



National Seroprevalence Study: Discussion of Different Approaches

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Surveillance Data

Necessary to:

- Determine (age- and risk-group specific) prevalence, incidence
- Burden of disease
- Evaluate impact of prevention
- Adapt public health action
- Generation of scientific hypotheses



Modelling hepatitis epidemic: Data

- Prevalence (age and risk group specific)
Also by geographical area?
- Incidence data
- Natural history data
Cohort studies; literature



Sero-prevalence: Methods

- Combining available information from (passive) surveillance programs, cohort studies or clinical trials with population based size of risk groups
- Testing residual sera (active disease-specific surveillance programs)
- National (population-based) seroprevalence studies

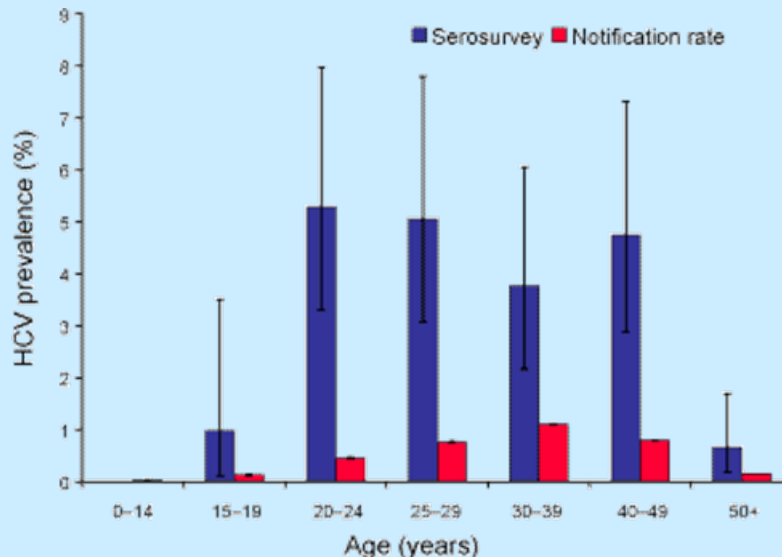
National Notifiable Diseases Surveillance system

Statistical modelling



Notification Hepatitis Data

- Surveillance systems still under development
- Cumulative hepatitis notification rate underestimates hepatitis prevalence
 - ✓ Under-reporting
 - ✓ Low levels of testing in some risk populations
 - ✓ Asymptomatic nature of acute hepatitis
 - ✓ Long latency period



Age distribution of hepatitis C as determined by serosurvey and cumulative notification rate (data from Australia)

Source: Amin J et al. Hepatitis C Prevalence – a nationwide Serosurvey; Communicable Diseases Intelligence Volume 28 Issue No4 – December



Reconstructing and predicting hepatitis C (or B) virus epidemic based on back calculation methods

- Combine existing statistics on the number of reported cases with a mathematical representation of the natural history of the HCV infection
- Reliable data on:
 - ✓ Primary HCC
 - ✓ Age and risk group specific prevalence (and incidence?) data
 - ✓ Staged model to describe the natural history



References

Deuffic S, et al: Modeling the hepatitis C virus epidemic in France. *Hepatology* 1999; 39: 1596-1601

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- Armstrong et al: The past incidence of hepatitis C virus infection: implications for future burden of chronic liver disease in the United States. *Hepatology* 2000; 31: 777-782
- Zou S et al. Prediction of hepatitis C burden in Canada. *Can J Gastroenterol* 2000; 14: 576-580
- Sypsa V et al: Reconstructing and predicting the hepatitis C virus epidemic in Greece: increasing trends of cirrhosis and hepatocellular carcinoma despite the decline in incidence of HCV infection. *Journal of Viral Hepatitis* 2004; 11: 366-374
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- Deuffic-Byrdan et al. Estimating the future health burden of chronic hepatitis C and human immunodeficiency virus infections in the United States. *Journal of Viral Hepatitis* 2007; 14: 107-115

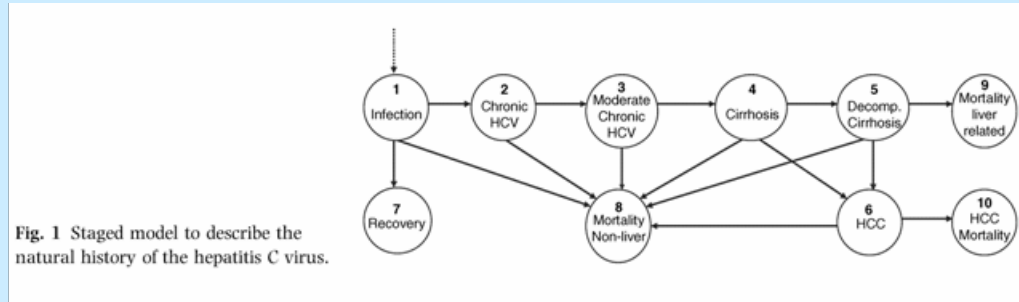


The burden of hepatitis C in England

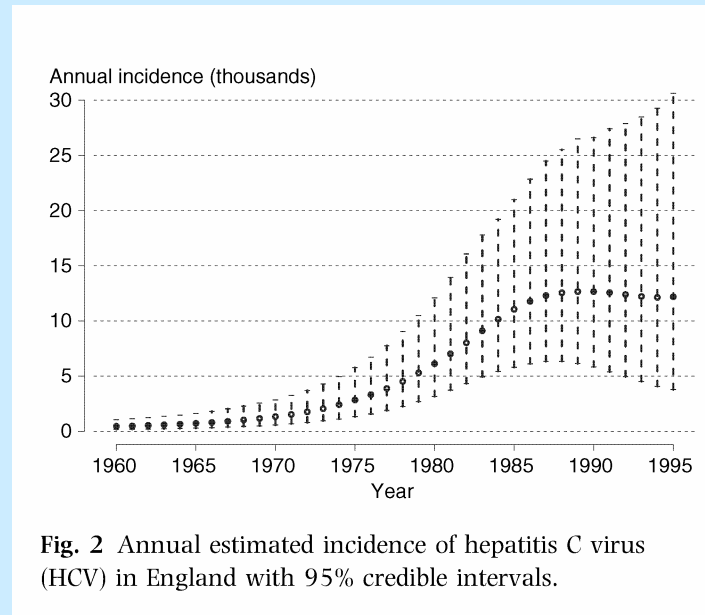
(Sweeting et al. *Journal of Viral Hepatitis* 2007; 14: 570-576)

Data: Primary HCC from Office of National Statistics

Prevalence from network of public health Laboratories (PHL)



Information on number of deaths over time is combined with disease progression to infer the number of infections that, over time, are consistent with the observed deaths





Data availability in Greece (1)

Limited population-based viral hepatitis seroprevalence studies

Population	Studies	Prevalence of HCV
A. General population-specific geographical areas	Gogos et al, 2003 Goritsas et al, 2000	0.5% - 1.25%
B. Specific groups		
Blood Donors	Zervou et al, 2003	0.61%
Healthy Workers	Sypsa et al, 2001 Mazokopakis et al, 2000	0.5% 0.4%
Hemodialysis patients	Stefanidis et al, 2004	23.6%
Parturients	Panagopoulos et al, 2004	0.8% (0.16-1.33)
Refugees	Roussos et al, 2003	2.3%
Prisoners	Giotakos et al, 2003	6.5%
Pregnant women	Raptopoulou et al, 2001	1.95%
GPs	Lionis et al, 2000	3.5%

National Statistic Service of Greece: Data on primary HCC of limited value



Data availability in Greece (2)

IDUs: EKTEPN (Greek Reitox Focal; www.ektepn.gr)

- HCV prevalence: 43.3%-61.7%
 - Different profiles of users screened at various programs due to different admission criteria
 - Substitution programmes (OKANA): 78.7%
 - Drug free programmes (KETHEA, 18ANO): 44.1%
 - Increase with age and years of injecting use

National HEPNET Cohort Study

- Data on age distribution, risk group, disease progression



Reconstructing and predicting hepatitis C virus epidemic in Greece

Estimate the number of persons who are currently infected with HCV and determine the distribution of transmission groups

Estimate the distribution of the onset years within each transmission group

Estimate HCV incidence curve



Data

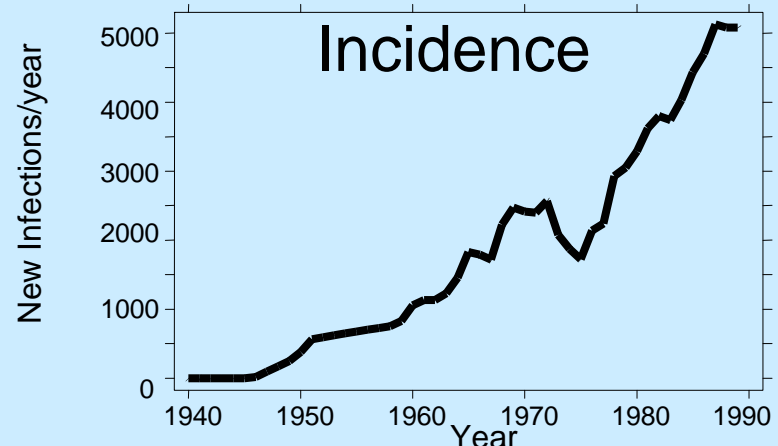
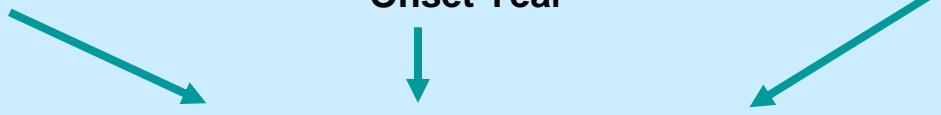
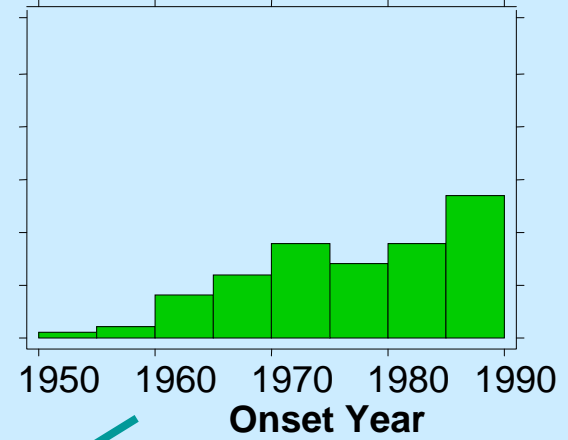
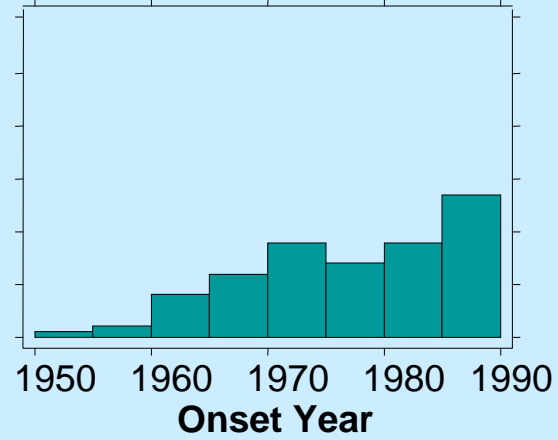
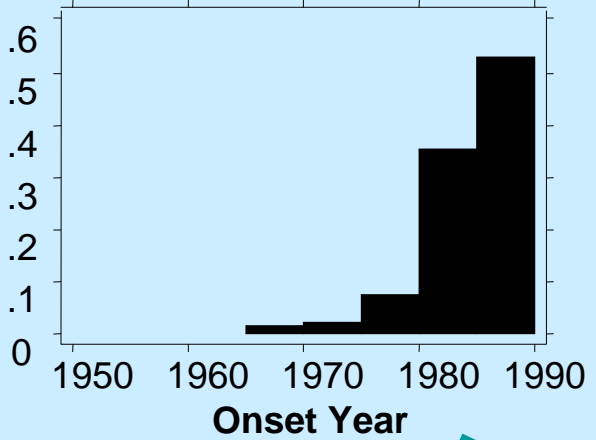
- Prevalence: 0.8%-1.4%
- Distribution of transmission groups among subjects with CHC: 943 patients enrolled in treatment studies
 - Adults 18-70 years
 - Histologically confirmed CHC
- Distribution of the onset years within each transmission group: 456 Greek patients enrolled in treatment studies with known date of infection

Prevalence 1%: 102.600 infected subjects on 1990

IDUS
24.1%

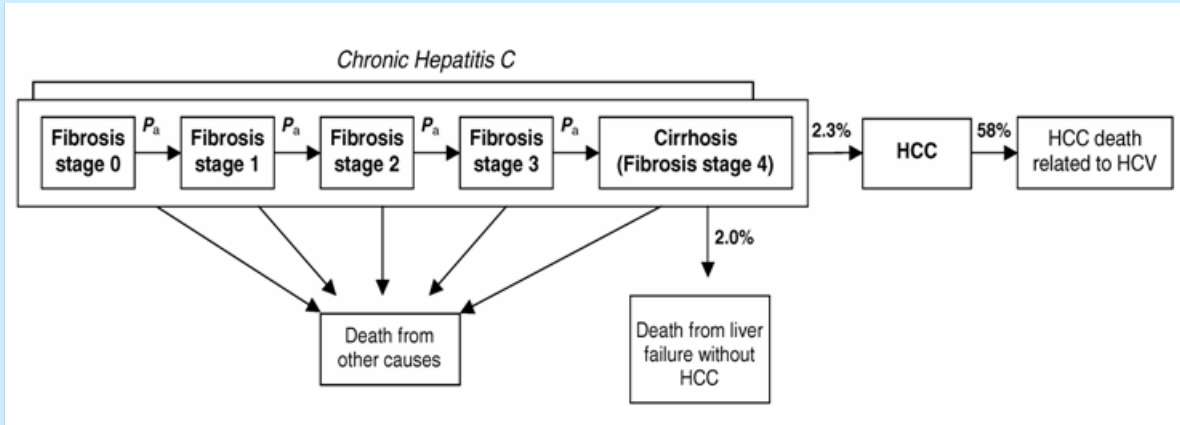
Transfusion
32.5%

Other/sporadic
43.4%

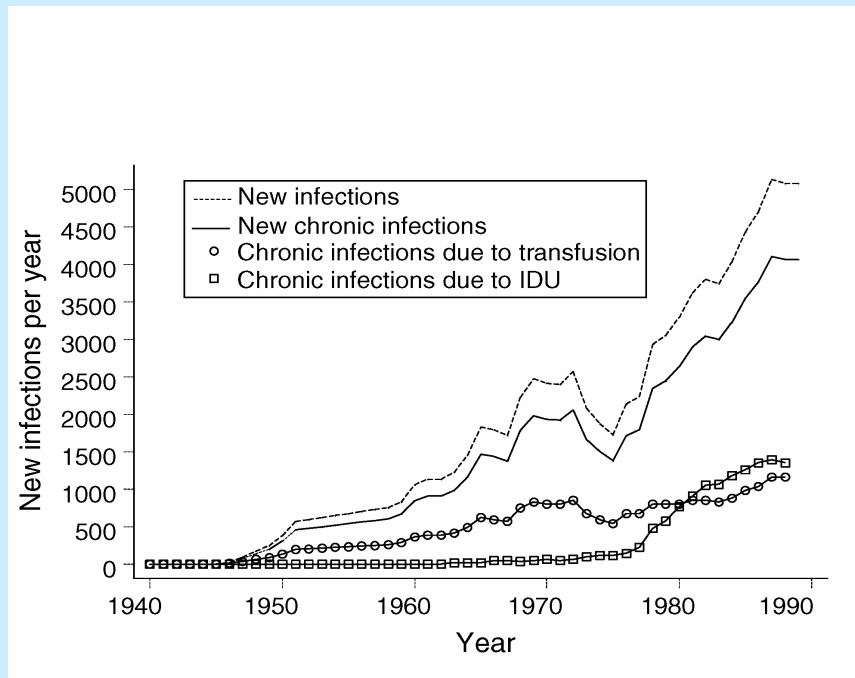




Reconstructing and predicting hepatitis C virus epidemic in Greece (2)



Natural History of HCV infection



Estimated incidence of HCV infection in Greece



Drawbacks

- Estimates depend heavily on the availability (and accuracy) of direct data on relevant parameters
- Model's assumptions validity

Greece:

- Accuracy of prevalence estimate
 - ✓ Distribution of transmission groups
 - ✓ Age distribution
- National HEPNET Cohort Study: Data on age distribution, risk group, disease progression **BUT DOES NOT** provide a (reliable) estimate of viral hepatitis prevalence



Sero-prevalence studies: A. Testing residual sera collected during routine laboratory testing

- Establish a national net of laboratories
- Set-up target numbers of sera to be tested (stratified by age and sex each year)

Prespecify the number of sera: The European Sero-Epidemiology Network – ESEN (~3500 samples – pre-specified age distribution)

References:

Osborne K et al. Ten years of serological surveillance in England and Wales: methods, results, implications and action. *International Journal of Epidemiology* 2000; 29: 362-368

Amin J et al. Hepatitis C Prevalence – a nationwide Serosurvey; *Communicable Diseases. Intelligence* Volume 28 Issue No4 –December

Nardone A et al. The comparative sero-epidemiology of varicella zoster virus in 11 countries countries in the European region



Testing residual sera collected during routine laboratory testing: Pros and Cons

- Pros
 - ✓ Serum specimens readily accessible
 - ✓ Cheap to collect sera
- Cons
 - ✓ May not be representative of the population
 - Overestimation (higher utilization of health services)
 - Differential selection bias (by transmission group?)
 - ✓ Lack of detailed information
 - ✓ Not possible to identify or control for potential biases
 - ✓ Selection bias depend on the public health system in each country



Testing residual sera collected during routine laboratory testing: methods to reduce selection bias

- Exclude recent repeat sera from the same individual
- Adjust for over-representation of some specific groups when selecting samples for testing
- Exclude sera from sexual health or liver (?) clinics

Pattern of HCV seroprevalence by age or sex should not be distorted by selection bias (transmission group?)



Sero-prevalence studies: B. Collect specimens as part of a population based survey

- Sampling procedures (weights?)
 - ✓ 3-stage sample design
 1. Geographical region
 2. Households within region
 3. Persons within household

Keep population age and sex distribution undisturbed

- Sample weights adjust for:
 - ✓ Oversampling (specific demographic groups; minorities)
 - ✓ Non-response
 - ✓ Differences between sample and population (differential uncoverage, response rates)
- Sample size estimation



Sero-prevalence studies: B. Collect specimens as part of a population based survey (2)

- Developing survey instruments
 - ✓ Questionnaires
 - Study design for?
 - ✓ Computer Assisted Personal Interviewing (?)
 - Difficult in Greece
 - ✓ Interviewers' education programs
 - ✓ Ethical Issues
 - Patient's Informed Consent Form
 - Confidentiality
- Checking responders
 - First approach by phone or by visiting home?
- Health Interview
- Sample collection
 - Collaboration with GPs, Local Hospitals
- Report of medical finding for each participant



Sero-prevalence studies: B. Collect specimens as part of a population based survey : Pros and Cons

- Pros
 - ✓ Population representative estimates
 - ✓ Generalization of the results
- Cons
 - ✓ Difficult to carry out
 - ✓ Expensive (funding?)
 - ✓ Non-response

Collaboration with- help from other experienced research teams

NHANES: www.cdc.gov/nchs/nhanes.htm

The Survey of Health, Ageing and Retirement in Europe (SHARE): www.share-project.org/

ESEN: www.hpa.org.uk/hpa/inter/esen2_menu.htm



NHANES (in Greece?)

- Aim: Prevalence of chronic conditions in Greek population
- Interview includes:
 - ✓ Demographic questions
 - ✓ Socioeconomic status
 - ✓ Dietary (only generally)
 - ✓ Medical examination (by trained medical personnel)
- Risk groups
- Diseases
 - ✓ Anemia
 - ✓ CDV
 - ✓ Diabetes
 - ✓ Infectious Diseases
 - ✓ Obesity
- Collaboration with other scientific societies



NHANES (in Greece?): Pros

- Estimate general health status of the population
- Project future diseases burden
- Design public health action
- Planning future costs for health

In a cost-benefit basis: The best choice



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