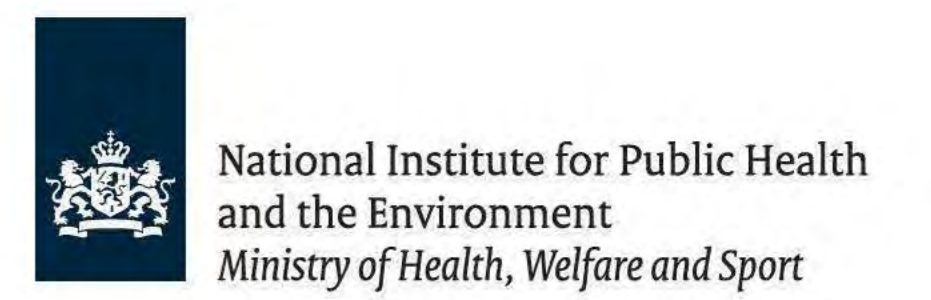


# Geotagging Hepatitis A Virus

## A dynamic tool for public health surveillance

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### BACKGROUND

- Hepatitis A is an acute liver disease caused by hepatitis A virus (HAV).
- Transmitted by oral-fecal route.
- Distributed worldwide, but infection depends on level of country endemicity (related socio-economic conditions and sanitation).
- Three genotypes (I, II, III) divided into A and B subtypes are known to infect humans.
- There is a genetic relatedness of HAV with geographical origin.
- Hepatitis A cases are mainly seen in travelers to endemic areas, and occasional infection linked to consumption of contaminated imported foods.
- The HAV NET database coordinated by RIVM, has been used to help to identify the source or track food-related clusters and outbreaks, improving the capacity of laboratory response, by using molecular and epidemiological information on HAV from different geographic origins.

### AIM

Our aim in this study was to analyse the suitability of the currently available hepatitis A database for detection of diffuse international foodborne outbreaks:

- Analyse genotyping target regions and length of the sequences available in the data-base.
- Evaluate the proportion of strain sequences that are linked to a specific country of infection (coverage and representativeness), HAV genotype diversity in each region, level of endemicity, mode of infection (e.g. travel related).
- Create a HAV NET website to diffuse the information about the aims of network and participation.

### METHODS

#### DATA

Hepatitis A data-base includes HAV sequences and epidemiological information from HAV NET Members combined with additional sequences retrieved from GenBank.

#### DATA ANALYSIS

1) **Sequence analysis** - Analysis of the sequence targets and lengths from HAV NET;

2) **Analysis of combined data** (epidemiological and molecular data)

Information linked with sequences was exported to Excel and data was analysed by geographic distribution, country of infection, possible transmission routes, and genotype diversity by geographic region.

Fields in HAV NET database

#### 1) Identification of the sequence data

- Provider (HAV NET, GenBank)

#### 2) Epidemiological data related with human case:

- Case identification and immune status.

- Possible transmission route (e.g. travel related)

#### 3) Molecular information

- Typed region and length of the fragment

#### 4) Geographic information of the sequence

- Suspected country of infection

- Level of endemicity

### RESULTS

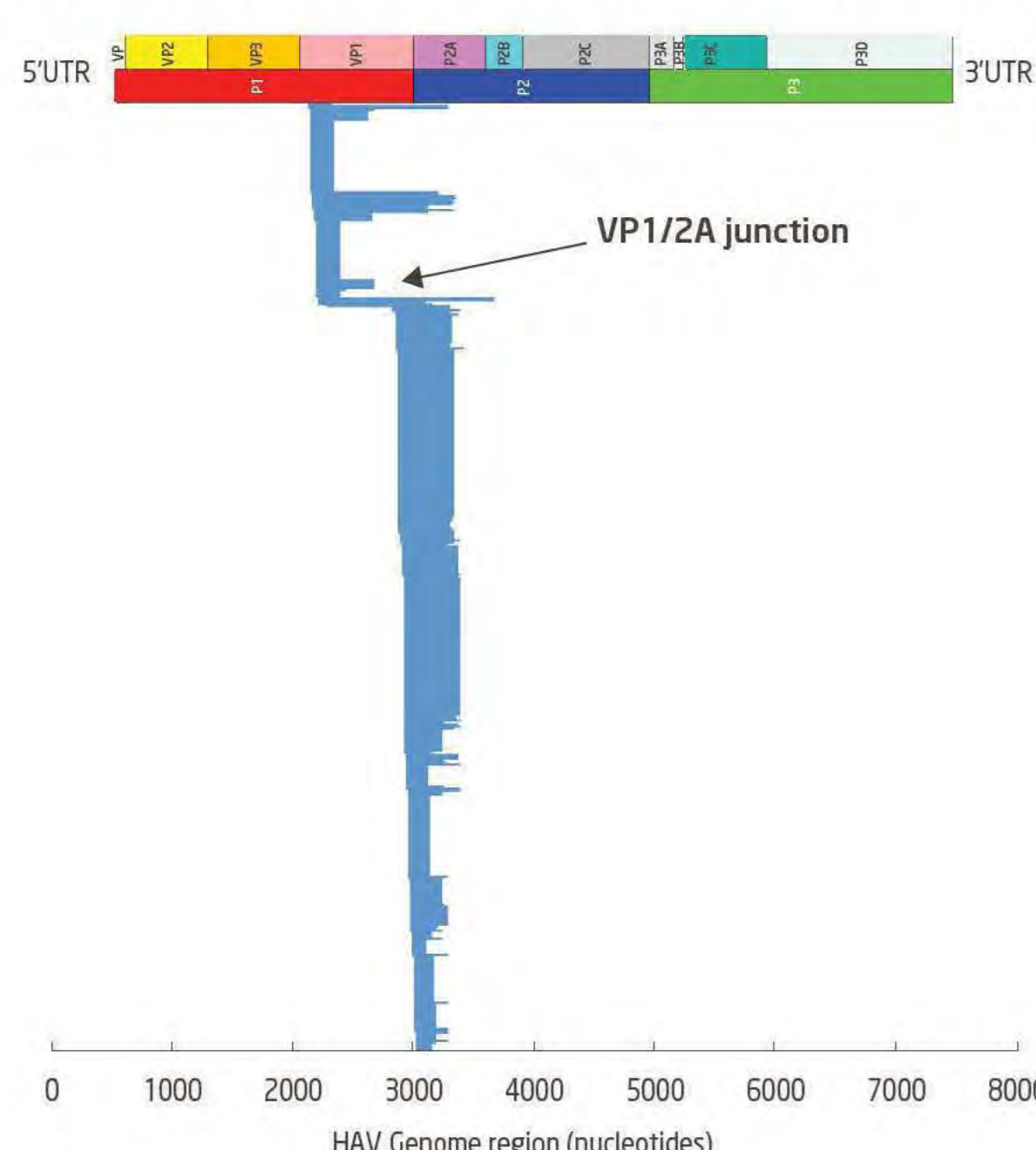
**DATA BASE**

- Total of sequences analysed in the data-base (N = 7120)
- Sequences from HAV NET (N = 1634) + GenBank (N = 5486)
- Period of time of sampling: 1957 - 2013

#### 1\_ Sequence analysis

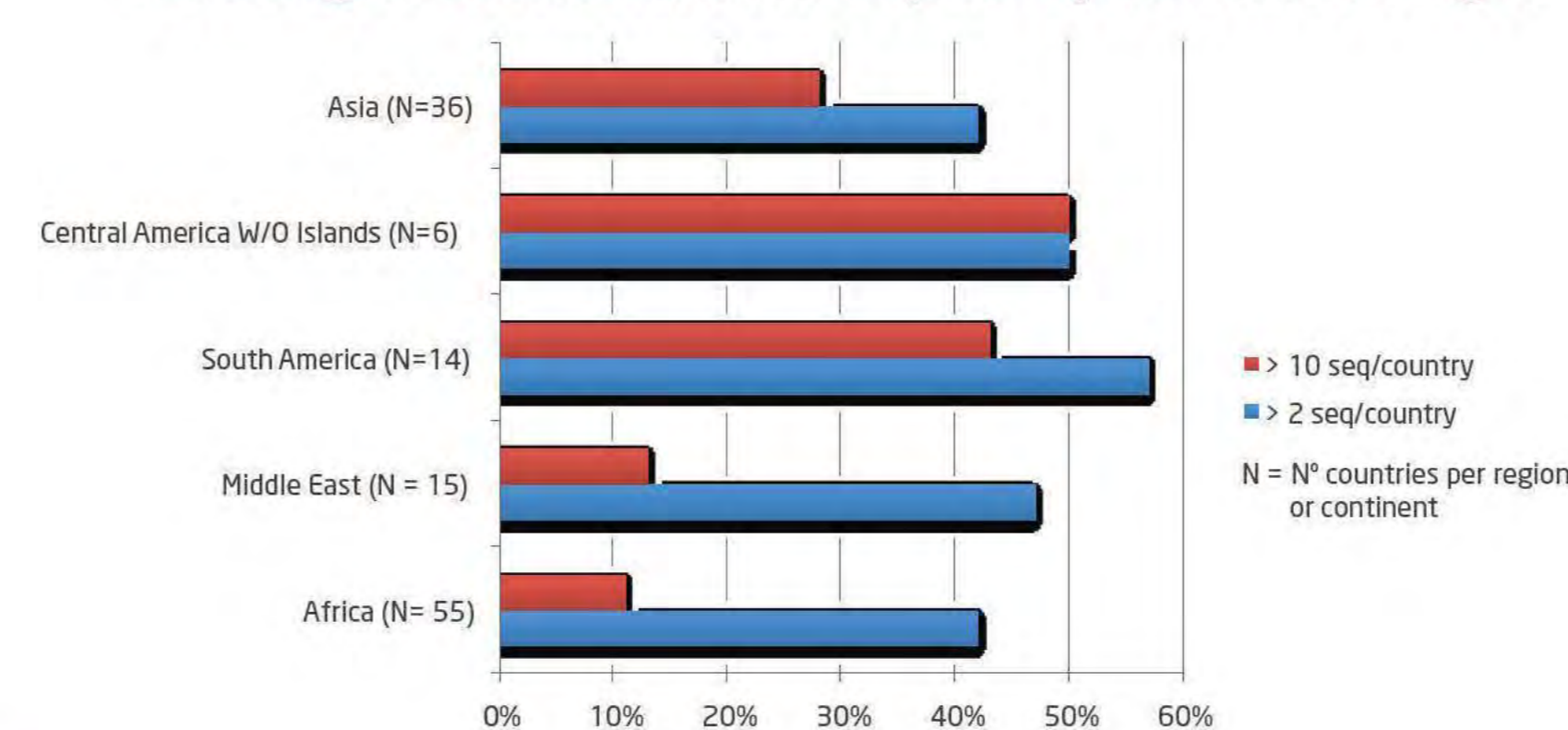
- Homogeneity in the target region used for typing from sequences from HAV NET members (73% sequences in V1/2A region).
- Different lengths of the fragments (>150 lengths; range 120 nt to 901 nt).

**FIG. 1** Genome Region used for genotype HAV (HAV NET N=1634 sequences)



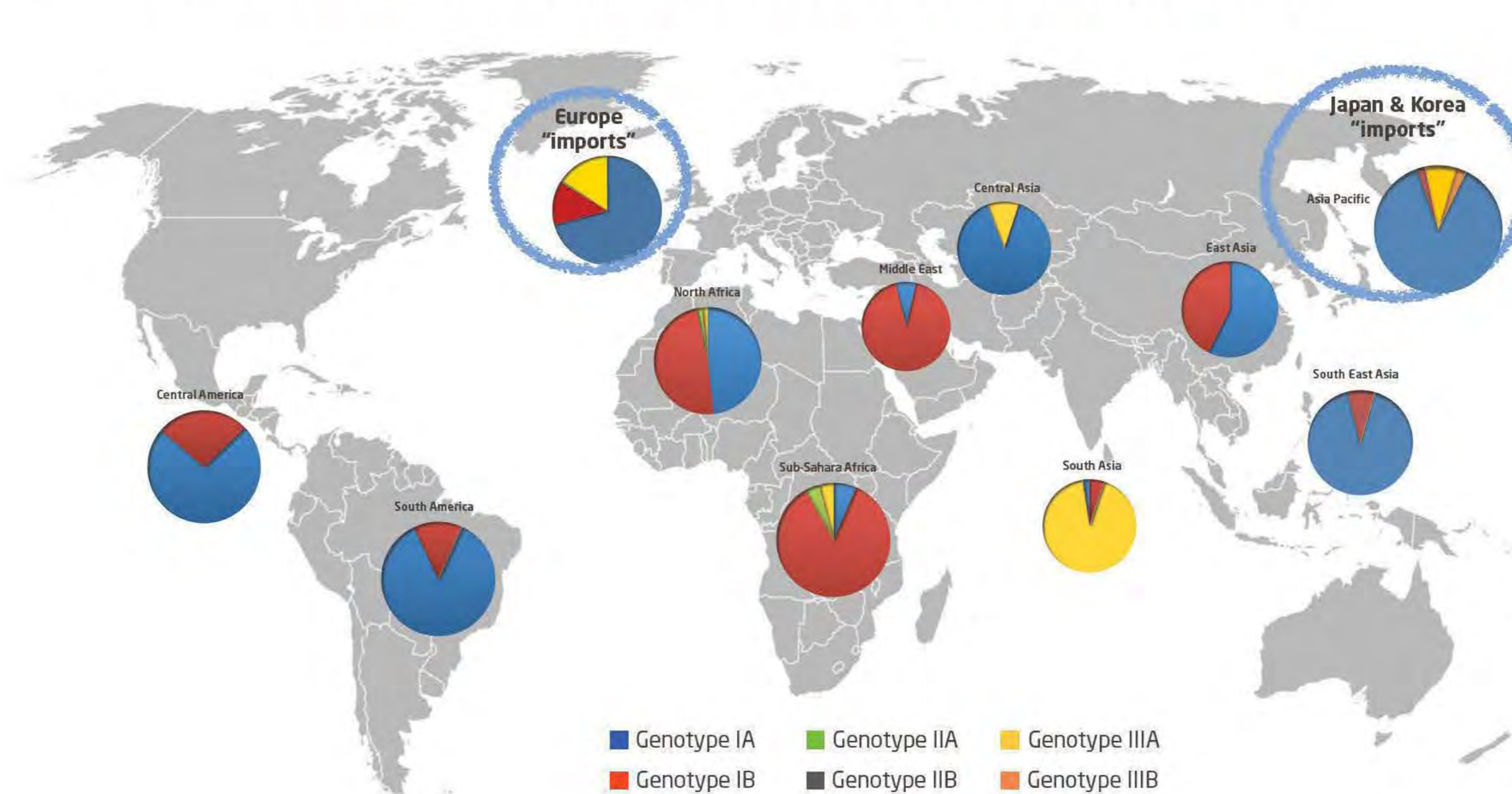
#### 2\_ Analysis of combined data

**FIG. 2** Percentage of countries with HAV sequences per continent or region



- Considering at least 2 HAV sequences by country, coverage ranges from 42-57% by continent or regions (fig 2);
- Of the total 67% (HAV NET = 942; GenBank = 3795) sequences have information on origin of infection (fig 3);
- Genotype IA (60%) is the most prevalent;
- Genotype IB (19.5%) is more prevalent in Africa and Middle East;
- Genotype IIIA (19.7%) is most prevalent in Asia (India, Afghanistan);
- Information on transmission route was available for 16% of these sequences (table 1);
- Travel related information indicates that the higher number of sequences are from High to High-medium endemic countries; Genotype IB counts for 55% of the sequences, mainly from travellers to North Africa and Turkey.

**FIG. 3** Genotype distribution based on HAV sequences linked to place "origin of infection"



**Table 1** Number of sequences with information on transmission route (N = 741)

Possible transmission route	HAV NET (N=637; 67%)	GenBank (N=104; 2.7%)
Travel related	277	51
Person-to-person (non-sexual contact)	219	3
Person-to-person (sexual contact)	102	19
IV drug users	14	11
Food and waterborne source	25	20

#### 3\_ HAV NETWeb site



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### CONCLUSION

- Available sequences have made it possible to identify and link outbreaks and their geographic origin internationally.
- Comparative analyses of sequences data, internationally, is hampered by lack of target standardisation.
- The currently available HAV NET database contains information from most continents and genotypes, but resolution in some geographic areas is limited by the number and the length of sequences.
- The lack of some epidemiological information was evident and can be limited for the understanding of HAV infection (e.g. transmission routes of some strains).

### RECOMMENDATIONS

- The resolution of HAV genotype-based cluster distribution can be greatly improved by more systematic collection of data, and target standardisation (region and length), through harmonization of genotyping protocols between laboratories.
- Geographic representation and coverage need to be increased to improve applicability of the database for support of public health investigations.

**References** Jacobsen H. The global prevalence of hepatitis A virus infection and susceptibility: A systematic Review. Geneva: World Health Organization; 2009. Available from: [http://whqlibdoc.who.int/hq20107WHO\\_IVB\\_10\\_01\\_eng.pdf](http://whqlibdoc.who.int/hq20107WHO_IVB_10_01_eng.pdf). / Koopmans et al. Early identification of common-source foodborne virus outbreaks in Europe. Emerg. Infect. Dis. 2003. 9:1136-1142. / Robertson BH et al., Genetic relatedness of hepatitis A strains recovered from different geographical regions. J.Gen.Virol. 1992. 73: 1365-1377.