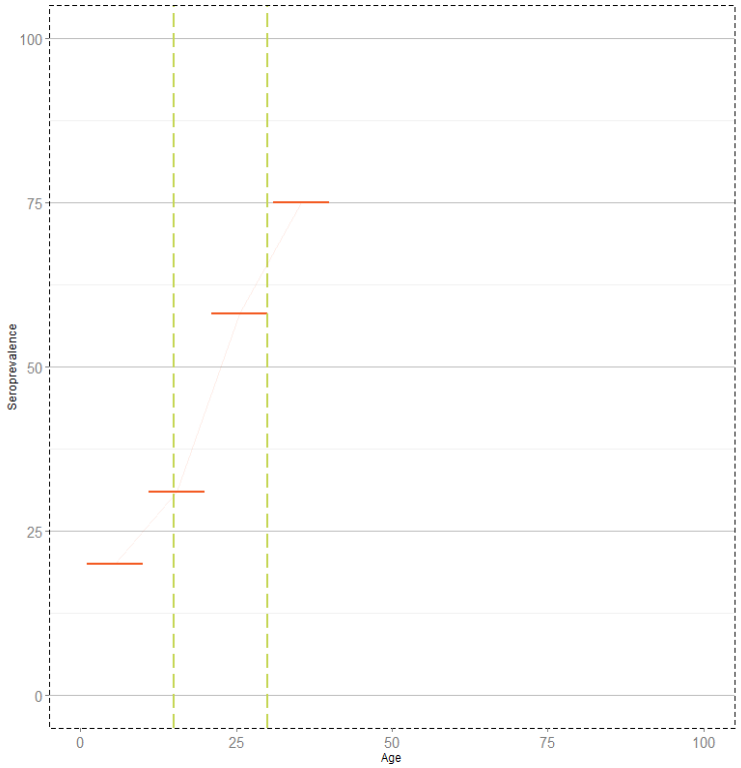
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence oscilated between 2 and 6/100 000 from 1989 to 2000 (Austria_Figure 2). The reported incidence based on TESSy data has been under 2/100 000 every year since 2006, although with a slightly increasing trend. This is consistent with a very low endemicity picture.

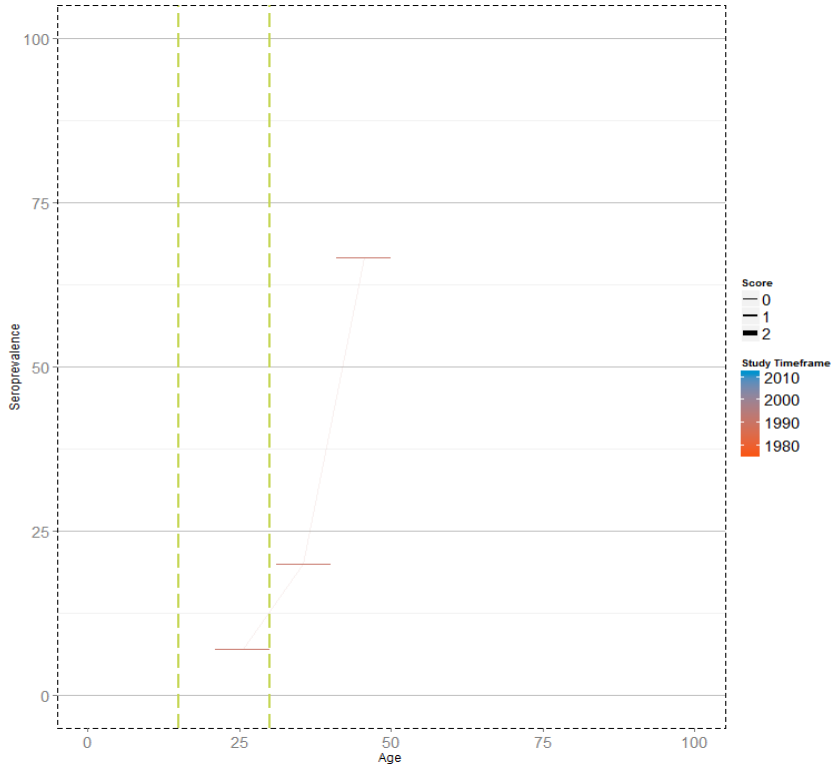
The susceptibility among adults was high during the 1990s (>70% at 30 years and around 30% at 50 years). Based on these data and the reported incidence below 2/100 000 during the last decade, the susceptibility among adults is nowadays likely to be high.

Austria_Figure 1 (panel a). Summary of seroprevalence in Austria, by age and time period.

Panel a.1: 1975–1989



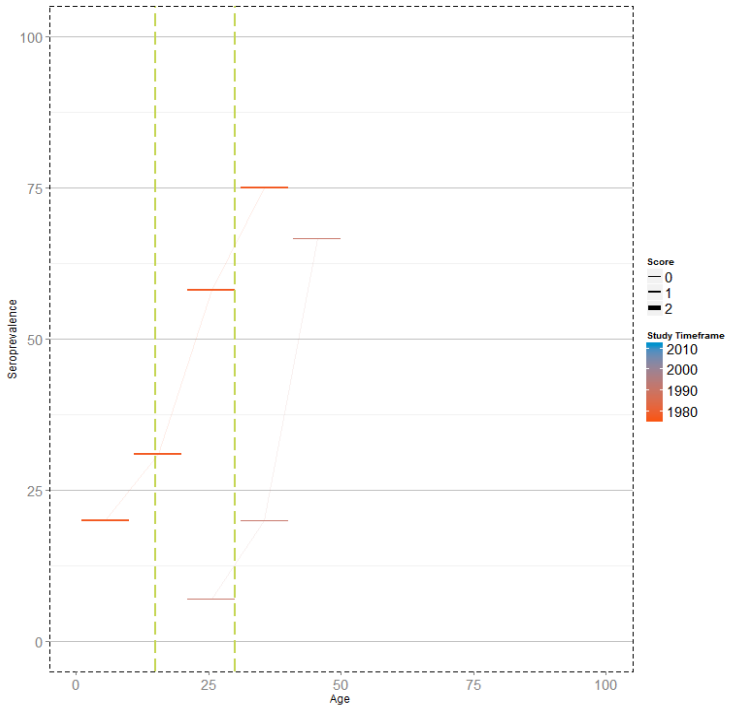
Panel a.2: 1990–1999



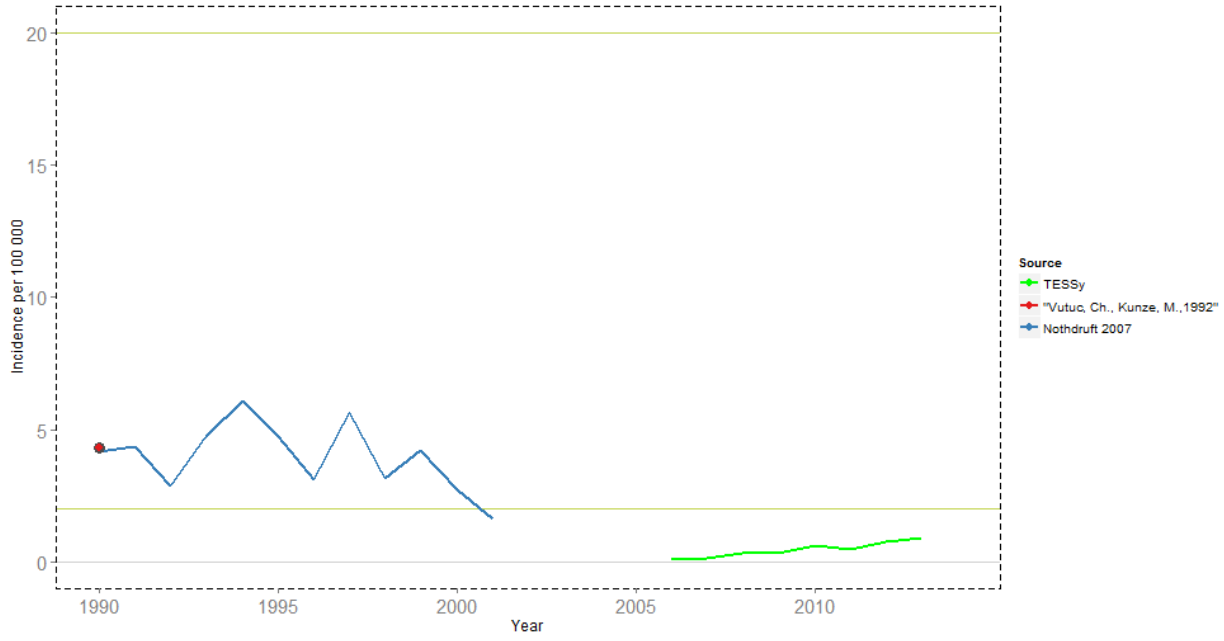
Panel a.3: 2000–2013

No data available

Austria_Figure 1 (panel b). Summary of seroprevalence in Austria, by age and time period (1975-2013).



Austria_Figure 2. Reported incidence of hepatitis A, Austria, 1989–2013



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Belgium

Population (January 2013):	11 161 642
Human development index (2013):	0.881
HAV vaccine recommendations:	HAV vaccination is not offered in the national childhood immunisation programme. Vaccination is recommended for: 1. travellers to endemic areas 2. MSM and bisexual men 3. candidates for liver transplantation and patients with chronic liver disease (including patients with hepatitis B and C) 4. haemophiliacs 5. contacts of HAV patients 6. staff and residents of institutions for patients with mental health conditions, people active in the food chain 7. children and adolescents of emigrants returning to their country of origin, close contacts adoptees from a country with high prevalence of hepatitis A.
Seroprevalence studies by quality score:	score 0:1 study score 1:6 studies; score 2: 2 studies
Seroprevalence studies timeframe:	1976–2003

Summary assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **high**

Five surveys conducted before 1990 estimated HAV seroprevalence in the under 30 years of age: three of these estimated seroprevalence over 50% and the remaining two, conducted in 1989, below 50%.

Belgium_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

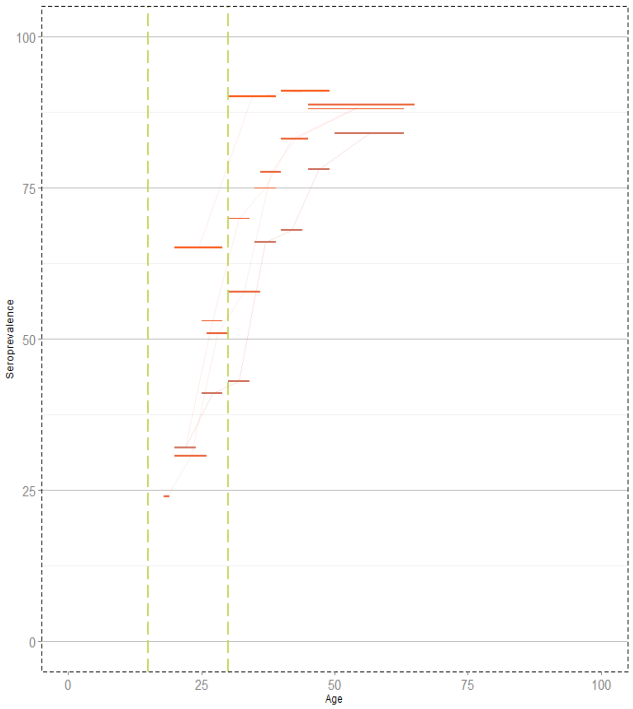
Three studies were conducted between 1990 and 2000 and all presented seroprevalence estimates below 50% by age 30. In 2003, HAV seroprevalence was 26% in the age group from 30 to 39 years. Therefore, Belgium is a very low endemicity country (Belgium_FFigure 1) and has likely been since the end of the 1980s.

The highest reported incidence was 7/100 000 in 1993, and has steadily been decreasing since (Belgium_FFigure 2). Incidence from TESSy data has been lower than 2/ 100 000 from 2008 and is consistent with a low/very low endemicity picture.

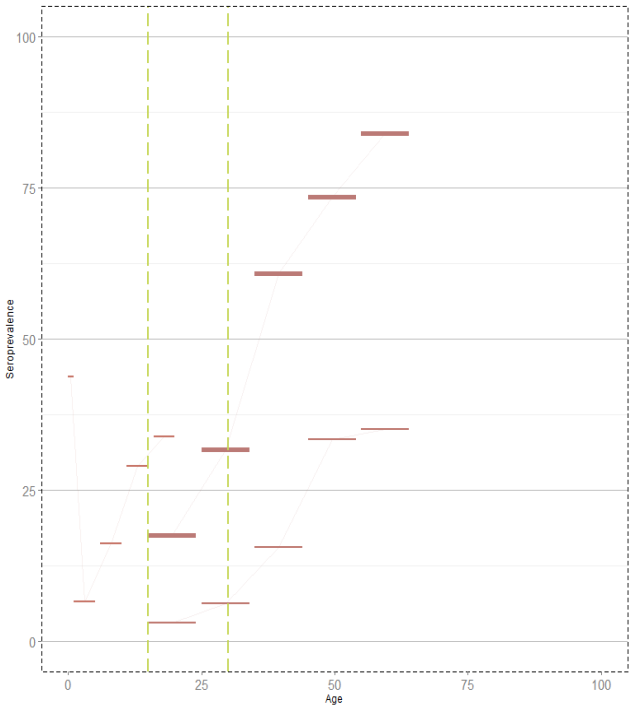
The susceptibility was estimated to be above 70% by the age of 30 and around 40% at the age of 50. Therefore the susceptibility in adults is considered to be high.

Belgium_Figure 1. Summary of seroprevalence in Belgium, by age and time period

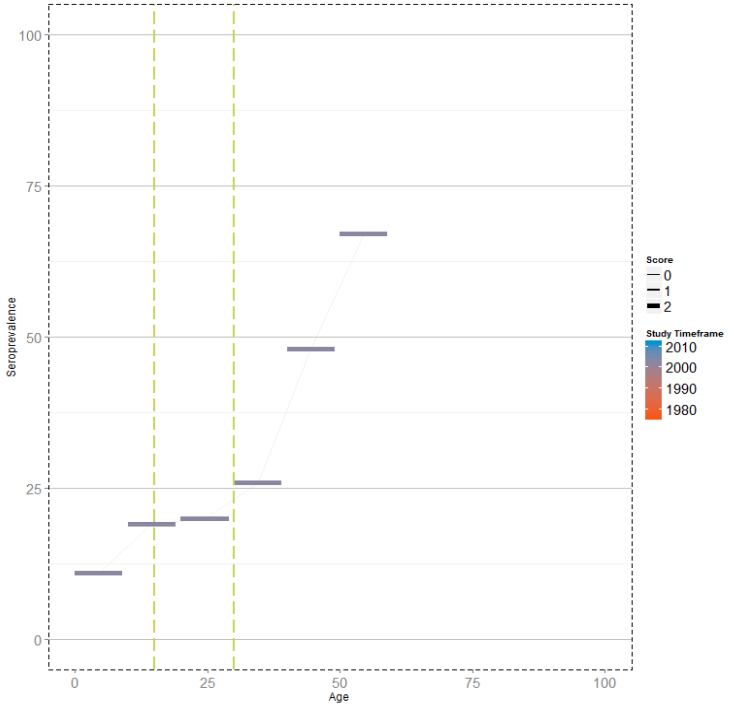
Panel a.1: 1975–1989



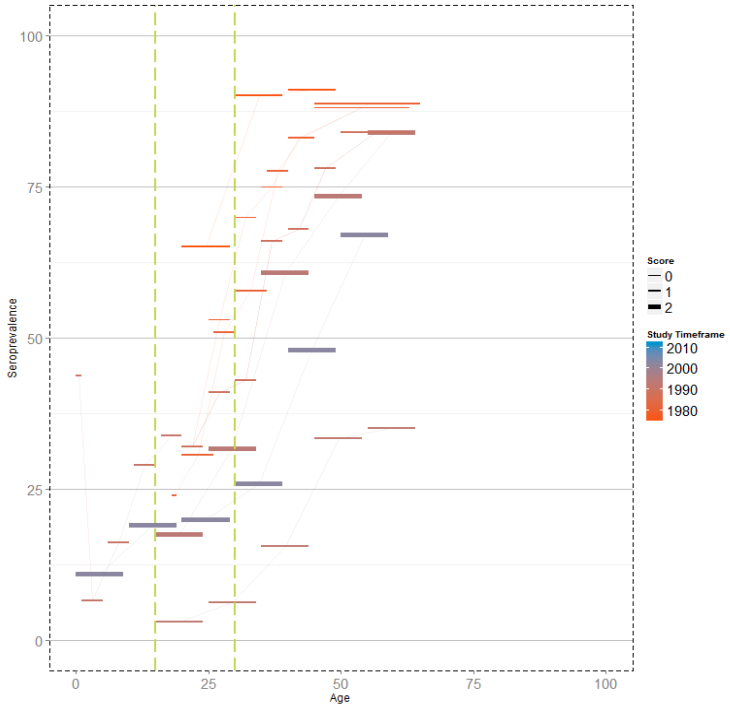
Panel a.2: 1990–1999



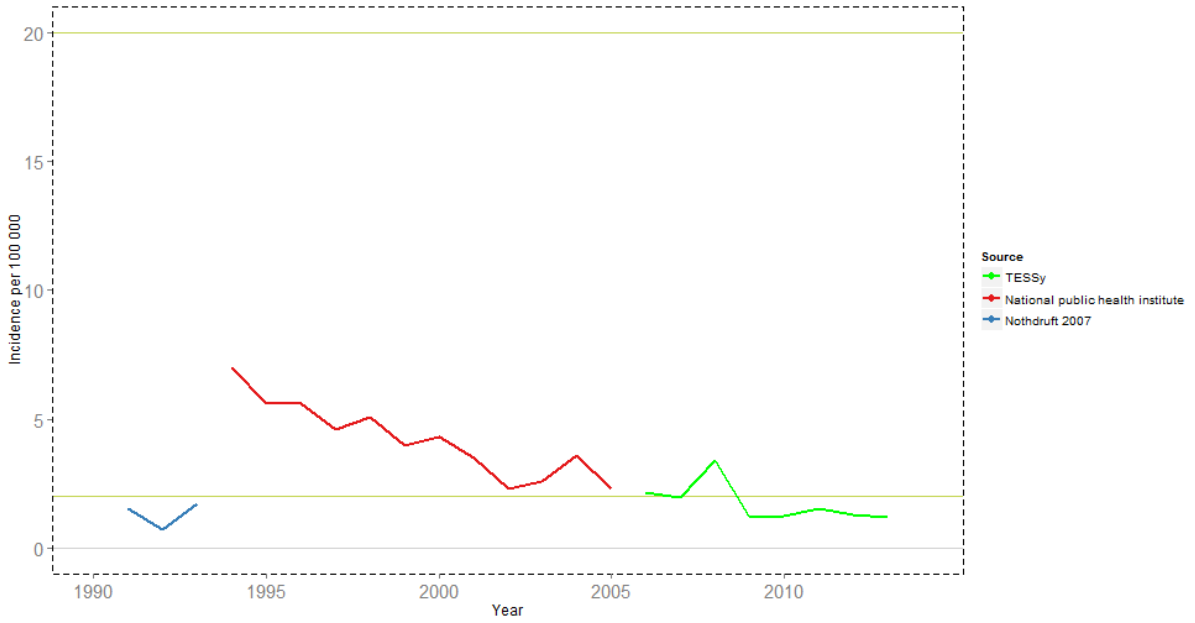
Panel a.3: 2000–2013



Belgium_Figure 1 (panel b). Summary of seroprevalence in Belgium, by age and time period (1975–2013)



Belgium_Figure 2. Reported incidence of hepatitis A, Belgium, 1990–2013



National data source: http://www.health.belgium.be/eportal

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Bulgaria

Population (January 2013):	7 284 552
Human development index (2013):	0.777
HAV vaccine recommendations:	HAV vaccination is recommended but not compulsory and as such not included in the National Immunisation schedule. Recommended for: 1. adults and children older than 12 months of age 2. patients with chronic liver disease 3. recipients of regular blood and blood components transfusion; 4. PWID 5. MSM 6. travelers to high endemicity countries 7. people with occupational increased risk for HAV infection, e.g. laboratory personnel, patients and personnel of institutions for mentally retarded people, sewage workers 8. Food handlers 9. for outbreak control.
Seroprevalence studies by quality score:	score 0: 2 study; score 1: 2 study; score 2: 0 studies
Seroprevalence studies timeframe:	1993–2011

Seroprevalence assessment: **low**
Incidence assessment: **intermediate**
Susceptibility in adults: **low**

One study conducted in 1985 in Bulgaria (Mikhailov 1993) estimated the HAV seroprevalence as below 5% at age 21 among a sample of 34 heterosexual men. After 2000, one single study was published in scientific literature (Vatev 2009), reporting a seroprevalence of more than 70% at 25 years (Bulgaria_FFigure 1) in a larger sample. Two additional grey literature studies conducted on and after 2000 consistently report a seroprevalence of about 22% by the age of 30. Bulgaria may be considered a country currently in transition phase from an intermediate endemicity and is classified as having a low endemicity profile, even though there are strong uncertainties due to the quality of the studies and the likelihood of intra-national variation of HAV seroprevalence.

Bulgaria_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989	*		
1990–1999			
2000–2013			

**This assessment is based on a study with a very small sample size (Mikhailov 1993).*

Incidence data are available for the period 1990 to thepresent with minor gaps (Bulgaria_FFigure 2). The study from Nothdruft et al. shows incidence levels below 100/100 000 during the 1990s, possibly corresponding to the epidemiological transition from high to intermediate endemicity. As TESSy data show, hepatitis A incidence has decreased to below 50 cases per 100 000 in the 2000s, but the country still experiences large outbreaks (2006 and 2011–2012) as clearly shown in FFigure 2.

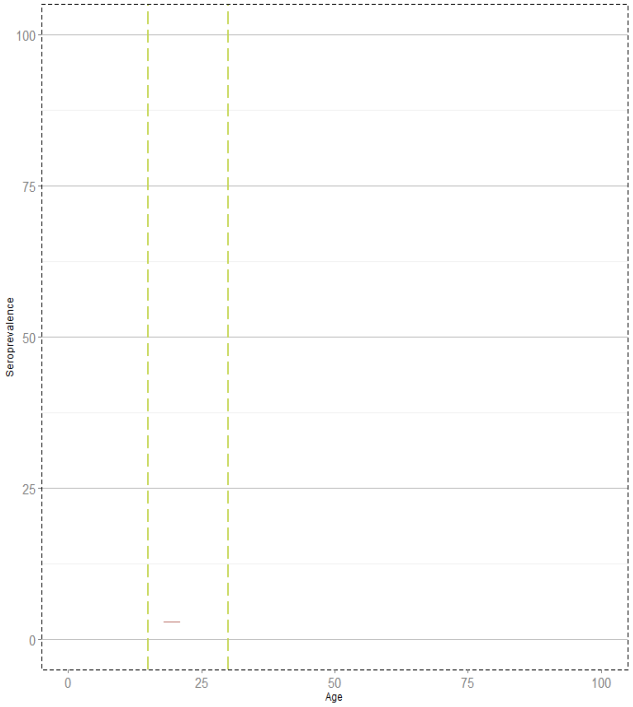
The susceptibility was estimated to be between 70–80% by the age of 30 and at the age of 50. Therefore the susceptibility in adults is deemed to be low.

Bulgaria_Figure 1 (panel a). Summary of seroprevalence in Bulgaria, by age and time period

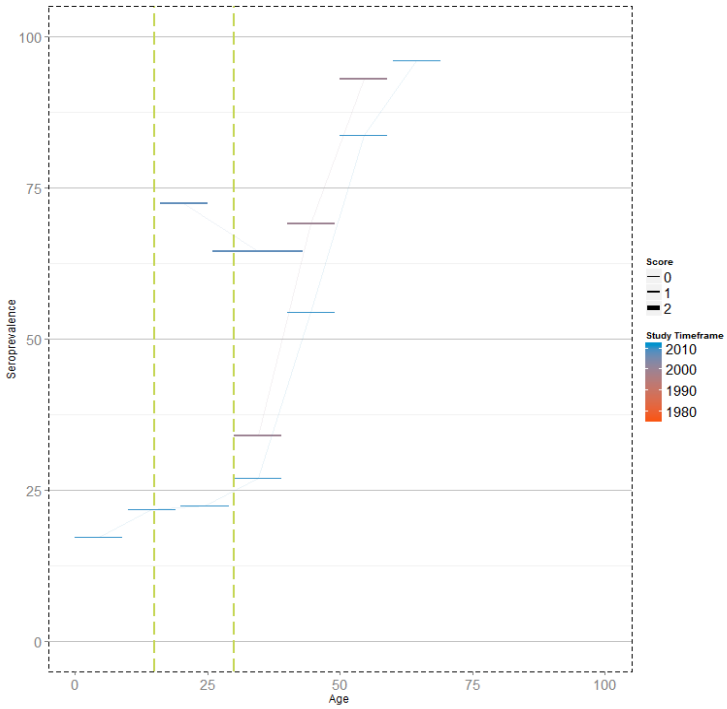
Panel a.1: 1975–1989

No data available

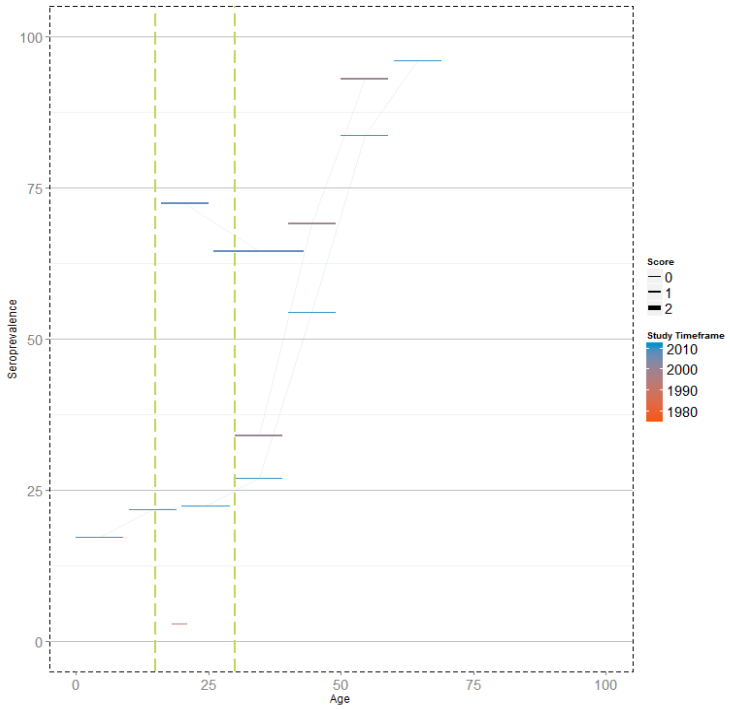
Panel a.2: 1990–1999



Panel a.3: 2000–2013



Bulgaria_Figure 1 (panel b). Summary of seroprevalence in Bulgaria, by age and time period (1975-2013)



Bulgaria_Figure 2. Reported incidence of hepatitis A, Bulgaria 1984–2013*

**National data source: personal communication from ECDC National Focal Point/Operational Contact Point, Bulgarian National Centre of Infectious and Parasitic Diseases*

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Croatia

Population (January 2013):	4 262 140
Human development index (2013):	0.812
HAV vaccine recommendations:	HAV vaccination is mainly recommended to travellers to endemic areas and to risk groups such as MSM. It is also used as outbreak control measure.
Seroprevalence studies by quality score:	score 0:1 studies; score 1:1 study score 2:0 studies
Seroprevalence studies timeframe:	1989–2009

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **high**

One 1989 study, including only children, estimated HAV seroprevalence be below 50%. in those under 16 years of age

A 2009 study estimated seroprevalence to be under 25% in those under 30 years of age. Therefore, Croatia is currently likely to be a very low endemicity country (Croatia_Figure 1).

Croatia_Table 1. Hepatitis A seroprevalence level by time period

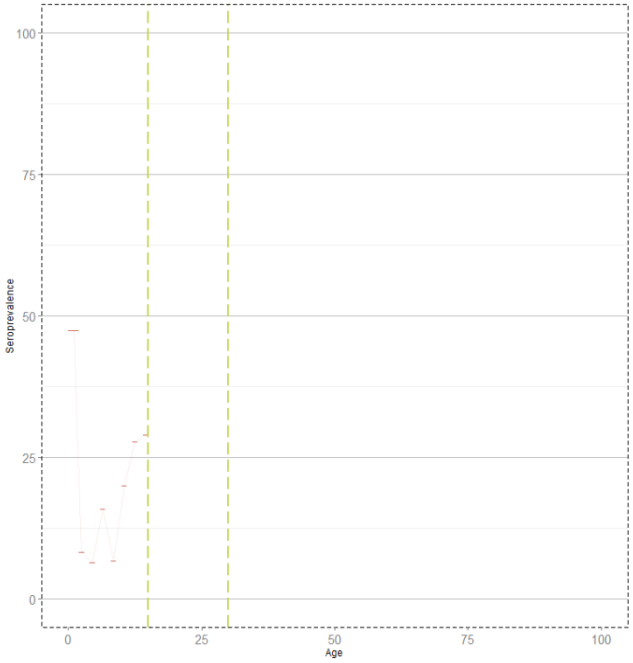
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989	*	*	
1990–1999			
2000–2013			

**The assessment cannot be completed as data are not available at 30 years of age.*

There is no incidence data available, and TESSy data is not available for Croatia since the country joined the European Union in 2013. Data from the National Health Institute show a steady decrease of hepatitis A incidence since the mid 1970s when it was well above 100 cases per 100 000. After a peak around 2000, the incidence has been as low as less than 1 case per 100 000 as shown in FFigure 2. Croatia is currently a country at very low incidence of HAV.

The susceptibility at 30 years is above 70%, while it declines to around 45% at the age of 50. Hence the susceptibility is high in the adult population.

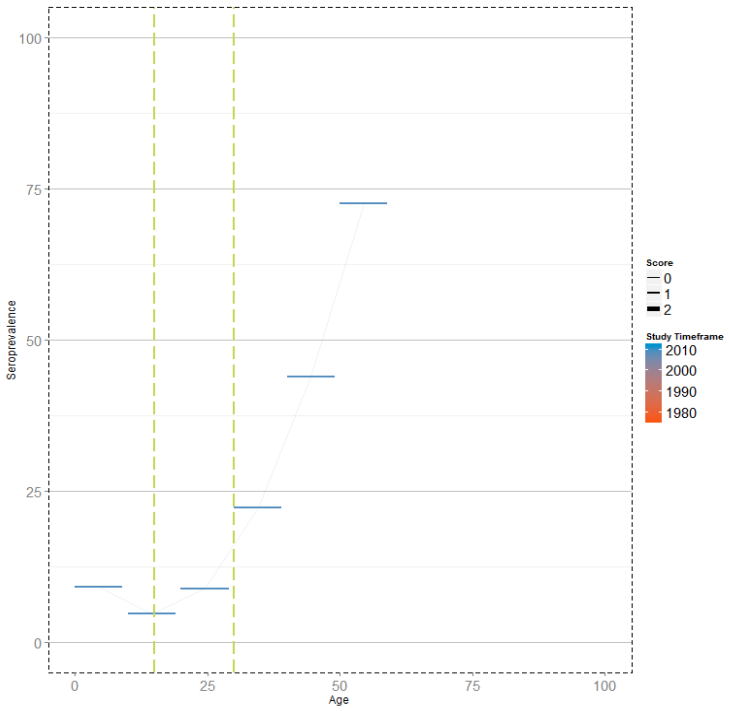
Panel a.1: 1975–1989



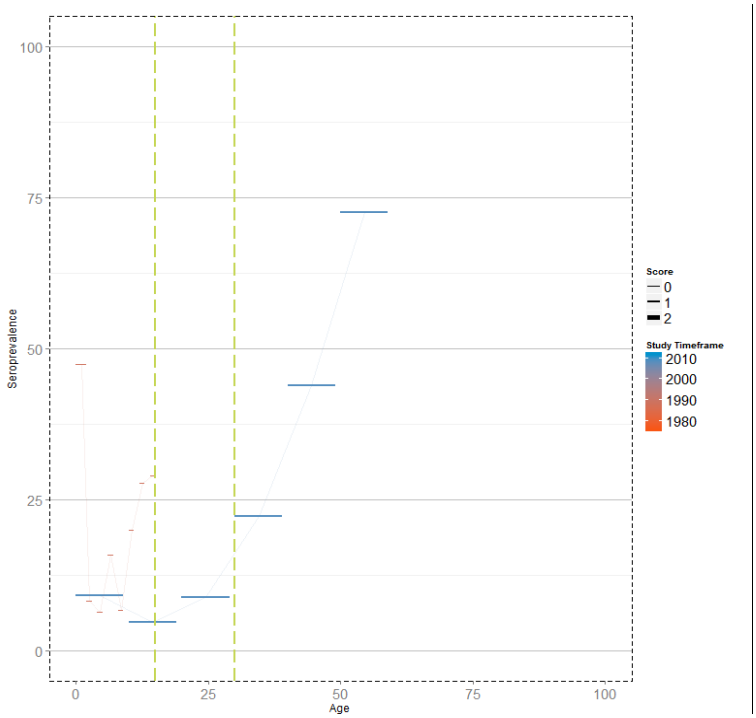
Panel a.2: 1990–1999

No data available

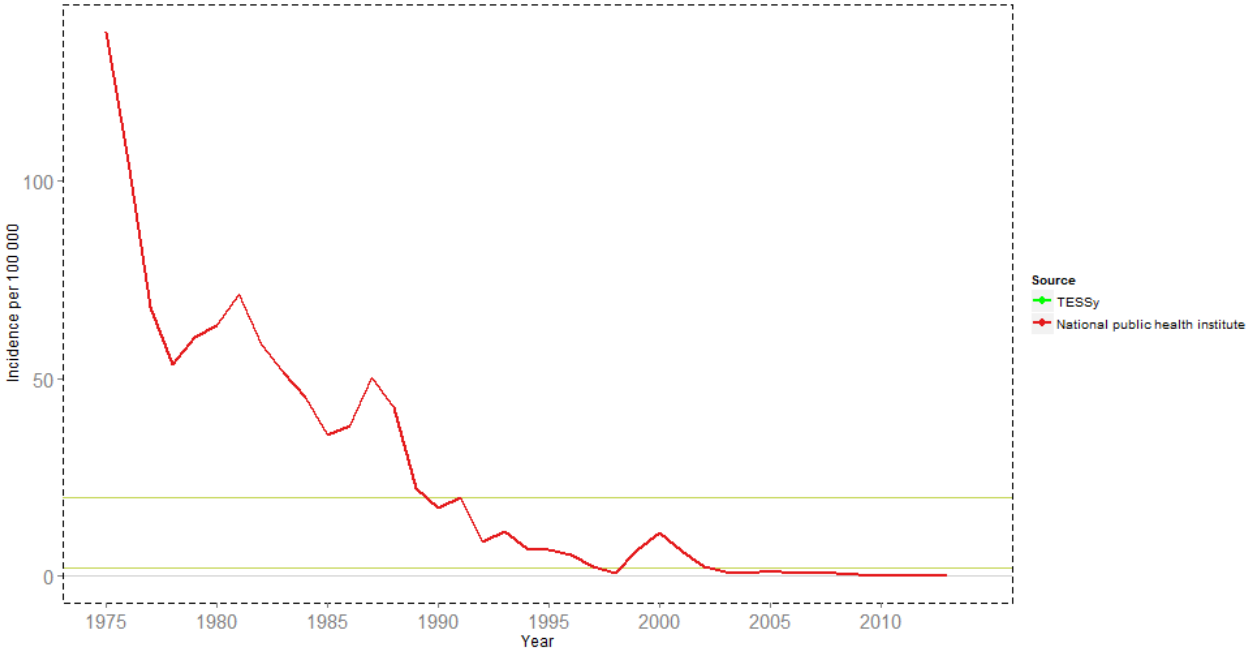
Panel a.3: 2000–2013



Croatia_Figure 1 (panel a). Summary of seroprevalence in Croatia, by age and time period.



Croatia_Figure 1 (panel b). Summary of seroprevalence in Croatia, by age and time period (1975-2013)



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Cyprus

Population (January 2013):	865 878
Human development Index (2013):	0.845
HAV vaccine recommendations:	HAV vaccination is recommended but not funded by the National Health System, with the exception of vaccination administered for medical conditions. Vaccination is given on specific indication only
Seroprevalence studies by quality score:	score 0: 1 studies score 1: 1 study score 2: 0 studies
Seroprevalence studies timeframe:	1975–1998

Seroprevalence assessment*: **very low**
Incidence assessment: **very low**
Susceptibility in adults*: **moderate**

**assessment based on data from the early 1990s*

The only article providing estimates seroprevalence among Cypriots is a study conducted in 1979 on a sample of 124 Turkish Cypriots and reports 100% prevalence by 30 years of age (Weiland 1979). After 1990, one study was retrieved providing data among children and soldiers in Cyprus. The estimated seroprevalence by age 18 are well below 10% (Cyprus_Figure 1). In the light of the available data, Cyprus in the 1990s could be considered a very low endemicity country, although with high likelihood of important geographical variation.

Cyprus_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

The reported incidence data obtained from TESSy show a very low incidence rate (≤ 0.5 cases per 100 000) in the period 2006 to the present (Cyprus_FFigure 2).

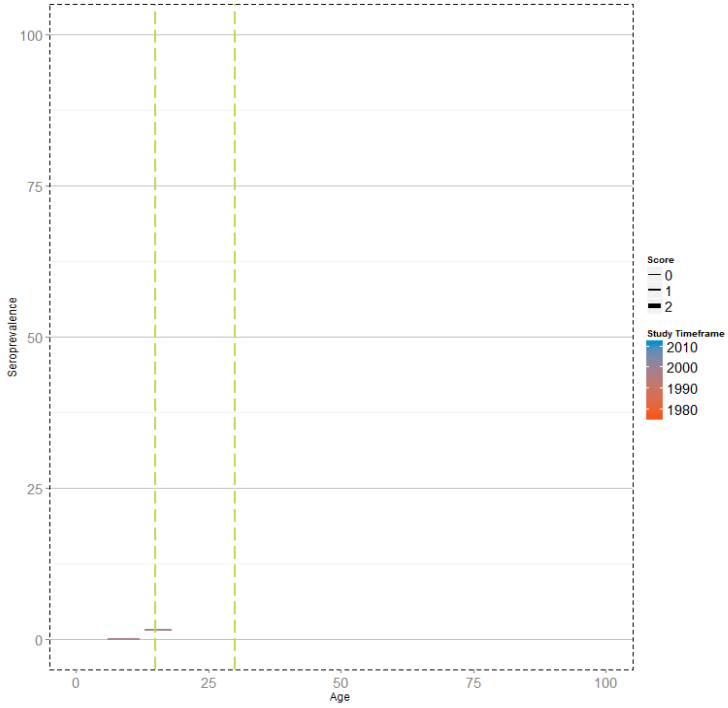
Considering the very low seroprevalence reported during the 1990s among individuals aged 18 years or below and the very low reported incidence in Cyprus after 2006, we expect young adults to be at high susceptibility at present. Nevertheless the data from previous decades indicates very high level of seroprevalence in the older birth cohorts.Therefore the overall susceptibility among adults is to be considered moderate.

Cyprus_Figure 1 (panel a). Summary of seroprevalence in Cyprus, by age and time period

Panel a.1: 1975–1989

No data available

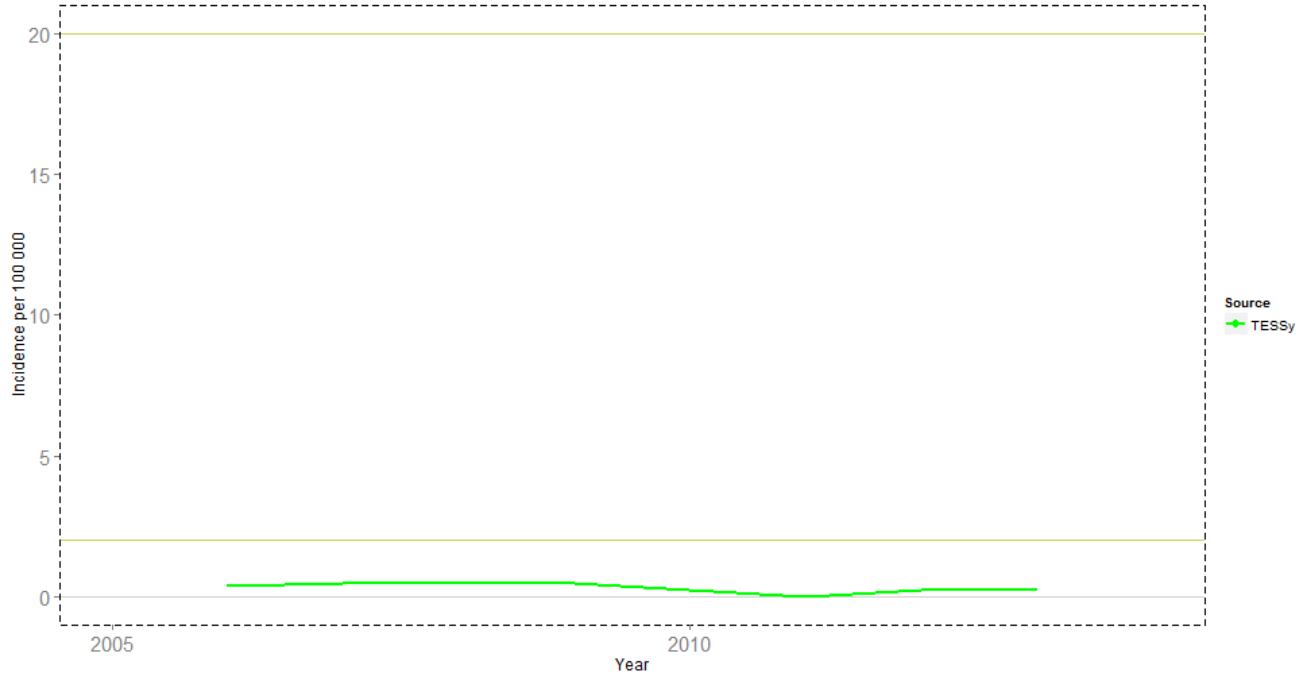
Panel a.2: 1990–1999



Panel a.3: 2000–2013

No data available

Cyprus_Figure 2. Reported incidence of hepatitis A, Cyprus, 2006–2013



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Czech Republic

Population (January 2013):	10 516 125
Human development Index (2013):	0.861
HAV vaccine recommendations:	HAV vaccination is recommended for susceptible individuals with no history of vaccination. Vaccination is mandatory for specific at risk groups
Seroprevalence studies by quality score:	score 0: 1 studies score 1: 5 studies score 2: 2 studies
Seroprevalence studies timeframe:	1992–2004

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **high**

No studies were identified estimating HAV seroprevalence before 1990 in the Czech Republic. Of the five studies investigating HAV seroprevalence in the period 1990 and 2000, two sampled military personnel only and three included the general population. All studies estimated the seroprevalence to be below 30% by 30 years of age (Czech Republic_FFigure 1). After 2000, the two studies retrieved provided very similar seroprevalence estimates. According to these, the HAV seroprevalence by the age of 30 was below 20%, reaching values above 50% in the age group 50–59. No epidemiological transition is evident from the graph in the recent decades. The Czech Republic is a very low endemicity country and has been so since the 1990s.

Czech Republic_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence suggests HAV was circulating in the country until the late 1980s (reported incidence above 20/100 000 until 1989) and has decreased since. According to TESSy and available studies (Hubalek 2005, Castkova 2009) reported incidence was well below 10/100 000 after 2000 (Czech Republic_FFigure 2). A ten-fold increase in reported incidence was registered during 2008–2009, as compared to the previous five-year period.

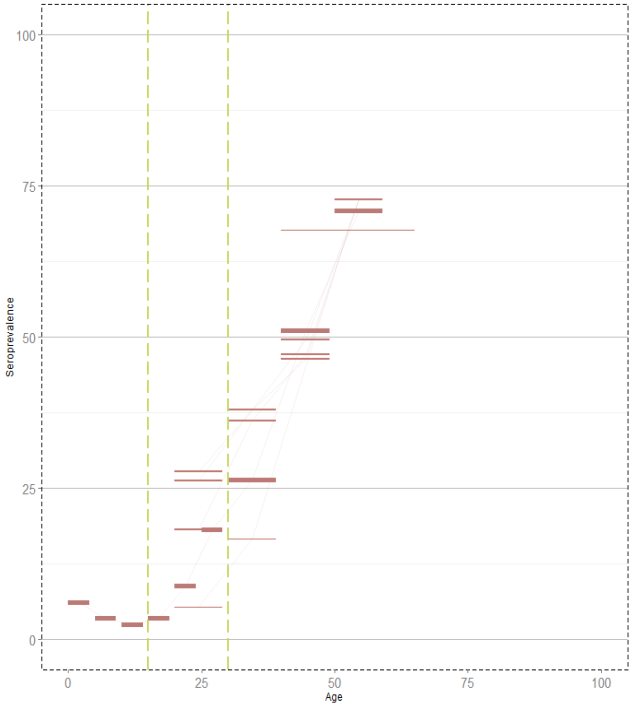
The susceptibility was estimated to be above 70% by the age of 30 and around 50% at the age of 50. Therefore the overall susceptibility in adults is considered high.

Czech Republic _Figure 1 (panel a). Summary of seroprevalence in Czech Republic, by age and time period

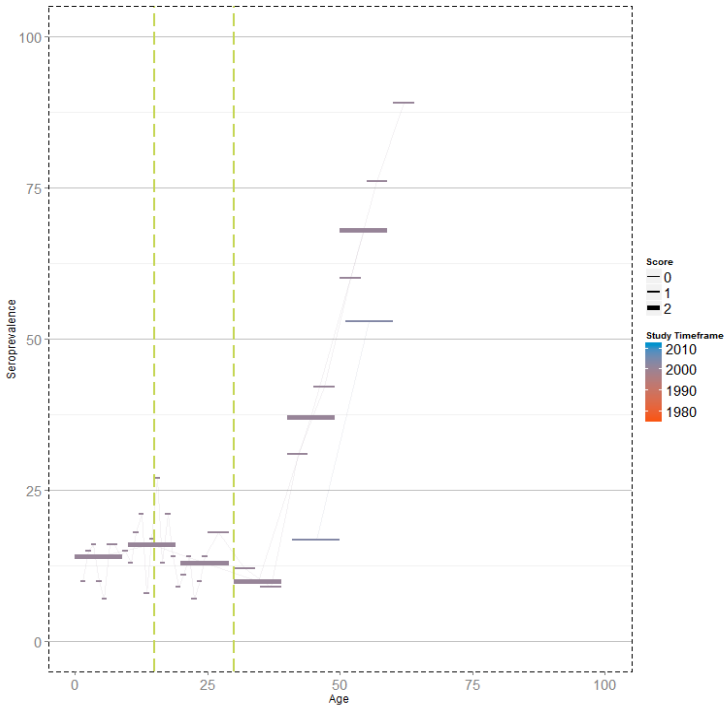
Panel a.1: 1975–1989

No data available

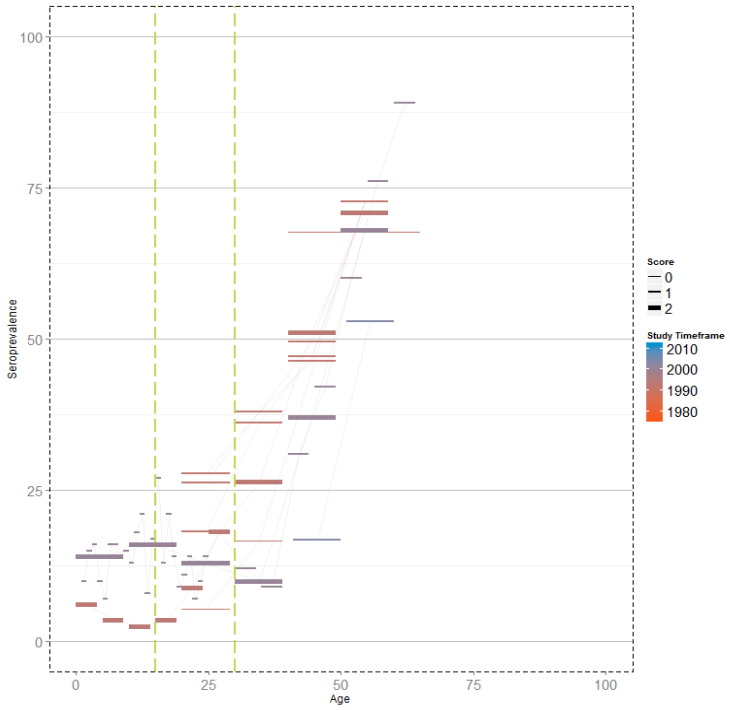
Panel a.2: 1990–1999



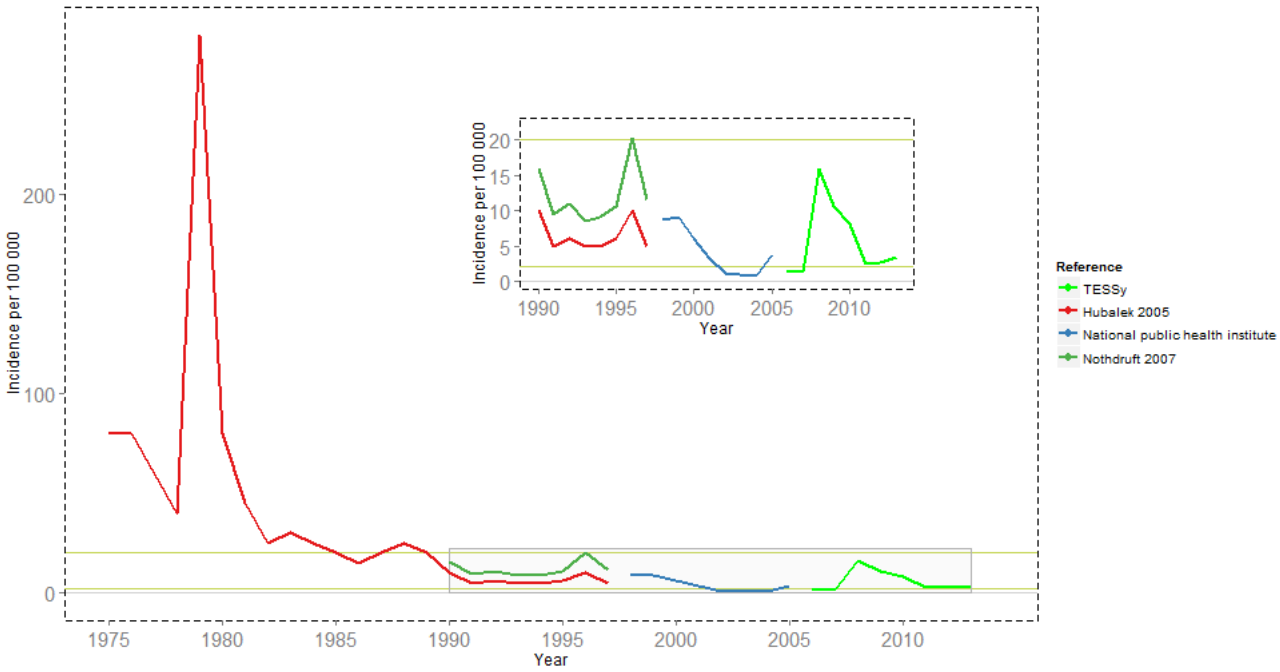
Panel a.3: 2000–2013



Czech Republic _Figure 1 (panel b). Summary of seroprevalence in Czech Republic 1975-2013, by age and time period



Czech Republic _Figure 2. Reported incidence of hepatitis A, Czech Republic, 1975–2013*



National data source: http://uzis.cz/en/catalogue/infectious-diseases

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Denmark

Population (January 2013):	5 602 628
Human development Index (2013):	0.899
HAV vaccine recommendations:	HAV vaccination is not included in the national childhood immunisation programme. Vaccination is recommended for: 1. travellers to endemic areas (not publically reimbursed). Contacts to cases of hepatitis A are offered free vaccination (postexposure). Vaccination is recommended to risk groups for hepatitis B in the form of the combined hep A/B vaccine.
Seroprevelance studies by quality score:	score 0: 1 study score 1: 2 studies score 2: 1 study
Seroprevelance studies timeframe:	1976–2003

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **very high**

Two studies conducted before 1990 estimated HAV seroprevalence in the under 30 years of age to be below 50%. No study estimated HAV seroprevalence in this age group between 1990 and 2000, but among 35–49 years old it was 15.9% according to one 1991 study. In 2003, HAV seroprevalence was 25% or less in all age groups. Therefore, Denmark is a very low endemicity country (Denmark_FFigure 1) and has likely been since at least the mid-1970s.

Denmark_Table 1. Hepatitis A seroprevalence level by time period

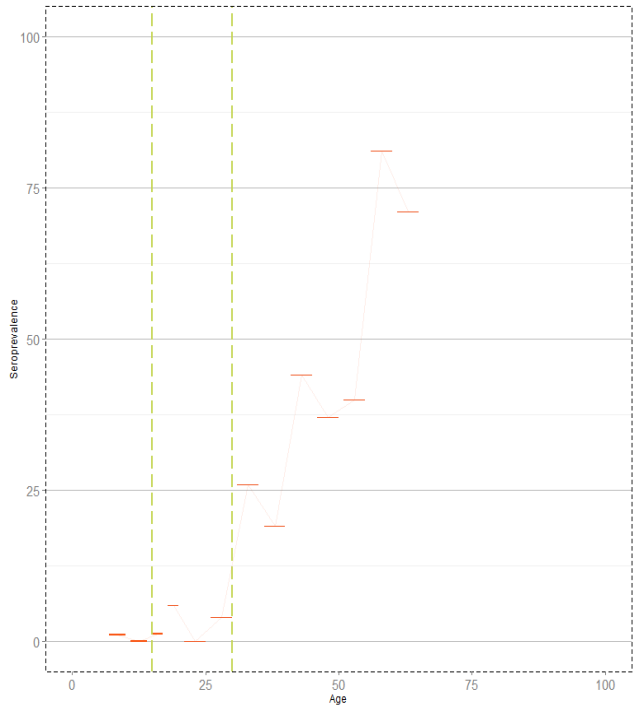
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence was already below 20/100 000 in the early 1980s, and has been decreasing since (Denmark_Figure 2). TESSy data is consistent with a very low endemicity picture; apart from an incidence slightly over 5 in 2007, reported incidence has been under 2/100 000 every year since at least 2006.

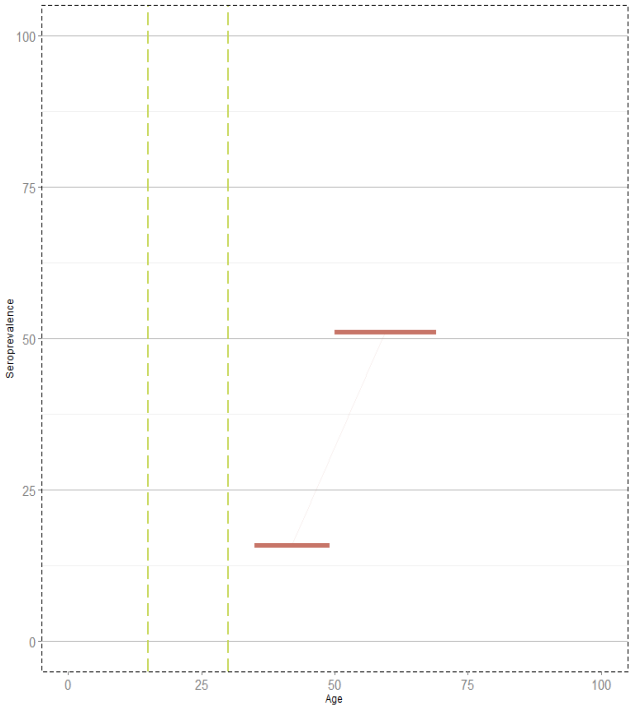
Susceptibility levels by 30 years are around 95% and by 60 years at least 75% are susceptible. Therefore, the susceptibility among adults is very high.

Denmark_Figure 1 (panel a). Summary of seroprevalence in Denmark, by age and time period

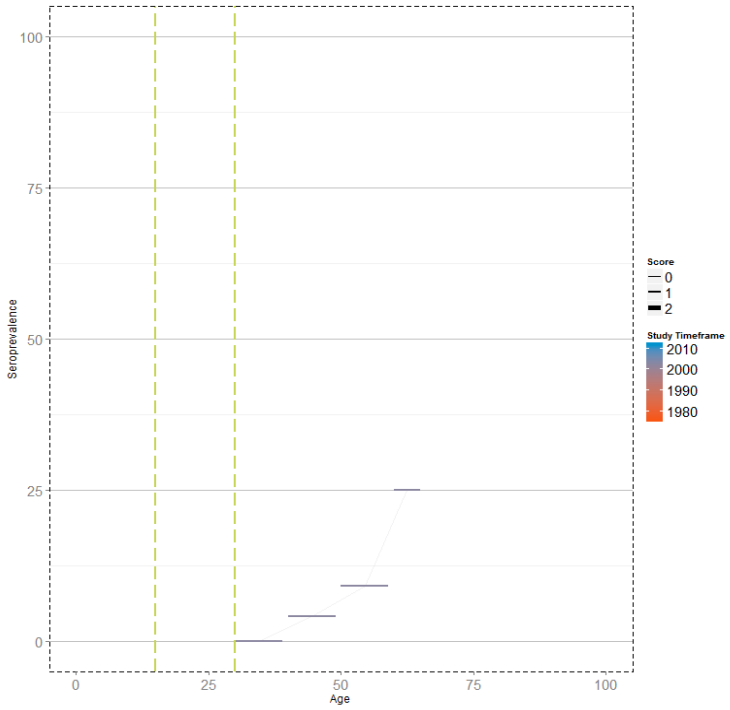
Panel a.1: 1975–1989



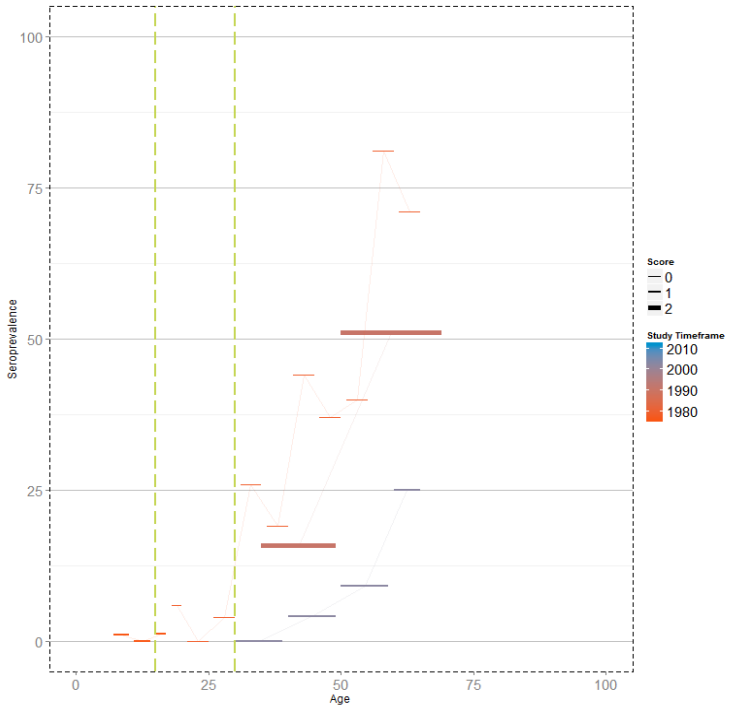
Panel a.2: 1990–1999



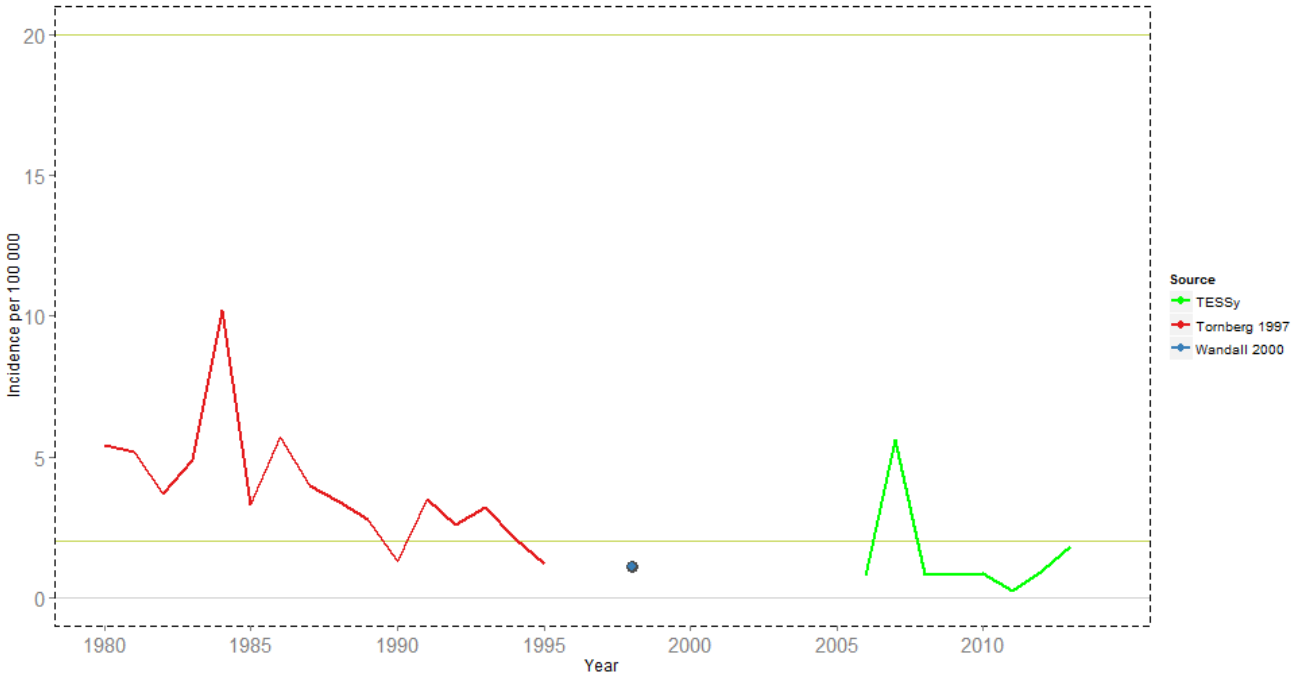
Panel a.3: 2000–2013



Denmark_Figure 1 (panel b). Summary of seroprevalence in Denmark, by age and time period (1975-2013



Denmark_Figure 2. Reported incidence of hepatitis A, Denmark, 1980–2013



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Estonia

Population (January 2013):	1 320 174
Human development Index (2013):	0.840
HAV vaccine recommendations:	HAV vaccination is not included in the national childhood immunisation programme. Vaccination is recommended for: 1. for the all population, especially for children and adults with chronic liver diseases (chronic hepatitis, cirrhosis, biliary atresia) 2. PWID 3. MSM 4. sewage workers 5. food business operators.
Seroprevalence studies by quality score: **Seroprevalence studies Timeframe:**	score 0: 0 studies score 1: 1 studies score 2: 0 studies 2002

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **high**

Only one study on HAV seroprevalence could be found on the Estonian population. According to this non-randomised study, conducted in 2002 among the general population, the HAV seroprevalence was around 40% at the age of 30 years; increasing to around 50% by the age of 50.Therefore, Estonia can be classified as a very low endemicity country in the present period.

Estonia_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2012			

Available incidence data from 1995 show a steady decrease from 250 cases per 100 000 to values mostly oscillating around 2 cases per 100 000 in the period 2006 to the present with a peak of 11 cases per 100 000 in 2011 (Estonia_Figure 1).

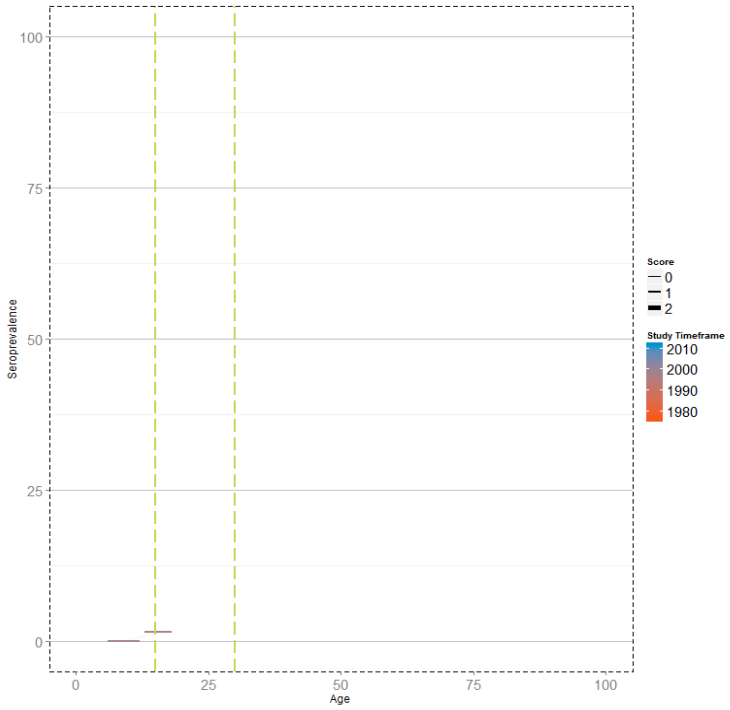
The susceptibility at 30 years is estimated to be around 60%, decreasing to around 50% in 50 year olds. Hence the overall susceptibility is estimated as high.

Estonia_Figure 1 (panel a). Summary of seroprevalence in Estonia, by age and time period.

Panel a.1: 1975–1989

No data available

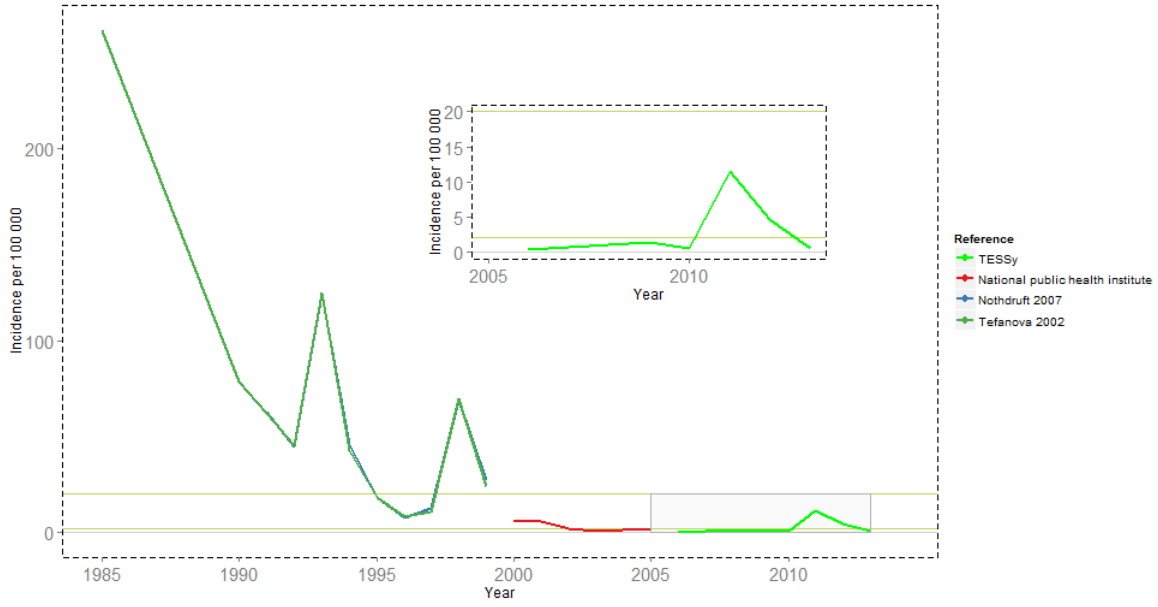
Panel a.2: 1990–1999



Panel a.3: 2000–2013

No data available

Estonia_Figure 2. Reported incidence of hepatitis A in Estonia, 1985–2013*



** National data source: personal communication from ECDC National Focal Point/Operational Contact Point, Estonian Health Board*

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Finland

Population (January 2013):	5 426 674
Human development Index (2013):	0.879
HAV vaccine recommendations:	The national vaccination programme covers HAV vaccination for haemophiliacs and PWID and their close contacts. In addition, vaccination is recommended for: 1. chronic liver patients, including HBV and HCV carriers 2. travelers to high endemicity countries 3. people with occupational increased risk for HAV infection, e.g. people working with children or refugees, sewage workers 4. for outbreak control
Seroprevalence studies by quality score:	score 0: 1 study score 1: 1 study score 2: 2 studies
Seroprevalence studies timeframe:	1978–1998

Seroprevalence assessment*: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **very high**

**this assessment is based on data from the 1990s*

The two studies published in Finland before 1990 (Ukkonen 1979, Pohjanpelto 1984) estimated an HAV seroprevalence of below 10% by the age of 30 years (Finland_Figure 1). For the period 1990–1999 we included two studies. Both estimated a HAV seroprevalence by age 30 years below 10%.

There are no studies conducted after 2000. Nevertheless, Finland has been a very low endemicity country since at least the late 1970s (Finland_table 1)**.**

Finland_Table 1. Hepatitis A seroprevalence level by time period

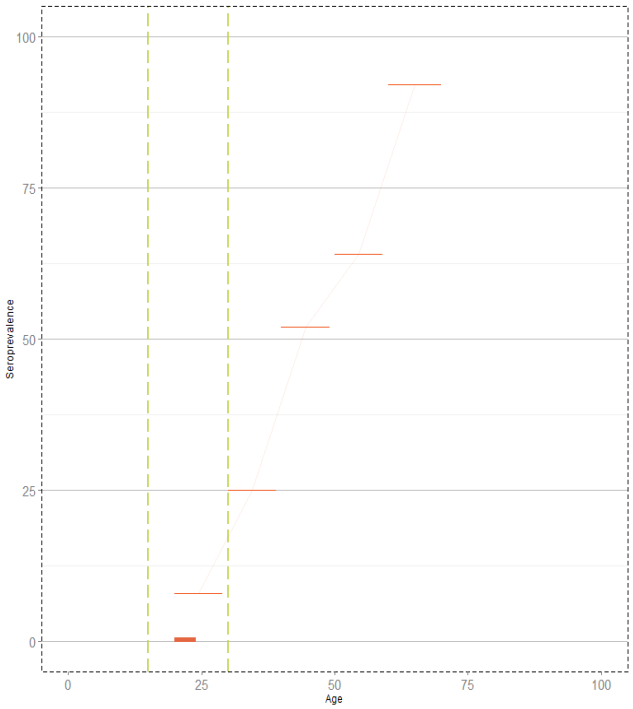
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

For the years where data are available (Finland_Figure 2), the incidence is very low and follows a decreasing trend, of 0.17 per 100 000 in 2012.

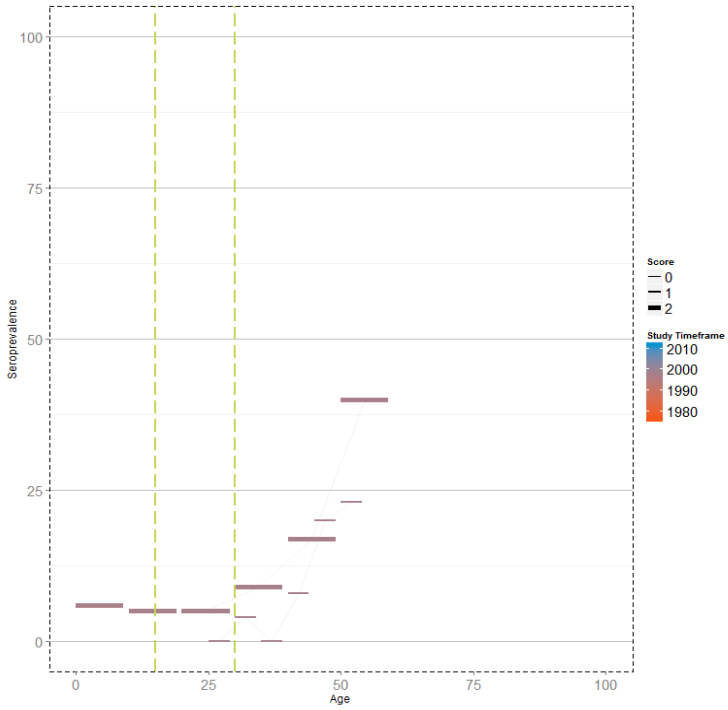
In the 1990s susceptibility levels by 30 years were around 90% and over 50% for those aged between 50–60 years.Considering the very low incidence profile of the country in the last years and the absence of sustained circulation of the virus, susceptibility in adults is likely to be very high in the present situation.

Finland_Figure 1 (panel a). Summary of seroprevalence in Finland, by age and time period

Panel a.1: 1975–1989



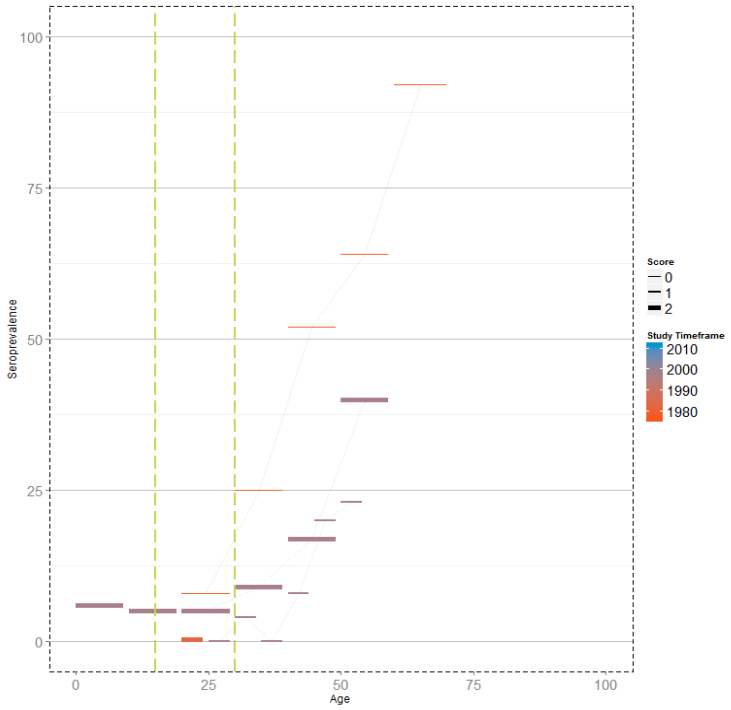
Panel a.2: 1990–1999



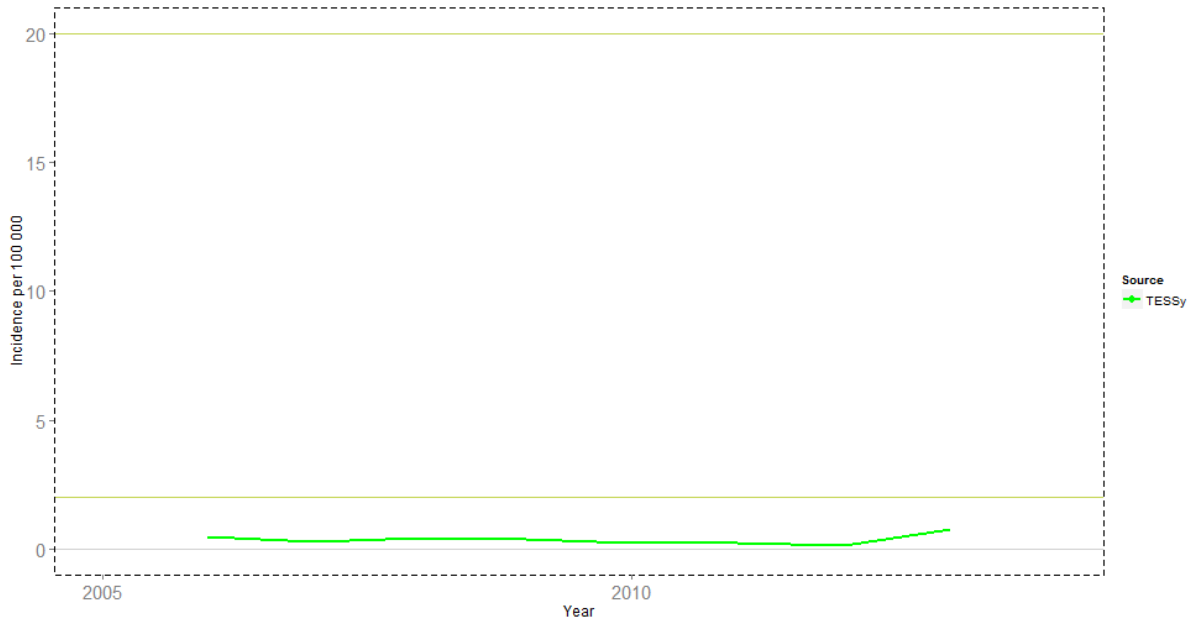
Panel a.3: 2000–2013

No data available

Finland_Figure 1 (panel b). Summary of seroprevalence in Finland, by age and time period (1975-2013)



Finland_Figure 2. Reported incidence of hepatitis A, Finland, 2006–2013



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France

Population (January 2013):	65 578 819
Human development Index (2013):	0.884
HAV vaccine recommendations:	France does not offer vaccination against hepatitis A in the national childhood immunisation programme. Vaccination is recommended for patients with: 1.chronic liver diseases or cystic fibrosis, 2.institutionalised children, 3.children aged 1 year or more born to a family with at least one parent originating from an endemic country and who are susceptible to stay in this country, 4.MSM and households contacts of HAV patients.
Seroprevalence studies by quality score:	score 0: 6 studies score 1: 12 studies score 2: 2 studies
Seroprevalence studies timeframe:	1977–2010

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **moderate**

Nine studies were conducted before 1990: four reports estimates HAV seroprevalence by 30 years of age and all estimates are above 50%; in the same time period, four studies report estimates by 15 years of age: three below 50% and one above 50% (74% in the age group 15-18) (Lemaire 1980). Nine studies were conducted from 1990 to 2000 with consistent results. Four of these report HAV seroprevalence estimates by 30 years of age and all estimates are below 50%. One of the two studies conducted after 2000 reports seroprevalence estimates in the adult general population to be below 30% by the age of 30 years (Lepoutre 2013). Therefore France can currently be defined as a very low endemicity country (France_Figure 1), with a transition from a higher endemicity level occurring in the 1980s.

France_Table 1. Hepatitis A seroprevalence level by time period

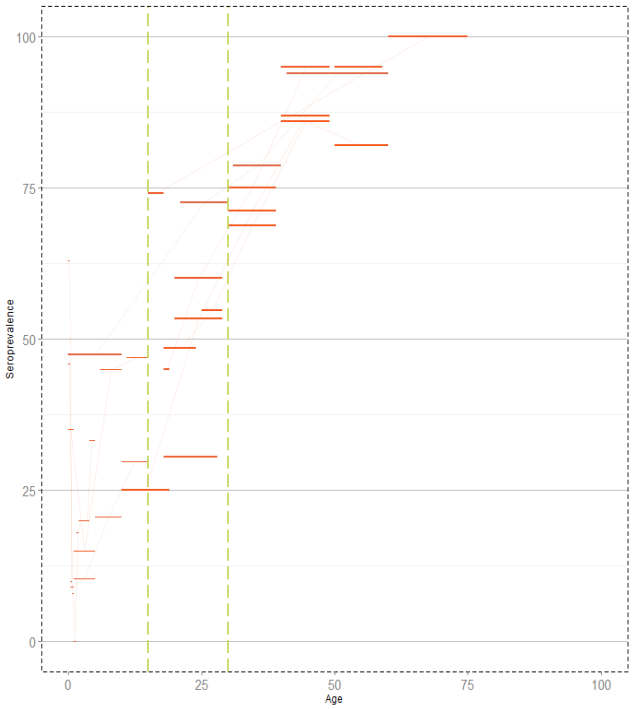
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence has been steadily declining from 15/100 000 in the early 1990s (France_Figure 2). TESSy data are consistent with a low/very low endemicity picture, with notification rate oscillating around 2/100 000 since 2006.

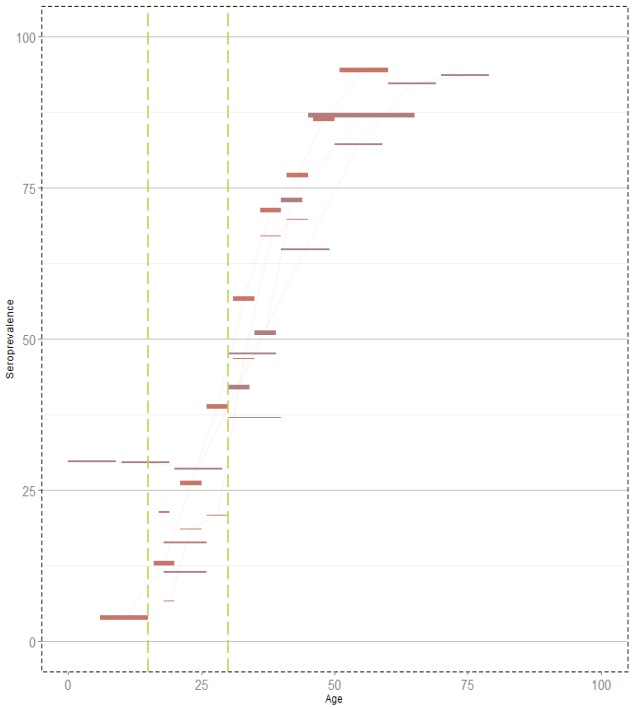
At the end of the 1990s, the susceptibility was estimated to be above 50% by the age of 30 and around 25% at the age of 50. Considering the current very low seroprevalence in young adults, and the incidence picture of the past years, the susceptibility in adults may today be considered moderate.

France_Figure 1 (panel a). Summary of seroprevalence in France, by age and time period.

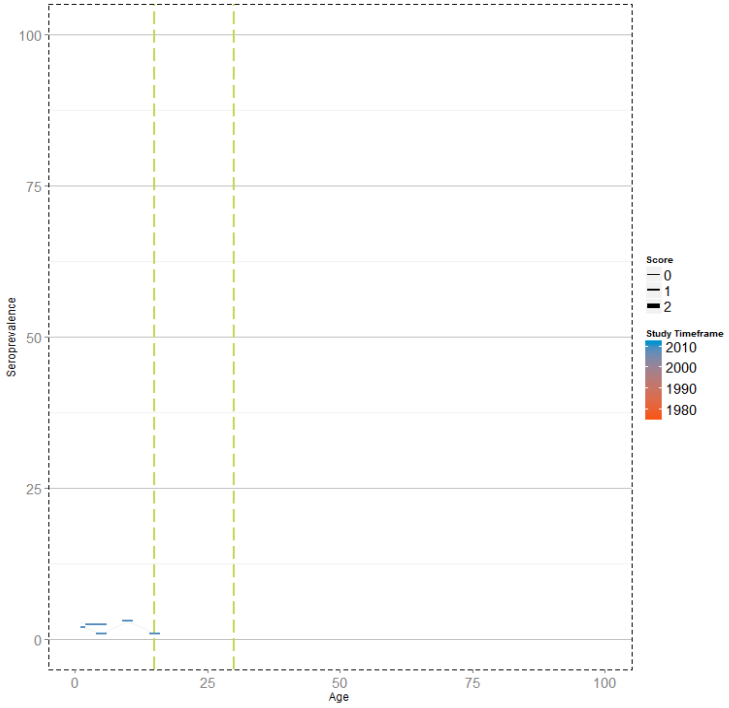
Panel a.1: 1975–1989



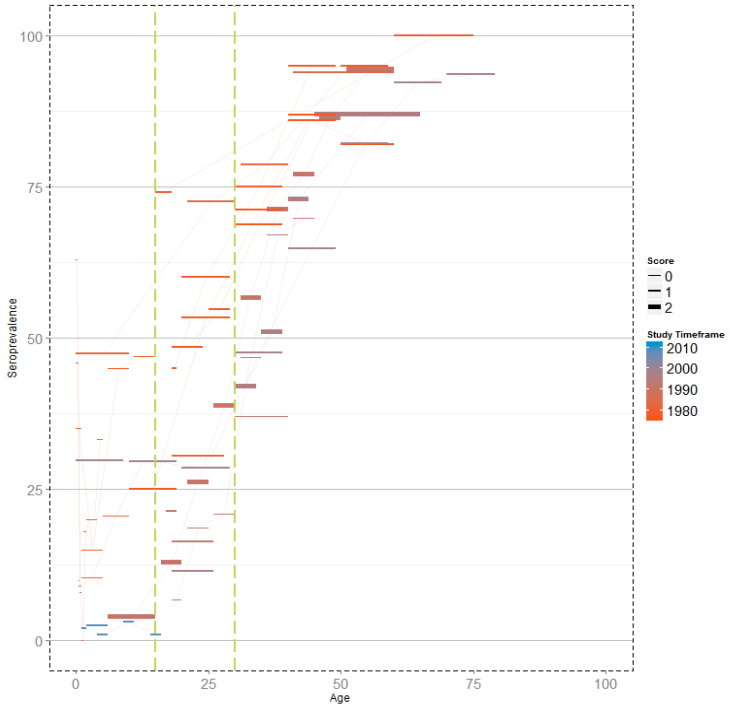
Panel a.2: 1990–1999



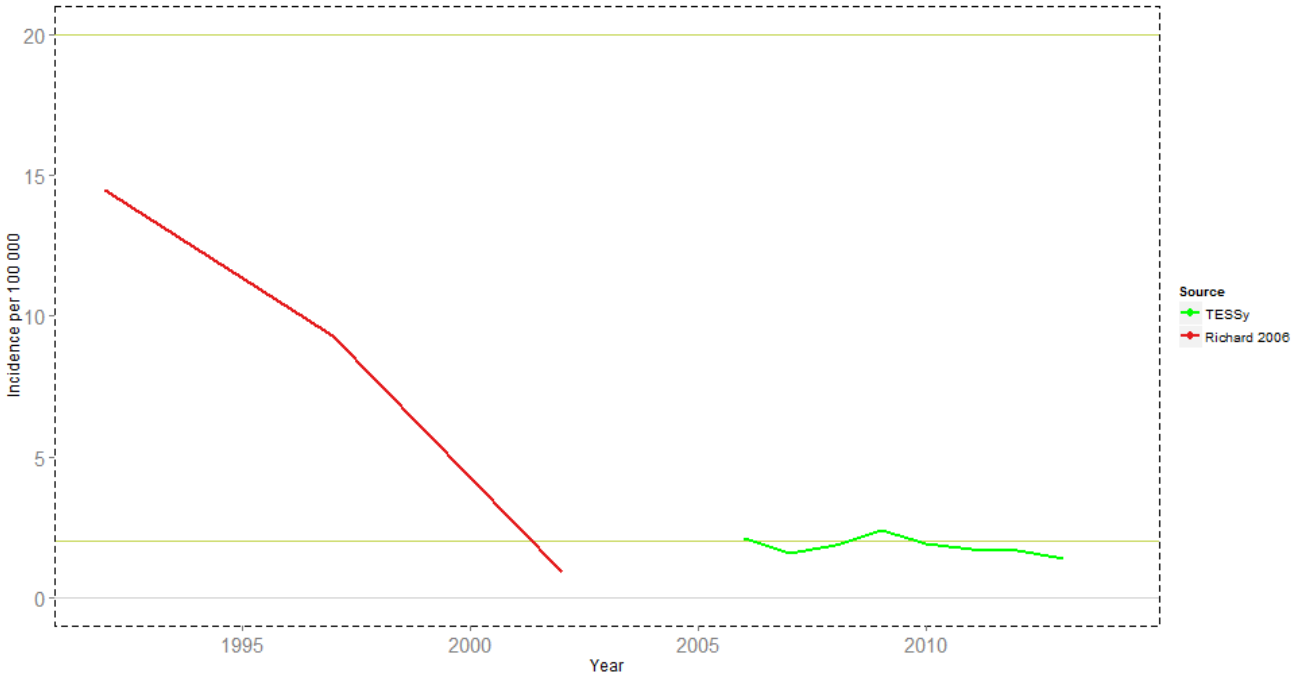
Panel a.3: 2000–2013



France_Figure 1 (panel b). Summary of seroprevalence in France, by age and time period (1975-2013)



France_Figure 2. Reported incidence of hepatitis A, France, 1990–2013



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Germany

Population (January 2013):	80 523 746
Human development Index (2013):	0.911
HAV vaccine recommendations:	HAV vaccination is not included within the National Immunization Programme. HAV vaccination is recommended for persons with specific indication or who are at higher risk for infection/disease: 1. MSM 2. highly transfused 3. residents of psychiatric institutions or comparable welfare facilities 4. health service workers and medical students 5. sewage workers 6. employees of children's day centres, children's homes 7. travellers to regions at high endemicity for HAV. HAV vaccine is also used as post-exposure prophylaxis.
Seroprevalence studies by quality score:	score 0: 7 studies score 1: 5 studies score 2: 4 study
Seroprevalence studies timeframe:	1975–2010

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **high**

Several studies estimating HAV seroprevalence were conducted in Germany before 1990, mostly during the 1970s. Ten studies provided estimates of seroprevalence at 15 and 30 years of age; all estimated prevalence below 35% by the age of 15 years, however seroprevalence ranged from 40% to 62% by the age of 30, depending on the studies (Germany_Figure 1). The six studies conducted during the 1990s provided comparable estimates, with an HAV seroprevalence of 30% or below by the age of 30 years, rising above 50% in those aged 50 and older (Germany_Figure 1). Two studies were published after 2000, of which one is the report of the German Health Interview and Examination Survey for Adults (DEGS1) (Poethko 2013). The studies provide HAV seroprevalence in the youth and adult population with estimates below 40% by the age of 30, a slight increase as compared to the previous decade.

Germany may be considered a very low endemicity country since the 1990s.

Germany_Table 1. Hepatitis A seroprevalence level by time period

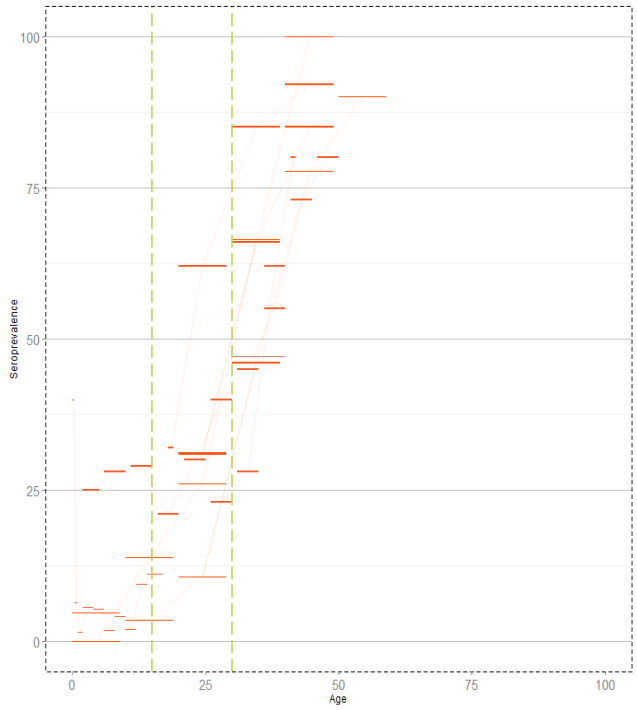
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Incidence data are available from 1990 (Germany_Figure 2) and show a marked decreasing trend from a reported rate of around 7/100 000 in mid 1990s to a reported rate consistently below 2/100 000 since 2006.

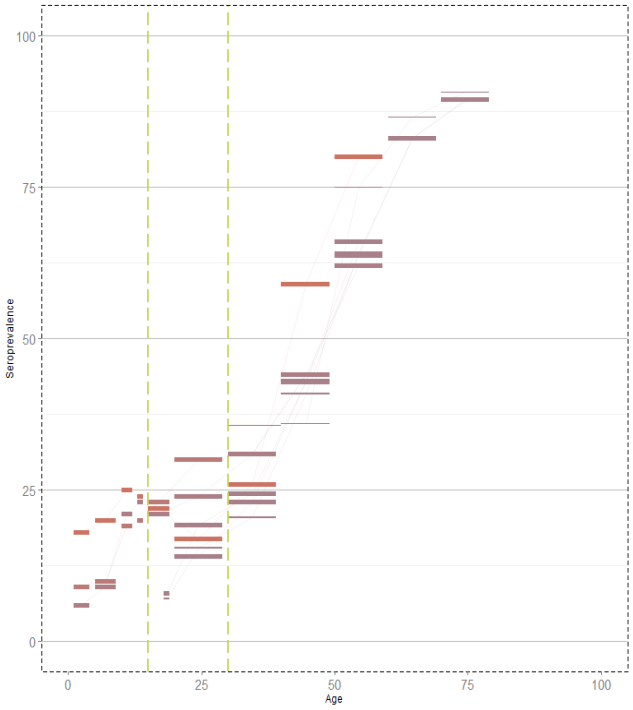
Based on the available data from the1990s, the susceptibility was estimated to be around 75% by the age of 30, and around 50% at the age of 50. Therefore the susceptibility among adults has been and is currently likely to be high.

Germany_Figure 1 (panel a). Summary of seroprevalence in Germany, by age and time period

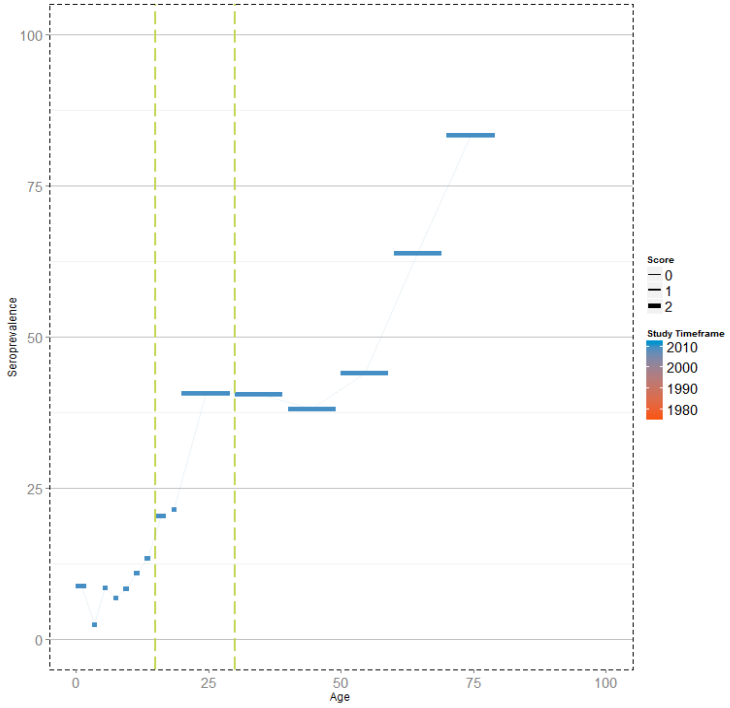
Panel a.1: 1975–1989



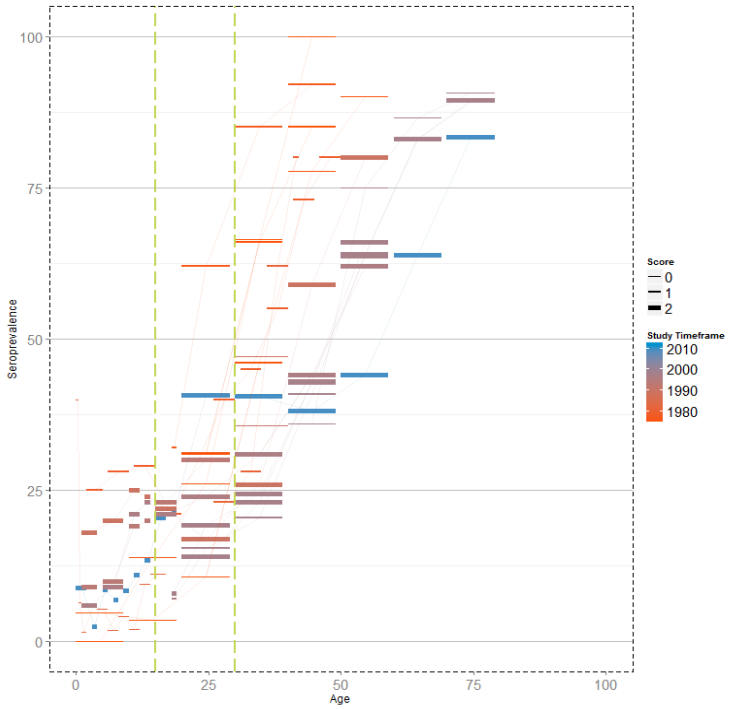
Panel a.2: 1990–1999



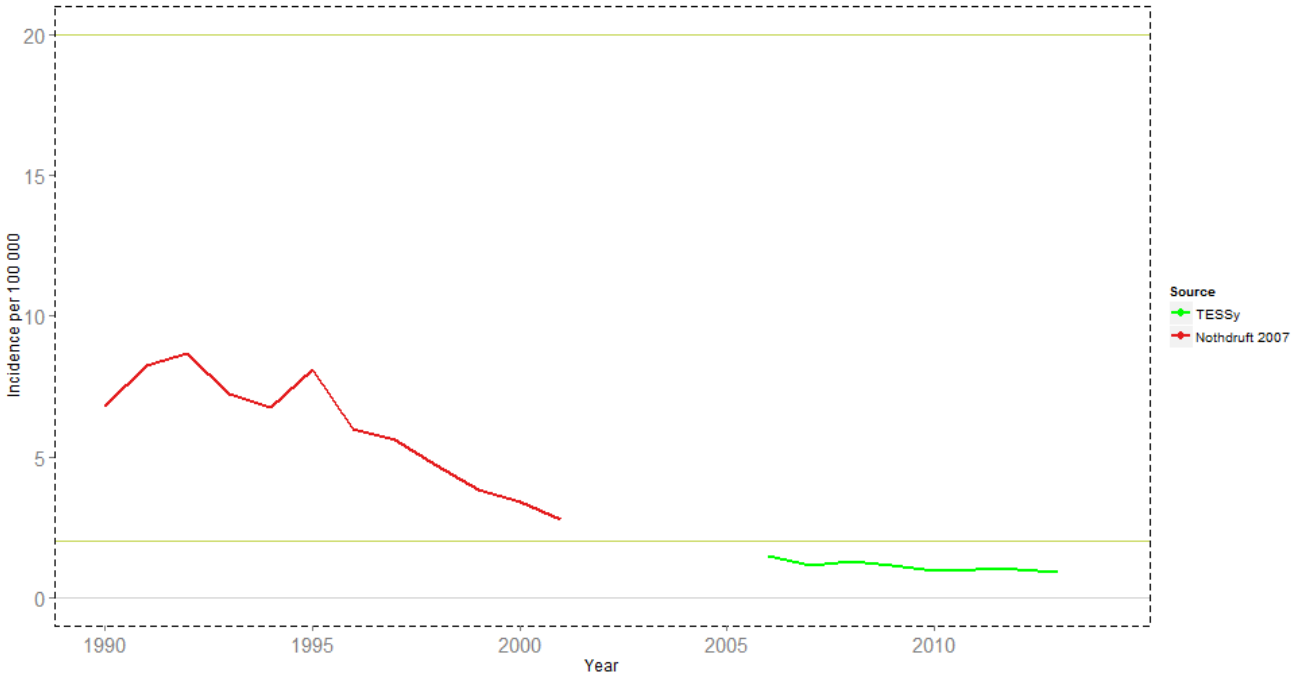
Panel a.3: 2000–2013



Germany_Figure 1 (panel b). Summary of seroprevalence in Germany, by age and time period (1975-2013)



Germany_Figure 2. Reported incidence of hepatitis A, Germany, 1990–2013



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Greece

Population (January 2013):	11 062 508
Human development Index (2013):	0.853
HAV vaccine recommendations:	As of January 2008, HAV vaccine is offered free of charge to all children above the age of 12 months within the National Immunization Programme. In addition HAV vaccination is recommended for adults who are at higher risk for infection/disease: 1. travellers to endemic countries with high/intermediate endemicity 2. MSM 3. PWID; 4. health service workers 5. professionals involved in handling and distribution of food In 2011 the estimated coverage of HAV vaccine was 62% in children below six, (Pavlopoulou, 2013).
Seroprevalence studies by quality score:	score 0: 4 studies score 1: 4 studies score 2: 0 studies
Seroprevalence studies timeframe:	1977–2007

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **moderate**

Few studies on the prevalence of HAV in children and young adults were conducted in Greece in the period 1977–1989. The seroprevalence estimates in the studies conducted are above 50% at the age of 30. Only one study conducted in 1982 (Papavangelou 1982) provides a seroprevalence estimate below 50% at the age of 15 (Greece_Figure 1). Out of 4 studies estimating HAV seroprevalence in Greece between 1990 and 1999, two gave information on the estimates of seroprevalence by 15 years old with estimates ranging from 6% to 32%. Two studies provided estimates for young adults aged 19–20 at 17%. One study (Lionis 1997) on Crete population, provided a seroprevalence estimate of 95% in the age group 45–64 years. Two studies were conducted in the period 2006–7, providing estimates of an HAV seroprevalence below 20% by 15 and by 30 years (Greece_Figure 1). Given the intra-country seroprevalence variability in Greece, it is challenging to assign an appropriate endemicity profile, although it is likely to be very low for most of the Greek territory.

Greece_Table 1. Hepatitis A seroprevalence level by time period

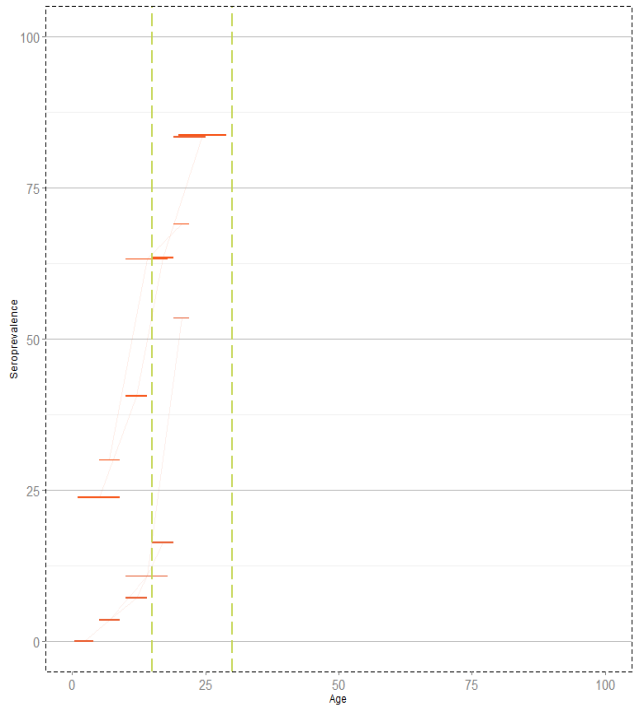
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

The reported incidence of hepatitis A in Greece is available from 1990 and shows fluctuation around 2/100 000 with a decreasing trend since 2007 (Greece_Figure 2).

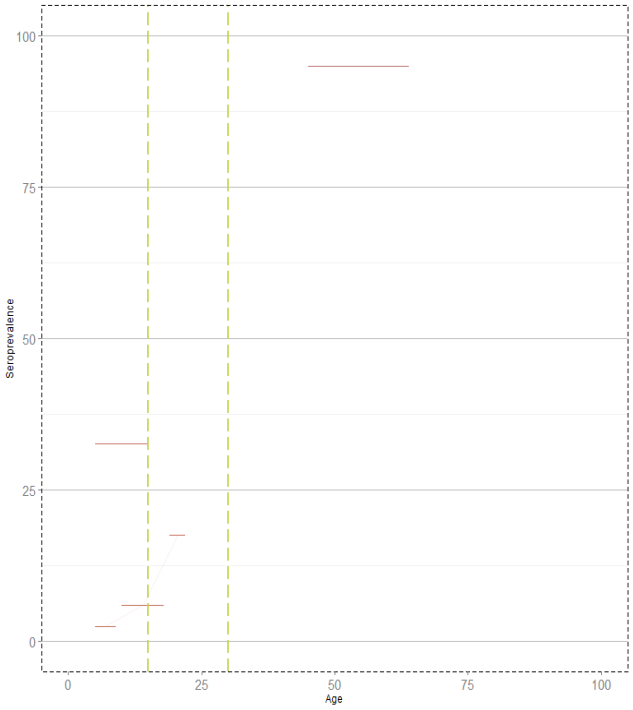
Data are too scarce to assess the susceptibility level in adults. However, considering the seroprevalence level in the past decades, and the likelihood of intra-country variability, the susceptibility in adults may today be considered moderate.

Greece_Figure 1 (panel a). Summary of seroprevalence in Greece, by age and time period.

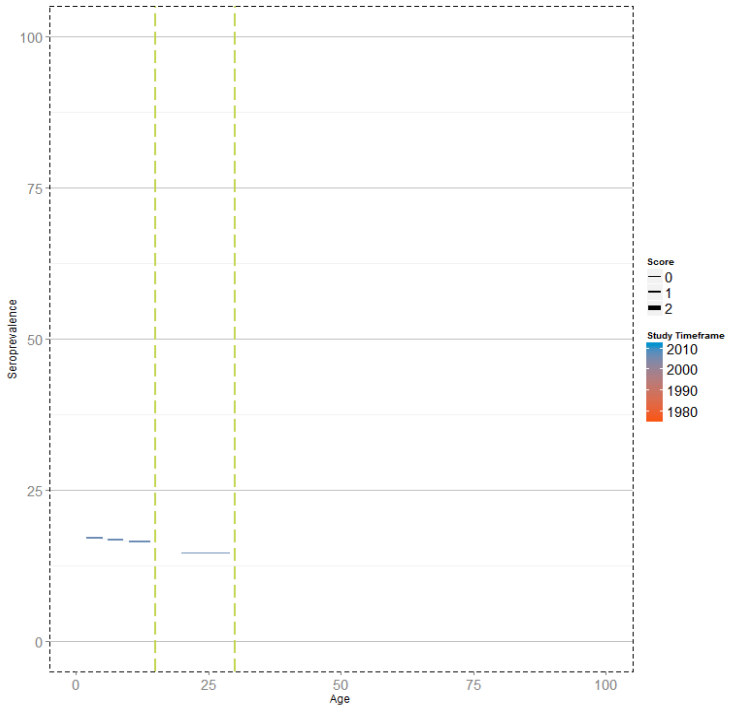
Panel a.1: 1975–1989



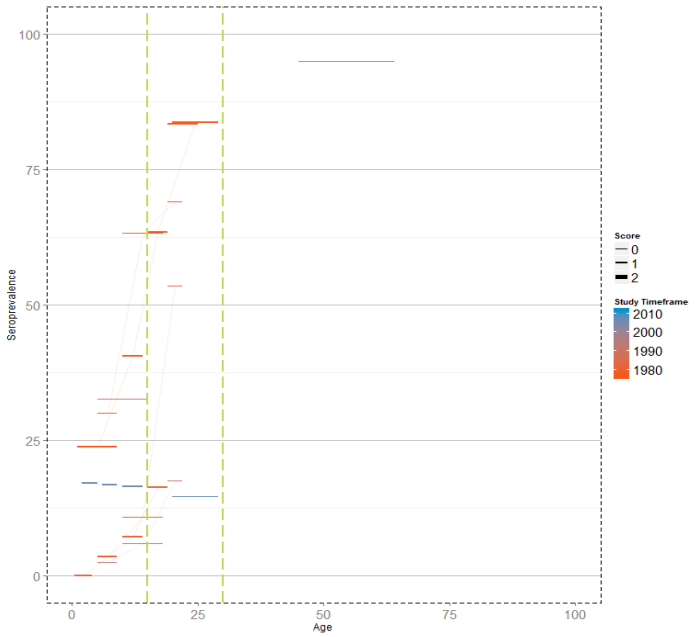
Panel a.2: 1990–1999



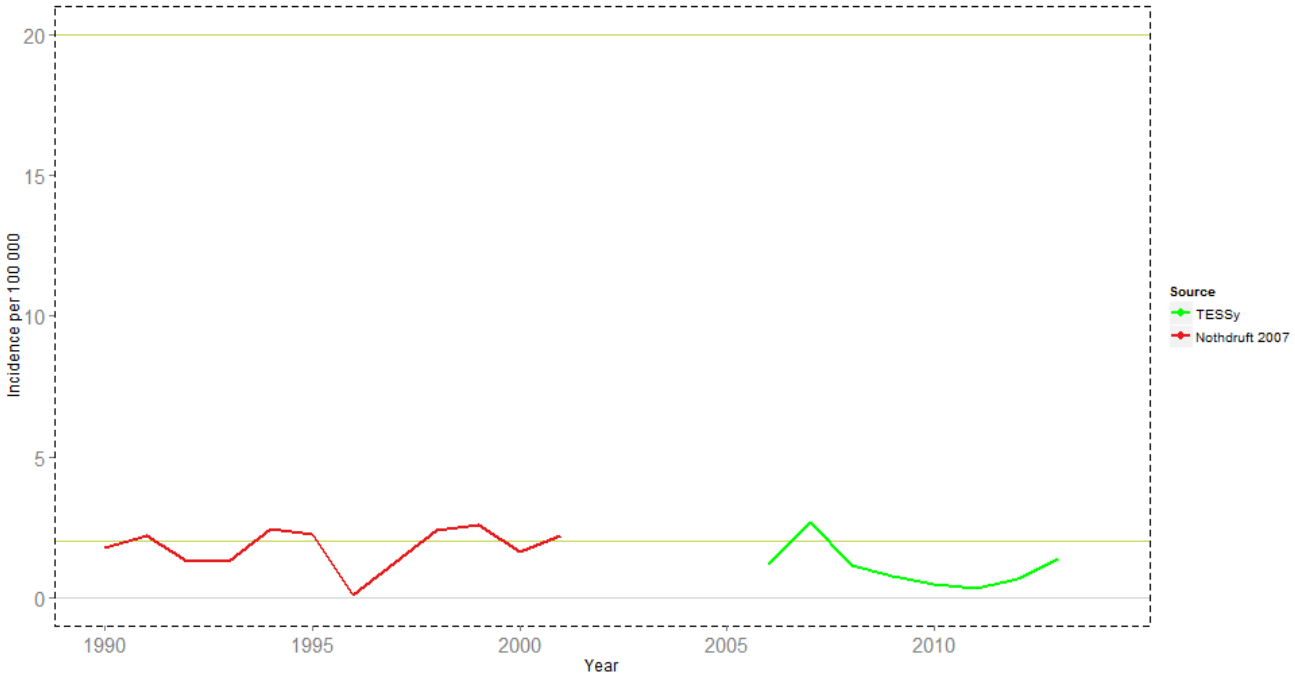
Panel a.3: 2000–2013



Greece_Figure 1 (panel b). Summary of seroprevalence in Greece, by age and time period (1975-2013)



Greece_Figure 2. Reported incidence of hepatitis A, Greece, 1990–2013



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Hungary

Population (January 2013):	865 878
Human development Index (2013):	0.818
HAV vaccine recommendations:	HAV vaccination is not included in the routine vaccination schedule for children. Vaccination is free of charge for close contacts of a HA patients. Vaccination is recommended for people belonging to high risk groups, such as: 1. travellers to endemic country 2. chronically ill people (e.g. haemophilic) 3. PLWD 4. MSM.
Seroprevalence studies by quality score:	score 0: 0 studies score 1: 0 studies score 2: 0 studies
Seroprevalence studies timeframe:	-

Seroprevalence assessment: **no data available**
Incidence assessment: **low**
Susceptibility in adults: **no data available**

No study on HAV seroprevalence could be found on the Hungarian population.

Hungary_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

The incidence data are available from the 1990s, although it is discontinuous. The data show a steady decrease from 24 cases per 100 000 in the mid-1990s to values oscillating around 2 cases per 100 000 in the period 2006 to present (Figure 2).

Hungary_Figure 1. Reported incidence of hepatitis A, Hungary, 1990–2013

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Iceland

Population (January 2013):	321 857
Human development Index (2013):	0.895
HAV vaccine recommendations:	HAV vaccination is not included in the General Childhood Vaccination Schedule. It is recommended for high risk groups and travellers.
Seroprevalence studies by quality score:	score 0: 1 study score 1: 1 study score 2: 0 studies
Seroprevalence studies timeframe:	1979–1987

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **very high**

Data for Iceland come from a study by Briem (Briem 1991) which included two assessments done in two different points in time (1979 and 1987). The estimates of HAV seroprevalence by the age of 30 are around 10% (Iceland_Figure 1). Iceland falls in the category of very low endemicity country.

Iceland_Table 1. Hepatitis A seroprevalence level by time period

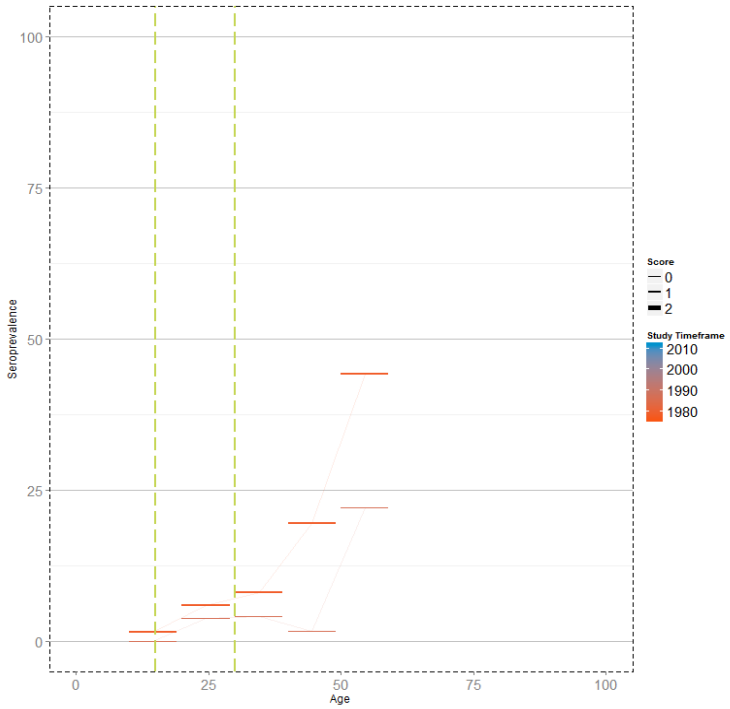
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

The incidence in Iceland is nowadays very low (Iceland_Figure 2). It was estimated as 2.2 per 100 000 in 1983; additionally, data reported by TESSy range from 0.31 to 1.25 per 100 000.

The susceptibility among adults is very high, at above 70% in all adult age groups.

Iceland_Figure 1 (panel a). Summary of seroprevalence in Iceland, by age and time period.

Panel a.1: 1975–1989



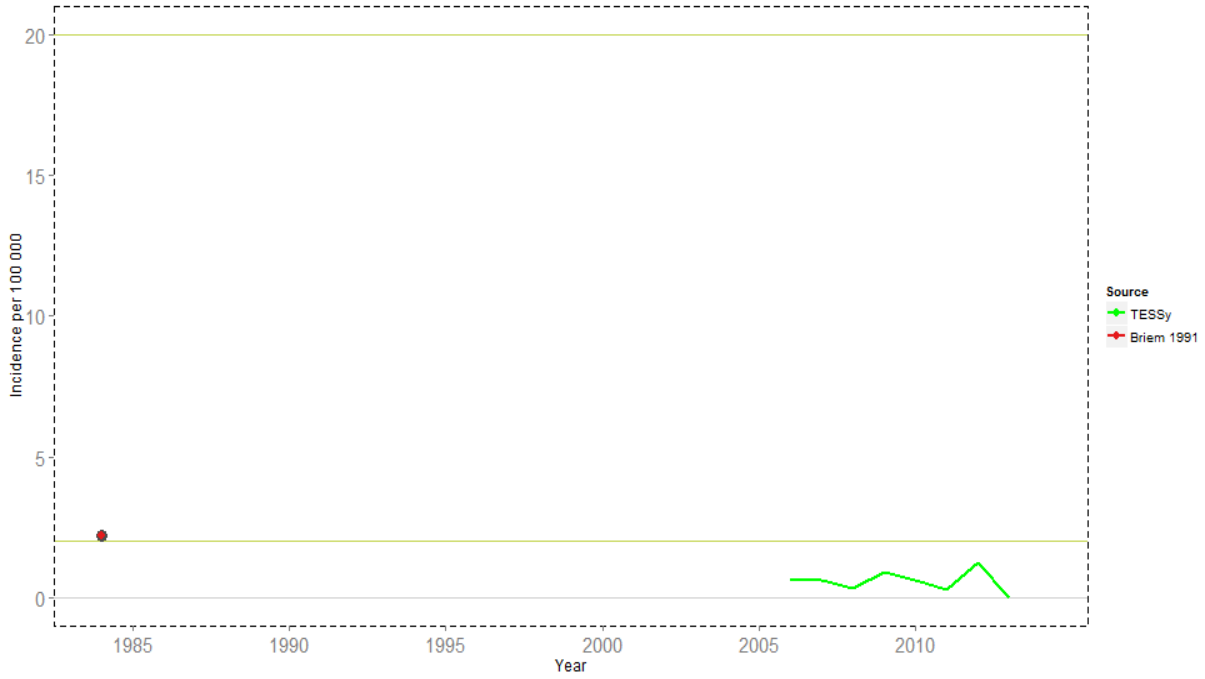
Panel a.2: 1990–1999

No data available

Panel a.3: 2000–2013

No data available

Iceland_Figure 2. Reported incidence of hepatitis A, Iceland, 1983–2013



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Ireland

Population (January 2013):	4 591 087
Human development Index (2013):	0.899
HAV vaccine recommendations:	Hepatitis A vaccine is not part of the routine childhood immunisation programme. The vaccine is recommended for: 1. travellers 2. persons with chronic liver disease, solid organ transplant recipients 3. haemophiliacs 4. PWID 5. MSM 6. institutionalised patients; people with occupational exposure, e.g. laboratory workers, sewage workers 7. close contacts of adoptees from countries with high or intermediate hepatitis A endemicity 8. for outbreak control.
Seroprevelance studies by quality score:	score 0: 2 study score 1: 0 studies score 2: 0 studies
Seroprevelance studies timeframe:	1985–1997

Seroprevalence assessment*: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **high**

*this assessment is based on data from 1997 and supported by current incidence levels

Only two studies were retrieved on HAV seroprevalence in Ireland. The first, conducted in 1985 among children, provides a HAV seroprevalence estimate of 23% by the age of 14 years. The second study reported seroprevalence upto 40% in the age group 20–29 years, and 71% in the age group 30–39 yrs in 1997 (Ireland_Figure 1). As more recent data are not available, and even though data are scarce, Ireland has been classified as a very low endemicity country based on data from the late 1990's.

Ireland_Table 1. Hepatitis A seroprevalence level by time period

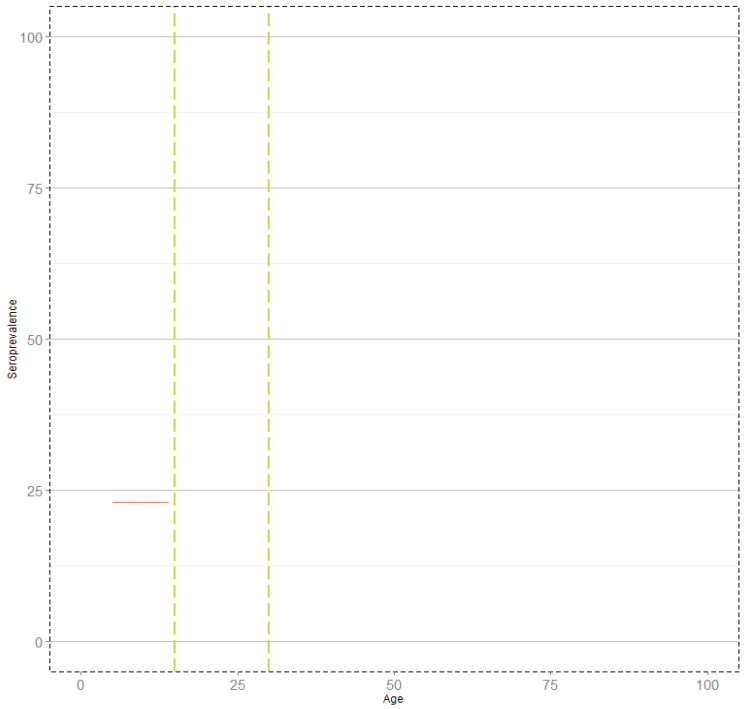
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported hepatitis A incidence between 2006 and 2012 was below 1 case per 100 000 for most of the period, with no evidence of disease outbreaks as clearly shown in Ireland_Figure 2. Such level of incidence, combined with seroprevalence assessed in 1997, suggest that Ireland could have recently transitioned towards very low endemicity.

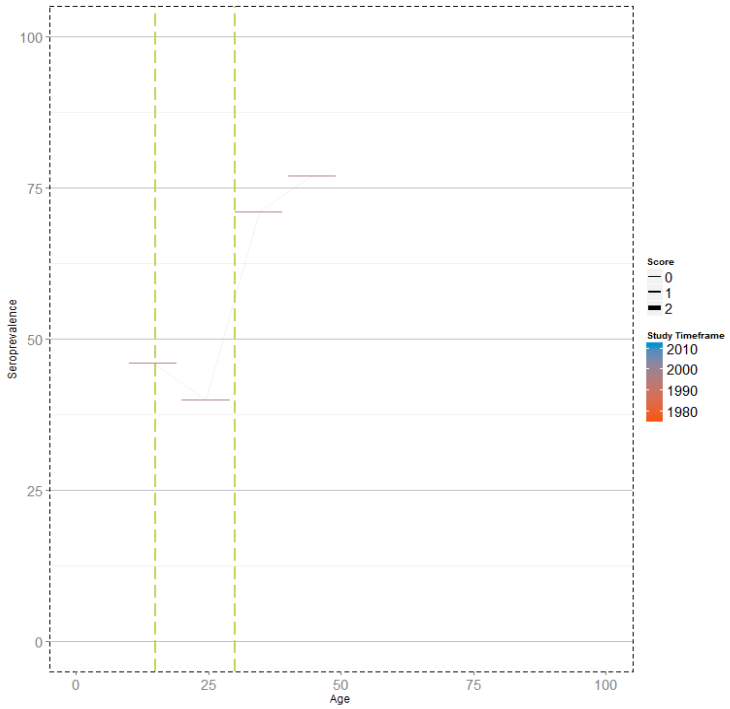
Estimated susceptibility in 1997 was around 50% at 30 years and around 20% at 50 years. At that time the susceptibility among adults was considered moderate. Considering the very low incidence profile of the country in the last decade, and the absence of sustained circulation of the virus, the susceptibility among adults is likely to be high in the present situation.

Ireland_Figure 1 (panel a). Summary of seroprevalence in Ireland, by age and time period.

Panel a.1: 1975–1989



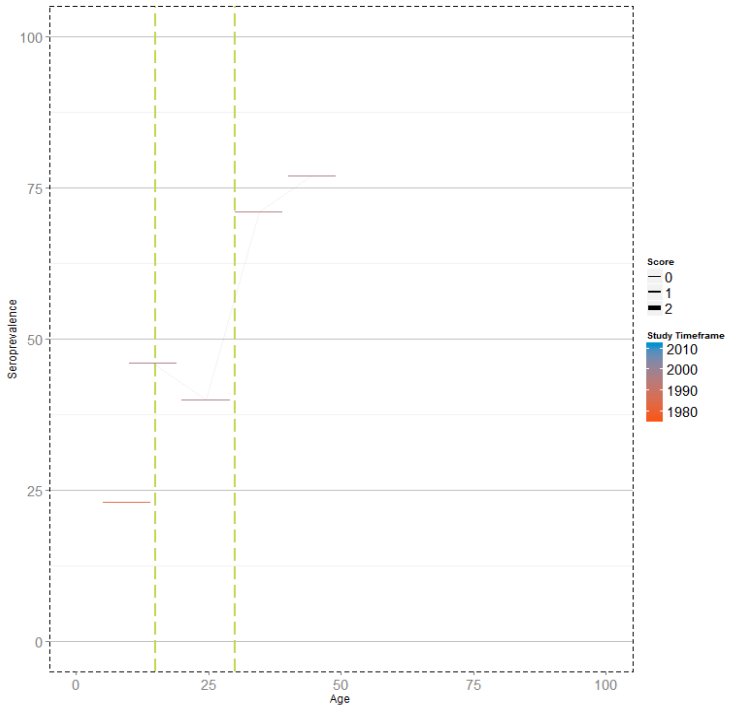
Panel a.2: 1990–1999



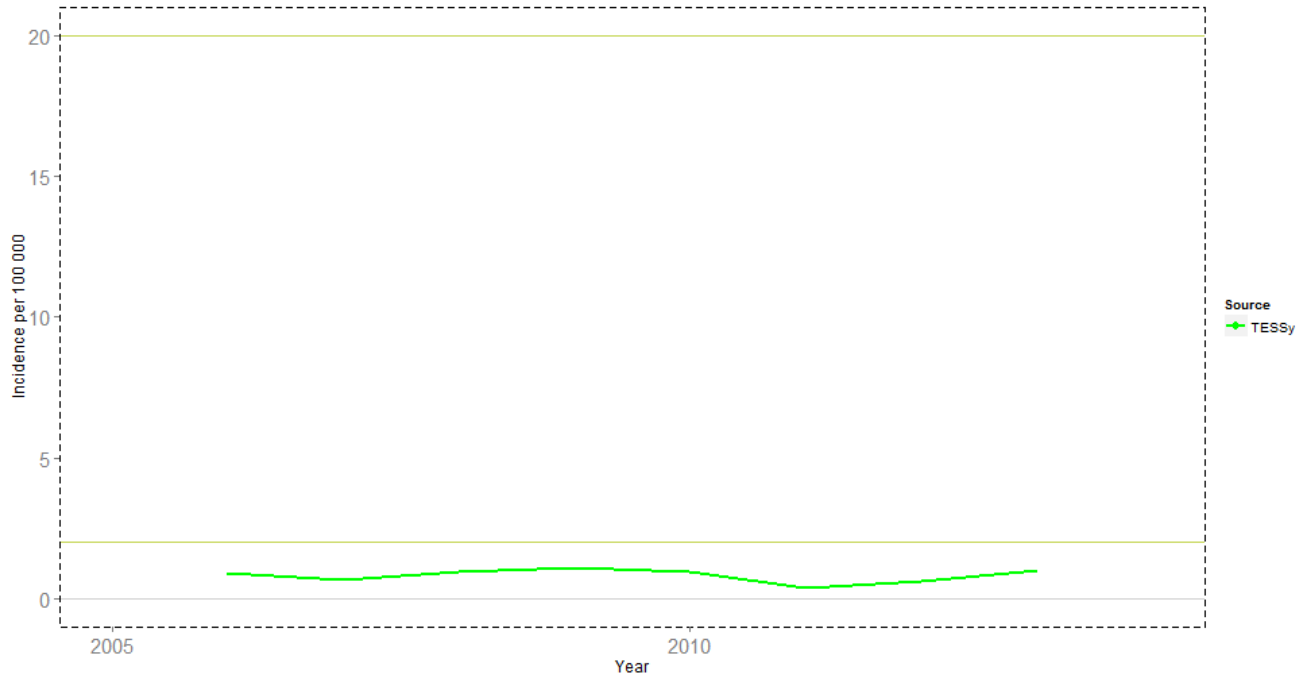
Panel a.3: 2000–2013

No data available

Ireland_Figure 1 (panel b). Summary of seroprevalence in Ireland, by age and time period (1975-2013)



Ireland_Figure 2. Reported incidence of hepatitis A, Ireland, 2006–2013



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Italy

Population (January 2013):	59 685 227
Human development Index (2013):	0.872
HAV vaccine recommendations:	HAV vaccination is recommended for specific groups: 1. patients with chronic liver disease and in therapy with coagulation factors 2. MSM 3. PWID 4. People with occupational exposure, e.g. lab personnel 5. 0–6 years old children of immigrant population visiting endemic countries. Universal children vaccination is offered free of charge in Puglia region only: since 1998 to all children 15–18 months of age and form 1998-2003 to 12-year-olds.
Seroprevalence studies by quality score: **Seroprevalence studies timeframe:**	score 0: 22 studies score 1: 36 studies score 2: 6 studies 1977–2011

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **moderate**

Before 1990, a total of 33 studies were included in the analysis. Of those that provide an estimate of HAV seroprevalence at 30 years of age, all but one report values above 50%. A marked geographical variability is reported at the age of 15, with a strong North-South gradient (Italy_Figure 1).

Similarily, high variability is observed between 1990 and 2000 around the age of 30. Out of 23 studies estimating HAV seroprevalence in this period, 10 give information on the age group up to 30, providing estimates ranging from 8 to 77%, with only three above 50%. No estimate above 50% is reported in the age group below 15 years (Italy_Figure 1).

After 2000, all studies estimated an HAV seroprevalence at less than 50% among adults aged 30. One cohort in 2008 in the Puglia region, aged 16–20, had an HAV seroprevalence estimated at 77%, due to universal children and adolescent vaccination started in 1998 in that region (Chironna 2012). Italy likely transitioned from intermediate to low endemicity in the 1980s, and from low to very low endemicity in the late 1980s (Italy_Figure 1) with an evident geographical gradient, with Northern regions transitioning at an earlier time. It remains a very low endemicity country.

Italy_Table 1. Hepatitis A seroprevalence level by time period

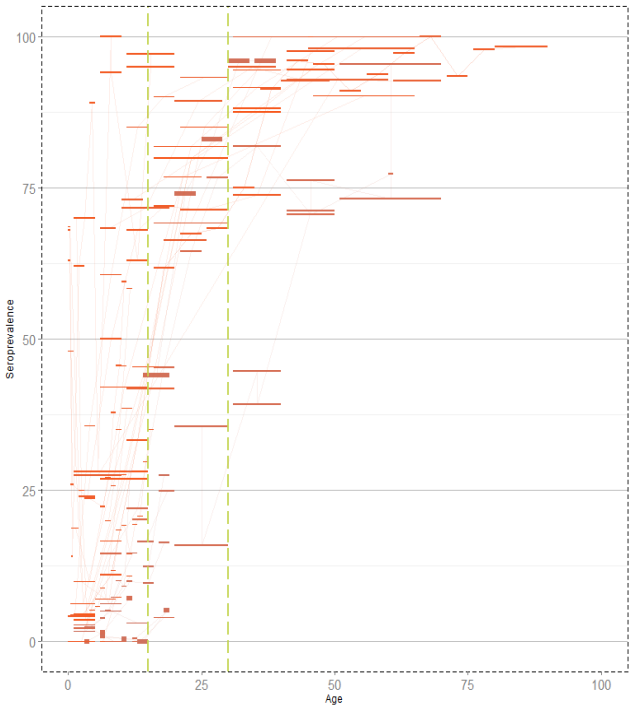
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence in TESSy is consistent with this finding, with less than 3 cases per 100 000 since 2006 (Italy_Figure 2).

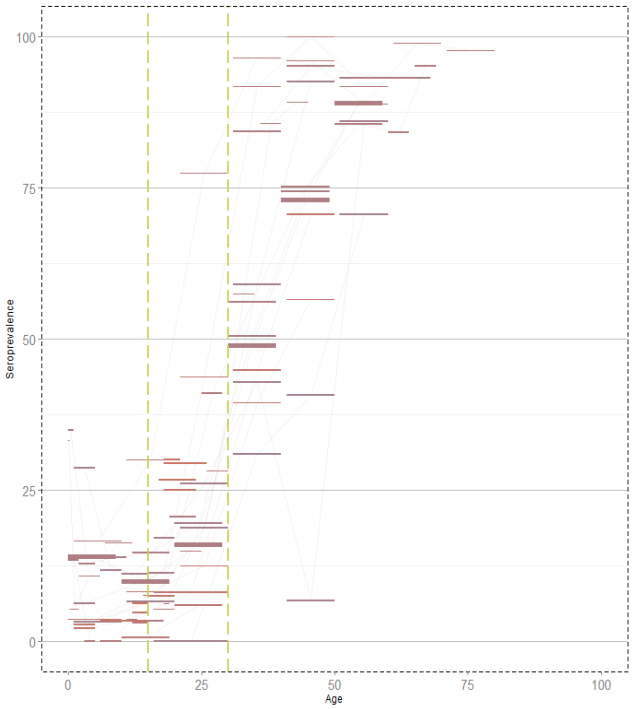
The susceptibility level by 30 years ranges from 80% and above in the Northern regions to around 60% in the Southern regions. Due to the large variability between studies from different regions the assessment of susceptibility among adults may be considered moderate.

Italy_Figure 1 (panel a). Summary of seroprevalence in Italy, by age and time period.

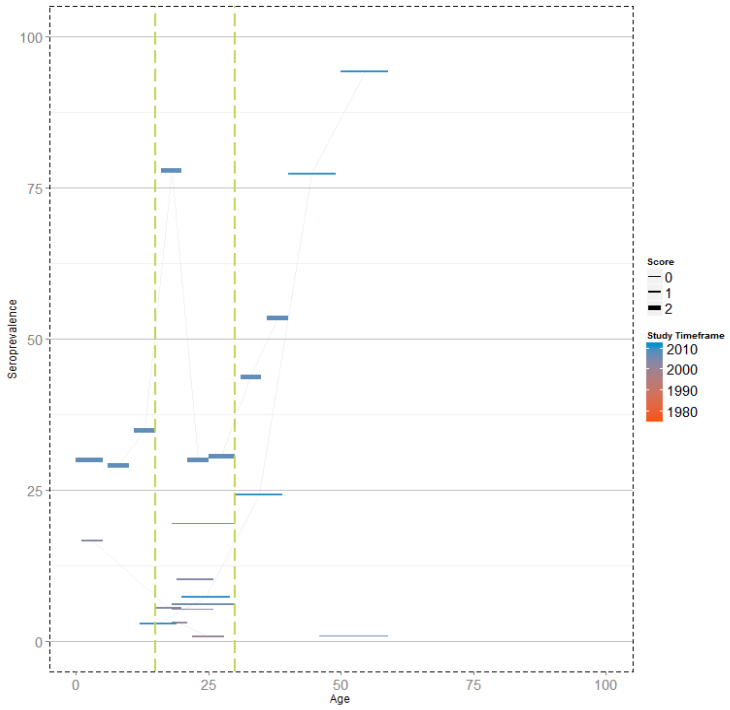
Panel a.1: 1975–1989



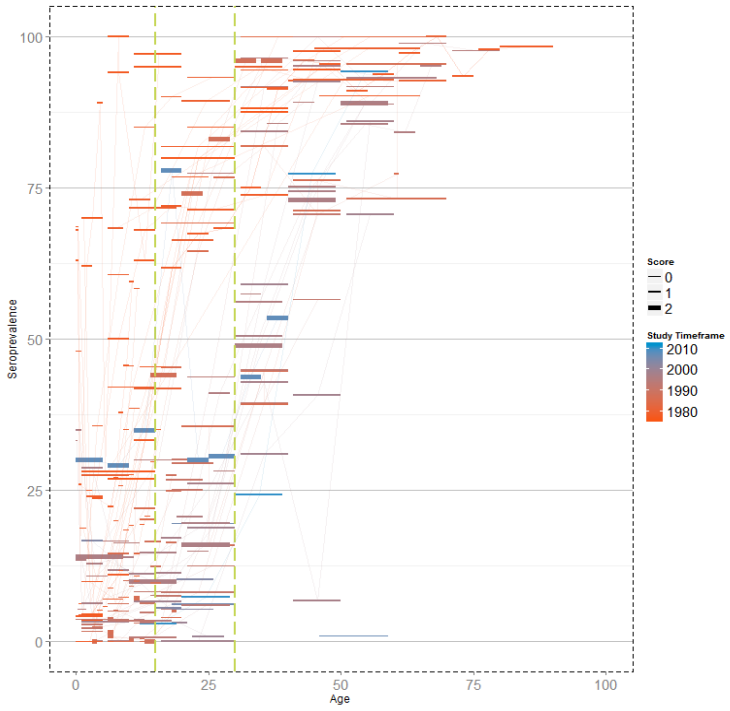
Panel a.2: 1990–1999



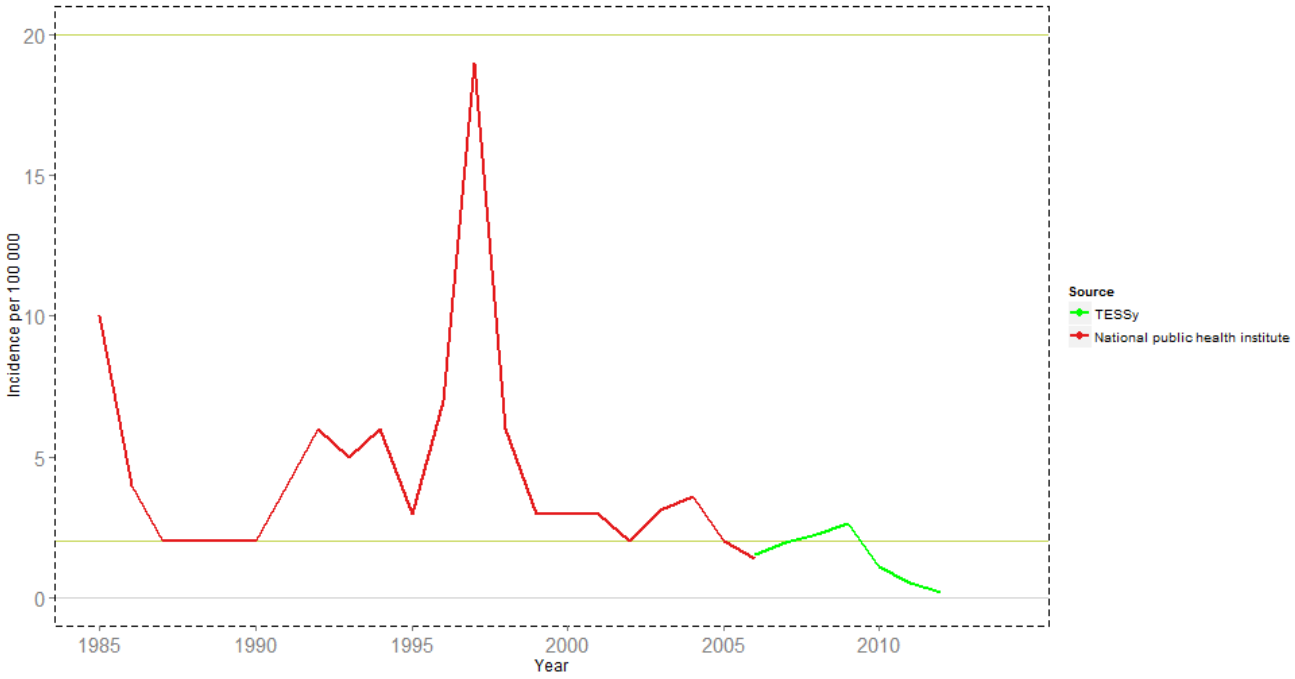
Panel a.3: 2000–2013



Italy_Figure 1 (panel b). Summary of seroprevalence in Italy, by age and time period (1975-2013)



Italy_Figure 2. Reported incidence of hepatitis A, Italy, 1985-2012*



National data source: www.iss.it

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Latvia

Population (January 2013):	2 023 825
Human development Index (2013):	LV: 0.810
HAV vaccine recommendations:	HAV vaccination is not included in the national childhood immunization programme. Vaccination is recommended for: 1. travellers to endemic areas 2. people infected with HBV or HCV 3. For outbreak control.
Seroprevalence studies by quality score:	score 0: 0 studies score 1: 0 studies score 2: 0 studies
Seroprevalence studies timeframe:	-

Seroprevalence assessment: **no data available**
Incidence assessment: **intermediate**
Susceptibility in adults: **no data available**

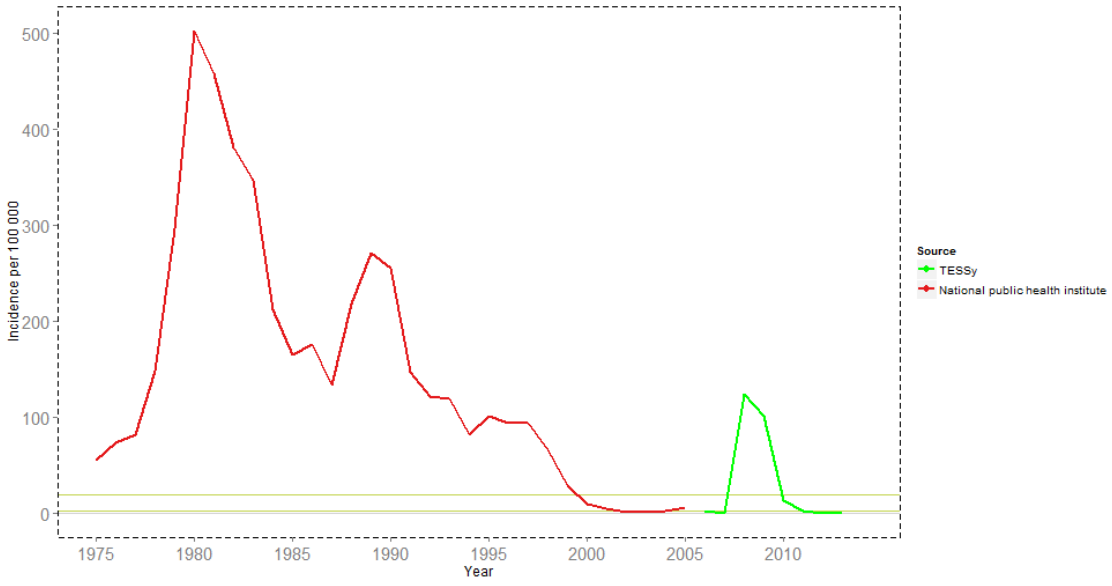
No study on HAV seroprevalence could be found on Latvian population.

Latvia_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Available incidence data from 1990 shows a steady decrease from more than 250 cases per 100 000 to 5 cases per 100 000 in 2001. Reported incidence in TESSy from 2006 to 2012 widely oscillates from less than 1 case per 100 000 in 2007 and 2012 to more than 100 cases per 100 000 in 2008 and 2009 (Latvia_Figure 2).

Latvia_Figure 1. Reported incidence of hepatitis A in Latvia, 1990-2013



National data source: personal communication from ECDC National Focal Point/Operational Contact Point, Centre for Disease Prevention and Control of Latvia

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Lithuania

Population (January 2013):	2 971 905
Human development Index (2013):	0.834
HAV vaccine recommendations:	HAV vaccination is not included in the national childhood immunization programme. Vaccination is recommended for: 1. contacts of HAV patients 2. travellers to endemic areas 3. high risk groups.
Seroprevalence studies by quality score:	score 0: 0 studies score 1: 0 study score 2: 1 study
Seroprevalence studies timeframe:	2003

Seroprevalence assessment: **low**
Incidence assessment: **low**
Susceptibility in adults: **moderate**

One study conducted in Lithuania in 2003, estimated HAV seroprevalence to be 55%in the age group 20–29 years and 30% in the age group 10–19 years. There were no available estimates by 30 years or older. Therefore, Lithuania, is likely to be a low endemicity country (Figure 1).

Lithuania_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence was above 20/100 000 until 1999 and it has been strongly decreasing since then (Figure 2). TESSy data are consistent with low/very low endemicity picture with a reported incidence oscillating around 2/100 000 since 2006.

In Lithuania, around 40% of the population is susceptible to HAV infection at age 30. Considering the reported incidence, virus circulation was sustained until late 1990s. Therefore, susceptibility levels among older age groups are very likely to be lower. Susceptibility in adults is to be considered moderate.

Lithuania_Figure 1 (panel a). Summary of seroprevalence in Lithuania, by age and time period.

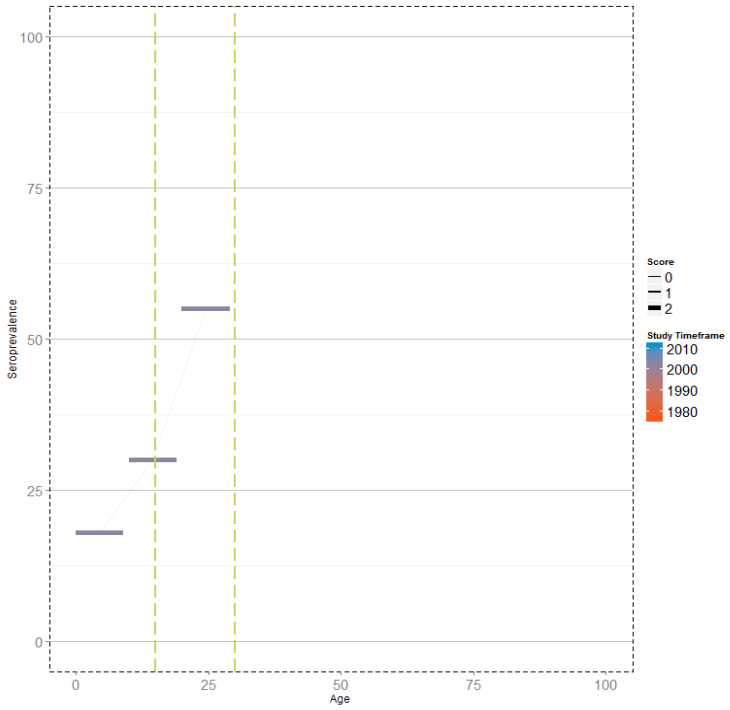
Panel a.1: 1975–1989

No data available

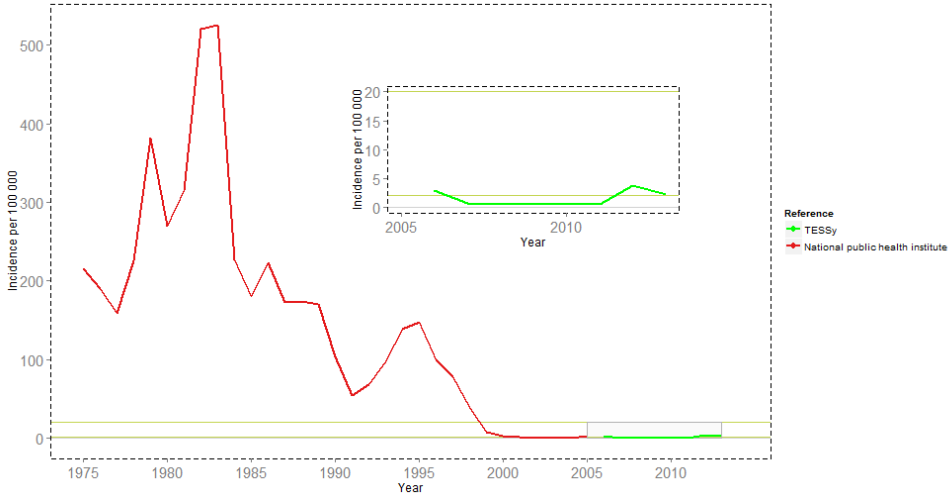
Panel a.2: 1990–1999

No data available

Panel a.3: 2000–2013



Lithuania_Figure 2. Reported incidence of hepatitis A in Lithuania, 1975–2013*



**National data source: personal communication from ECDC National Focal Point/Operational Contact Point, Centre of Infectious Diseases and AIDS of Lithuania*

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Luxembourg

Population (January 2013):	537 039
Human Development Index (2013):	0.881
HAV vaccine recommendations:	Hepatitis A vaccine is not part of the routine childhood immunisation programme. The vaccine is recommended for: 1. child-care workers and workers in collective institutions 2. personnel in the food sector 3. personnel in water-treatment plants 4. travellers to endemic countries.
Seroprevalence studies by quality score:	score 0: 0 study score 1: 1 study score 2: 0 studies
Seroprevalence studies timeframe:	2000–2001

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **high**

The only study published in Luxembourg (Mossong 2006) reported seroprevalence in 2001 below 50% in all age groups considered; seroprevalence was less than 20% up to 19 years of age. No other study was available. According to the available data Luxembourg should be considered a very low endemicity country.

Luxembourg_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

As TESSy data show, reported hepatitis A incidence between 2006 and 2012 was below 1 case per 100 000; according to Nothdruft (2007). The country experienced some disease outbreaks during the 1990's. The current level of incidence is in line with the very low endemicity level assessed through the seroprevalence survey in 2001.

The susceptibility among adults is high, with more than 60% susceptible individuals by age 30, and about 50% by the age of 50.

Luxembourg_Figure 1 (panel a). Summary of seroprevalence in Luxembourg, by age and time period.

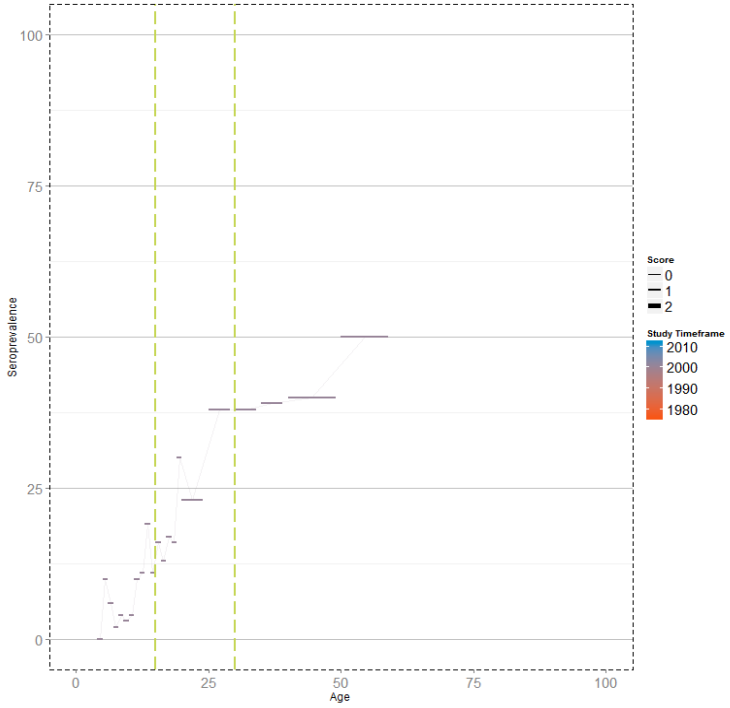
Panel a.1: 1975–1989

No data available

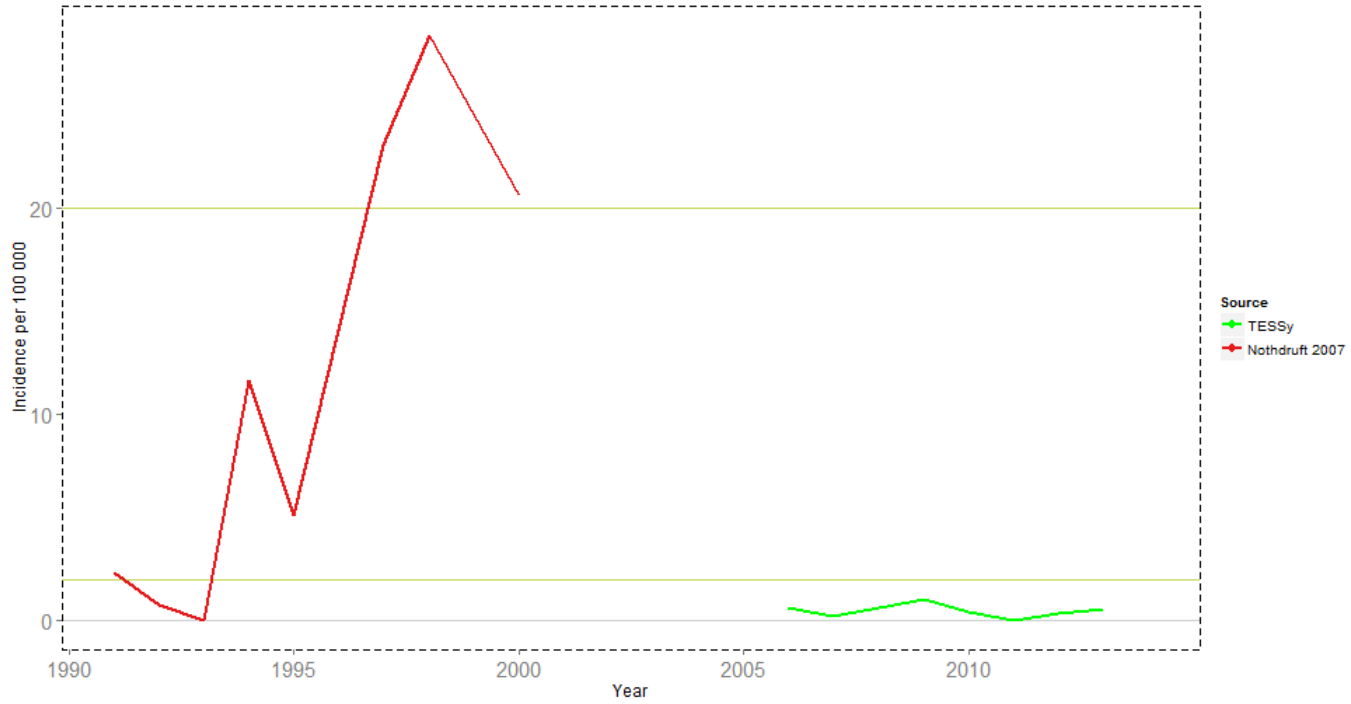
Panel a.2: 1990–1999

No data available

Panel a.3: 2000–2013



Luxembourg_Figure 2. Reported incidence of hepatitis A, Luxembourg, 1990–2013



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Malta

Population (January 2013):	421 364
Human development Index (2013):	0.829
HAV vaccine recommendations:	HAV vaccine is usually recommended for the management of contacts of cases and for outbreak control. It is also recommended for: 1. travellers to regions with a high prevalence of hepatitis A 2. people with occupational exposure, e.g. sewage workers.
Seroprevalence studies by quality score:	score 0: 0 studies score 1: 0 studies score 2: 1 study
Seroprevalence studies timeframe:	2004

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Risk of infection >30 years: **moderate**

The only data available for Malta comes from the study of Kurkela et al. (Kurkela 2012). The reported seroprevalence of HAV is below 50% by 30 years of age and below 25% by 15 years (Figure 1). Malta falls in the category of very low endemicity countries.

Malta_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Incidence data is available from 1989 until 2001 from one study (Nothdruft 2007) and from 2006 until 2012 from TESSy (Figure 2). The incidence is low, ranging from 0.53 to 3.81 per 100 000, and shows a subtle declining trend with peaks every 3–5 years.

The susceptibility among adults is moderate, as data show susceptibility levels around 70% by 30 years. Almost all individuals over 60 are seropositive.

Malta_Figure 1 (panel a). Summary of seroprevalence in Malta, by age and time period.

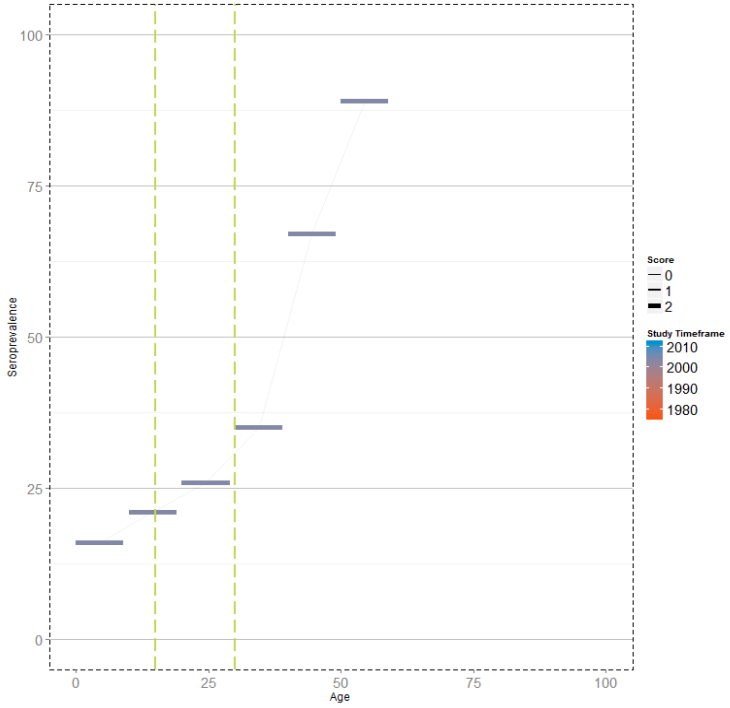
Panel a.1: 1975–1989

No data available

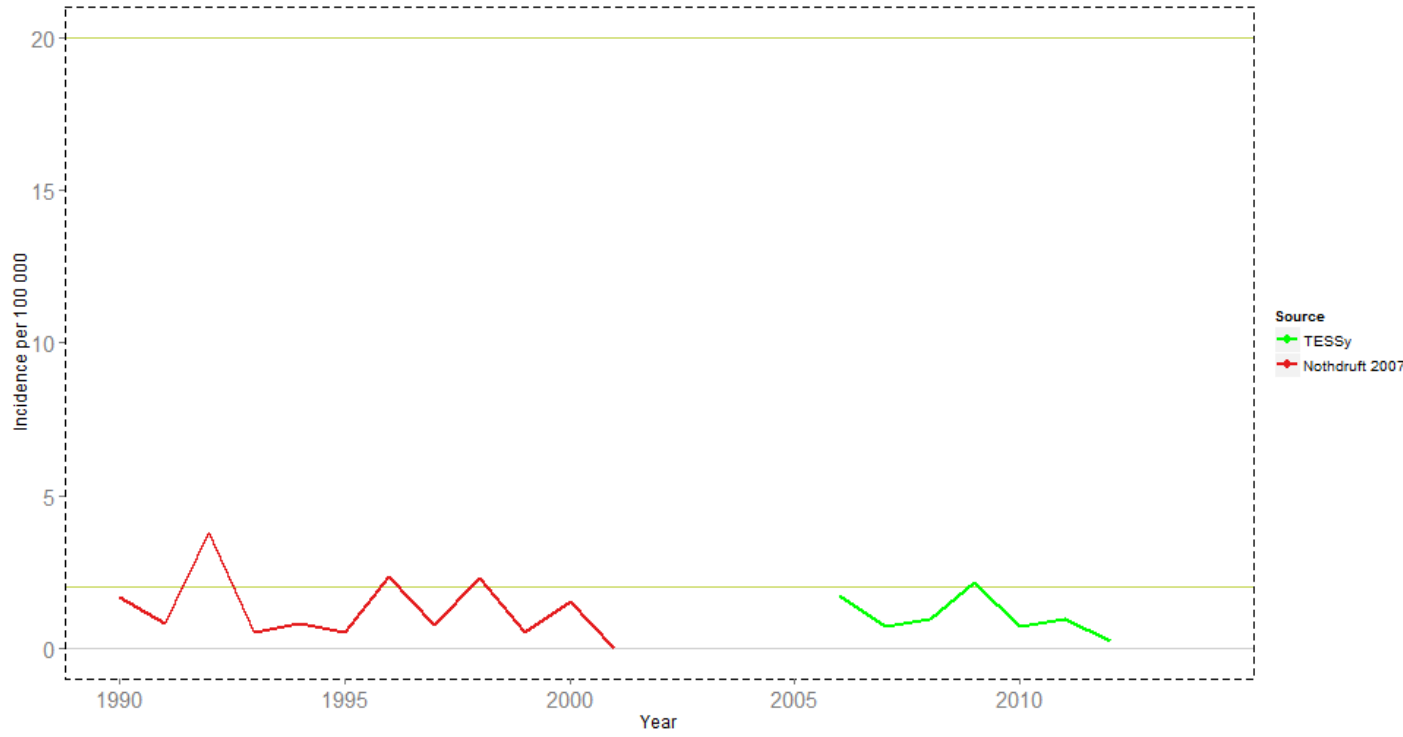
Panel a.2: 1990–1999

No data available

Panel a.3: 2000–2013



Malta_Figure 2. Reported incidence of hepatitis A, Malta, 1989–2013



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Netherlands

Population (January 2013):	16 779 575
Human development Index (2013):	0.915
HAV vaccine recommendations:	Hepatitis A vaccine is not part of the routine childhood immunisation programme.
Seroprevalence studies by quality score:	score 0: 0 study score 1: 3 study score 2: 2 studies
Seroprevalence studies timeframe:	1977–2004

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **high**

Seroprevalence levels reported in 1977 (Frezner 1979) indicate low endemicity levels, with about 36% seropositivity among 20–29 years old and 64% among 30–39 years old. One study (Termorshuizen 2000) conducted in 1999 reported 20% seroprevalence in the age group 15–49. Two studies published after 2000 both suggest that the Netherlands should be considered a very low endemicity country. Transition from low to very low endemicity most likely happened during the early 1990s.

Netherlands_Table 1. Hepatitis A seroprevalence level by time period

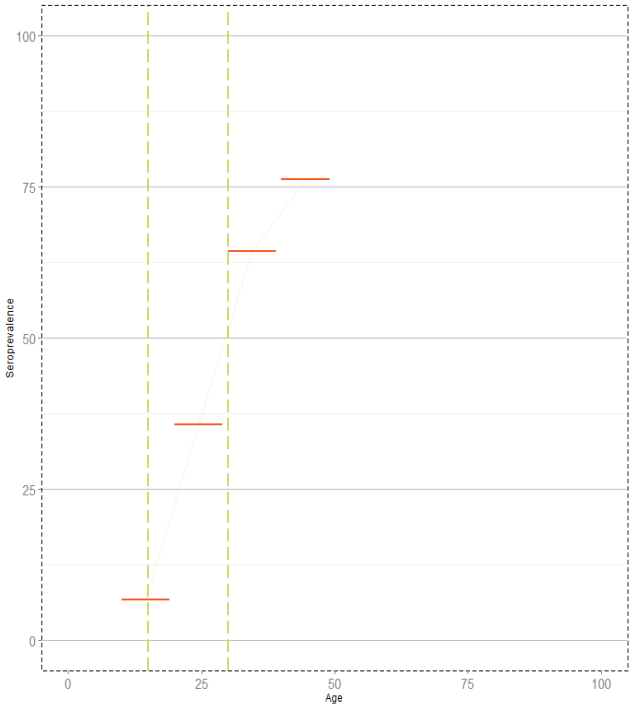
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Studies published since the 1990s report incidence levels always below 10 cases per 100 000 (Figure 2). Between 2006 and 2012, TESSy data show reported hepatitis A incidence to be below 2 cases per 100 000. The current level of incidence is in line with the very low endemicity level assessed through seroprevalence surveys.

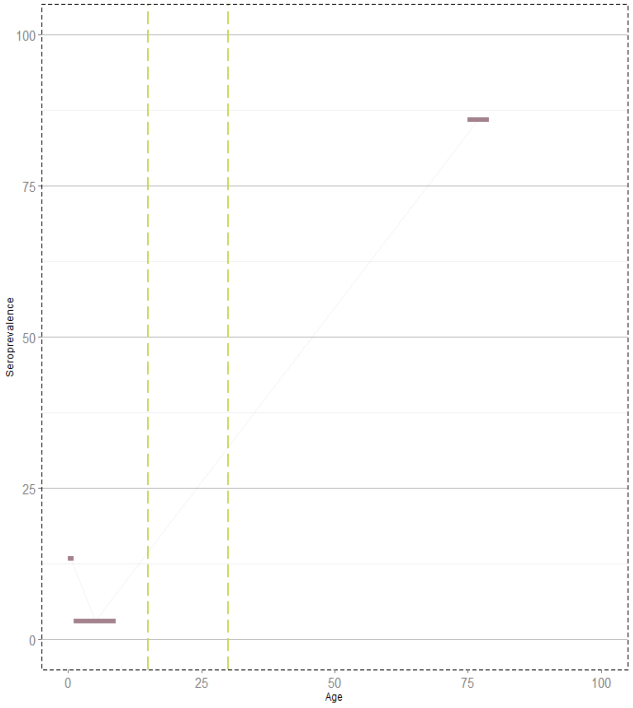
The susceptibility among adults has to be considered high, with at least 60% susceptible population by 30 years and around 40% susceptibility at 50 years of age.

Netherlands_Figure 1 (panel a). Summary of seroprevalence in the Netherlands, by age and time period.

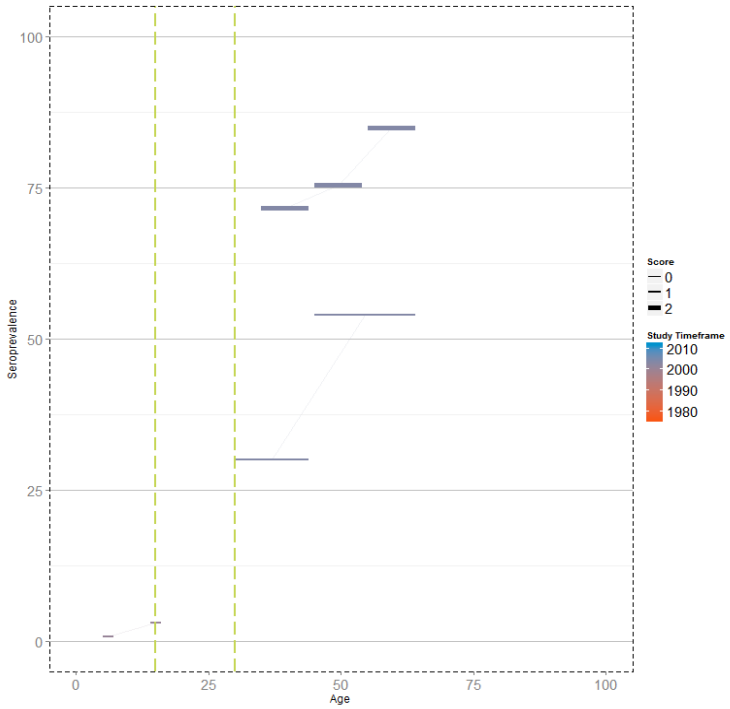
Panel a.1: 1975–1989



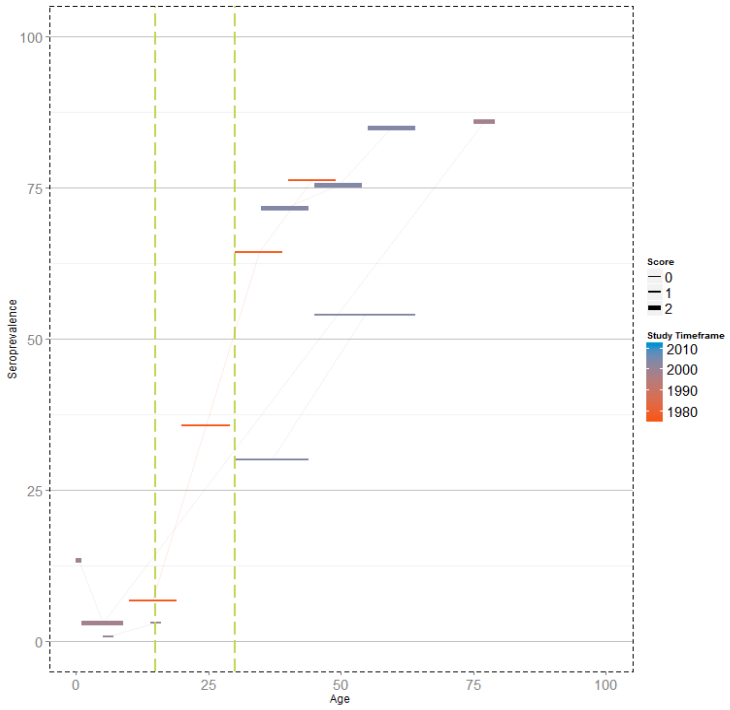
Panel a.2: 1990–1999



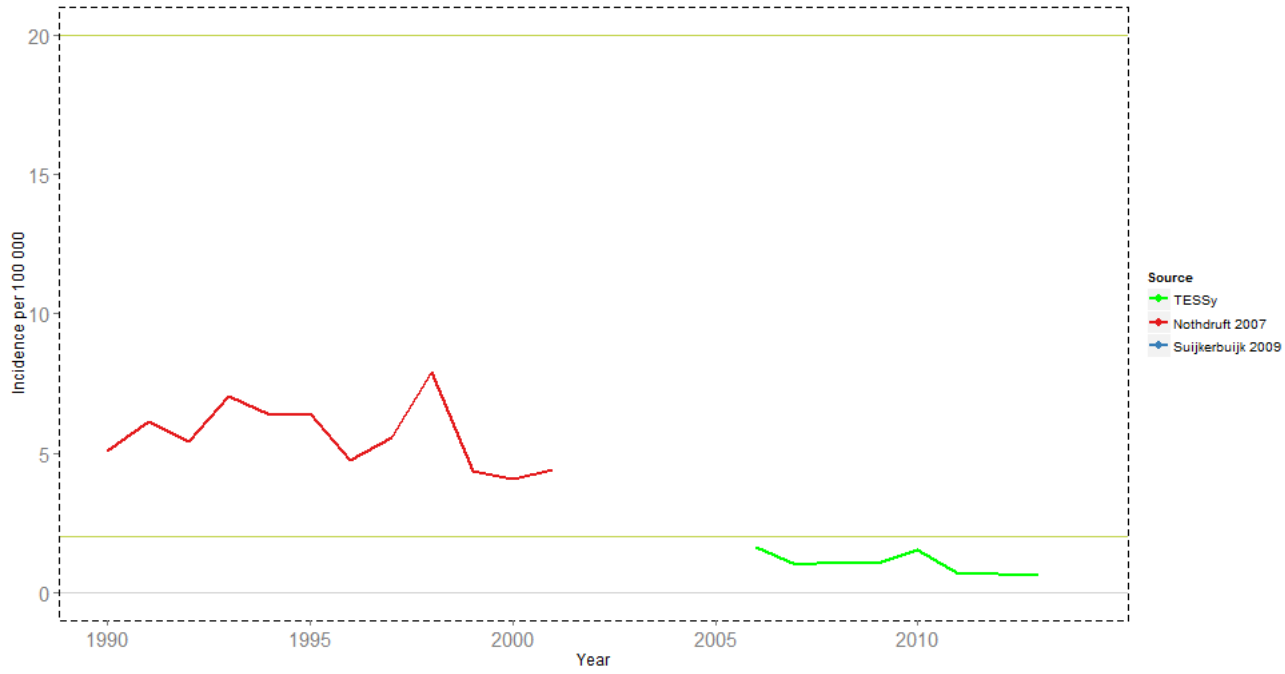
Panel a.3: 2000–2013



Netherlands_Figure 1 (panel b). Summary of seroprevalence in the Netherlands, by age and time period (1975-2013)



Netherlands_Figure 2. Reported incidence of hepatitis A, the Netherlands, 1989–2013



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Norway

Population (January 2013):	5 051 275
Human development Index (2013):	0.944
HAV vaccine recommendations:	HAV vaccination is not included in the national childhood immunisation programme. Vaccination is recommended for: 1. travellers to endemic areas 2. migrants visiting friends and relatives in their former country of residence 3. PWID 4. patients with chronic liver disease 5. Haemophiliacs 6. For outbreak control (free vaccination). Vaccination is recommended to risk groups for hepatitis B in the form of the combined hep A/B vaccine.
Seroprevalence studies by quality score:	score 0: 2 studies; score 1: 0 studies; score 2: 0 studies
Seroprevalence studies timeframe:	1975–1976

Seroprevalence assessment*: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **very high**

**this assessment is based on data from the 1970s*

Norway_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

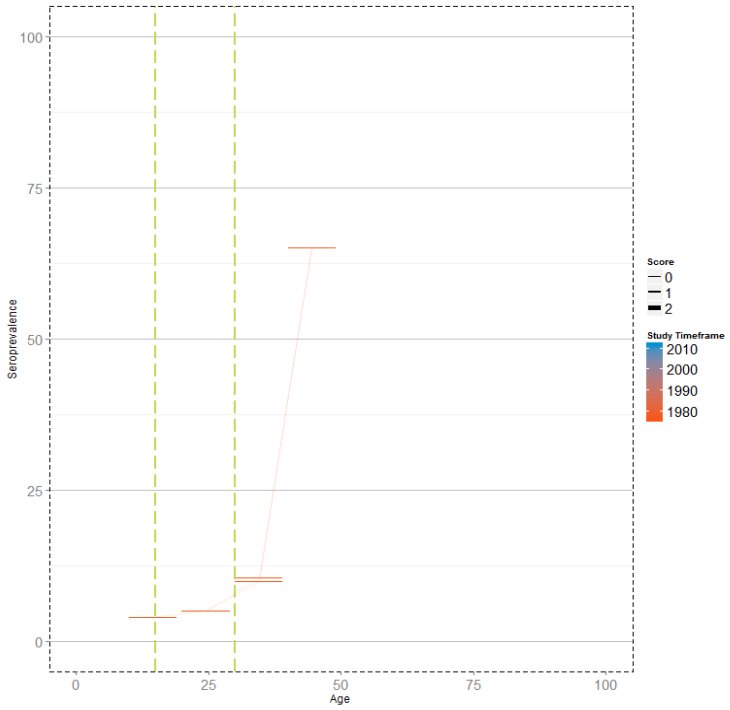
One study conducted in 1976 estimated HAV seroprevalence in the age group 30–39 years to be 10.5%; the seroprevalence estimates were 5% or below in those younger than 30 years of age and 65% in the age group 40–49 This was the only available study for Norway. Based on this, Norway is to be considered a very low endemicity country (Figure 2) and has likely been so since at least the mid-1960s.

Reported incidence from 1975–2005 has been below 1 and 5/100 000 with a steep peak in 1999 of 22/100 000 (Figure 1). TESSy data are consistent with a very low endemicity picture, showing an incidence ≤1/100 000 every year since at least 2006.

In 1976, the susceptibility level was above 70% at 30 years and around 40% at 50 years old. Considering the very low incidence profile of the country in the last decade and the absence of sustained circulation of the virus, the susceptibility, in the non-vaccinated population, is likely to be very high in the present situation.

Norway_Figure 1 (panel a). Summary of seroprevalence in Norway, by age and time period.

Panel a.1: 1975–1989

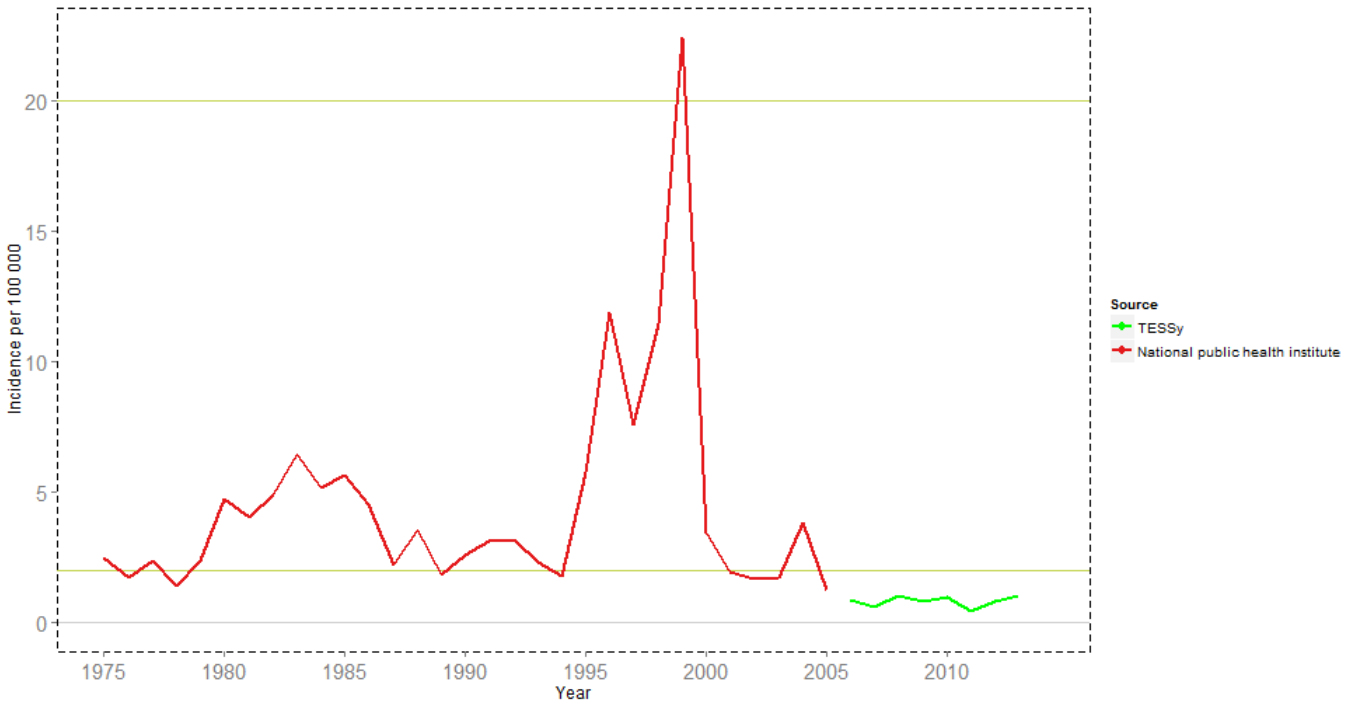


Panel a.2: 1990–1999

No data available Panel a.3: 2000–2013

No data available

Norway_Figure 2. Reported incidence of hepatitis A, Norway, 1975–2013*



National data source: www.fhi.no

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Poland

Population (January 2013):	38 533 299
Human development Index (2013):	0.834
HAV vaccine recommendations:	HAV vaccination is a recommended vaccination and not founded by National Health System. It is recommended for: 1. travelers to high endemicity countries 2. food handlers 3. susceptible children 4. people with occupational risks, e.g. sewage workers 5. PWID 6. MSM 7. hemophiliacs 8. HIV positive people and 9. patients with chronic liver disease.
Seroprevalence studies by quality score:	score 0: 3 studies score 1: 1 study score 2: 0 studies
Seroprevalence studies timeframe:	1985–1999

Seroprevalence assessment*: **very low**
Incidence assessment: **low**
Susceptibility in adults: **moderate**

**this assessment is based on data from the 1990s and supported by latest incidence levels*

One study conducted before 1990 estimated HAV seroprevalence at 68% in the age group 20–29 and at 89.5%. in the age group 30–39 years. No estimates are available among children; nevertheless the endemicity level was likely to be intermediate. Of the four surveys conducted between 1990 and 1999, the one conducted in 1999 estimated HAV seroprevalence below 50%. By the age 30. Among the others, only one study conducted in 1990 presented an estimated prevalence above 50%. by age 15 For these reasons it is likely that Poland transitioned from an intermediate to very low endemicity level during the 1990s (Figure 1). No study estimated HAV seroprevalence after 1999.

Poland_Table 1. Hepatitis A seroprevalence level by time period

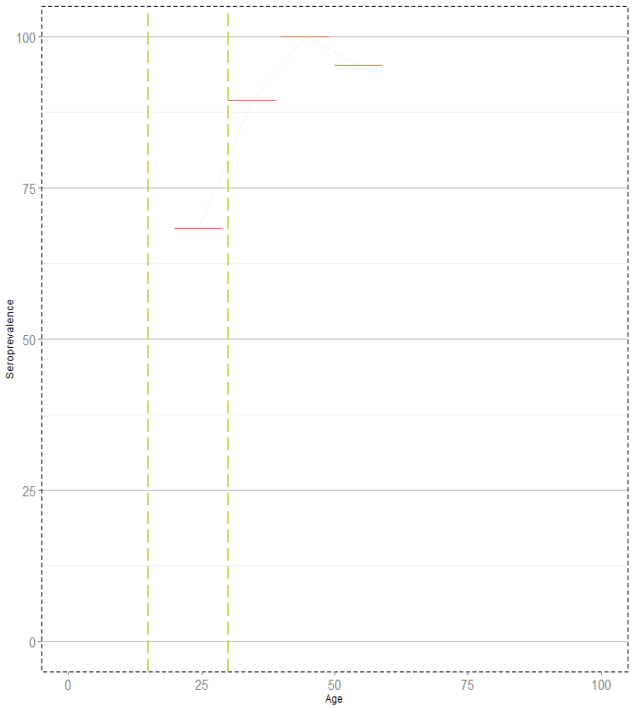
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence was below 20/100 000 since 1997 (Figure 2). TESSy data are consistent with a very low endemicity picture with reported incidence below 2/100 000 since at least 2006.

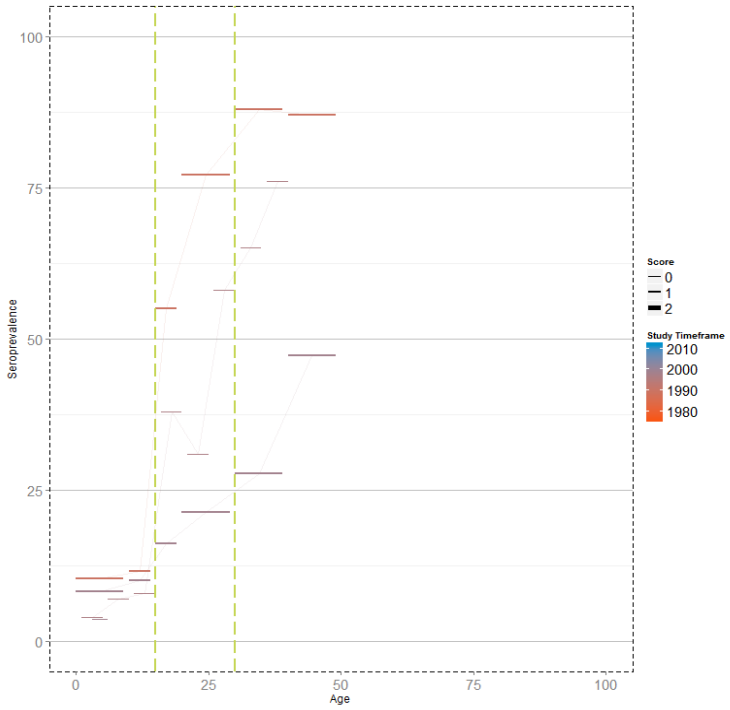
At the end of the 1990s, the susceptibility was estimated to range from 35%–70% by the age of 30 and to range from 40% to less than 25% at the age of 50. Considering the incidence picture of the past years, the susceptibility in adults may be considered moderate.

Poland_Figure 1 (panel a). Summary of seroprevalence in Poland, by age and time period.

Panel a.1: 1975–1989



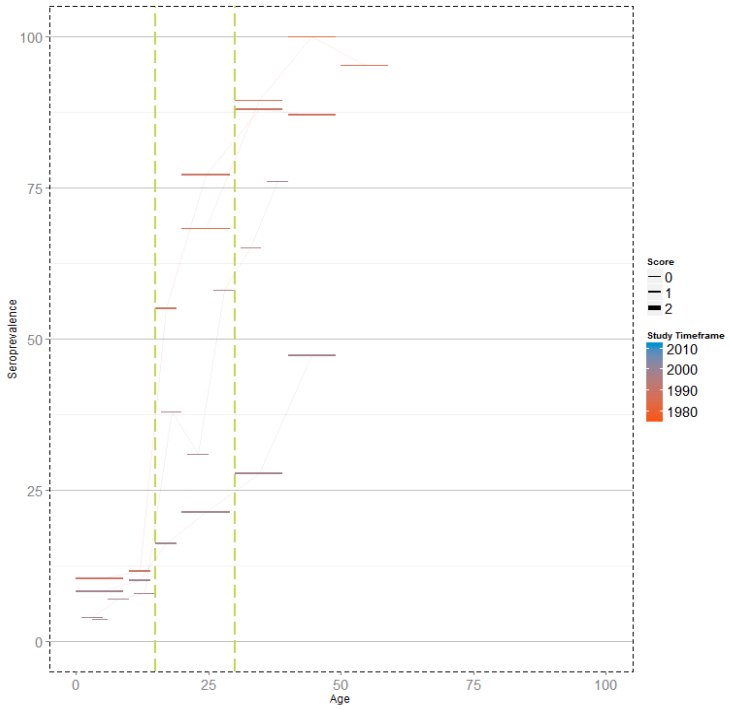
Panel a.2: 1990–1999



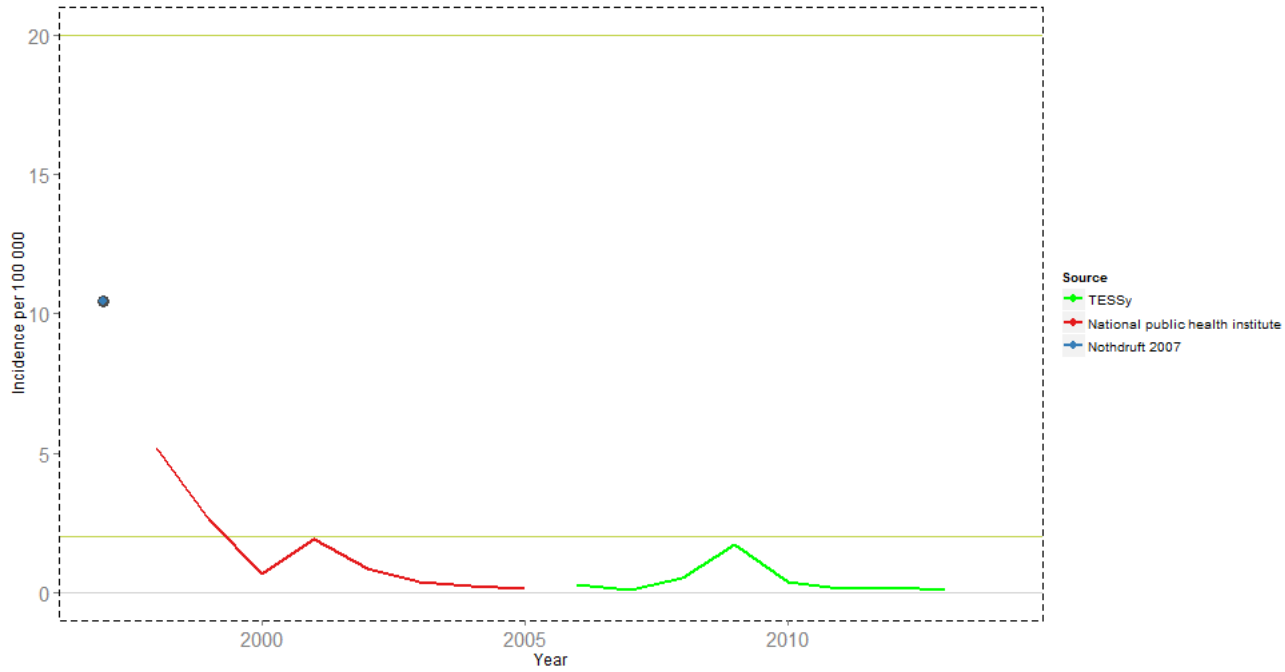
Panel a.3: 2000–2013

No data available

Poland_Figure 1 (panel b). Summary of seroprevalence in Poland, by age and time period (1975–2013)



Poland_Figure 2. Reported incidence of hepatitis A, Poland, 1997–2013*



National data source: http://www.pzh.gov.pl/oldpage/epimeld/index_p.html#04

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Portugal

Population (January 2013):	10 487 289
Human development Index (2013):	0.822
HAV vaccine recommendations:	HAV vaccination is recommended for: 1. travellers to high or intermediate endemic countries 2. adolescents and adults with chronic liver disease 3. for outbreak control.
Seroprevalence studies by quality score:	score 0: 3 studies; score 1: 3 studies; score 2: 2 studies
Seroprevalence studies timeframe:	1983–2007

Seroprevalence assessment: **low**
Incidence assessment: **very low**
Susceptibility in adults: **low**

The only study published in Portugal before 1990 (Lecour 1984), estimated an HAV seroprevalence to be above 50% by 15 years with less than 90% seroprevalence by10 years (Figure 1).

Out of 5 studies estimating HAV seroprevalence in Portugal between 1990 and 1999, only three provided estimates of seroprevalence by 30 and 15 years old. The seroprevalence estimates are above 50% in all 3 studies by the age of 30; while only one study reports seroprevalence above 50% by the age of 15 (Figure 1).

Two studies conducted after 2000 estimated HAV seroprevalence to be around or over 50% by the age of 30 . Therefore, Portugal likely transitioned from intermediate to low endemicity in the 1990s (Figure 1), and remains a low endemicity country after 2000**.**

Portugal_Table 1. Hepatitis A seroprevalence level by time period

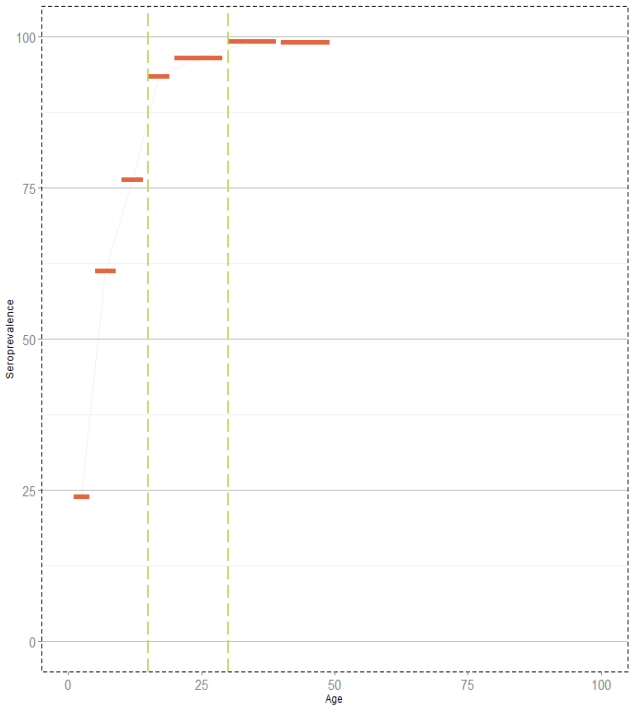
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported incidence data in Portugal is available from TESSy (Figure 2) since 2006. It shows a very low incidence below 0.5 per 100 000.

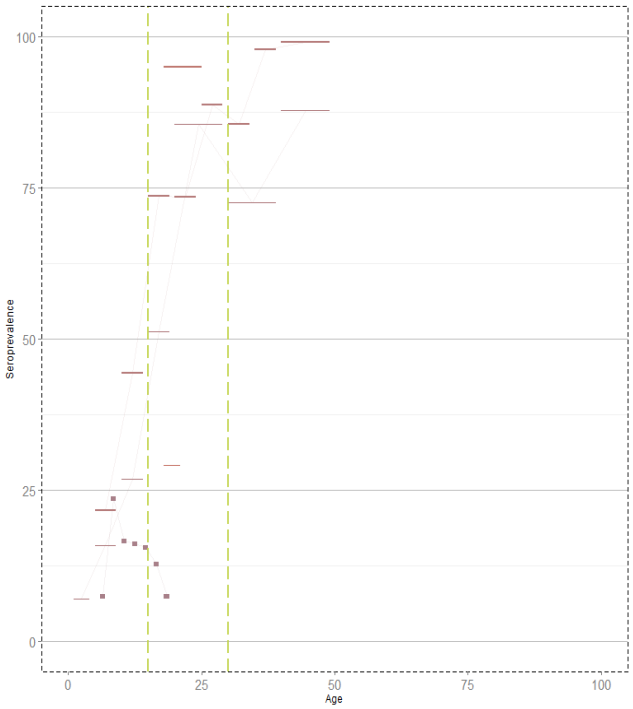
The susceptibility among adults is low, as susceptibility levels by 30 years are around 20% and by 50 years old less than 10% are susceptible.

Portugal_Figure 1 (panel a). Summary of seroprevalence in Portugal, by age and time period.

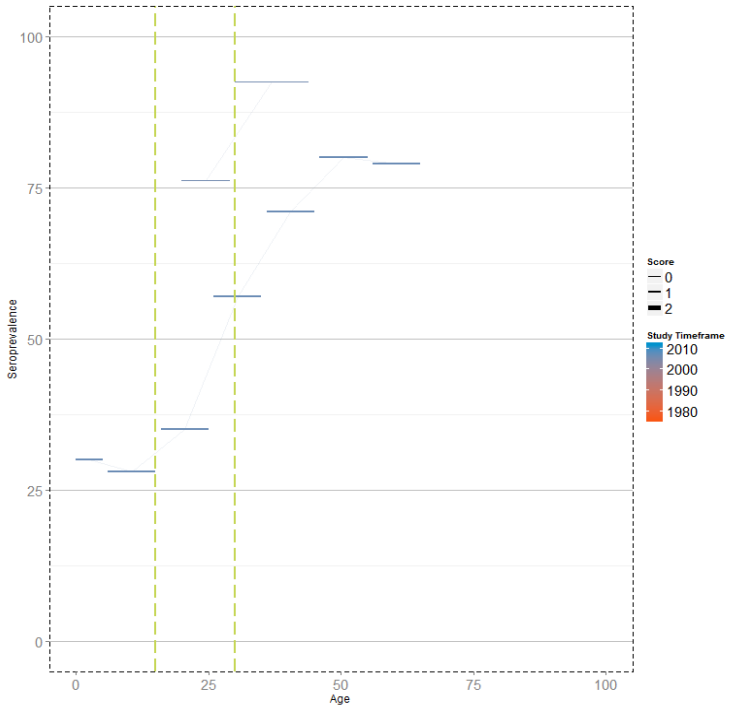
Panel a.1: 1975–1989



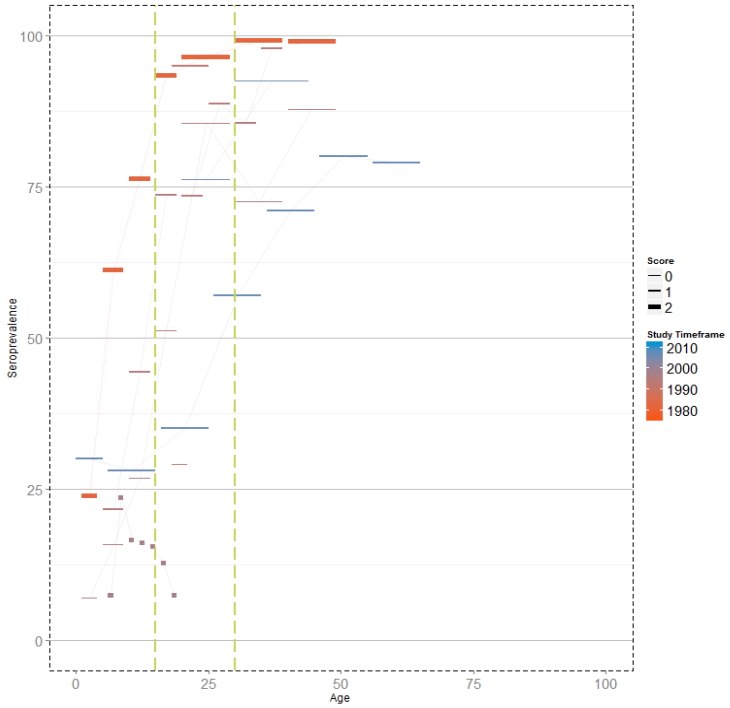
Panel a.2: 1990–1999



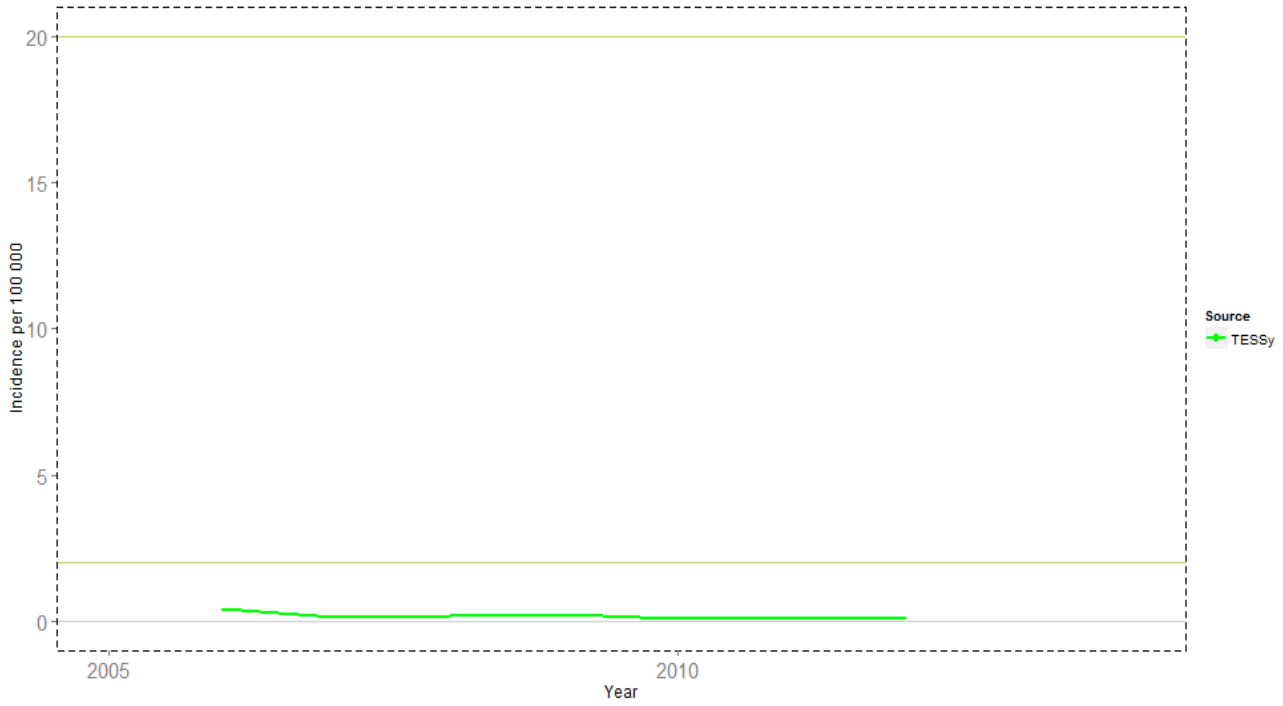
Panel a.3: 2000–2013



Portugal_Figure 1 (panel b). Summary of seroprevalence in Portugal, by age and time period (1975–2013).



Portugal_Figure 2. Reported incidence of hepatitis A, Portugal, 1989–2013.



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Romania

Population (January 2013):	20 020 074
Human development Index (2013):	0.785
HAV vaccine recommendations:	HAV vaccination is not included in the National Immunization Programme. HAV vaccination is utilised as an intervention measure for children in an outbreak/epidemic situation.
Seroprevalence studies by quality score:	score 0: 4 studies; score 1: 0 studies; score 2: 1 study
Seroprevalence studies timeframe:	1980–2002

Seroprevalence assessment: **intermediate**
Incidence assessment: **intermediate**
Risk of infection >30 years: **low**

HAV seroprevalence studies conducted in Romania over the period 1980–2002 show very similar patterns of the presence of anti-HAV antibodies in the population increasing with age. No epidemiological transition is evident over this period (Figure 1). In more details, the most recent study from Kurkela et al. (Kurkela 2012) reports a seroprevalence of 45% in children below 10; increasing to 62% in children aged 10–19, and reaching 90% in those aged 30 and older. This profile is characteristic of a country at intermediate endemicity.

Romania_Table 1. Hepatitis A seroprevalence level by time period

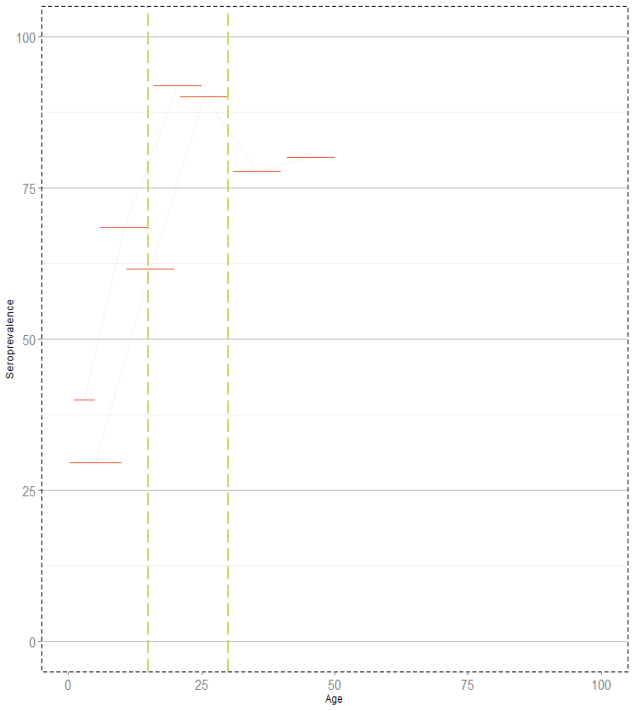
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

The incidence of acute hepatitis A in Romania is available from 1990 and shows a steep decrease over the decade from almost 300/100 000 to values comprised between 50 and 100/100 000 at the turn of the century. Since 2006, incidence is reported at below 50/100 000 with a decreasing trend (Figure 2).

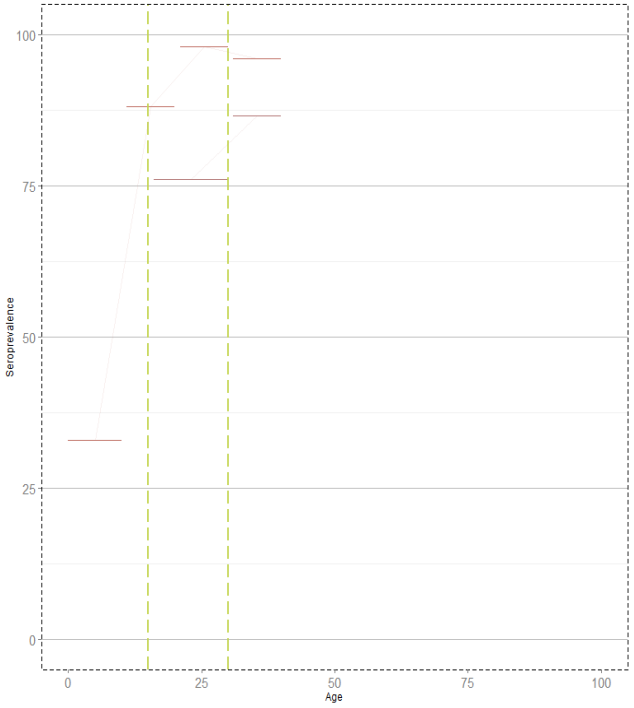
The susceptibility among adults is low, as susceptibility levels are below 25%.by 30 years and older

Romania_Figure 1 (panel a). Summary of seroprevalence in Romania, by age and time period

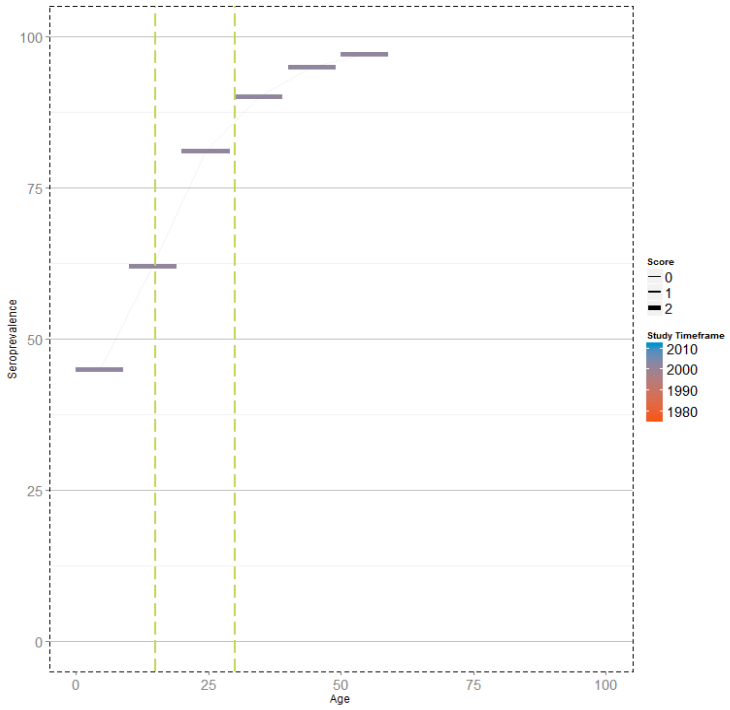
Panel a.1: 1975–1989



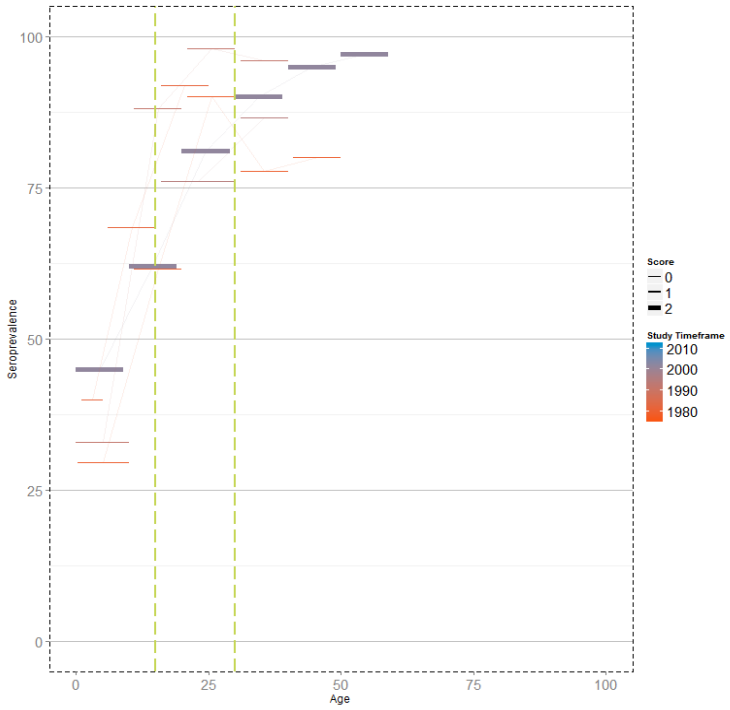
Panel a.2: 1990–1999



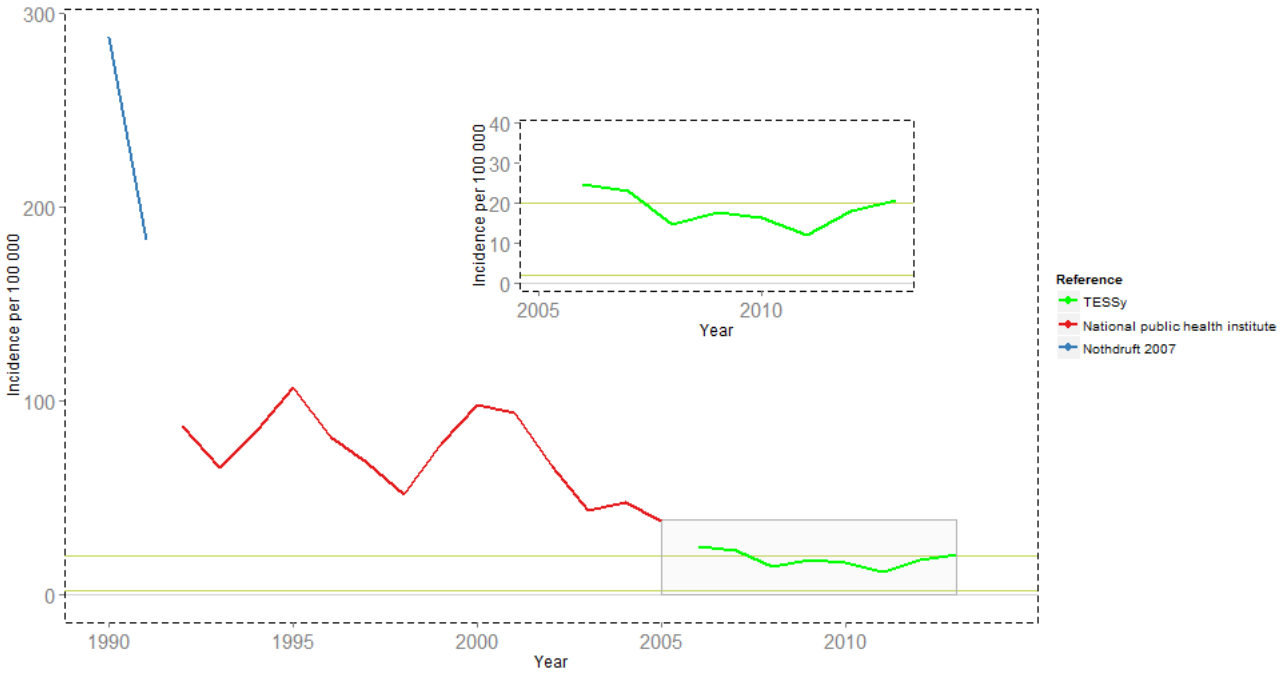
Panel a.3: 2000–2013



Romania_Figure 1 (panel b). Summary of seroprevalence in Romania, by age and time period (1975-2013)



Romania_Figure 2. Reported incidence of hepatitis A, Romania, 1990-2013*



**National data source: personal communication from ECDC National Focal Point/Operational Contact Point, National Institute of Public Health*

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Slovakia

Population (January 2013):	5 410 836
Human development Index (2013):	0.830
HAV vaccine recommendations:	HAV vaccination is not included in the National Immunisation Schedule. It is recommended and fully covered by public health insurance for children aged 2 living in places with low social-hygienic standard, and for all older children in the case of an outbreak (contacts of cases). The vaccination is recommended and paid for by employers for the following professionals: staff of regional public health institutes and laboratories, sewage workers, professional soldiers, military of Slovakia, police officers including prison and court guards, railway police, employees of asylum centres, fire and rescue service employees. The vaccine is also recommended for travellers to endemic countries.
Seroprevalence studies by quality score:	score 0: 0 study score 1: 0 study score 2: 2 study
Seroprevalence studies timeframe:	2002–2003

Seroprevalence assessment: **very low**
Incidence assessment: **intermediate**
Susceptibility in adults: **moderate**

The only study available (Kurkela 2012), complemented by unpublished data from the National Institute of Health (Figure 1), indicates a seroprevalence in Slovakia of 30% or below at the age of 30 in a random sample of the population in 2003. Based on these findings, Slovakia has been classified as a very low endemicity country since at least the early 2000s. Nevertheless caution should be applied when assessing the endemicity level, as a slightly different picture is obtained from the reported incidence data (Figure 2).

Slovakia_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

The HAV reported incidence has been decreasing constantly in Slovakia since the mid-1990s, from over 30/100 000 to less than 10/100 000 in 2006–2007. Nevertheless a steep rise in incidence was reported over the years 20082010, reaching rates over 26/100 000 in two consecutive years.

The susceptibility was estimated to be about 70% by the age of 30 and between 40% and 20% at the age of 50. Therefore the susceptibility in adults is considered moderate.

Slovakia_Figure 1 (panel a). Summary of seroprevalence in Slovakia, by age and selected time period.

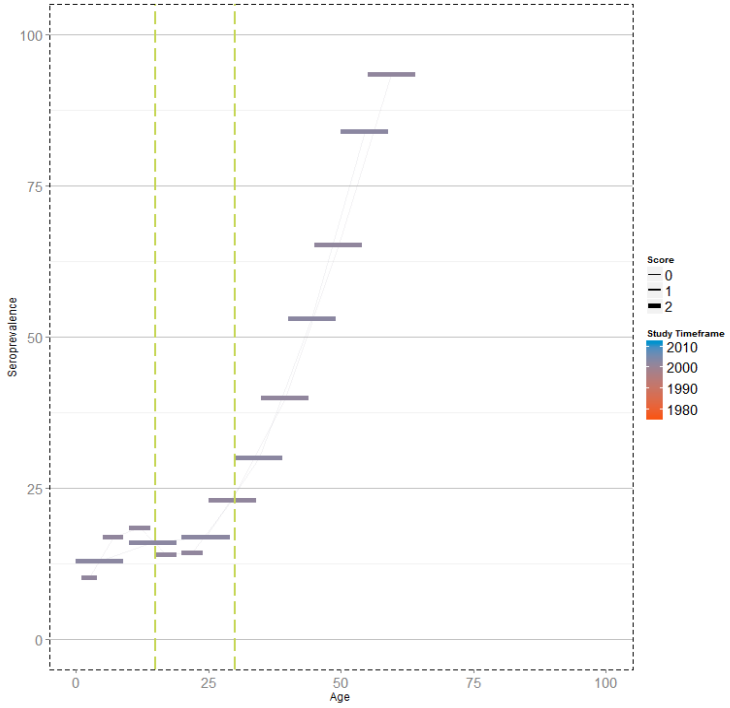
Panel a.1: 1975–1989

No data available

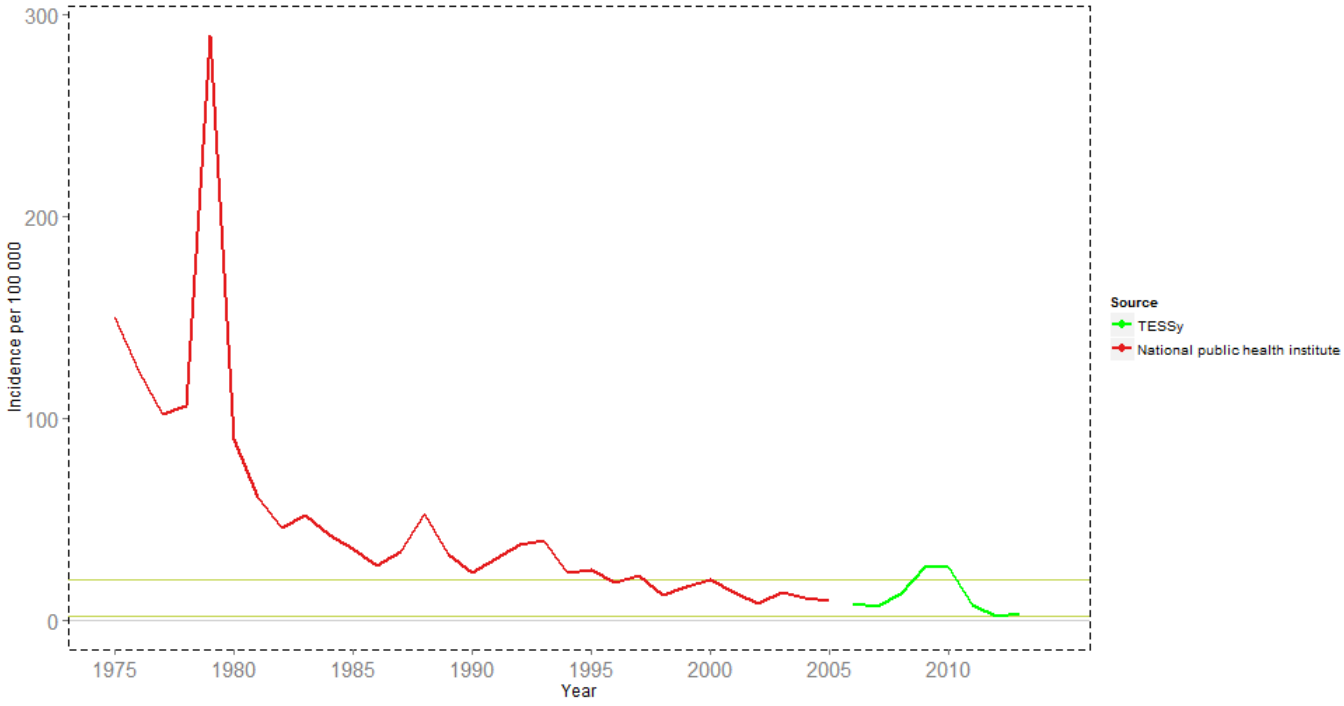
Panel a.2: 1990–1999

No data available

Panel a.3: 2000–2013



Slovakia_Figure 2. Reported incidence of hepatitis A, Slovakia, 1990–2013*



**National data source: personal communication from ECDC National Focal Point/Operational Contact Point, Public Health Authority of the Slovak Republic*

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Slovenia

Population (January 2013):	2 058 821
Human development Index (2013):	0.874
HAV vaccine recommendations:	Vaccination against hepatitis A is recommended for: 1. preschool children and students with medical conditions predisposing for severe HA 2. adults with medical condition predisposing for severe HA3. people with occupational exposure, e.g. sewage workers, laboratory personnel 4. travellers to endemic countries. Vaccination is covered by National Health Insurance for groups 1 and 2, by the employee for group 3 and self-paid for group 4.
Number of seroprevalence studies by quality score:	score 0: 0 studies; score 1: 1 study; score 2: 0 studies
Seroprevalence study timeframe:	1995–2012

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **moderate**

The one study published in Slovenia, compares the HAV seroprevalence in blood donors in the country in1995 and 2012 (Jovanovic 2012) (Figure 1). In 1995,the HAV seroprevalence in Slovenian blood donors was 31% in the age group 26–35 year. In 2012 the HAV seroprevalence among blood donors was 16% in the same age group. An additional study conducted in 2005 among the general population provides an estimate at 20% or below at 30 years, and of above 70% at 50 years. Slovenia is currently a very low endemicity country.

Slovenia_Table 1. Hepatitis A seroprevalence level by time period

	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

According to the incidence data presented in Figure 2, the reported infection rate in the population has been decreasing consistently since the early 1990s from values above 20/100 000 to values below 5/100 000 in the second half of the decade. Since 2005, the reported incidence rate has been consistently below 1/100 000.

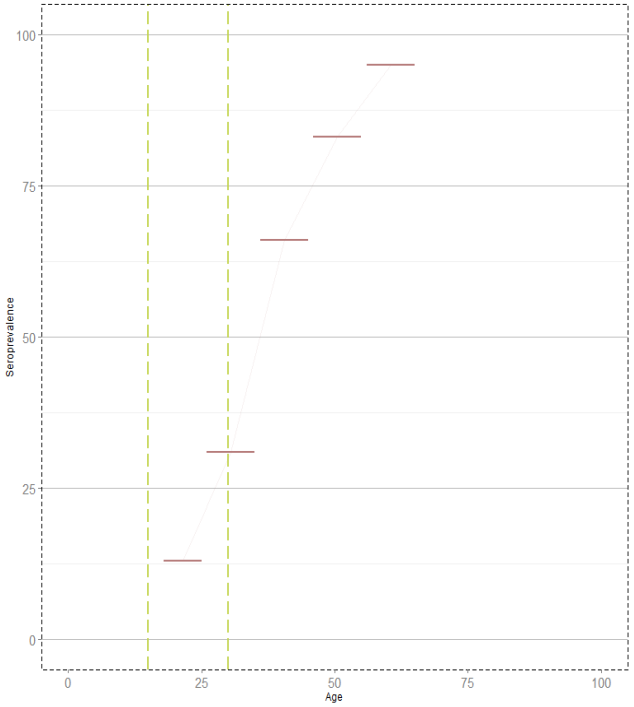
The susceptibility among adults is moderate, as susceptibility levels are above 70% at age of 30, and decreasing to less than 30% at the age of 50.

Slovenia_Figure 1 (panel a). Summary of seroprevalence in Slovenia, by age and time period.

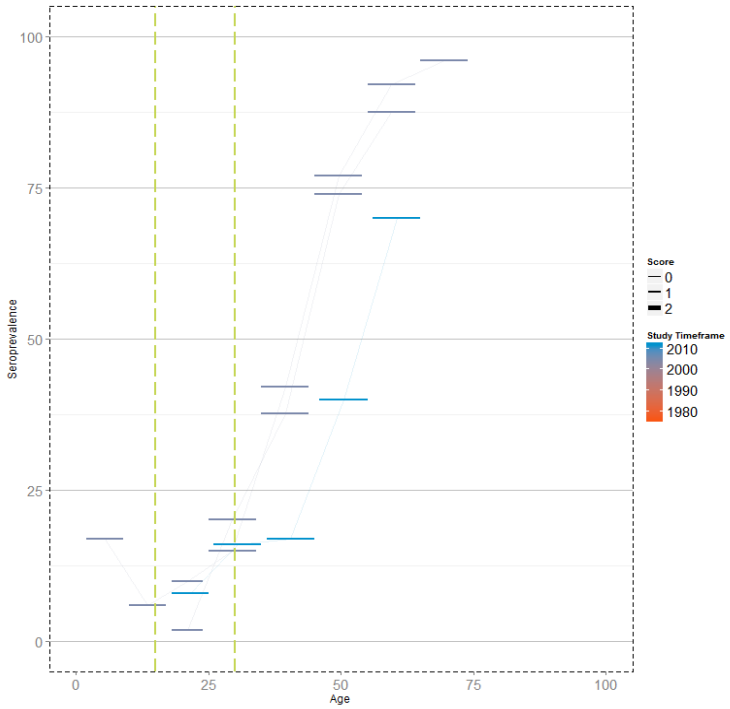
Panel a.1: 1975–1989

No data available

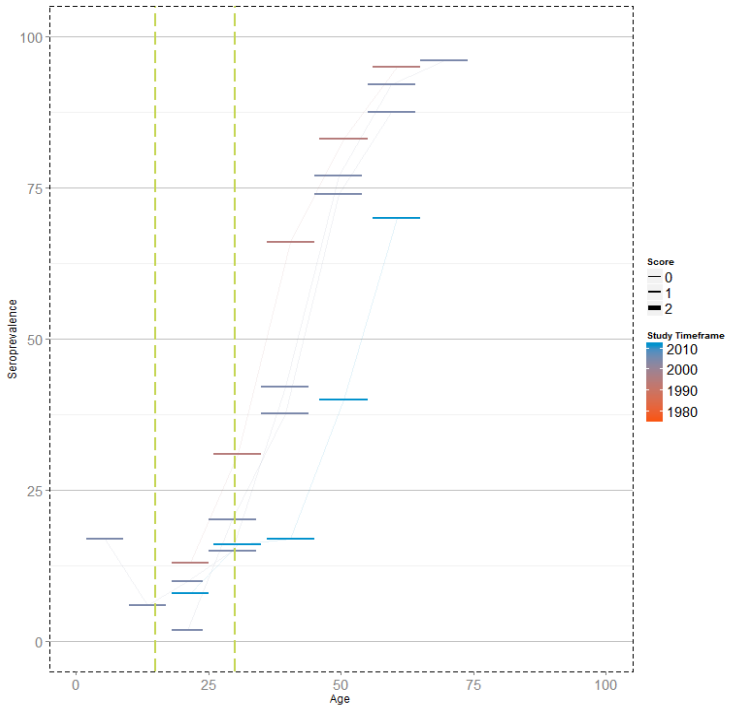
Panel a.2: 1990–1999



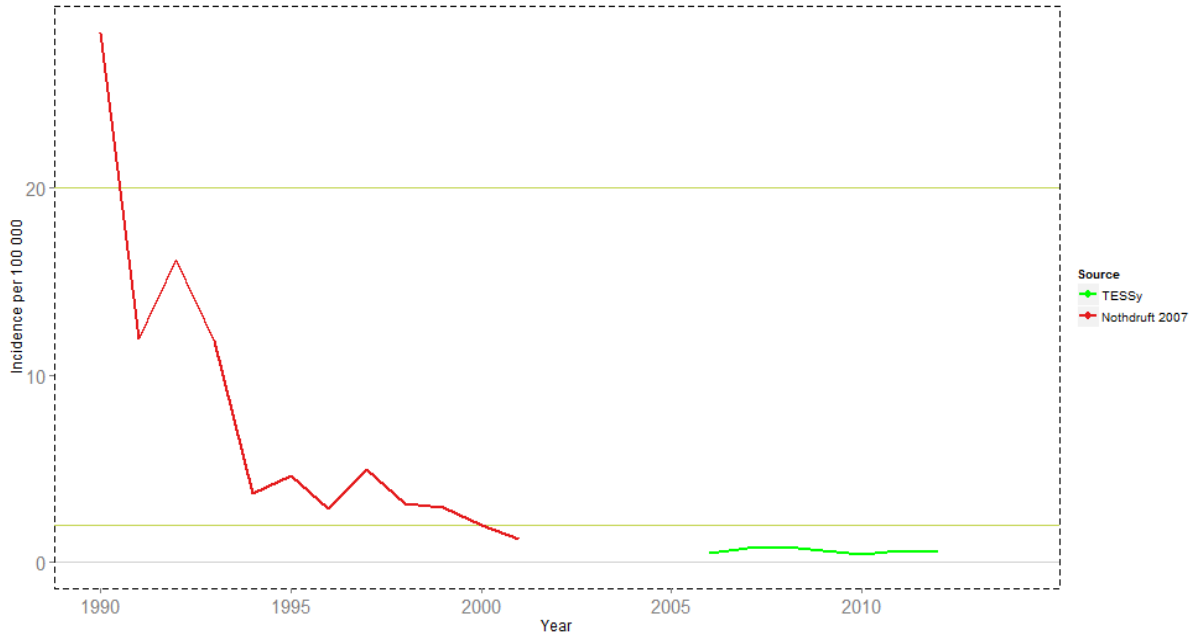
Panel a.3: 2000–2013



Slovenia_Figure 1 (panel b). Summary of seroprevalence in Slovenia, by age and time period (1975-2013). .



Slovenia_Figure 2. Reported incidence of hepatitis A, Slovenia, 2006–2013.



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Spain

Population (January 2013):	46 727 890
Human development Index (2013):	0.869
HAV vaccine recommendations:	HAV vaccination is universally recommended and covered for children aged between 15 and 24 months in Ceuta and Melilla (13 years old catch-up), and; for children aged between 12 months and 6 years old in Catalonia (11-12 years old catch-up). Vaccination is recommended for: 1. travellers to endemic areas 2. patients with chronic hepatic disease (including asymptomatic VHB patients) 3. household contacts of an HAV patient 4. haemophiliacs 5. institutionalised children 6. people with occupational exposure, e.g. nursery staff, healthcare workers, sewage workers 7. MSM 8. PWID.
Seroprevelance studies by quality score:	score 0: 19 studies; score 1: 21 studies; score 2: 13 studies
Seroprevelance studies timeframe:	1977–2013

Seroprevalence assessment: **very low**
Incidence assessment: **low**
Susceptibility in adults: **moderate**

A total of 24 studies were included for the period 1975–1990 andall estimated a HAV seroprevalence above 50%. by age 30 years On the other hand, only three studies of lower quality estimated the seroprevalence to be over 50% by age of 15 (Figure 1).

For the period 1991–1999 we included 31 studies. Seven of these reported seroprevalence by age 30, three estimated seroprevalence levels above 50% and four below 50%. No study estimated seroprevalence over 50% by age 15 (Figure 1).

A total of 15 studies were included from 2000 onwards. All estimated a HAV seroprevalence at less than 50% by 30 years old and less than 20% at the age of 15. Therefore, Spain, likely transitioned from low to very low endemicity in the 1990s and remains a very low endemicity country after 2000**.**

Spain_Table 1. Hepatitis A seroprevalence level by time period

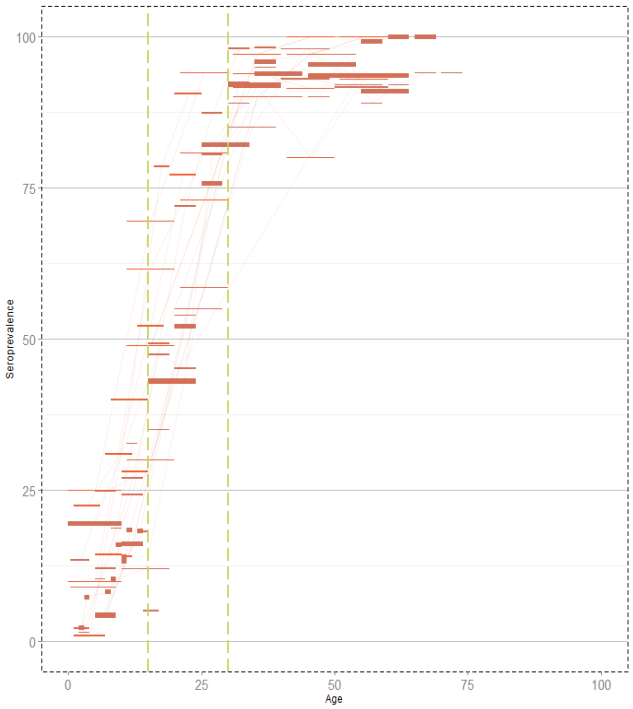
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Incidence data (Figure 2) are available from TESSy and two published studies since 2005. The incidence has been low to very low, ranging from 1.1 to 5.5 per 100 000 over the period.

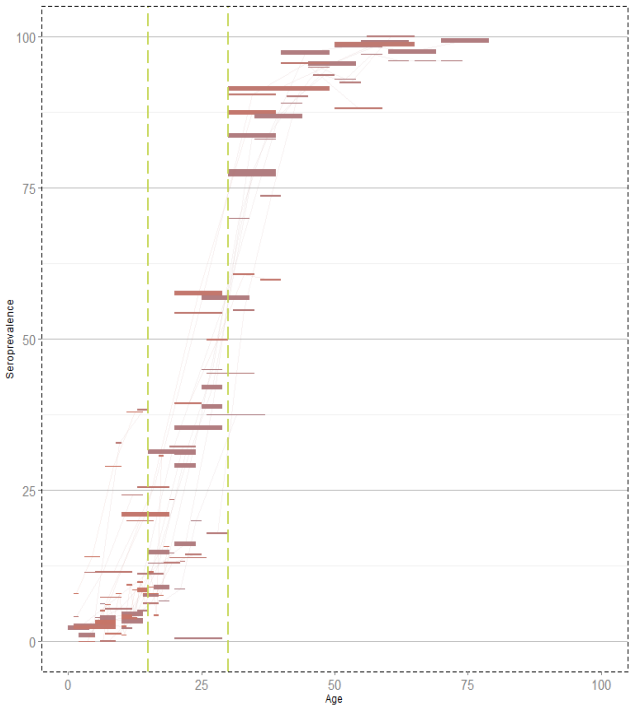
The susceptibility among adults is moderate, as susceptibility levels are around 60–70%, by 30 years of age however the susceptibility quota steeply decreases and less than 20% are susceptible after age 45.

Spain_Figure 1 (panel a). Summary of seroprevalence in Spain, by age and time period.

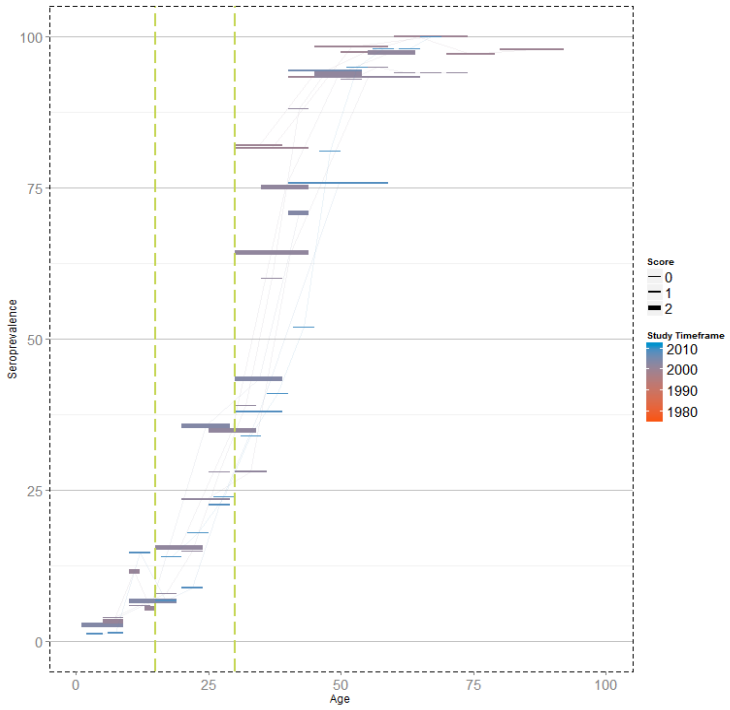
Panel a.1: 1975–1989



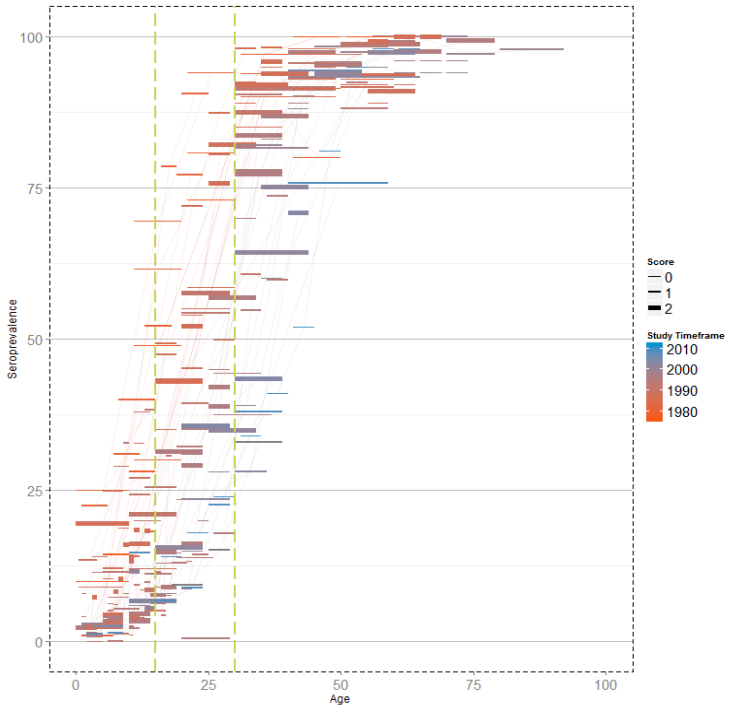
Panel a.2: 1990–1999



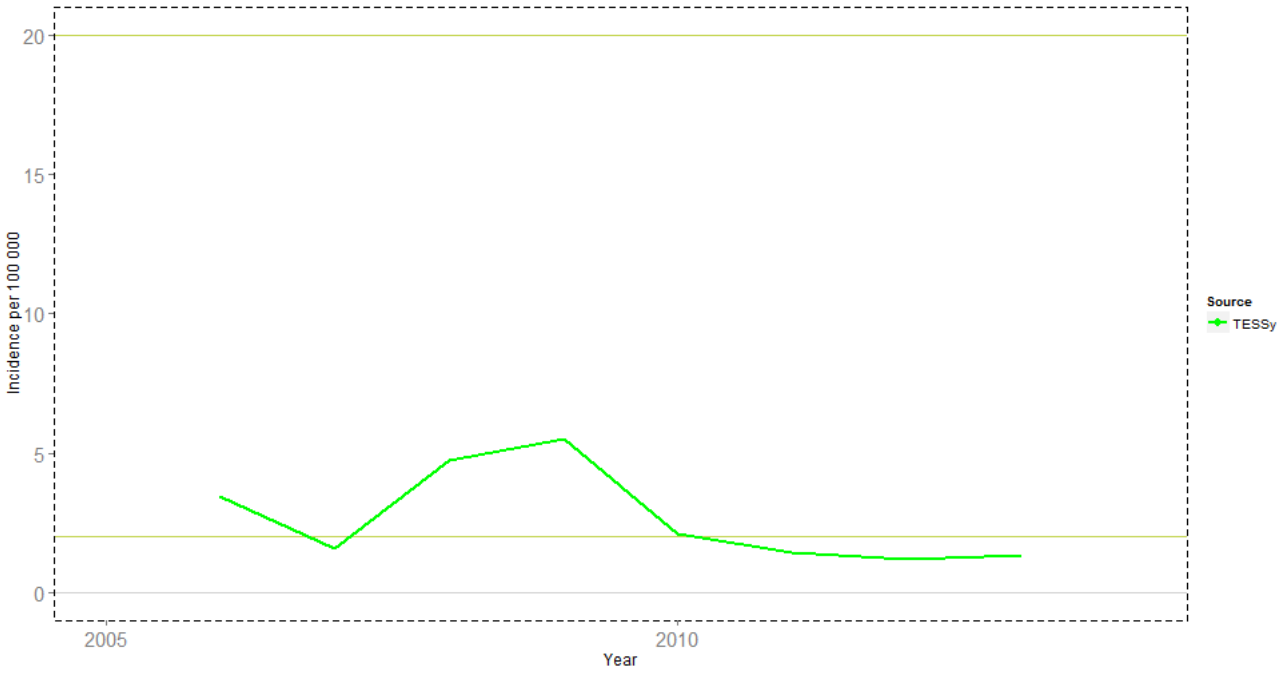
Panel a.3: 2000–2013



Spain_Figure 1 (panel b). Summary of seroprevalence in Spain, by age and time period (1975-2013).



Spain_Figure 2. Reported incidence of hepatitis A, Spain, 2005–2013.



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Sweden

Population (January 2013):	9 555 893
Human development Index (2013):	0.898
HAV vaccine recommendations:	Hepatitis A vaccine is not part of the routine childhood immunisation programme. Vaccination is recommended for (not publically funded): 1. travellers to endemic areas 2. children of immigrant populations visiting endemic countries of origin, 3. individuals with chronic hepatitis B and C 4. sewage workers (funded by the employer) 5. contacts of cases of hepatitis A are offered free vaccination (first dose)(postexposure). Vaccination is recommended to certain risk groups for hepatitis B in the form of the combined hepatitis A/B vaccine.
Seroprevalence studies by quality score:	score 0: 0 study score 1: 2 study score 2: 1 studies
Seroprevalence study timeframe:	1977–1991

Seroprevalence assessment*: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **very high**

**this assessment is based on data from the 1990s*

Two studies (Iwarson 1978, Froesner 1979) reported seroprevalence levels of less than10% in the age groups up to 39 years. One study (Bottiger 1997) conducted in 1991 reported very low seroprevalence, below 10%, in the adult population. Sweden should be considered a country that is likely at a very low endemicity level since the 1940s.

Sweden_Table 1. Hepatitis A seroprevalence level, by time period

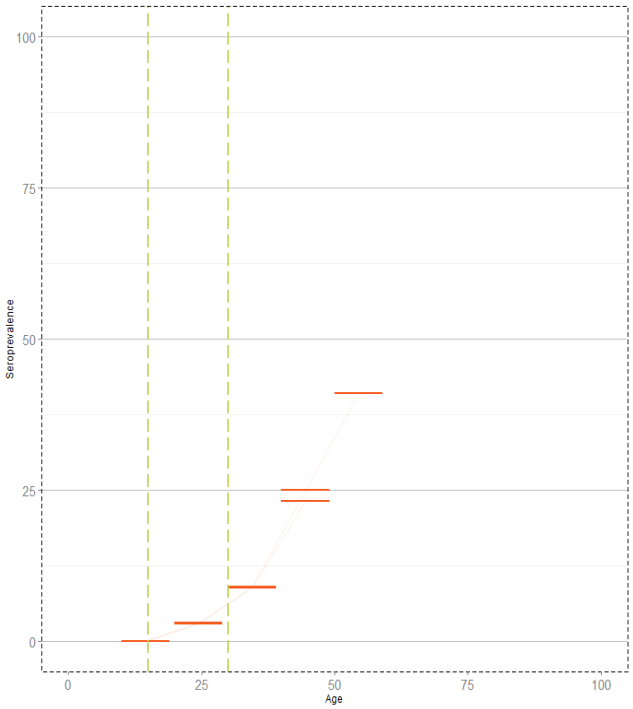
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported hepatitis A incidence has been low since 1985 (between 3 and 8 cases per 100 000) and has remained very low during the past years, below 2 cases per 100 000. The current level of incidence is in line with the very low endemicity level assessed through seroprevalence surveys.

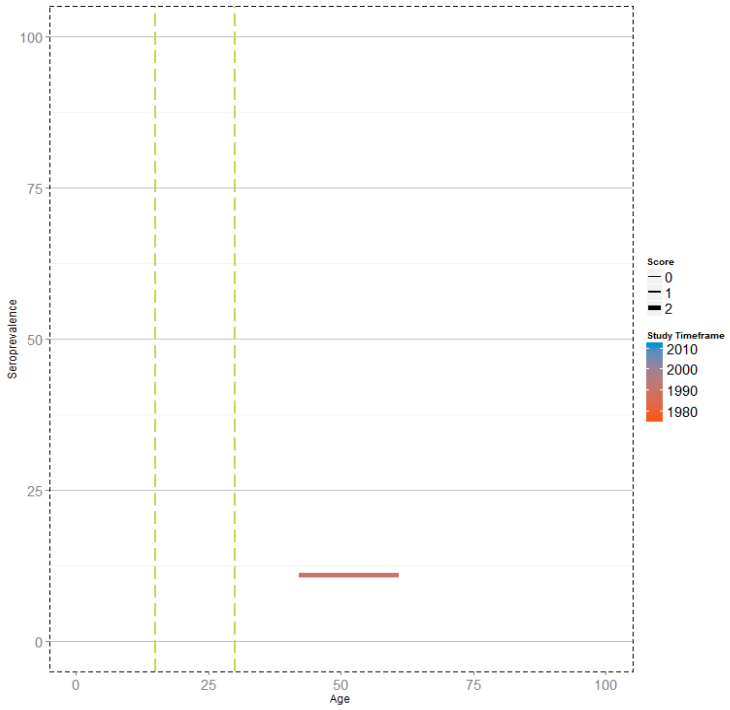
The susceptibility among adults has to be considered very high, with more than70% of adult population susceptible to HAV infection.

Sweden_Figure 1 (panel a). Summary of seroprevalence in Sweden, by age and time period.

Panel a.1: 1975–1989



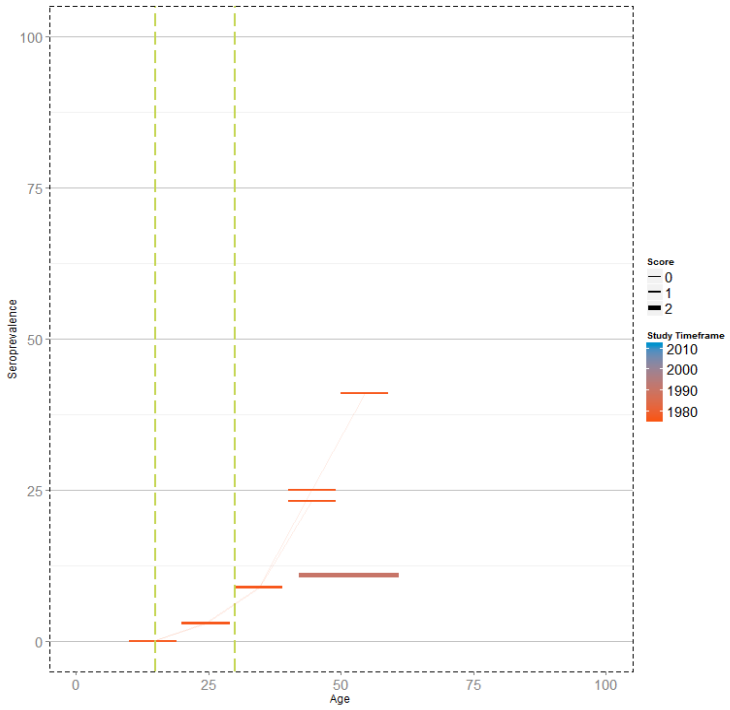
Panel a.2: 1990–1999



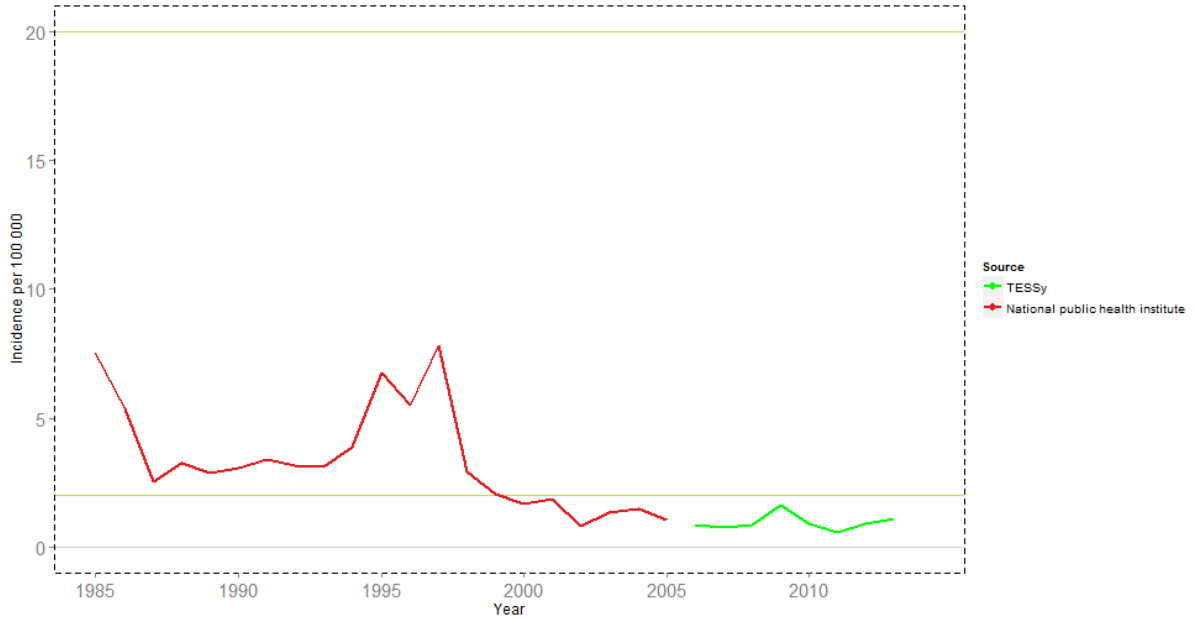
Panel a.3: 2000–2013

No data available

Sweden_Figure 1 (panel b). Summary of seroprevalence in Sweden, by age and time period (1975-2013). .



Sweden_Figure 2. Reported incidence of hepatitis A, Sweden, 1985–2013



National data source: personal communication from ECDC National Focal Point/Operational Contact Point, Public Health Agency of Sweden

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United Kingdom

Population (January 2013):	63 905 297
Human development Index (2013):	0.892
HAV vaccine recommendations:	Hepatitis A vaccine is not part of the routine childhood immunisation programme. Vaccination is recommended to: 1. people travelling to countries at high or intermediate endemicity 2. patients with chronic liver disease 3. haemophiliacs 4. MSM 5. PWID 6. People with occupational exposure, e.g. laboratory staff, sewage workers 7. close contacts for outbreak control.
Seroprevalence studies by quality score:	*score 0:* 5 study; *score 1:* 5 study; *score 2:* 5 studies
Seroprevalence study timeframe:	1985–2003

Seroprevalence assessment: **very low**
Incidence assessment: **very low**
Susceptibility in adults: **high**

One study (Scott 1989) reported a seroprevalence level of 66% in 1988 in the age group 30–39 years; in the same period other studies (Gay 1994, Tettmar 1987, Bernal 1996) reported seroprevalence levels of less than50% by 30 years of age. All studies conducted from 1990 to 2003 reported seroprevalence levels below 30% by 30 years of age. Therefore, the UK should be considered a country with a very low endemicity level that probably transitioned to such a level during the 1980s.

UK_table 1. Hepatitis A seroprevalence level by time period

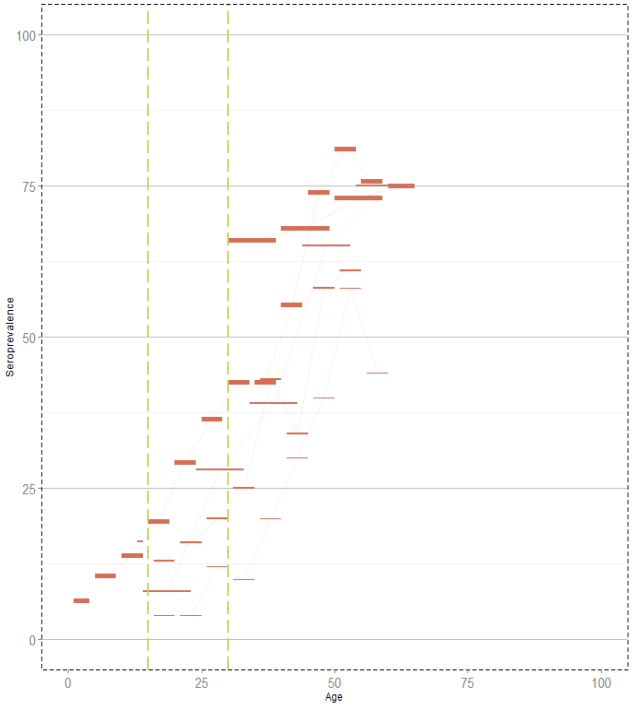
	Very low endemicity	Low endemicity	Intermediate endemicity
1975–1989			
1990–1999			
2000–2013			

Reported hepatitis A incidence has been below 5 cases per 100 000 since 1995, with no evidence of large outbreaks. Since 2004 it remains around 1 case per 100 000. The current level of incidence is in line with the very low endemicity level assessed through seroprevalence surveys.

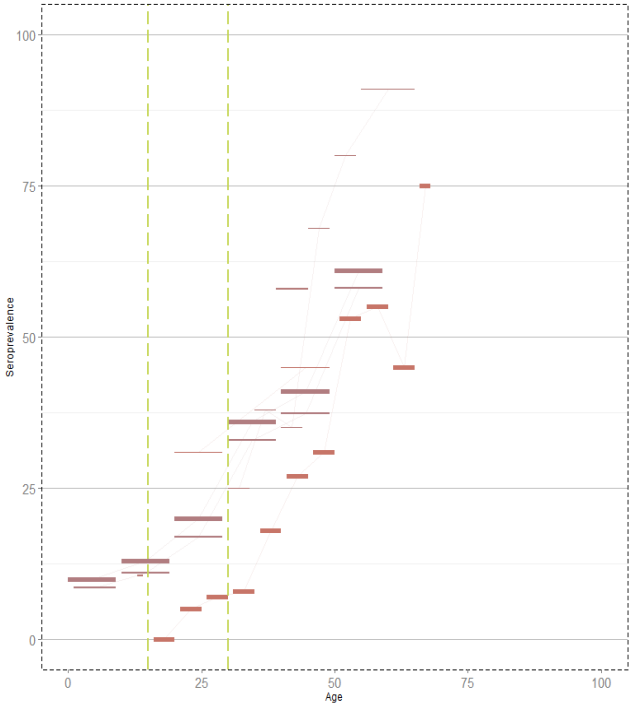
In 2000, the susceptibility was estimated to be above 60% by the age of 30 and in the 1990s around 40% at the age of 50. Considering the current very low seroprevalence in young adults and the incidence picture of the past years, the susceptibility in adults may be considered high at the present time.

United_Kingdom_Figure 1 (panel a). Summary of seroprevalence in the UK, by age and time period.

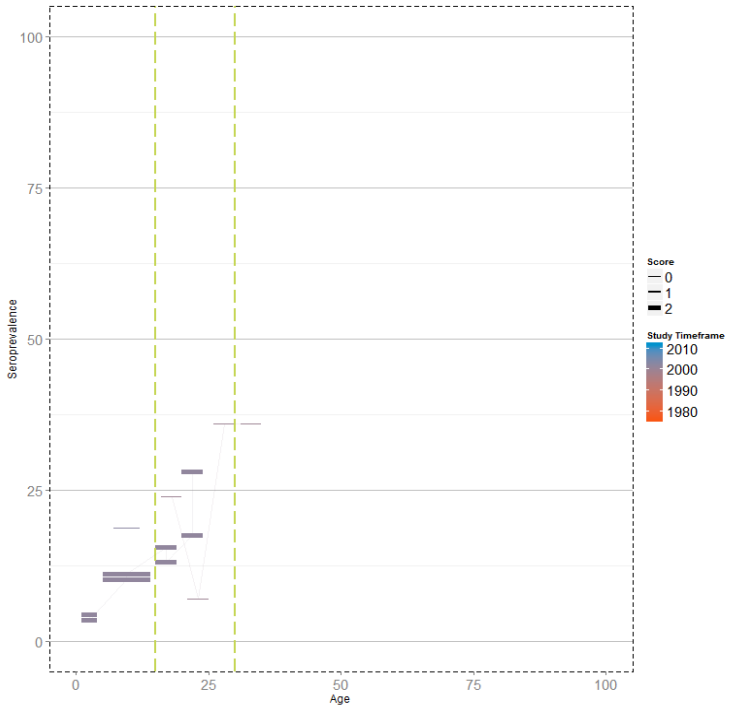
Panel a.1: 1975–1989



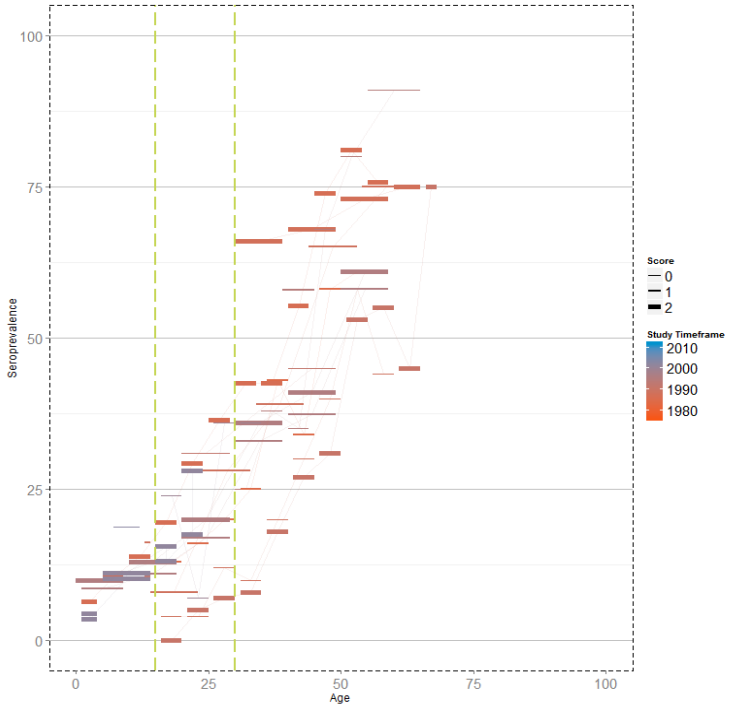
Panel a.2: 1990–1999



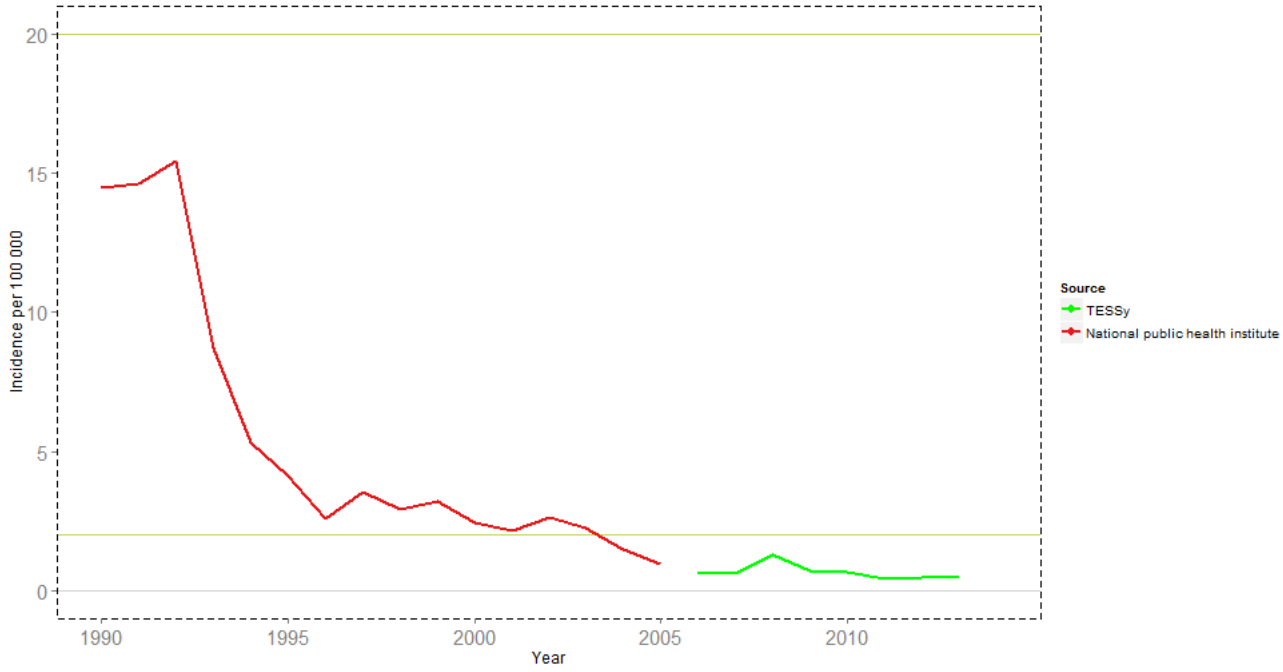
Panel a.3: 2000–2013



United_Kingdom_Figure 1 (panel b). Summary of seroprevalence in the UK, by age and time period (1975-2013). .



United_Kingdom_Figure 2. Reported incidence of hepatitis A, UK, 1989–2013



National data source: https://www.gov.uk/government/organisations/public-health-england

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Annex 2. Search strategies for HAV seroprevalence

PUBMED

Concept 1:	Boolean operator	Concept 2:	Boolean operator	Concept 3:
OR		OR		OR
"Prevalence"[Mesh] "prevalence studies"[Title/Abstract] "prevalence study"[Title/Abstract] "Prevalence"[Title] "Incidence"[Mesh] "incidence studies"[Title/Abstract] "incidence study"[Title/Abstract] "Incidence"[Title] "Seroepidemiologic Studies"[Mesh] "seroprevalence"[Title/Abstract] "seroprevalences"[Title/Abstract] "seroepidemiologic"[Title/Abstract] "seroepidemiological"[Title/Abstract] "seroepidemiology"[Title/Abstract] "sero epidemiologic"[Title/Abstract] "sero epidemiological"[Title/Abstract] "sero epidemiology"[Title/Abstract] "serosurvey"[Title/Abstract] "serosurveys"[Title/Abstract] serolog*[Title] epidemiolog*[Title]	AND	"Hepatitis A Antibodies"[Mesh] "Hepatitis A virus"[Mesh] "Hepatitis A Antigens"[Mesh] "hav"[Title] "hepatitis a virus"[Title/Abstract] "hepatitis a viruses"[Title/Abstract] "infectious hepatitis a"[Title/Abstract] "hepatitis a virus antibodies"[Title/Abstract] "hepatitis a virus antibody"[Title/Abstract] "hepatitis a virus antigen"[Title/Abstract] "hepatitis a virus antigens"[Title/Abstract] "hepatitis a virus hav"[Title/Abstract] "hepatitis a virus infection"[Title/Abstract] "anti hav"[Title/Abstract] "hav antibodies"[Title/Abstract] "hav antibody"[Title/Abstract] "hav infection"[Title/Abstract] "hav infections"[Title/Abstract] "hav infectivity"[Title/Abstract] "viral hepatitis a"[Title/Abstract] "hepatitis a"[Title/Abstract]	NOT	outbreak*[Title]

Publication date from 1975/01/01 to 2014/06/30

EMBASE

Concept 1:	Boolean operator	Concept 2:	Boolean operator	Concept 3:
OR		OR		OR
'prevalence'/exp 'prevalence studies':ab,ti 'prevalence study':ab,ti 'prevalence':ti 'incidence'/exp 'incidence studies':ab,ti 'incidence study':ab,ti incidence:ti 'seroepidemiology'/exp seroepidemiolog*:ab,ti 'seroepidemiologic studies':ab,ti 'seroepidemiologic study':ab,ti 'sero epidemiology':ab,ti 'sero epidemiologic':ab,ti 'sero epidemiological':ab,ti seroprevalenc*:ab,ti seroepidemiologic*:ab,ti serosurvey*:ab,ti serolog*:ti epidemiolog*:ti	AND	'hepatitis a antibody'/exp 'hepatitis a antibodies':ab,ti 'hepatitis a antibody':ab,ti 'hepatitis a virus'/exp 'hepatitis a virus':ab,ti 'hepatitis a viruses':ab,ti 'hepatitis a antigen'/exp 'hepatitis a antigen':ab,ti 'hepatitis a antigens':ab,ti 'hepatitis a virus antigen':ab,ti 'infectious hepatitis a':ab,ti 'hepatitis a virus antigens':ab,ti 'hepatitis a virus hav':ab,ti 'hepatitis a virus infection':ab,ti 'anti hav':ab,ti 'hav antibodies':ab,ti 'hav antibody':ab,ti 'hav infection':ab,ti 'hav infections':ab,ti 'hav infectivity':ab,ti 'viral hepatitis a':ab,ti hav:ti 'hepatitis a':ti	NOT	outbreak*:ti
(seropositiv* NEAR/5 'hepatitis a'):ab,ti (serolog* NEAR/5 'hepatitis a'):ti (seroepidemiolog* NEAR/5 'hepatitis a'):ab,ti (epidemiolog* NEAR/5 'hepatitis a'):ti (seropositiv* NEAR/15 hav):ab,ti (serolog* NEAR/15 hav):ti (seroepidemiolog* NEAR/15 hav):ab,ti (epidemiolog* NEAR/15 hav):ti	NOT	outbreak*:ti		

[embase]/lim AND [1975-2014]/py

Annex 3. Expert Panel: Terms of Reference and composition

Changes

This is the first version. No changes.

Glossary of Terms

The glossary of terms is given in Table 1.

Table 1. Glossary of terms.

Term	Description
CDC	Centers for Diseases Control and Prevention
FWD	Food- and Waterborne Diseases and Zoonoses
EC	European Commission
EP	Expert Panel
EU	European Union
ECDC	European Centre for Disease Prevention and Control
HAV	Hepatitis A Virus
HA	Hepatitis A
MSs	Member States
VHPB	Viral Hepatitis Prevention Board
WHO	World Health Organization

Background

The notification rate in the EU for HAV has been steadily decreasing over the last 15 years, from 14.0 in 1997 to 2.51 per 100 000 population in 2011[5], despite some countries still experiencing high notification rates. This most likely reflects improved living conditions, as HAV seroprevalence rates are strongly correlated with socioeconomic status and access to clean water and sanitation.

The highest notification rates in the EU are reported among the under 15 years old. There is a marked seasonal pattern with a peak in the autumn, which may reflect increases following travel to endemic countries during summer holidays. In the absence of vaccination, the low incidence in the EU population can result in a high proportion of susceptible individuals.

Food-borne transmission of HAV has been implicated in several outbreaks in recent years. Between 2007 and 2011, EFSA and ECDC reported 11 outbreaks with strong evidence of hepatitis A as the causative agent. In 2013–2014 two large multi-country outbreaks of HAV linked to consumption of frozen berries raised concern on the potential for re-emerging risk of hepatitis A in the EU/EEA

In light of the outbreaks occurring in the EU/EEA and the changes in the epidemiology of HAV with a shift to older ages, an assessment of the epidemiological situation in the EU/EEA would be of interest in order to understand the situation and evaluate potential vaccine recommendations.

In this context, in 2014 ECDC started the project 'Guidance on hepatitis A prevention and control with a focus on post-exposure prophylaxis, vaccination policies, and seroprevalence in the EU/EEA'. The project aims at assessing the epidemiological situation of hepatitis A in EU/EEA in order to inform potential vaccine recommendations. ECDC is currently performing a systematic review to retrieve and analyse all available evidence on seroprevalence and incidence of hepatitis A in the EU/EEA for the period 1975–2013. The findings shall be used to identify the pattern of hepatitis A endemicity profiles across the EU/EEA using the framework developed by the World Health Organization (WHO)[6], based on age- specific HAV seroprevalence.

[5] ECDC Annual Epidemiological Report, 2013. Available at: http://www.ecdc.europa.eu/en/publications/Publications/annual-epidemiological-report-2013.pdf

[6] WHO position paper on hepatitis A vaccines – June 2012. Available at: http://www.who.int/wer/2012/wer8728_29.pdf?ua=1

The project general objectives are to:

- assess and describe HAV endemicity across the EU/EEA, by providing:
  - geographical endemicity pattern
  - secular HAV endemicity pattern
- propose tailored vaccination strategies for different HAV endemicity profiles in the EU/AA as defined according to the WHO framework.

Expected outcomes of the project are:

- a full report on the epidemiology of HAV in the EU/EEA;
- a guideline for vaccination against HAV as a prevention and control measure in the EU/EEA, and;
- at least one peer-reviewed article.

In the frame of this project, ECDC will establish and manage a multi-sectorial Expert Panel (EP) composed of experts on hepatitis A (HEPA) and vaccination programmes. The HEPA EP shall provide expert opinion in interpretation and presentation of the findings from the systematic reviews on HAV seroprevalence and incidence in the EU/EEA and contribute to proposing tailored vaccination strategies for different HAV endemicity profiles occurring in the EU/EEA.

Composition of the Expert Panel

The EP will consist of ten invited experts on hepatitis A and vaccination from EU/EEA and non-EU countries, and representatives of the main international stakeholders such as the World Health Organization, Centre for Diseases Control and Prevention (CDC) or the Viral Hepatitis Prevention Board (VHPB). The EP will also include ECDC staff members responsible for the implementation of the project.

EP members will participate in their capacity as individual experts. The EP may also agree to include other members or observers, such as additional HAV experts from Member States or third countries, members of the Food- and Waterborne Diseases and zoonoses Network (FWD-Net), representatives of the European Commission or other EU agencies, as the need may arise and following agreement with ECDC.

The chair of the EP shall be an ECDC staff member together with an external member of the EP. ECDC may invite additional ECDC staff members, observers and external experts to take part in the EP meetings. The secretariat of the EP shall be provided by the ECDC.

Tasks of the Expert Panel

The EP shall discuss and make suggestions and proposals to the ECDC project team on the development of the project 'Guidance on hepatitis A prevention and control with a focus on post-exposure prophylaxis, vaccination policies, and seroprevalence in the EU/EEA'. The EP will contribute to the finalisation of the systematic review report and will be responsible together with ECDC project team for the development of a guidelines for vaccination against HAV as a prevention and control measure in the EU/EEA.

The main tasks of the EP will be to:

- review and provide inputs on the findings from the systematic review and the attribution of HAV endemicity profiles
- provide inputs and agree on the main conclusions for the final report
- review the final draft report
- contribute to the formulation of tailored vaccination strategies for different HAV endemicity profiles in the EU/AA
- contribute to the development of the 'Guideline for vaccination against HAV as a prevention and control measure in the EU/EEA' by providing expert inputs and reviewing the guideline draft (scheduled for 2015)
- closely liaise with ECDC project team and serve as a continuous forum for discussion during the implementation of the project.

Members of the EP shall be included in the authorship of the ECDC guideline document. Inclusion in the authorship of the peer-reviewed articles will be subject to individual contribution to the preparation of the manuscripts and in line with the criteria set forth by the International Committee of Medical Journals Editors (ICMJE), http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

Selection procedure

The selection procedure for invitation to participate in the EP is proposed by ECDC. The invitation to participate and become nominated as an expert in the EP is based on the following criteria, and previously recognised expertise on HAV and vaccination programmes:

- HAV public health experts identified through previous participation to ECDC initiatives
- identification via the ECDC Expert Database
- representatives from key stakeholders e.g., WHO, CDC, VHPB, European Commission.

Ideally, in selecting the composition of the EP, the aim is to have a balance, to the extent possible, between gender, Eastern and Western European countries, high and low endemicity countries, large and small countries as well as countries implementing different vaccination strategies, including universal routine vaccination against HAV.

Declaration of interest

Members of the EP will be invited to sign up in the ECDC Expert Directory (http://ecdc.europa.eu/en/aboutus/external_experts/Pages/external_experts.aspx).

Members will be requested to declare any interest by completing and signing ECDC standard Declaration of Interest. This can be done by following the online procedure through the ECDC Expert Directory webpage. The signed declaration of interest shall be submitted before the participation to the first EP meeting and shall be renewed on annual bases for the duration of the membership. The declaration of interest will be screened by the ECDC compliance officer and if any conflict of interest is identified the EP member will be contacted regarding possible mitigating measures

Duration

The expected duration of the membership is 18 months. The membership may be extended in case of need, as decided and communicated by ECDC.

Schedule overview

The first meeting of the EP is planned in October 2014. The project is expected to end by December 2015 the latest. In particular, the following applies:

- The EP is convened by ECDC and meets at ECDC premises in Stockholm;
- The EP members will be invited to participate to an introductory teleconference in the second half of September 2014 (week 39 or 40);
- The EP will meet for the first time on 6–7 October 2014 to discuss on the findings from the systematic review and to start formulating tailored vaccination strategies for different HAV endemicity profiles;
- Further inputs may be requested to support the finalisation of the systematic review report (November 2014-January 2015);
- Publication of the report on the systematic review of HAV seroprevalence and incidence in the EU/EEA (February 2015);
- For 2015, another meeting is planned, to be defined, to eventually provide expert advice and inputs on the development of the 'Guideline for vaccination against HAV as a prevention and control measure in the EU/EEA' (May/June 2015). Other relevant topics for discussion during this meeting could be prioritised by the panel;
- Further opinions or advice may be requested to support the finalisation guideline (June-August 2015);
- Release of the guideline (autumn 2015)

EP members are invited to participate on voluntary basis in the guideline and/or peer-reviewed articles drafting process.

In between the physical meetings, communication with and between the members of the EP will be maintained by a dedicated workspace in the ECDC extranet, emails and/or teleconferences.

Contact information

Any questions related to the project should be addressed to ECDC.

Members of the panel

Name	Country
Mira Kojouharova	Bulgaria
Roman Chilbek	Czech Republic
Jördis Ott	Germany
Manolis Galanakis	Greece
Daniel Shouval	Israel
Caterina Rizzo	Italy
Vytauthas Usonis	Lithuania
Denisa Janta	Romania
Angela Dominguez	Spain
Ingrid Uhno	Sweden
Noel Nelson	United States

With the additional participation of Vana Papaevangelou (Greece) and Valeria Alfonsi (Italy).

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