Background document

VHPB Country meeting

Prevention and control of Viral Hepatitis in Belgium and Luxembourg: lessons learnt and the way forward

BRUSSELS, BELGIUM
7-8 November 2017

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Content

This pre-meeting document contains general background information of the countries and the reported current hepatitis situation. Furthermore a list of selected abstracts/ references from a Pubmed MEDLINE search on different search terms. The references are ranged by publication year (most recent first) and for each year in alphabetical order of the first author's name.
This document should guide you in the preparation of the meeting, it should not be considered as complete literature review, but hopefully it will give an overview of what has been published on the topics of the meeting

1. Belgium

1.1. General background

(Source World factbook https://www.cia.gov/library/publications/resources/the-world-factbook/geos/en.html) and Wikipedia http://en.wikipedia.org/wiki)

Belgium: officially the Kingdom of Belgium, is a sovereign state in Western Europe bordered by France, the Netherlands, Germany, Luxembourg, and the North Sea. It is a small, densely populated country which covers an area of 30,528 square kilometres and has a population of about 11 million people. Straddling the cultural boundary between Germanic and Latin Europe, Belgium is home to two main linguistic groups: the Dutch-speaking, mostly Flemish community, which constitutes about 59 percent of the population, and the French-speaking, mostly Walloon population, which comprises 40 percent of all Belgians. Additionally, there is a small 1 percent group of German-speakers who live in the East Cantons.

	Demographics data
Population	11,491,346 (July 2017 est.)
GDP (PPP) per capita	$45,000 (2016 est.)
GDP	$467 billion (2016 est.)
Unemployment rate	8.4% (2016 est.)
Population growth	0.7% (2017 est.)
Birth rate:	11.3 births/1,000 population (2017 est.)
Death rate:	9.7 deaths/1,000 population (2017 est.)
Net migration rate	5.4 migrant(s)/1,000 population (2017 est.)
Health expenditures	10.6% of GDP (2014)
Physicians density:	2.97 physicians/1,000 population (2014)
Life expectancy at birth	total population: 81 years

1.2. Hepatitis

1.2.1. VHPB survey

VHPB survey on prevention and control of viral hepatitis in 53 European countries in 2014 – November 2014
(http://www.vhpb.org/files/html/Meetings_and_publications/Other_VHPB_documents/SURVEY2014.pdf)

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PREVENTION AND CONTROL OF VIRAL HEPATITIS IN EUROPE IN 2014: THE CASE OF BELGIUM

Country profile

- Population (in millions) (year): 11,2 (2014)[a]
- Gross national income per capita (int $) (year): 40 280 (2013)[b]
- Most recent seroprevalence data:

	% HBsAg + (year)	% Anti-HCV + (year)
General population	0.7% (2003)[c]	0.1% (2003)[c]
Blood donors (first time)	0.08% (2008)[d]	0.04% (2008)[d]
Pregnant women	-	-
Risk groups:		
Injecting drug users	2.7% (2007)[d]	55% (1995)[1]
Haemodialysis patients	-	6.8% (2000)[2]
Health care workers	-	0.4% (2000)[3]

Screening[e]

Recommended for following groups:	Hep B	Hep C
Blood and organ donors	Yes (since year ?)	Yes (since year ?)
Pregnant women	Not at national level	Yes
Injecting drug users	No	Yes (since year ?)
STI clinic patients	No	No
Haemodialysis patients	Yes (since year ?)	Yes (since year ?)
Health care workers	Yes (since year?)	No
Men having sex with men	No	No
Prison population	No	No
Migrants	No	No
Others	No	No

National plan

There is a written action plan for hepatitis C (period 2014-2019) but no written national strategy for hepatitis B or viral hepatitis.[f]

Vaccination programs

Hepatitis A[4,g]		Target	Since/Period
Universal	No		
Risk group	Yes	Contacts of hepatitis A patients, travellers, male homo- and bisexuals, liver patients, occupational risk, staff and residents in institutions for mentally disabled, people working in the food chain, contacts of a recently adopted child from an endemic country	2001
Hepatitis B[c,h]			
Universal	Yes	Infant Adolescent (12y)	1999-ongoing 1999-2011
Catch-up	Yes	Adolescent (12-18y)	2012-ongoing
Risk group	Yes	Occupational risk; neonates born to HBsAg+ mothers, haemodialysis patients; chronic liver patients, STI patients, multiple sex partners, MSM, IDU, household contacts HBsAg+ patient; immunsupressed patients, travellers to HBV endemic area	1988; 1991; 2002

Treatment

National guidelines for clinicians available	
Hepatitis B	Yes (2007)[5]
Hepatitis C	Yes (2003, 2012)[6]
Drugs available for hepatitis C treatment*,f	
Ribavirirn	Yes
Pegylated interferon	Yes
Interferon alpha	Yes
Telaprevir	Yes
Boceprevir	Yes
Simeprevir	No
Sofosbuvir	No
Others: *(specify)*	No
Number of patients treated for hepatitis B	?
Number of patients treated for hepatitis C	710 (2010)[7]

*included on the national essential medicines list or subsidized by the government

Impact

Figure 1: Hepatitis B vaccination coverage [i] and impact on hepatitis B incidence [j,k]

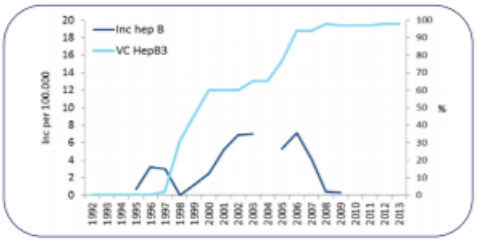
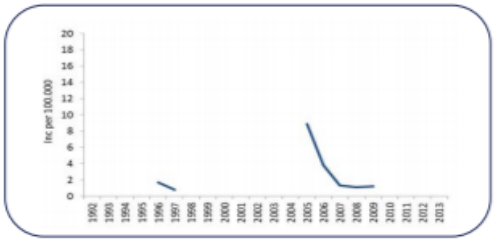


Figure 2: Introduction of activities and impact on hepatitis C incidence [j,k]



Specific issues and future challenges

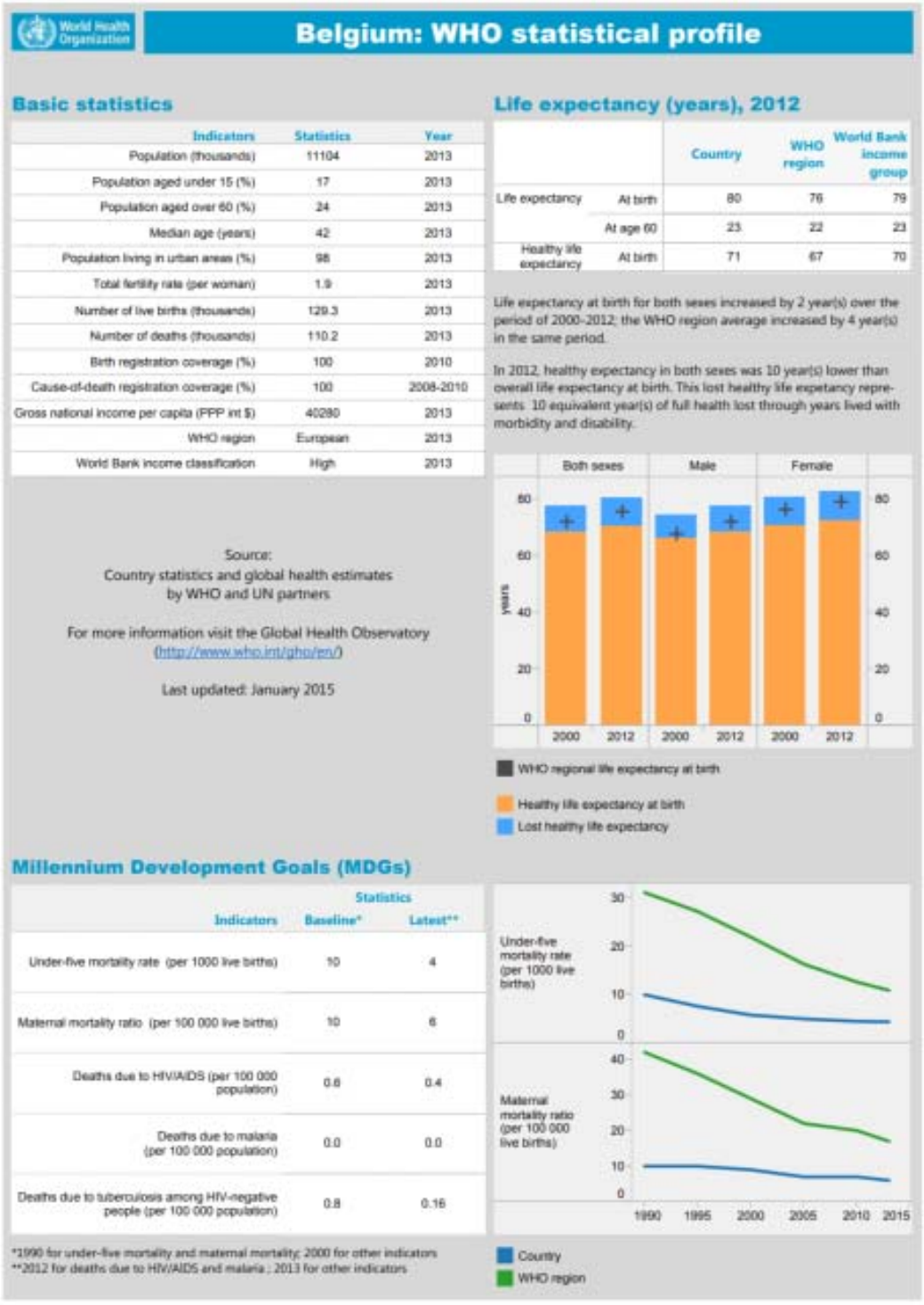
To complete by country if wanted.....

VHPB

Country contact:

1.2.2 WHO data

(http://www.who.int/gho/countries/alb.pdf?ua=1)



Belgium: WHO statistical profile

Basic statistics

Indicators	Statistics	Year
Population (thousands)	11104	2013
Population aged under 15 (%)	17	2013
Population aged over 60 (%)	24	2013
Median age (years)	42	2013
Population living in urban areas (%)	98	2013
Total fertility rate (per woman)	1.9	2013
Number of live births (thousands)	129.3	2013
Number of deaths (thousands)	110.2	2013
Birth registration coverage (%)	100	2010
Cause-of-death registration coverage (%)	100	2008-2010
Gross national income per capita (PPP int $)	40280	2013
WHO region	European	2013
World Bank income classification	High	2013

Source:
Country statistics and global health estimates
by WHO and UN partners

For more information visit the Global Health Observatory
(http://www.who.int/gho/en/)

Last updated: January 2015

Life expectancy (years), 2012

		Country	WHO region	World Bank income group
Life expectancy	At birth	80	76	79
	At age 60	23	22	23
Healthy life expectancy	At birth	71	67	70

Life expectancy at birth for both sexes increased by 2 year(s) over the period of 2000–2012; the WHO region average increased by 4 year(s) in the same period.

In 2012, healthy expectancy in both sexes was 10 year(s) lower than overall life expectancy at birth. This lost healthy life expetancy represents 10 equivalent year(s) of full health lost through years lived with morbidity and disability.

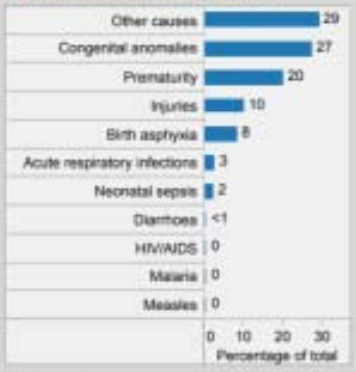
Millennium Development Goals (MDGs)

Indicators	Statistics Baseline*	Statistics Latest**
Under-five mortality rate (per 1000 live births)	10	4
Maternal mortality ratio (per 100 000 live births)	10	6
Deaths due to HIV/AIDS (per 100 000 population)	0.6	0.4
Deaths due to malaria (per 100 000 population)	0.0	0.0
Deaths due to tuberculosis among HIV-negative people (per 100 000 population)	0.8	0.16

*1990 for under-five mortality and maternal mortality; 2000 for other indicators
**2012 for deaths due to HIV/AIDS and malaria ; 2013 for other indicators

Belgium: WHO statistical profile

Distribution of causes of deaths in children under-5, 2013



DTP3 immunization among 1-year-olds

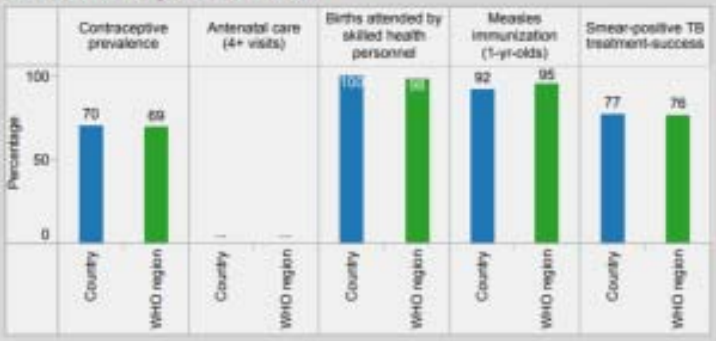
Children aged under-5 stunted

Country
WHO region

Source: Country statistics and global health estimates by WHO and UN partners
For more information visit the Global Health Observatory (http://www.who.int/gho/en/)
Last updated: January 2015

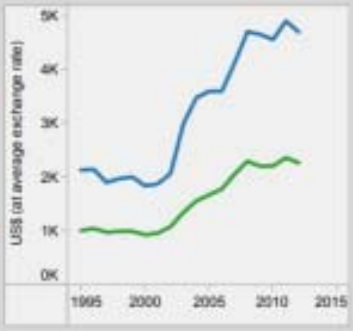
Utilisation of health services*

*Data refer to the latest year available from 2007.

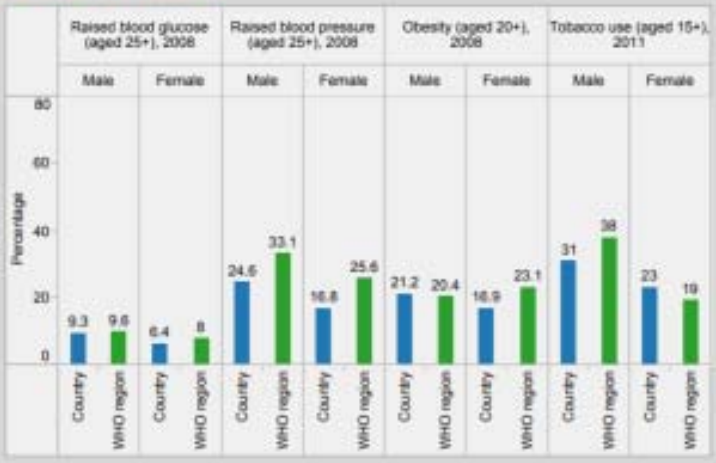


... Data not available or applicable

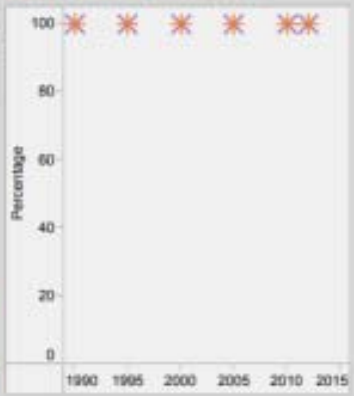
Per capita total expenditure on health



Adult risk factors



Population using improved water and sanitation



+ Improved drinking-water sources
× Improved sanitation facilities

Belgium: WHO statistical profile

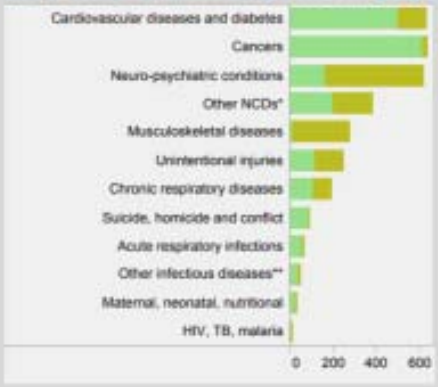
Top 10 causes of death

Ischaemic heart disease was the leading cause of death, killing 11.5 thousand people in 2012

Burden of disease, 2012

Disability-adjusted life years (DALYs) are the sum of years of life lost due to premature mortality (YLL) and years of healthy life lost due to disability (YLD).

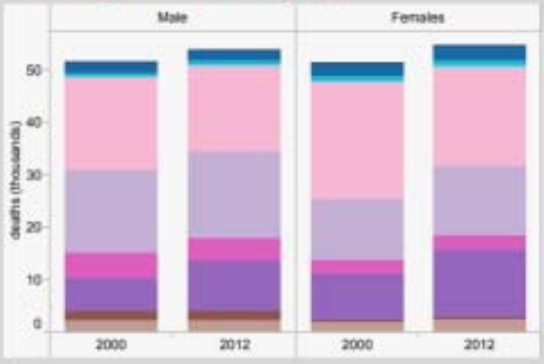
DALYs, YLL and YLD (thousands) by broad cause group



*Other noncommunicable diseases (NCDs) including non-malignant neoplasms; endocrine, blood and immune disorders; sense organ, digestive, genitourinary, and skin diseases; oral conditions; and congenital anomalies.
** Infectious diseases other than acute respiratory diseases, HIV, TB and malaria.

YLL YLD

Deaths by broad cause group



Causes
- HIV, TB, malaria
- Acute respiratory infections
- Other infectious diseases
- Maternal, neonatal, nutritional
- Cardiovascular diseases and diabetes
- Cancers
- Chronic respiratory diseases
- Other NCDs
- Suicide, homicide and conflict
- Unintentional injuries

Probability of dying, 2012

Probability of dying between relevant exact ages, for a person experiencing the 2012 age-specific mortality risks throughout their life.

Before age 15, all causes	Male	2%
	Female	2%
Before age 70, all causes	Male	34%
	Female	21%
Between ages 15 and 49, from maternal causes	Female	0%
Between ages 30 and 70, from 4 major noncommunicable diseases (NCDs)–	Both sexes	12%

–Cancers, cardiovascular diseases, chronic respiratory diseases and diabetes

Source: Country statistics and global health estimates by WHO and UN partners
For more information visit the Global Health Observatory (http://who.int/gho/mortality_burden_disease/en/)
Last updated: January 2015

WHO CISID database info (http://data.euro.who.int/cisid/?TabID=399572)

Hepatitis A

6011 - Hepatitis A - Number of cases											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Belgium	225	217	365								

Hepatitis B Incidence (cases per 100 000 population)

9009 - Hepatitis B - Incidence (cases per 100 000 population)											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Belgium		1.39	4.33					0.9			

9008 - Hepatitis B - Number of cases											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Belgium		146	459					97			

Hepatitis C Incidence (Cases per 100 000 population)

6015 - Hepatitis C - Incidence (cases per 100 000 population)											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Belgium		4.2	9.25								

6014 - Hepatitis C - Number of cases											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Belgium		442	980								

Immunization coverage

Source: http://www.who.int/immunization/monitoring_surveillance/data/en/

	Country	Immunization coverage %	2017	2016	2015	2014	2013	2012	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000	1999	1998
BEL	Belgium	HepB3	97	98	98	98	98	97	97	97	98	94	94	77	64	64	60	60	60		31	2
LUX	Luxembour	HepB3	94	94	94	94	94	95	95	95	94	87	95	95		49	95					49

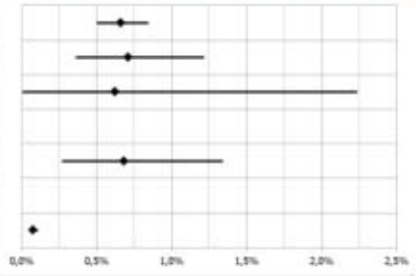
1.2.3 ECDC data

3.2 Belgium

HbsAg prevalence

Author (year of publication)	Population	Sampling period	Risk of bias score	Sample size	Sampling method	Sampling description	Age range
Quoilin et al. (2007)	General population	2002	4	Standardised	Random	Region of Flanders	Standardised
Quoilin et al. (2007)	General population	2002	4	1,830	Random	Region of Flanders	0 to >65
Nardone et al. (2009)	General population	2002–2003	3	321	Convenience	Residual lab samples representative of location and gender	16 to 39
Nardone et al. (2009)	General population	2002–2003	3	1,175	Convenience	Residual lab samples representative of location and gender	1 to 15
Council of Europe	First-time blood donors	2011	N/A	53,524	N/A	N/A	N/A

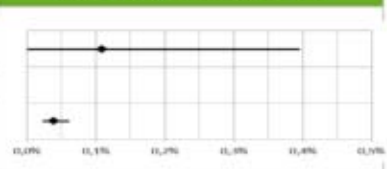
Author (year of publication)	Sampling period	Estimate (95% CI)	Sample size	Forest plot of estimates and 95% CI
General population				
Quoilin et al. (2007)	2002	0.7% (0.5–0.8)	Standardised	
Quoilin et al. (2007)	2002	0.7% (0.4–1.2)	1,830	
Nardone et al. (2009)	2002–2003	0.6% (0.1–2.2)	321	
General population – children				
Nardone et al. (2009)	2002–2003	0.7% (0.3–1.3)	1,175	
First-time blood donors				
Council of Europe	2011	0.08% (0.05–0.1)	53,524	



Anti-HCV prevalence

Author (year of publication)	Population	Sampling period	Risk of bias score	Sample size	Sampling method	Sampling description	Age range
Quoilin et al. (2007)	General population	2002	4	1,830	Random	Region of Flanders	0 to >65
Council of Europe	First-time blood donors	2011	N/A	53,524	N/A	N/A	N/A

Author (year of publication)	Sampling period	Estimate (95% CI)	Sample size	Forest plot of estimate and 95% CI
General population				
Quoilin et al. (2007)	2002	0.1% (0.0–0.4)	1,830	
First-time blood donors				
Council of Europe	2011	0.04% (0.02–0.06)	53,524	



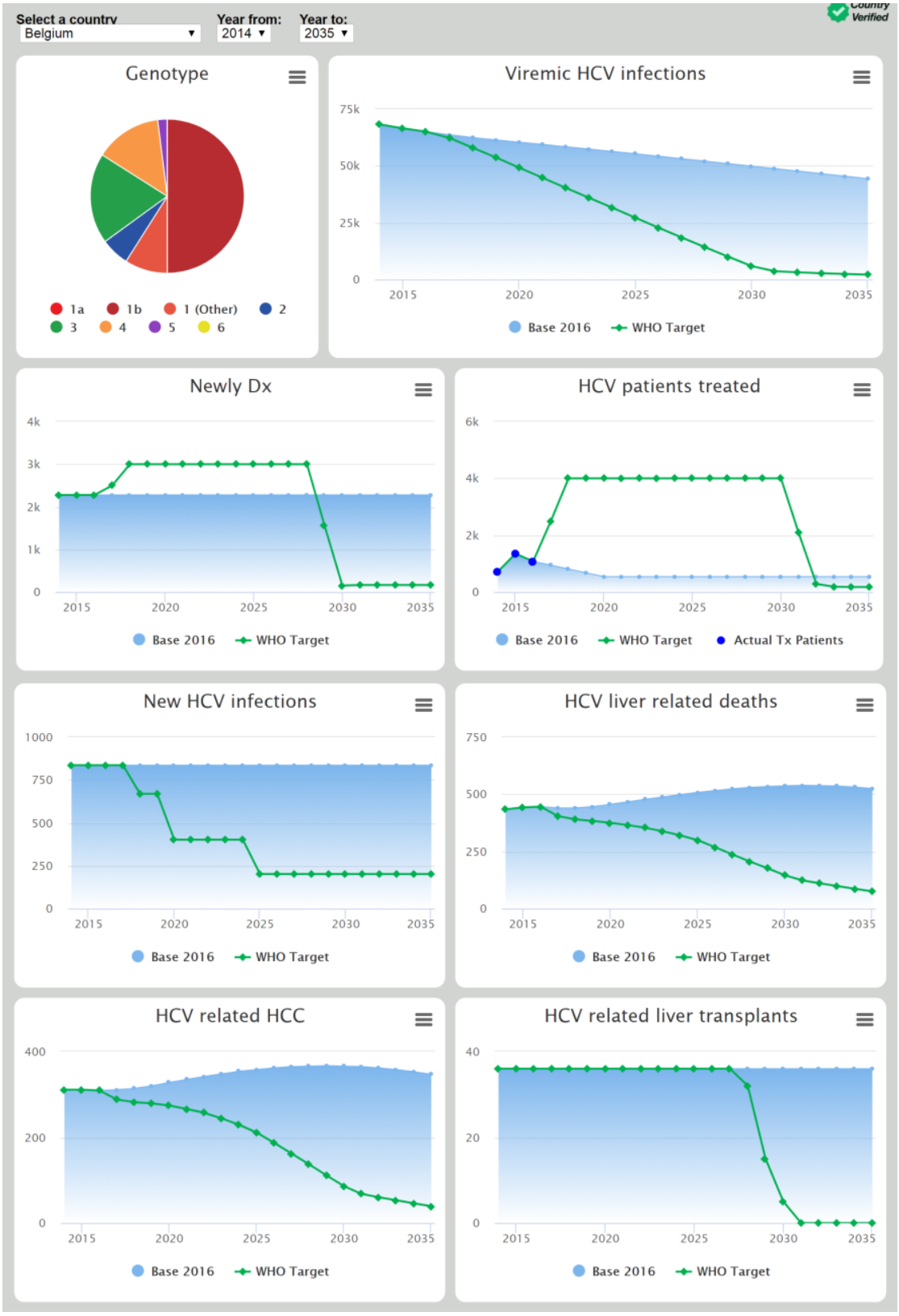
HBsAg and anti-HCV prevalence: PWID

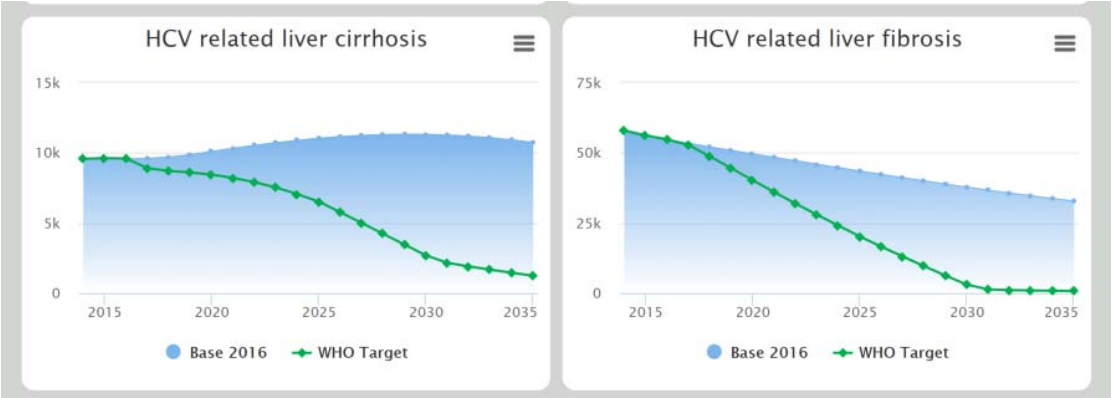
Source	Sampling period	Virological marker	Testing settings and sample size (if available)	Estimated prevalence range (no CI available)
EMCDDA	2013	HBsAg	Drug treatment services in Antwerp and the Flanders region. N=N/A	0.0% to 1.58%
EMCDDA	2013	Anti-HCV	Drug treatment and harm reduction services in Antwerp and the Flanders region. N=N/A	7.5% to 73.5%

source: ECDC Systematic review on hepatitis Band C prevalence in the EU/EEA 2016.
https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/systematic-review-hepatitis-B-C-prevalence.pdf

1.2.4 Centre of disease control - Polaris observatory

http://polarisobservatory.org/polaris_view/hepC.htm




HCV related liver cirrhosis
15k
10k
5k
0
2015
2020
2025
2030
2035
Base 2016
WHO Target
HCV related liver fibrosis
75k
50k
25k
0
2015
2020
2025
2030
2035
Base 2016
WHO Target

1.3 Presentation related Pubmed abstracts -Belgium

Pubmed MEDLINE search on {(Hepatitis) AND **(Belg*)** } in all [Abstract/title] and filter:**'last 10 years'** on was performed.
The references were manually sorted in the different subject in an EndNote database.
The references are listed by publication year (recent first).

1.3.1 Surveillance, epidemiology of viral hepatitis in Belgium (session 3)

Hepatitis A

Kurkela, S., Pebody, R., Kafatos, G., Andrews, N., Barbara, C., Bruzzone, B., Butur, D., Caplinskas, S., Davidkin, I., Hatzakis, A., et al. "**Comparative hepatitis A seroepidemiology in 10 European countries**." Epidemiol Infect **2012** 140(12): 2172-2181.Health Protection Agency, Health Protection Services, Colindale, London, UK.

The WHO recommends hepatitis A virus (HAV) immunization according to level of transmission and disease burden. We aimed to identify susceptible age groups by standardized serosurveys to inform HAV vaccination policy in participating countries: Belgium, Czech Republic, England, Finland, Germany, Italy, Lithuania, Malta, Romania, and Slovakia. Each country tested national serum banks (n = 1854-6748), collected during 1996-2004, for anti-HAV antibodies. Local laboratory results were standardized to common units. Forty-one per cent of those aged <30 years and 6% of those aged >/=30 years were susceptible to HAV in Romania; compared to 70-94% and 26-71%, respectively, elsewhere. Romania reported high HAV incidence in children and young adults. Other countries reported HAV disease primarily in older risk groups. The results suggest low level of HAV transmission in most of Europe. Romania, however, appeared as an area with intermediate transmission. Vaccination of risk groups in countries with high susceptibility of young and middle-aged adults needs to be continued.

Robesyn, E., Micalessi, M. I., Quoilin, S., Naranjo, M. and Thomas, I. "**Cluster of hepatitis A cases among travellers returning from Egypt, Belgium, September through November 2008**." Euro Surveill **2009** 14(3).Flemish Agency for Care and Health, Department of Public Health Surveillance, Infectious Disease Control Unit, Brussels, Belgium

Following a European alert by France, we detected a hepatitis A cluster in Belgian travellers returning from Egypt. Our investigation supports the hypothesis of a common source outbreak, linked to Nile river cruises. The outbreak also suggests the need to consider an intensification of the vaccination policy for travellers to hepatitis A endemic countries.

Robesyn, E., De Schrijver, K., Wollants, E., Top, G., Verbeeck, J. and Van Ranst, M. "**An outbreak of hepatitis A associated with the consumption of raw beef**." J Clin Virol **2009** 44(3): 207-210.Department of Public Health Surveillance, Flemish Agency for Care and Health, Belgium.

BACKGROUND: In July 2004, a sharp increase of hepatitis A, a notifiable disease in Belgium, was detected. OBJECTIVES: We investigated the outbreak in order to identify the source and take appropriate action. STUDY DESIGN: We conducted an outbreak investigation which included a matched case-control study to analyse the association with a range of food items and food providers. A phylogenetic analysis was used to study the relation between the outbreak cases

and the identified source. RESULTS: We registered 269 cases of hepatitis A. Consumption of raw beef (OR 16.0; 95% CI 2.1-120.7) was the most probable way of infection. A food handler working at an epidemiologically linked meat distribution plant had contracted hepatitis A 1 month before the start of the outbreak. HAV strains from the food handler and the patients involved in the outbreak were monophyletically related. CONCLUSIONS: Since serological immunity in Belgium is decreasing over time, foodborne outbreaks of hepatitis A are a substantial risk. In this outbreak, a single food handler, at the level of the distribution chain, has been identified as the most likely source, through cross-contamination of raw beef. This outbreak investigation suggests the need to consider vaccination against hepatitis A in food handlers.

Hepatitis E

HUMAN

Van Hoecke, F., Van Maerken, T., De Boulle, M., Geerts, A., Vlierberghe, V., Colle, I. and Padalko, H. E. "**Hepatitis E seroprevalence in east and west Flanders, Belgium**." Acta Gastroenterol Belg **2012** 75(3): 322-324.Department of Clinical Chemistry, Microbiology and Immunology, (2) Department of Hepatology and Gastroenterology, Ghent University Hospital, Ghent, Belgium.

BACKGROUND AND STUDY AIM: Hepatitis E virus (HEV) infection is increasingly recognized as a cause of hepatitis in developed countries. The goal of this study is to provide an estimate of the seroprevalence of HEV in Belgium, more precisely in East and West Flanders, since data for this country are currently lacking. PATIENTS AND METHODS: One hundred patients presenting at the gynecological (mainly fertility center) or orthopedic clinics of our hospital were randomly selected to be tested for anti-HEV IgG antibodies using a sensitive indirect ELISA and, in the case of a borderline result, a strip immunoassay. RESULTS: The anti-HEV IgG seroprevalence was found to be 14%. CONCLUSIONS: The observed seroprevalence rate suggests that HEV infection is not an uncommon occurrence in Belgium. Comparisons with published seroprevalence data of other Western European countries should be made with caution due to differences in the analytical performance of anti-HEV IgG assays.

Seivert, M., Belaiche, J. and Delwaide, J. "**[Hepatitis E: a Third World's hepatitis found in Belgium]**." Rev Med Liege **2008** 63(9): 549-553.

Hepatitis E virus is the second cause of acute viral hepatitis of oral-fecal origin in the world. This virus has a vast distribution throughout the world and manifests itself either in epidemic or endemic-sporadic form in many developing countries. Usually, the cases of HEV infection in industrialized countries are observed after a history of travel in an endemic area. However, an increasing number of cases have been attributed to a HEV zoonotic form transmitted by swine. HEV infection can lead to deadly fulminant hepatic failure in 1-4% in the common population, but the mortality incidence reaches 20% in case of third trimester pregnant women infection. The diagnosis of HEV infection can be made using serological tests but today, RT-PCR is considered as the gold standard test. Unfortunately, this technique is not widely available in Belgium yet. There is no treatment for HEV infection, only prophylactic measures as hygiene and sewage treatment can stop epidemics. Recently, a new vaccine, still in research phase, has showed promising outcomes.

ANIMAL- Zoonosis

Thiry, D., Mauroy, A., Saegerman, C., Licoppe, A., Fett, T., Thomas, I., Brochier, B., Thiry, E. and Linden, A. "**Belgian Wildlife as Potential Zoonotic Reservoir of Hepatitis E Virus**." Transbound Emerg Dis **2017** 64(3): 764-773.

Hepatitis E is an acute human liver disease in healthy individuals but may become chronic in immunocompromised patients. It is caused by the hepatitis E virus (HEV) and can have a zoonotic origin, particularly in high-income countries. In this study, 383 sera from wild boars were selected for serology; for virological analyses, 69 sera and 61 livers from young wild boars were used. A total of 189 and 235 sera of, respectively, red deer and roe deer were collected for serological analysis. For virological analyses, 84 and 68 sera and 29 and 27 livers from, respectively, red and roe deer were sampled. An apparent seroprevalence of 34% (95% CI 29.71-39.46) was

found in wild boars, of 1% (95% CI 0-2.4) in red deer and 3% (95% CI 0.8-4.2) in roe deer. To assess the ELISA screening prevalence, Western blot (WB) analyses were carried out, a receiver operating characteristic curve analysis was performed and different scenarios with varying ELISA specificities relative to WB were analysed. Seroprevalence remained high whatever the scenario in the wild boar population. In wild boar, 4 of 69 sera and 4 of 61 livers were detected as positive for HEV RNA. All sequences obtained from sera belonged to genotype HEV-3. HEV RNA, belonging to genotype HEV-3, was detected in one of 29 red deer livers. Wild boar can be considered as a host reservoir of the virus in Belgium. However, in contrast to the epidemiological role played by them in other countries, the low prevalence in deer makes these species an unlikely reservoir. This evidence needs further investigation to determine in which situation deer can serve as reservoir. These results also raise the question of the dynamics of HEV infection between wild fauna, domestic pigs and humans.

Thiry, D., Mauroy, A., Saegerman, C., Thomas, I., Wautier, M., Miry, C., Czaplicki, G., Berkvens, D., Praet, N., van der Poel, W., et al. "**Estimation of hepatitis E virus (HEV) pig seroprevalence using ELISA and Western blot and comparison between human and pig HEV sequences in Belgium**." Vet Microbiol **2014** 172(3-4): 407-414.

Zoonotic transmission of hepatitis E virus (HEV) is of special concern, particularly in high income countries were waterborne infections are less frequent than in developing countries. High HEV seroprevalences can be found in European pig populations. The aims of this study were to obtain prevalence data on HEV infection in swine in Belgium and to phylogenetically compare Belgian human HEV sequences with those obtained from swine. An ELISA screening prevalence of 73% (95% CI 68.8-77.5) was determined in Belgian pigs and a part of the results were re-evaluated by Western blot (WB). A receiver operating characteristic curve analysis was performed and scenarios varying the ELISA specificity relative to WB were analysed. The seroprevalences estimated by the different scenarios ranged between 69 and 81% and are in agreement with the high exposure of the European pig population to HEV. Pig HEV sequences were genetically compared to those detected in humans in Belgium and a predominance of genotype 3 subtype f was shown in both swine and humans. The high HEV seroprevalence in swine and the close phylogenetic relationships between pig and human HEV sequences further support the risk for zoonotic transmission of HEV between humans and pigs.

Presentation related references:

Overview of surveillance system and epidemiology of hepatitis A, D and E

Provided by speaker: Steven Van Gucht

Thiry, D., Mauroy, A., Saegerman, C., Licoppe, A., Fett, T., Thomas, I., Brochier, B., Thiry, E. and Linden, A. "**Belgian Wildlife as Potential Zoonotic Reservoir of Hepatitis E Virus**." Transbound Emerg Dis **2017** 64(3): 764-773.

Hepatitis E is an acute human liver disease in healthy individuals but may become chronic in immunocompromised patients. It is caused by the hepatitis E virus (HEV) and can have a zoonotic origin, particularly in high-income countries. In this study, 383 sera from wild boars were selected for serology; for virological analyses, 69 sera and 61 livers from young wild boars were used. A total of 189 and 235 sera of, respectively, red deer and roe deer were collected for serological analysis. For virological analyses, 84 and 68 sera and 29 and 27 livers from, respectively, red and roe deer were sampled. An apparent seroprevalence of 34% (95% CI 29.71-39.46) was found in wild boars, of 1% (95% CI 0-2.4) in red deer and 3% (95% CI 0.8-4.2) in roe deer. To assess the ELISA screening prevalence, Western blot (WB) analyses were carried out, a receiver operating characteristic curve analysis was performed and different scenarios with varying ELISA specificities relative to WB were analysed. Seroprevalence remained high whatever the scenario in the wild boar population. In wild boar, 4 of 69 sera and 4 of 61 livers were detected as positive for HEV RNA. All sequences obtained from sera belonged to genotype HEV-3. HEV RNA, belonging to genotype HEV-3, was detected in one of 29 red deer livers. Wild boar can be considered as a host reservoir of the virus in Belgium. However, in contrast to the

epidemiological role played by them in other countries, the low prevalence in deer makes these species an unlikely reservoir. This evidence needs further investigation to determine in which situation deer can serve as reservoir. These results also raise the question of the dynamics of HEV infection between wild fauna, domestic pigs and humans.

Ho, E., Deltenre, P., Nkuize, M., Delwaide, J., Colle, I., Michielsen, P. and Belgian Association for the Study of the, L. "**Coinfection of hepatitis B and hepatitis delta virus in Belgium: a multicenter BASL study. Prospective epidemiology and comparison with HBV mono-infection**." J Med Virol **2013** 85(9): 1513-1517.

Epidemiological data on hepatitis delta virus (HDV) infection in Belgium are lacking. A multicenter questionnaire-based registry on HDV infection was collated between March 1, 2008 and February 28, 2009. It consisted of patients coinfected with hepatitis B virus (HBV) and HDV. The data samples were compared to those of a concurrent registry on HBV infection. Prospective data of patients with HBV-HDV coinfection were collected. Active HBV replication is defined as HBeAg positivity or HBV DNA > 2,000 IU/ml. Forty-four patients from 15 centers were registered. A comparison of 29 patients infected with HDV (registered in the concurrent HBV registry) was made against 785 HBV mono-infected patients. The seroprevalence of patients coinfected with HBV and HDV in Belgium is reported to be 3.7% (29/785), consisting solely of the HBV-HDV coinfected patients in the HBV registry. This rises to 5.5% (44/800) if all patients infected with HDV from the two registries combined are included. The patients coinfected with HBV and HDV had higher ($P < 0.05$) ALT values and more advanced liver disease (Metavir score >/=F2), but had less active HBV replication and lower HBV DNA titers when compared with the patients infected only with HBV. Additionally, the majority of HBV-HDV coinfected patient was male, and 13.6% (6/44) of the patients that were coinfected HBV and HDV were also infected with HCV. In conclusion, this study provided much needed epidemiological data on the current state of HDV infection in Belgium.

Van Hoecke, F., Van Maerken, T., De Boulle, M., Geerts, A., Vlierberghe, V., Colle, I. and Padalko, H. E. "**Hepatitis E seroprevalence in east and west Flanders, Belgium**." Acta Gastroenterol Belg **2012** 75(3): 322-324.

BACKGROUND AND STUDY AIM: Hepatitis E virus (HEV) infection is increasingly recognized as a cause of hepatitis in developed countries. The goal of this study is to provide an estimate of the seroprevalence of HEV in Belgium, more precisely in East and West Flanders, since data for this country are currently lacking. PATIENTS AND METHODS: One hundred patients presenting at the gynecological (mainly fertility center) or orthopedic clinics of our hospital were randomly selected to be tested for anti-HEV IgG antibodies using a sensitive indirect ELISA and, in the case of a borderline result, a strip immunoassay. RESULTS: The anti-HEV IgG seroprevalence was found to be 14%. CONCLUSIONS: The observed seroprevalence rate suggests that HEV infection is not an uncommon occurrence in Belgium. Comparisons with published seroprevalence data of other Western European countries should be made with caution due to differences in the analytical performance of anti-HEV IgG assays.

Hakze-van der Honing, R. W., van Coillie, E., Antonis, A. F. and van der Poel, W. H. "**First isolation of hepatitis E virus genotype 4 in Europe through swine surveillance in the Netherlands and Belgium**." PLoS One **2011** 6(8): e22673.

Hepatitis E virus (HEV) genotypes 3 and 4 are a cause of human hepatitis and swine are considered the main reservoir. To study the HEV prevalence and characterize circulating HEV strains, fecal samples from swine in the Netherlands and Belgium were tested by RT-PCR. HEV prevalence in swine was 7-15%. The Dutch strains were characterized as genotype 3, subgroups 3a, 3c and 3f, closely related to sequences found in humans and swine earlier. The HEV strains found in Belgium belonged to genotypes 3f and 4b. The HEV genotype 4 strain was the first ever reported in swine in Europe and an experimental infection in pigs was performed to isolate the virus. The genotype 4 strain readily infected piglets and caused fever and virus shedding. Since HEV4 infections have been reported to run a more severe clinical course in humans this observation may have public health implications.

Mina, T., Amini-Bavil-Olyaee, S., Shirvani-Dastgerdi, E., Trovao, N. S., Van Ranst, M. and Pourkarim, M. R. "**15year fulminant hepatitis B follow-up in Belgium: Viral evolution and signature of demographic change**." Infect Genet Evol **2017** 49: 221-225.

Fulminant hepatitis among different clinical outcomes of hepatitis B virus infection is very rare and manifests high mortality rate, however it has not been investigated in Belgian inhabitants yet. In the frame of a retrospective study between 1995 and 2010, 80 serum samples (in some cases serial samples) archived in Biobank, were collected from 24 patients who had clinically developed fulminant infection of hepatitis B virus. In total, 33 hepatitis B virus (HBV) strains (31 full-length genome and 2 partial viral genes) of different HBV genotypes and subgenotypes including A2, B2, D1, D2, D3 and E, were amplified, sequenced and phylogenetically analyzed. HBV isolated strains from native and exotic patients were characterized by genome variations associated with viral invasiveness. Although several mutations at nucleotide and protein levels were detected, evolutionary analyses revealed a negative selective pressure over the viral genomes. This study revealed influence of immigration through a steady change in the viral epidemiological profile of the Belgian population.

Ho, E., Deltenre, P., Nkuize, M., Delwaide, J., Colle, I. and Michielsen, P. "**Coinfection of hepatitis B and hepatitis delta virus in Belgium: a multicenter BASL study. Prospective epidemiology and comparison with HBV mono-infection**." J Med Virol **2013** 85(9): 1513-1517.

Epidemiological data on hepatitis delta virus (HDV) infection in Belgium are lacking. A multicenter questionnaire-based registry on HDV infection was collated between March 1, 2008 and February 28, 2009. It consisted of patients coinfected with hepatitis B virus (HBV) and HDV. The data samples were compared to those of a concurrent registry on HBV infection. Prospective data of patients with HBV-HDV coinfection were collected. Active HBV replication is defined as HBeAg positivity or HBV DNA > 2,000 IU/ml. Forty-four patients from 15 centers were registered. A comparison of 29 patients infected with HDV (registered in the concurrent HBV registry) was made against 785 HBV mono-infected patients. The seroprevalence of patients coinfected with HBV and HDV in Belgium is reported to be 3.7% (29/785), consisting solely of the HBV-HDV coinfected patients in the HBV registry. This rises to 5.5% (44/800) if all patients infected with HDV from the two registries combined are included. The patients coinfected with HBV and HDV had higher ($P < 0.05$) ALT values and more advanced liver disease (Metavir score >/=F2), but had less active HBV replication and lower HBV DNA titers when compared with the patients infected only with HBV. Additionally, the majority of HBV-HDV coinfected patient was male, and 13.6% (6/44) of the patients that were coinfected HBV and HDV were also infected with HCV. In conclusion, this study provided much needed epidemiological data on the current state of HDV infection in Belgium.

De Vroey, B., Moreno, C., Laleman, W., van Gossum, M., Colle, I., de Galocsy, C., Langlet, P., Robaeys, G., Orlent, H., Michielsen, P., et al. "**Hepatitis B virus and hepatitis C virus infections in Belgium: similarities and differences in epidemics and initial management**." Eur J Gastroenterol Hepatol **2013** 25(5): 613-619.

INTRODUCTION: Nationwide studies comparing patients with hepatitis B and C virus (HBV and HCV) infections are mandatory for assessing changes in epidemiology. AIM: The aim of this study was to compare epidemiological data and initial management of newly diagnosed patients with persistent HBV (HBsAg positive) or HCV (detectable HCV RNA) infection in Belgium. PATIENTS AND METHODS: Data were extracted from two Belgian observational databases. RESULTS: A total of 655 patients (387 HBV and 268 HCV) were included. Compared with HCV patients, HBV patients were younger, more frequently men, more often of Asian or African origin (43 vs. 10%, $P<0.0001$), and less frequently contaminated by transfusion or intravenous drug use (9 and 6% vs. 34 and 44%, $P<0.0001$). Viral replication was assessed in 89% of HBV patients. Compared with HCV patients, HBV patients more frequently had normal alanine aminotransferase (ALT) levels (65 vs. 29%, $P<0.0001$), less frequently underwent liver biopsy (29 vs. 67%, $P<0.0001$), and were less often considered for antiviral therapy (25 vs. 54%, $P<0.0001$). When taking only HBV patients with detectable viral replication into consideration, results remained unchanged. During the multivariate analysis, ALT was a major factor for performing liver biopsy or considering antiviral therapy in both

groups. CONCLUSION: HBV and HCV screening policies should be targeted toward immigrants and intravenous drug users, respectively. Guidelines recommending systematic search for viral replication should be reinforced in HBV patients. HBV patients less frequently underwent liver biopsy and were less often considered for antiviral therapy compared with HCV patients. Despite the lack of sensitivity and specificity, ALT remains a pivotal decision-making tool for liver biopsy and antiviral therapy in both infections.

Deltenre, P., Laleman, W., Van Gossum, M., Lenaerts, A., Colle, I., Michielsen, P., Adler, M., Delwaide, J., Assene, C., Reynaert, H., et al. "**HBV infection in Belgium: results of the BASL observatory of 1,456 HBsAg carriers**." Acta Gastroenterol Belg **2012** 75(1): 35-41.Hopital de Jolimont, Haine-Saint-Paul, Belgium.

INTRODUCTION: Nationwide studies are mandatory to assess changes in the epidemiology of HBV infection in Europe. AIM: To describe epidemiological characteristics of HBsAg-positive patients, especially inactive carriers, and to evaluate how practitioners manage HBV patients in real life. METHODS: Belgian physicians were asked to report all chronically infected HBV patients during a one-year period. RESULTS: Among 1,456 patients included, 1,035 (71%) were classified into one of four phases of chronic infection: immune tolerance (n = 10), HBeAg-positive hepatitis (n = 248), HBeAg-negative hepatitis (n = 420) and inactive carrier state (n = 357 HBeAg-negative patients with ALT <upper limit of normal (ULN) and HBV DNA <2,000 IU/mL). Using less restrictive criteria for ALT (1-2 ULN) or HBV DNA (2,000-20,000 IU/mL), 93 unclassified patients were added to the group of inactive carriers. These 93 additional inactive carriers were younger, more frequently males, with similar risk factors for HBV infection and histological features compared to inactive carriers according to recent guidelines. Recent guidelines on management of HBV patients were generally followed, but systematic HBV DNA measurements and HDV co-infection screening should be reinforced. CONCLUSION: In Belgium, an inactive carrier state was a common form of chronic HBV infection. Using less restrictive criteria for classification of inactive carriers did not modify their main characteristics and seemed better adapted to clinical practice. Recent guidelines on management of HBV patients should be reinforced.

Pourkarim, M. R., Amini-Bavil-Olyaee, S., Verbeeck, J., Lemey, P., Zeller, M., Rahman, M., Maes, P., Nevens, F. and Van Ranst, M. "**Molecular evolutionary analysis and mutational pattern of full-length genomes of hepatitis B virus isolated from Belgian patients with different clinical manifestations**." J Med Virol **2010** 82(3): 379-389.

Molecular evolutionary patterns of 62 HBV full-length genomes obtained from Belgian patients were characterized. Phylogenetic analysis revealed diverse HBV subgenotypes including A2 and A6 (46.8%), D1-D4 (38.8%), E (9.7%), C1 (1.6%), and B2 (1.6%). The study population consisted of patients with different ethnic origin (Caucasian, Turkish, Asian, Arab, and African). One HBV D/C recombinant isolate was identified, which encoded subtype adw2. An HBV subgenotype D4 with an aberrant subtype ayw4 was detected. Although none of the genotypes was associated with a specific disease outcome, several nucleotide substitutions, deletions and insertions were observed within the HBV preS1/S and X genes, particularly among patients with active chronic hepatitis B infection and patients with cirrhosis. Within the immunological domain of the HBsAg gene, the most frequent substitutions were sT125M and sT118A. High rates of precore and basal core promoter mutations were detected in patients infected with genotype D of HBV. Almost half of the patients who received lamivudine therapy for at least 1 year had HBV variants associated with lamivudine drug resistance. In conclusion, the most common HBV genotypes in West Europe (A and D) also prevail in Belgium. The highest degree of genetic diversity was detected in HBV genotype D. In addition, this study reveals the circulation of exotic HBV genotypes B, C, and E in Belgium. J. Med. Virol. 82:379-389, 2010. (c) 2010 Wiley-Liss, Inc.

Pourkarim, M. R., Verbeeck, J., Rahman, M., Amini-Bavil-Olyaee, S., Forier, A. M., Lemey, P., Maes, P. and Van Ranst, M. "**Phylogenetic analysis of hepatitis B virus full-length genomes reveals evidence for a large nosocomial outbreak in Belgium**." J Clin Virol **2009** 46(1): 61-68.

BACKGROUND: Hepatitis B virus (HBV) is primarily transmitted from mother to child, by sexual contact, intravenous drug abuse, or unsafe health care-related injection practices. Despite increased safety efforts, nosocomial acquired hepatitis B infection remains problematic. OBJECTIVES: A large HBV outbreak was investigated comprising 36 patients with acute HBV

infection in a primary care physician's practice. STUDY DESIGN: In a retrospective study (2003-2008), 36 serum samples from patients with acute HBV infection were collected. They had received several injections by the same physician at least 3 months before the onset of clinical symptoms. As a control group, sera were collected from HBV patients from other physicians from the same province. Full-length HBV genomes were amplified and were phylogenetically analysed. RESULTS: HBV complete genomes of 32 patients were successfully amplified and sequenced, and clustered together with the reference genotype A, subgenotype A2 strains. We also analysed 26 control HBV genotype A samples. All 32 HBV strains from the patient group clustered in a monophyletic branch with a bootstrap value of 100, whereas the control samples branched separately in another clade. The genetic distance value showed small differences within the patients group, whereas the rate within the control group was seven times higher. These observations confirm that the source of transmission was clearly different in both groups. CONCLUSION: Maximum likelihood analysis and genetic distance calculations based on the full-length genomes of HBV strains isolated from patients and controls provided strong evidence for a common nosocomial source of infection for all 32 patient cases.

Hepatitis C

Newsum, A. M., Stolte, I. G., van der Meer, J. T., Schinkel, J., van der Valk, M., Vanhommerig, J. W., Buve, A., Danta, M., Hogewoning, A. and Prins, M. "**Development and validation of the HCV-MOSAIC risk score to assist testing for acute hepatitis C virus (HCV) infection in HIV-infected men who have sex with men (MSM)**." Euro Surveill **2017** 22(21).

Current guidelines recommend hepatitis C virus (HCV) testing for HIV-infected men who have sex with men (MSM) with ongoing risk behaviour, without specifying the type of risk behaviour. We developed and validated the HCV-MOSAIC risk score to assist HCV testing in HIV-infected MSM. The risk score consisted of six self-reported risk factors identified using multivariable logistic regression using data from the Dutch MOSAIC study (n = 213, 2009-2013). Area under the ROC curve (AUC), sensitivity, specificity, post-test-probability-of-disease and diagnostic gain were calculated. The risk score was validated in case-control studies from Belgium (n = 142, 2010-2013) and the United Kingdom (n = 190, 2003-2005) and in cross-sectional surveys at a Dutch sexually transmitted infections clinic (n = 284, 2007-2009). The AUC was 0.82; sensitivity 78.0% and specificity 78.6%. In the validation studies sensitivity ranged from 73.1% to 100% and specificity from 56.2% to 65.6%. The post-test-probability-of-disease ranged from 5.9% to 20.0% given acute HCV prevalence of 1.7% to 6.4%, yielding a diagnostic gain of 4.2% to 13.6%. The HCV-MOSAIC risk score can successfully identify HIV-infected MSM at risk for acute HCV infection. It could be a promising tool to improve HCV testing strategies in various settings.

Nkuize, M., Mulkay, J. P., Moreno, C., Lasser, L., Michielsen, P., de Galocsy, C., Scheen, R., Assene, C. and Delwaide, J. "**Ethnic epidemiological profiles and antiviral therapy among patients infected with hepatitis C virus genotype 4: a multicenter study from Belgium**." Acta Gastroenterol Belg **2015** 78(4): 365-372

BACKGROUND: Hepatitis C virus genotype 4 (HCV-4) is the most prevalent genotype in Central Africa. AIM: To compare epidemiology, clinical characteristics and any differences in access to HCV therapy in two populations of HCV-4 patients residing in Belgium. METHODS: This multicenter study selected 473 HCV-4 patients from seven hospital databases and compared them according to ethnic origin, i.e., Black African (n=331) or not (n=142), for epidemiological, clinical, biological and histological characteristics. Interleukin 28B polymorphism (CC-genotype) was evaluated in a second cohort of 69 Black African and 30 non-Black African patients. RESULTS: Compared to other patients, the Black African patients were more likely to be female and were older, commonly overweight, frequently had abnormal glucose metabolism and arterial hypertension ; they were less likely to have dyslipidemia, a history of alcohol consumption or ALT elevation. The route of infection was more frequently unknown in Black African than in other patients. Black African patients had more HCV-4 subtypes, were less frequently of IL28B CC-genotype and had less severe liver fibrosis. The proportion of patients who received antiviral treatment was similar in the two groups.

CONCLUSION: In this Belgian cohort, patients with HCV-4 infection were more frequently of Black African origin than of other origin. Infected Black African patients were more commonly -female, older at diagnosis, and had more co-morbidities than other patients; they also had less advanced liver fibrosis than infected non-Black African patients and fewer had a CC genotype.

Van Damme, P., Laleman, W., Starkel, P., Van Vlierberghe, H., Vandijck, D., Hindman, S. J., Razavi, H. and Moreno, C. "**Hepatitis C epidemiology in Belgium**." Acta Gastroenterol Belg **2014** 77(2): 277-279

BACKGROUND: The burden of hepatitis C virus (HCV) infection is significant and is increasing with the aging population. The results of a modeling study that included Belgium, along with many other countries, was published in April 2014. An in depth discussion surrounding the epidemiology of HCV in Belgium will be presented here. METHODS: A systematic literature review was conducted to assess the historical and current clinical burden of HCV in Belgium. Two expert panels were convened to discuss the strengths and limitations surrounding the available data and to generate consensus regarding the best estimates for total number of HCV cases, number of cases diagnosed, and the number of patients treated and cured, including potential HCV control strategies. RESULTS: Although no national studies exist, there were an estimated 70,000 (10,000-91,000) viremic HCV infections in 1994. By 2010 there were an estimated 22,900 individuals diagnosed with viremic HCV, and in 2011 approximately 710 patients were treated annually. An estimated 13% of liver transplants were attributable to HCV in 2011. Genotype 1 predominated (59%), followed by genotypes 3 (19%) and 4 (14%). CONCLUSIONS: Estimates of HCV prevalence, diagnosed cases and liver transplants due to HCV were available through published studies. However these publications were subject to bias and were occasionally outdated. Improved estimates of HCV prevalence would be useful for informing treatment, prevention and policy efforts in Belgium.

De Vroey, B., Moreno, C., Laleman, W., van Gossum, M., Colle, I., de Galocsy, C., Langlet, P., Robaeys, G., Orlent, H., Michielsen, P., et al. "**Hepatitis B virus and hepatitis C virus infections in Belgium: similarities and differences in epidemics and initial management**." Eur J Gastroenterol Hepatol **2013** 25(5): 613-619.Department of Hepatogastroenterology, Hopital de Jolimont, Haine-Saint-Paul, Belgium.

INTRODUCTION: Nationwide studies comparing patients with hepatitis B and C virus (HBV and HCV) infections are mandatory for assessing changes in epidemiology. AIM: The aim of this study was to compare epidemiological data and initial management of newly diagnosed patients with persistent HBV (HBsAg positive) or HCV (detectable HCV RNA) infection in Belgium. PATIENTS AND METHODS: Data were extracted from two Belgian observational databases. RESULTS: A total of 655 patients (387 HBV and 268 HCV) were included. Compared with HCV patients, HBV patients were younger, more frequently men, more often of Asian or African origin (43 vs. 10%, P<0.0001), and less frequently contaminated by transfusion or intravenous drug use (9 and 6% vs. 34 and 44%, P<0.0001). Viral replication was assessed in 89% of HBV patients. Compared with HCV patients, HBV patients more frequently had normal alanine aminotransferase (ALT) levels (65 vs. 29%, P<0.0001), less frequently underwent liver biopsy (29 vs. 67%, P<0.0001), and were less often considered for antiviral therapy (25 vs. 54%, P<0.0001). When taking only HBV patients with detectable viral replication into consideration, results remained unchanged. During the multivariate analysis, ALT was a major factor for performing liver biopsy or considering antiviral therapy in both groups. CONCLUSION: HBV and HCV screening policies should be targeted toward immigrants and intravenous drug users, respectively. Guidelines recommending systematic search for viral replication should be reinforced in HBV patients. HBV patients less frequently underwent liver biopsy and were less often considered for antiviral therapy compared with HCV patients. Despite the lack of sensitivity and specificity, ALT remains a pivotal decision-making tool for liver biopsy and antiviral therapy in both infections.

Putzeys, V., Gerard, C., Bastens, B., Wain, E., Bataille, C., Defrance, P., Belaiche, J., Delwaide, J., Belaiche, J., Delwaide, J., et al. "**Hepatitis C of genotype 2: the role of medical invasive exams**." Acta Gastroenterol Belg **2011** 74(2): 277-280.C.H.U. Sart Tilman, Liege, Belgium.

BACKGROUND AND AIM: Hepatitis C virus genotype 2 is the third in order of

frequency in Belgium. The aim of this study was to better define the genotype 2 carriers' epidemiology characteristics. METHODS: In a database comprising 1726 viremic hepatitis C virus patient from the south part of Belgium, the files of 98 genotype 2 carriers were reviewed. RESULTS: There was a strong association between genotype 2 and the mode of transmission. The rate of contamination by invasive medical exams was very high (23%), and statistically different from the one of the others genotypes. Eligibility for antiviral therapies and the rate of sustained viral response were high. CONCLUSION: HCV genotype 2 was highly associated with transmission by invasive medical exams.

Verbeeck, J., Kwanten, L., D'Heygere, F., Beguin, A., Michiels, S., Desombere, I., Leroux-Roels, G., Lemey, P., Nevens, F. and Van Ranst, M. "**HCV genotype distribution in Flanders and Brussels (Belgium): unravelling the spread of an uncommon HCV genotype 5a cluster**." Eur J Clin Microbiol Infect Dis **2010** 29(11): 1427-1434.

In order to study the hepatitis C virus (HCV) epidemiology in Flanders, Belgium, the HCV genotype of 2,301 patients diagnosed with HCV between 2001 and 2009 was determined. HCV genotyping was conducted using the Versant LiPA 1.0 or Versant LiPA 2.0 assay. To explore the transmission history of a remarkable cluster of the rarely found HCV genotype 5a, face-to-face interviews based on detailed questionnaires and maximum likelihood phylogenetic analysis were performed. HCV genotype 1 was the most prevalent genotype in all provinces, followed by HCV genotype 3 in East Flanders, Antwerp, Flemish Brabant and Limburg. In Brussels, HCV genotype 4 was the second most prevalent genotype. This observation is due to the immigration of patients from the Middle East and Africa. Remarkably, a cluster of HCV genotype 5a was found in West Flanders, where it represents the second most prevalent genotype, accounting for 26.2% of HCV infections. We could not identify one major transmission source explaining the whole HCV genotype 5a epidemic. Instead, several smaller possible transmission chains were identified and confirmed phylogenetically. Overall, the HCV genotype 5a epidemic in West Flanders seems to be mainly associated with blood transfusion and unsafe medical practices.

De Maeght, S., Henrion, J., Bourgeois, N., de Galocsy, C., Langlet, P., Michielsen, P., Reynaert, H., Robaeys, G., Sprengers, D., Orlent, H., et al. "**A pilot observational survey of hepatitis C in Belgium**." Acta Gastroenterol Belg **2008** 71(1): 4-8.CH Jolimont, Haine Saint Paul. s.dm@scarlet.be

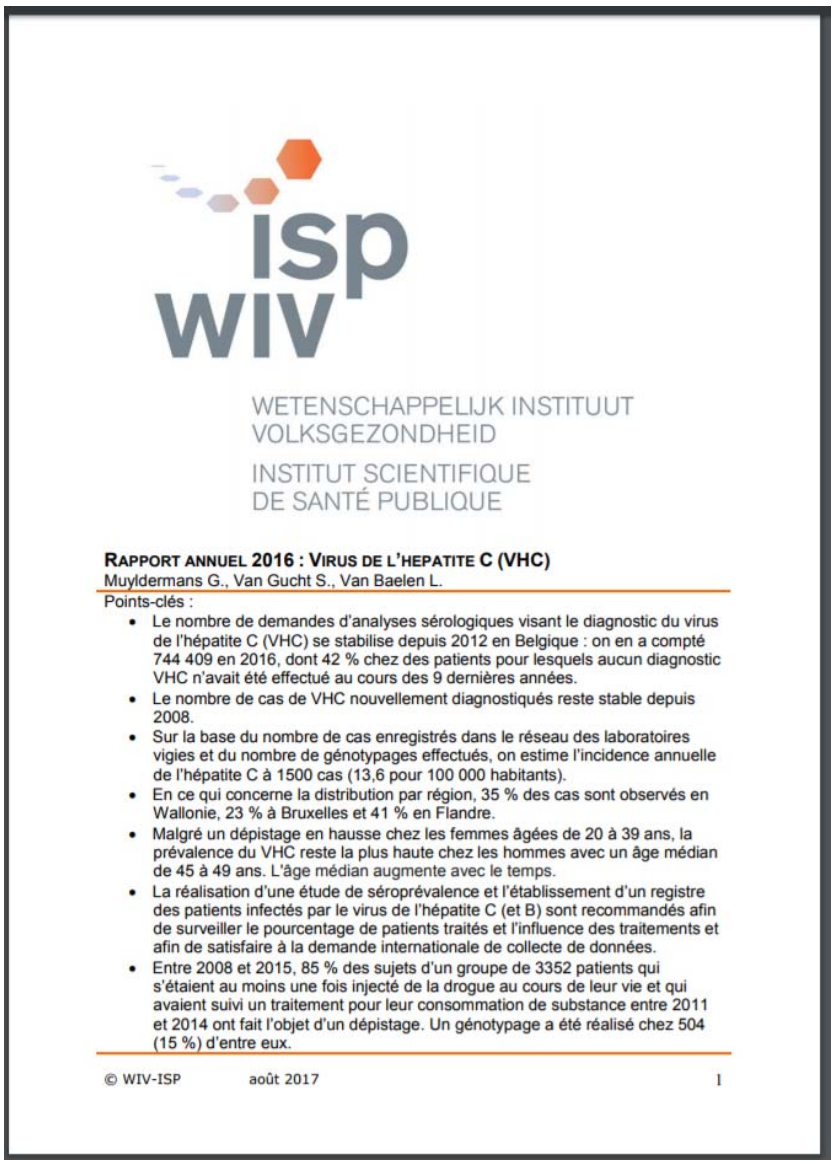
AIM OF THE STUDY: There is a lack of epidemiological data on hepatitis C (HCV) infected patients in Belgium. Therefore our purpose was to address this important question and to evaluate the feasibility of a national HCV observatory. PATIENTS AND METHODS: From November 2003 to November 2004, every new patient prospectively seen for HCV antibody positivity in 9 Belgian hospital centres was recorded and a standardised 10-items questionnaire was completed during the consultation, including a Quality of Live (QOL) visual analogue scale. RESULTS: Three hundred and eighteen consecutive patients were recruited. Fifty five percent were male with a median age of 45 y (11-87 y). The main risk factors for infection were IV drug use (27%), blood transfusion (23%), and invasive medical procedure (11%). On the QOL scale, ranging from 0 and 100, mean value was 61 +/- 31. Transaminases were abnormal in 66% with a median elevation 2 times above normal value. HCV RNA was positive in 87% with a viral load above 800 000 IU/ml in 42%. Genotype 1 was predominant (59%), followed by genotypes 3 (19%) and 4 (14%). A liver biopsy was performed in 190 patients, with minimal fibrosis (METAVIR F0-F1) in 43%, moderate fibrosis (F2) in 35% and advanced stages (F3-F4) in 22%. Antiviral treatment was not considered in 53% because of normal ALT (30%), old age (7%), minimal histological stage (6%) or patient refusal (4%). CONCLUSIONS: This study highlights the feasibility of a national HCV survey using a simple questionnaire. This pilot study could be generalised throughout Belgium, and, if repeated, could allow a regular assessment of the changes in epidemiology and management of HCV infection in our country.

Presentation related references:

Overview of surveillance system and epidemiology of hepatitis B and C

Provided by speaker: Gaëtan Muyldermans

Muyldermans G. Van Gucht S., Van Baelen L. Yearly annual epidemiologic report, (2016) – Instituut for public health (available in NL/FR)
https://nrchm.wiv-isp.be/fr/centres_ref_labo/hepatitis_b_d_d_e_et_viruses/Rapports/rapport%20HCV%202016.pdf



WETENSCHAPPELIJK INSTITUUT VOLKSGEZONDHEID

INSTITUT SCIENTIFIQUE DE SANTÉ PUBLIQUE

RAPPORT ANNUEL 2016 : VIRUS DE L'HEPATITE C (VHC)

Muyldermans G., Van Gucht S., Van Baelen L.

Points-clés :

- Le nombre de demandes d'analyses sérologiques visant le diagnostic du virus de l'hépatite C (VHC) se stabilise depuis 2012 en Belgique : on en a compté 744 409 en 2016, dont 42 % chez des patients pour lesquels aucun diagnostic VHC n'avait été effectué au cours des 9 dernières années.
- Le nombre de cas de VHC nouvellement diagnostiqués reste stable depuis 2008.
- Sur la base du nombre de cas enregistrés dans le réseau des laboratoires vigies et du nombre de génotypages effectués, on estime l'incidence annuelle de l'hépatite C à 1500 cas (13,6 pour 100 000 habitants).
- En ce qui concerne la distribution par région, 35 % des cas sont observés en Wallonie, 23 % à Bruxelles et 41 % en Flandre.
- Malgré un dépistage en hausse chez les femmes âgées de 20 à 39 ans, la prévalence du VHC reste la plus haute chez les hommes avec un âge médian de 45 à 49 ans. L'âge médian augmente avec le temps.
- La réalisation d'une étude de séroprévalence et l'établissement d'un registre des patients infectés par le virus de l'hépatite C (et B) sont recommandés afin de surveiller le pourcentage de patients traités et l'influence des traitements et afin de satisfaire à la demande internationale de collecte de données.
- Entre 2008 et 2015, 85 % des sujets d'un groupe de 3352 patients qui s'étaient au moins une fois injecté de la drogue au cours de leur vie et qui avaient suivi un traitement pour leur consommation de substance entre 2011 et 2014 ont fait l'objet d'un dépistage. Un génotypage a été réalisé chez 504 (15 %) d'entre eux.

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1.3.2 Viral hepatitis Disease burden (session 4)

Starkel, P., Vandijck, D., Laleman, W., Van Damme, P., Moreno, C., Blach, S., Razavi, H. and Van Vlierberghe, H. "**The Disease Burden of Hepatitis C in Belgium : An update of a realistic disease control strategy**." Acta Gastroenterol Belg **2015** 78(2): 228-232

BACKGROUND: This manuscript serves as an update to position papers published in 2014 based on the available Belgian hepatitis C virus (HCV) epidemiological data. METHODS: Building on the current standard of care (2015 : 900 >/= F3 patients treated with 70-85% SVR), four new scenarios were developed to achieve the goals of near viral elimination and prevention of HCV associated morbidity and mortality by 2026 and 2031. Increases in treatment efficacy were assumed in 2016 (90% SVR) and 2017 (95% SVR). RESULTS: Scenario 1: Treating 6,670 patients annually by 2018 (>/= F0 beginning in 2017) and diagnosing 3,790 patients annually by 2020, a 90% reduction in viremic cases and advanced outcomes was observed by 2026. Scenario 2: Treating 4,300 patients annually by 2018 (>/= F0 beginning in 2020) without increasing the number diagnosed, a 90% reduction in viremic cases and 85%-95% reduction in advanced outcomes was observed by 2031. Scenario 3: Treating 5,000 >/= F2 patients annually by 2018, and diagnosing 3,620 patients annually by 2020, a 90% reduction in advanced outcomes and 50% reduction in viremic cases was observed by 2026. Scenario 4: Treating 3,100 >/= F2 patients annually by 2018 without increasing the number diagnosed, a 90%-95% reduction in advanced outcomes and 55% reduction in viremic cases was observed by 2031. CONCLUSIONS: Scenario 2 would provide the most favorable balance of outcomes (90% reduction in viremic prevalence and advanced outcomes) and realistic requirements for implementation (gradual increase in treatment, delayed incorporation of patients with no/mild fibrosis).

Starkel, P., Vandijck, D., Laleman, W., Van Damme, P., Moreno, C., Hindman, S., Razavi, H. and Van Vlierberghe, H. "**The disease burden of hepatitis C in Belgium: development of a realistic disease control strategy.**" Acta Gastroenterol Belg **2014** 77(2): 280-284

BACKGROUND: Novel direct antiviral agents (DAAs) will become available soon with higher sustained viral response (SVR), fewer side-effects and higher compliance. Our aim was to evaluate different realistic strategies to control the projected increase in HCV-related disease burden in Belgium. METHODS: Based on literature review, expert opinions and historical assumptions, HCV-disease progression and mortality in Belgium was modeled to 2030. Strategies exploring the impact of increased treatment, treatment delay, and treatment restrictions were developed. RESULTS: Although the overall HCV prevalence is decreasing in Belgium, the burden of advanced stage HCV, including cirrhosis and hepatocellular carcinoma (HCC), is expected to increase under current treatment and cure rates. By increasing SVR to 90% from 2016 onward and the number of treated cases (from 710 to 2,050), in 2030 the cases with cirrhosis, decompensated cirrhosis and HCC would be significantly lower than in 2013. This strategy was found most efficient when applied to F2-F4 cases. To obtain comparable outcomes with F0-F4 cases, 3,490 patients should be treated. A two year delayed access to the DAAs increased HCV related morbidity and mortality by 15% relative to our strategy. CONCLUSIONS: Considering the evolving burden of HCV disease and the need for efficacious usage of healthcare resources, primary application of new DAAs in Belgium should focus on patients with significant and advanced fibrosis (F2-F4), providing these new drugs without delay upon availability and increasing access to therapy.

Nevens, F., Colle, I., Michielsen, P., Robaeys, G., Moreno, C., Caekelbergh, K., Lamotte, M. and Wyffels, V. "**Resource use and cost of hepatitis C-related care**." Eur J Gastroenterol Hepatol **2012** 24(10): 1191-1198.

BACKGROUND: Chronic hepatitis because of the hepatitis C virus (CHC) is a major health problem that can lead to decompensated cirrhosis, hepatocellular carcinoma, and eventually death, all of which are associated with significant healthcare costs. AIM: To update the cost of care of CHC according to the different severity stages of the disease in a west European country (Belgium). METHODS: Medical records of 157 patients, who were referred to the medical specialist at different stages of disease, were reviewed to identify the medical costs over a follow-up period of 3 years or 2 years in the case of liver transplantation (LT). Six disease stages were defined on the basis of histology (Metavir classification) and/or clinical data. RESULTS: In

comparison with mild disease, the cost increased 1.6 times in the case of decompensated cirrhosis, 1.9 times in the case of hepatocellular carcinoma, and 3.4 in the case of LT. The costs for medication, hospitalization, and ambulatory care were, respectively, on the one hand, 81, 8, and 11% for mild disease and, on the other, 18, 79, and 3% for LT. In the case of a sustained viral response, the cost of follow-up within 3 years decreased by 45% for patients with mild and moderate disease. CONCLUSION: Antiviral treatment is the most important factor governing cost in mild and moderate disease, but once complications of CHC occur, hospitalization costs far exceed the cost of antiviral therapy. Already during the first 3 years of follow-up, sustained viral response decreased the cost significantly. Treatment of patients with CHC in an early stage has the potential to be cost-effective.

Presentation related references:

Chronic viral hepatitis and liver disease in Belgium

Provided by speaker: Pierre Deltenre

1. Deuffic-Burban S, Deltenre P, Buti M, Stroffolini T, Parkes J, Mühlberger N, Siebert U, Moreno C, Hatzakis A, Rosenberg W, Zeuzem S, Mathurin P. Predicted effects of treatment for HCV infection vary among European countries. Gastroenterology 2012;143:974-85.

   BACKGROUND & AIMS: The dynamics of hepatitis C virus (HCV) infection, as well as screening practices and access to therapy, vary among European countries. It is important to determine the magnitude of the effects of such differences on incidence and mortality of infection. We compared the dynamics of infection and screening and treatment practices among Belgium, France, Germany, Italy, Spain, and the United Kingdom. We also assessed the effects of treatment with pegylated interferon and additional effects of triple therapy with protease inhibitors. METHODS: We created a country-specific Markov model of HCV progression based on published epidemiologic data (on HCV prevalence, screening, genotype, alcohol consumption among patients, and treatments) and reports of competitive and hepatocellular carcinoma mortality for the 6 countries. The model was used to predict the incidence of HCV-related cirrhosis and its mortality until 2021 for each country. RESULTS: From 2002 to 2011, antiviral therapy reduced the cumulative incidence of cirrhosis by 7.1% and deaths by 3.4% overall. Reductions in incidence and mortality values ranged from 4.0% and 1.9%, respectively, in Italy to 16.3% and 9.0%, respectively, in France. From 2012 to 2021, antiviral treatment of patients with HCV genotype 1 infection that includes protease inhibitor-based triple therapy will reduce the cumulative incidence of cirrhosis by 17.7% and mortality by 9.7% overall. The smallest reduction is predicted for Italy (incidence reduced by 10.1% and mortality by 5.4%) and the highest is for France (reductions of 34.3% and 20.7%, respectively). CONCLUSIONS: Although HCV infection is treated with the same therapies in different countries, the effects of the therapies on morbidity and mortality vary significantly. In addition to common guidelines that are based on virologic response-guided therapy, there is a need for public health policies based on population-guided therapy.

2. De Vroey B, Moreno C, Laleman W, van Gossum M, Colle I, de Galocsy C, Langlet P, Robaeys G, Orlent H, Michielsen P, Delwaide J, Reynaert H,

D'Heygere F, Sprengers D, Bourgeois S, Assene C, Vos B, Brenard R, Adler M, Henrion J, Deltenre P. HBV and HCV infections in Belgium: similarities and differences in epidemics and in initial management. Eur J Gastroenterol Hepatol 2013;25:613-19.

INTRODUCTION: Nationwide studies comparing patients with hepatitis B and C virus (HBV and HCV) infections are mandatory for assessing changes in epidemiology. AIM: The aim of this study was to compare epidemiological data and initial management of newly diagnosed patients with persistent HBV (HBsAg positive) or HCV (detectable HCV RNA) infection in Belgium. PATIENTS AND METHODS: Data were extracted from two Belgian observational databases. RESULTS: A total of 655 patients (387 HBV and 268 HCV) were included. Compared with HCV patients, HBV patients were younger, more frequently men, more often of Asian or African origin (43 vs. 10%, P<0.0001), and less frequently contaminated by transfusion or intravenous drug use (9 and 6% vs. 34 and 44%, P<0.0001). Viral replication was assessed in 89% of HBV patients. Compared with HCV patients, HBV patients more frequently had normal alanine aminotransferase (ALT) levels (65 vs. 29%, P<0.0001), less frequently underwent liver biopsy (29 vs. 67%, P<0.0001), and were less often considered for antiviral therapy (25 vs. 54%, P<0.0001). When taking only HBV patients with detectable viral replication into consideration, results remained unchanged. During the multivariate analysis, ALT was a major factor for performing liver biopsy or considering antiviral therapy in both groups. CONCLUSION: HBV and HCV screening policies should be targeted toward immigrants and intravenous drug users, respectively. Guidelines recommending systematic search for viral replication should be reinforced in HBV patients. HBV patients less frequently underwent liver biopsy and were less often considered for antiviral therapy compared with HCV patients. Despite the lack of sensitivity and specificity, ALT remains a pivotal decision-making tool for liver biopsy and antiviral therapy in both infections.

3. Vandenbulcke H, Moreno C, Colle I, Knebel JF, Francque S, Sersté T, George C, de Galocsy C, Laleman W, Delwaide J, Orlent H, Lasser L, Trépo E, Van Vlierberghe H, Michielsen P, van Gossum M, de Vos M, Marot A, Doerig C, Adler M, Henrion J, Deltenre P. Alcohol intake increases the risk of hepatocellular carcinoma in patients with HCV-related compensated cirrhosis: a prospective study. J Hepatol 2016;65:543-61.

BACKGROUND & AIMS: Whether alcohol intake increases the risk of complications in patients with HCV-related cirrhosis remains unclear. The aim of this study was to determine the impact of alcohol intake and viral eradication on the risk of hepatocellular carcinoma (HCC), decompensation of cirrhosis and death. METHODS: Data on alcohol intake and viral eradication were prospectively collected in 192 patients with compensated HCV-related cirrhosis. RESULTS: 74 patients consumed alcohol (median alcohol intake: 15g/day); 68 reached viral eradication. During a median follow-up of 58months, 33 patients developed HCC, 53 experienced at least one decompensation event, and 39 died. The 5-year cumulative incidence rate of HCC was 10.6% (95% CI: 4.6-16.6) in abstainers vs. 23.8% (95% CI: 13.5-34.1) in consumers (p=0.087), and 2.0% (95% CI: 0-5.8) vs. 21.7% (95% CI: 14.2-29.2) in patients with and without viral eradication (p=0.002), respectively. The lowest risk of HCC was observed for patients without alcohol intake and with viral eradication (0%) followed by patients with alcohol intake and viral eradication (6.2% [95% CI: 0-18.4]),

patients without alcohol intake and no viral eradication (15.9% [95% CI: 7.1-24.7]), and patients with alcohol intake and no viral eradication (29.2% [95% CI: 16.5-41.9]) (p=0.009). In multivariate analysis, lack of viral eradication and alcohol consumption were associated with the risk of HCC (hazard ratio for alcohol consumption: 3.43, 95% CI: 1.49-7.92, p=0.004). Alcohol intake did not influence the risk of decompensation or death. CONCLUSIONS: Light-to-moderate alcohol intake increases the risk of HCC in patients with HCV-related cirrhosis. Patient care should include measures to ensure abstinence. LAY SUMMARY: Whether alcohol intake increases the risk of complications in patients with HCV-related cirrhosis remains unclear. In this prospective study, light-to-moderate alcohol intake was associated with the risk of hepatocellular carcinoma in multivariate analysis. No patients who did not use alcohol and who reached viral eradication developed hepatocellular carcinoma during follow-up. The risk of hepatocellular carcinoma increased with alcohol intake or in patients without viral eradication and was highest when alcohol intake was present in the absence of viral eradication. Patients with HCV-related cirrhosis should be strongly advised against any alcohol intake. Patient care should include measures to ensure abstinence.

4. Marot A, Henrion J, Knebel JF, Moreno C, Deltenre P. Alcoholic liver disease confers a worse prognosis than HCV infection and non-alcoholic fatty liver among patients with cirrhosis. In press (PlosOne). [No Abstract]

1.3.3 Prevention of viral hepatitis (session 5)

Vaccin - Hepatitis A

Luyten, J., Van de Sande, S., de Schrijver, K., Van Damme, P. and Beutels, P. "**Cost-effectiveness of hepatitis A vaccination for adults in Belgium**." Vaccine **2012** 30(42): 6070-6080.Centre for Health Economics Research and Modelling Infectious Diseases, Vaccine and Infectious Disease Institute, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Antwerp, Belgium. Jeroen.Luyten@ua.ac.be

Hepatitis A vaccination targeting adults (or adult risk-groups like e.g. travellers, health care workers, soldiers or teachers) could be considered an alternative to a universal infant or adolescent vaccination program in low endemic countries. We estimated the current disease burden of hepatitis A in Belgium, and evaluated whether adult vaccination is cost-effective. We used a Markov cohort model to simulate the costs and effects of (1) vaccination of adults and (2) serological screening of adults and vaccination of susceptibles and compared these with the current situation. The results indicated that these expanded vaccination strategies are not cost-effective in the epidemiological circumstances of a typical low-endemic western country. In order to gain 1 quality-adjusted life year the health care payer would have to pay 185,000euro for vaccination and 223,000euro for screening and vaccination of seronegatives. For adult vaccination to be cost-effective, risk-groups would need to be exposed to a force of infection that is 3.5-4 times higher than currently estimated in the general population; or the total costs of vaccination would have to drop with approximately 75%.

Vaccin - Hepatitis B

Robert, E., Dramaix, M. and Swennen, B. "**Vaccination coverage for infants: cross-sectional studies in two regions of Belgium**." Biomed Res Int **2014** 2014: 838907.

Research Center of Epidemiology, Biostatistics and Clinical Research, School of Public Health, Universite Libre de Bruxelles, Route de Lennik 808, 1070 Brussels, Belgium.

METHODS AND OBJECTIVES: To estimate infant vaccination coverage in the French-speaking region of Belgium (Wallonia) and in the Brussels-Capital Region, two cross-sectional studies were performed in 2012. A face-to-face questionnaire was administered by trained investigators. The objective was to evaluate infant vaccination coverage retrospectively in 18- to 24-month-old children. These studies offered the opportunity to assess some factors influencing vaccine uptake in infants. RESULTS AND DISCUSSION: Approximately 99% of the children had received the first dose of IPV-DTaP, 90% the fourth dose, 94% the MMR vaccine, 97% the first dose of pneumococcal vaccine, and 90% the third dose. In both regions, when fitting a logistic model, the most associated factor was attendance at maternal and child clinics (MCH). No association was observed between vaccination coverage and the mother's level of education. For the last immunization session, where the mother was a Belgian native and when she worked more hours, child was better immunized, but only in Brussels. CONCLUSION: Coverage for the fourth dose of hexavalent vaccine (DTaP-IPV-HBV/Hib) needs to be increased. Indeed, additional effort is needed to increase HIB and pertussis coverage rates because the herd immunity threshold for these two diseases has not been reached.

Theeten, H., Hutse, V., Hoppenbrouwers, K., Beutels, P. and P, V. A. N. D. "**Universal hepatitis B vaccination in Belgium: impact on serological markers 3 and 7 years after implementation**." Epidemiol Infect **2014** 142(2): 251-261.Center for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerp, Belgium.

Scientific Institute of Public Health, Virology Section, Brussels, Belgium.

Centre of Youth Health Care, University of Leuven, Belgium.

Hepatitis B virus (HBV) can be eliminated by effective universal vaccination. In Belgium, a free-of-charge HBV vaccination programme in infants with catch-up in adolescents was introduced in 1999. To evaluate the effects in <20-year-olds, seroprotection (anti-HBs >11 mIU/ml, according to the assay) and markers of infection (anti-HBc, HBsAg) were assessed in 2443 residual sera collected 7-8 years after implementation of the programme. The maximal prevalence of a solely anti-HBs seroprotective ('vaccinated') serostatus was 82.9% at age 1 year and 60.5% at age 13 years. A clear increase was found in age cohorts targeted by the campaign after a similar serosurvey conducted 4 years earlier. The prevalence of HBV infection remained unchanged at a low level (1.8% in 2006) similar to pre-vaccination data (1993-1994). We conclude that universal HBV vaccination has achieved overall high levels of vaccine-induced immunity, despite regional variations, which may give rise to pockets of susceptible young adults in the future.

Vaccine coverage

Flanders – Report NL

Studie van de vaccinatiegraad in Vlaanderen
2016

Uitgevoerd in opdracht van:

VLAAMSE OVERHEID
Vlaams Agentschap Zorg en Gezondheid
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VaxInfo

Résultats

Couvertures vaccinales et types de vaccins utilisés

Le schéma recommandé en FWB prévoit l'administration de 9 doses de vaccins réparties en 5 consultations médicales décrites dans le tableau ci-dessous qui présente le calendrier vaccinal en vigueur depuis 2010.

Tableau 1. Calendrier vaccinal en FWB

Calendrier	Séance	Vaccin
à 8 semaines	1	DTPa-IPV-Hib-VHB1 + Pneumo1 + (Rotavirus)
à 12 semaines	2	DTPa-IPV-Hib-VHB2 + (Rotavirus)
à 16 semaines	3	DTPa-IPV-Hib-VHB3 + Pneumo2 + (Rotavirus)
à 12 mois	4	RRO + Pneumo3
à 15 mois	5	DTPa-IPV-Hib-VHB4+ MénC

Les vaccins nécessaires sont distribués par la FWB et sont donc gratuits pour les parents, à l'exception du vaccin contre le Rotavirus qui n'est pas disponible gratuitement mais remboursé en partie.

Le tableau ci-dessous présente les taux de couvertures pour ces différentes doses. Les quatre premières lignes du tableau représentent la couverture selon le schéma recommandé et réalisé avec les types de vaccins distribués par la FWB.
Plus de 98% des enfants reçoivent la première dose de vaccin Hexavalent et plus de 97% leur première dose de Pneumocoque.
Pour les vaccins Rotavirus (3 dernières lignes), trois quarts des enfants vaccinés l'ont été avec le Rotarix®, un quart avec le Rotateq®.

Tableau 2. Couverture vaccinale selon le type de vaccin disponible en Fédération Wallonie-Bruxelles

Vaccin	1ère séance	2ème séance	3ème séance	4ème séance	5ème séance
	8 semaines	12 semaines	16 semaines	12 mois	15 mois
Hexavalent	**98.8** (98.0-99.8)	**98.5** (97.5-99.5)	**98.2** (97.0-99.3		**92.3** (90.1-94.5)
Pneumocoque	**97.6** (96.3-98.9)		**96.9** (95.4-98.3)	**92.9** (90.7-95.0)	
RRO				**95.6** (93.9-96.4)	
Méningocoque					**91.2** (88.8-93.6)
Rotarix®	**69.0** (65.2-72.9)	**67.0** (63.1-71.0)			
RotaTeq®	**21.2** (17.8-24.7)	**20.3** (17.0-23.7)	**20.1** (16.8-23.5)		
Total Rotavirus			**87,1**		

Près de 87% des enfants ont reçu les 9 doses recommandées et un peu moins de 80% le schéma complet incluant le vaccin contre le Rotavirus.

Par ailleurs, peu d'enfants dans l'enquête ont reçu un schéma différent de celui recommandé par la FWB. Les vaccins Tétravalent et Hib, IPV et hépatite B ont été administrés à moins de 1% de l'échantillon.

De façon générale, les taux de protection trouvés en Wallonie, ne sont pas éloignés des objectifs de l'OMS et ceux trouvés dans la littérature.

Presentation related references

Vaccination program in Belgium

Provided by speaker: Geert Top (Flanders) – Ingrid Morales(Wallonia)

Presentation related references

Clinics, Treatment and Prevention of viral hepatitis E.

Provided by speaker: Thomas Vanwolleghem

1. Euro Surveill. 2017;22(16):pii=30514.

Domanovic, D., Tedder, R., Blumel, J., Zaaijer, H., Gallian, P., Niederhauser, C., Sauleda Oliveras, S., O'Riordan, J., Boland, F., Harritshoj, L., et al. "**Hepatitis E and blood donation safety in selected European countries: a shift to screening?**" Euro Surveill **2017** 22(16).

The public health implications of hepatitis E virus (HEV) in Europe have changed due to increasing numbers of hepatitis E cases and recent reports of chronic, persistent HEV infections associated with progression to cirrhosis in immunosuppressed patients. The main infectious risk for such immunosuppressed patients is exposure to undercooked infected pork products and blood transfusion. We summarised the epidemiology of HEV infections among blood donors and also outlined any strategies to prevent transfusion-transmitted HEV, in 11 European countries. In response to the threat posed by HEV and related public and political concerns, most of the observed countries determined seroprevalence of HEV in donors and presence of HEV RNA in blood donations. France, Germany, Spain and the United Kingdom (UK) reported cases of transfusion-transmitted HEV. Ireland and the UK have already implemented HEV RNA screening of blood donations; the Netherlands will start in 2017. Germany and France perform screening for HEV RNA in several blood establishments or plasma donations intended for use in high-risk patients respectively and, with Switzerland, are considering implementing selective or universal screening nationwide. In Greece, Portugal, Italy and Spain, the blood authorities are evaluating the situation. Denmark decided not to implement the HEV screening of blood donations.

2. N Engl J Med 2014;370:1111

Kamar, N., Izopet, J., Tripon, S., Bismuth, M., Hillaire, S., Dumortier, J., Radenne, S., Coilly, A., Garrigue, V., D'Alteroche, L., et al. "**Ribavirin for chronic hepatitis E virus infection in transplant recipients**." N Engl J Med **2014** 370(12): 1111-1120.

BACKGROUND: There is no established therapy for hepatitis E virus (HEV) infection. The aim of this retrospective, multicenter case series was to assess the effects of ribavirin as monotherapy for solid-organ transplant recipients with prolonged HEV viremia. METHODS: We examined the records of 59 patients who had received a solid-organ transplant (37 kidney-transplant recipients, 10 liver-transplant recipients, 5 heart-transplant recipients, 5 kidney and pancreas-transplant recipients, and 2 lung-transplant recipients). Ribavirin therapy was initiated a median of 9 months (range, 1 to 82) after the diagnosis of HEV infection at a median dose of 600 mg per day (range, 29 to 1200), which was equivalent to 8.1 mg per kilogram of body weight per day (range, 0.6 to 16.3). Patients received ribavirin for a median of 3 months (range, 1 to 18); 66% of the patients received ribavirin for 3 months or less. RESULTS: All the patients had HEV viremia when ribavirin was initiated (all 54 in whom genotyping was performed had HEV genotype 3). At the end of therapy, HEV clearance was observed in 95% of the patients. A recurrence of HEV replication occurred in 10 patients after ribavirin was stopped. A sustained virologic response, defined as an undetectable serum HEV RNA level at least 6 months after cessation of ribavirin therapy, occurred in 46 of the 59 patients (78%). A sustained virologic response was also observed in 4 patients who had a recurrence and were re-treated for a

longer period. A higher lymphocyte count when ribavirin therapy was initiated was associated with a greater likelihood of a sustained virologic response. Anemia was the main identified side effect and required a reduction in ribavirin dose in 29% of the patients, the use of erythropoietin in 54%, and blood transfusions in 12%. CONCLUSIONS: This retrospective, multicenter study showed that ribavirin as monotherapy may be effective in the treatment of chronic HEV infection; a 3-month course seemed to be an appropriate duration of therapy for most patients.

3. Lancet, 2014. **384**(9956): p. 1766-73.

Hewitt, P. E., Ijaz, S., Brailsford, S. R., Brett, R., Dicks, S., Haywood, B., Kennedy, I. T., Kitchen, A., Patel, P., Poh, J., et al. "**Hepatitis E virus in blood components: a prevalence and transmission study in southeast England**." Lancet **2014** 384(9956): 1766-1773.

BACKGROUND: The prevalence of hepatitis E virus (HEV) genotype 3 infections in the English population (including blood donors) is unknown, but is probably widespread, and the virus has been detected in pooled plasma products. HEV-infected donors have been retrospectively identified through investigation of reported cases of possible transfusion-transmitted hepatitis E. The frequency of HEV transmission by transfusion and its outcome remains unknown. We report the prevalence of HEV RNA in blood donations, the transmission of the virus through a range of blood components, and describe the resulting morbidity in the recipients. METHODS: From Oct 8, 2012, to Sept 30, 2013, 225,000 blood donations that were collected in southeast England were screened retrospectively for HEV RNA. Donations containing HEV were characterised by use of serology and genomic phylogeny. Recipients, who received any blood components from these donations, were identified and the outcome of exposure was ascertained. FINDINGS: 79 donors were viraemic with genotype 3 HEV, giving an RNA prevalence of one in 2848. Most viraemic donors were seronegative at the time of donation. The 79 donations had been used to prepare 129 blood components, 62 of which had been transfused before identification of the infected donation. Follow-up of 43 recipients showed 18 (42%) had evidence of infection. Absence of detectable antibody and high viral load in the donation rendered infection more likely. Recipient immunosuppression delayed or prevented seroconversion and extended the duration of viraemia. Three recipients cleared longstanding infection after intervention with ribavirin or alteration in immunosuppressive therapy. Ten recipients developed prolonged or persistent infection. Transaminitis was common, but short-term morbidity was rare; only one recipient developed apparent but clinically mild post-transfusion hepatitis. INTERPRETATION: Our findings suggest that HEV genotype 3 infections are widespread in the English population and in blood donors. Transfusion-transmitted infections rarely caused acute morbidity, but in some immunosuppressed patients became persistent. Although at present blood donations are not screened, an agreed policy is needed for the identification of patients with persistent HEV infection, irrespective of origin, so that they can be offered antiviral therapy. FUNDING: Public Health England and National Health Service Blood and Transplant.

4. EFSA journal doi: 10.2903/j.efsa.2017.4886

Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen

EFSA Panel on Biological Hazards (BIOHAZ),Antonia Ricci, Ana Allende, Declan Bolton, Marianne Chemaly, Robert Davies,Pablo Salvador Fernandez Escamez, Lieve Herman, Kostas Koutsoumanis, Roland Lindqvist,Birgit Nørrung, Lucy Robertson, Giuseppe Ru, Moez Sanaa, Marion Simmons,Panagiotis Skandamis, Emma Snary, Niko Speybroeck, Benno Ter Kuile, John Threlfall,Helene Wahlstr€om, Ilaria Di Bartolo, Reimar Johne, Nicole Pavio, Saskia Rutjes,Wim van der Poel, Petra Vasickova, Michaela Hempen, Winy Messens, Valentina Rizzi, Franxesca Latronico, Ronsina Girones

Hepatitis E virus (HEV) is an important infection in humans in EU/EEA countries, and over the last 10 years more than 21,000 acute clinical cases with 28 fatalities have been notified with an overall 10-fold increase in reported HEV cases; the majority (80%) of cases were reported from France, Germany and the UK. However, as infection in humans is not notifiable in all Member States, and surveillance differs between countries, the number of reported cases is not

comparable and the true number of cases would probably be higher. Food-borne transmission of HEV appears to be a major route in Europe; pigs and wild boars are the main source of HEV. Outbreaks and sporadic cases have been identified in immune-competent persons as well as in recognised risk groups such as those with preexisting liver damage, immunosuppressive illness or receiving immunosuppressive treatments. The opinion reviews current methods for the detection, identification, characterisation and tracing of HEV in food-producing animals and foods, reviews literature on HEV reservoirs and food-borne pathways, examines information on the epidemiology of HEV and its occurrence and persistence in foods, and investigates possible control measures along the food chain. Presently, the only efficient control option for HEV infection from consumption of meat, liver and products derived from animal reservoirs is sufficient heat treatment. The development of validated quantitative and qualitative detection methods, including infectivity assays and consensus molecular typing protocols, is required for the development of quantitative microbial risk assessments and efficient control measures. More research on the epidemiology and control of HEV in pig herds is required in order to minimise the proportion of pigs that remain viraemic or carry high levels of virus in intestinal contents at the time of slaughter. Consumption of raw pig, wild boar and deer meat products should be avoided.

5.J Hepatol 2016 ;65:200

Debing, Y., Moradpour, D., Neyts, J. and Gouttenoire, J. "**Update on hepatitis E virology: Implications for clinical practice**." J Hepatol **2016** 65(1): 200-212.

Hepatitis E virus (HEV) is a positive-strand RNA virus transmitted by the fecal-oral route. The 7.2kb genome encodes three open reading frames (ORF) which are translated into (i) the ORF1 polyprotein, representing the viral replicase, (ii) the ORF2 protein, corresponding to the viral capsid, and (iii) the ORF3 protein, a small protein involved in particle secretion. Although HEV is a non-enveloped virus in bile and feces, it circulates in the bloodstream wrapped in cellular membranes. HEV genotypes 1 and 2 infect only humans and cause mainly waterborne outbreaks. HEV genotypes 3 and 4 are widely represented in the animal kingdom and are transmitted as a zoonosis mainly via contaminated meat. HEV infection is usually self-limited but may persist and cause chronic hepatitis in immunocompromised patients. Reduction of immunosuppressive treatment or antiviral therapy with ribavirin have proven effective in most patients with chronic hepatitis E but therapy failures have been reported. Alternative treatment options are needed, therefore. Infection with HEV may also cause a number of extrahepatic manifestations, especially neurologic complications. Progress in the understanding of the biology of HEV should contribute to improved control and treatment of HEV infection.

Presentation related references

Hepatitis A outbreak: epidemiology and management

Provided by speaker: Naïma Hammami

1. European Centre for Disease Prevention and Control. Epidemiological update: hepatitis A outbreak in the EU/EEA mostly affecting men who have sex with men. 2017, https://ecdc.europa.eu/en/news-events/epidemiological-update-hepatitis-outbreak-eueea-mostly-affecting-men-who-have-sex-men , accessed on 25 October 2017.
2. European Centre for Disease Prevention and Control. Rapid risk assessment: Hepatitis A outbreaks in the EU/EEA mostly affecting men who have sex with men, 2nd update, 19 May 2017. https://ecdc.europa.eu/en/publications-

data/rapid-risk-assessment-hepatitis-outbreaks-eueea-mostly-affecting-men-who-have-0 , accessed on 25 October 2017.
3. European Centre for Disease Prevention and Control. Rapid Risk Assessment: Potential public health risks related to communicable diseases at the WorldPride festival in Madrid, 23 June–2 July 2017. https://ecdc.europa.eu/en/rapid-risk-assessment-worldpride-festival-spain , accessed on 25 October 2017.
4. Federaal Kenniscentrum voor de Gezondheidszorg 2008. Evaluatie van universele en doelgroep hepatitis A vaccinatie opties in België. *KCE reports vol. 98A.* https://kce.fgov.be/sites/default/files/atoms/files/d20081027388.pdf , accessed on 25 October 2017.

1.3.4 Hepatitis in different risk groups (session 6)

Co-infections

Gunter, J., Callens, S., De Wit, S., Goffard, J. C., Moutschen, M., Darcis, G., Meuris, C., van den Bulcke, C., Fombellida, K., Del Forge, M., Razavi H., Wyndham-Thomas C."**Prevalence of non-infectious comorbidities in the HIV-positive population in Belgium: a multicenter, retrospective study**." Acta Clin Belg **2017**: 1-4.a

OBJECTIVES: In Belgium, eleven AIDS Reference Centers (ARCs) and seven AIDS Reference Laboratories diagnose and treat HIV-positive individuals and track patients under care. As AIDS-related deaths are avoided and the HIV-positive population ages, non-infectious comorbidities (NICMs), such as cardiovascular disease, renal disease and certain cancers, play a larger role in the quality and length of patients' lives. This study aims to characterize the HIV-positive population in Belgium in terms of the prevalence of key NICMs. METHODS: We performed a retrospective study of 5787 HIV-positive patients under follow-up at four ARCs across Belgium between 1st of June 2014 and 1st of July 2016. RESULTS: The mean age of patients under follow-up was 46.7 (SD = 11.6) years, and the mean nadir CD4 count was 268.8 cells/mm3 (SD = 189.5). The prevalence of diabetes mellitus, arterial hypertension and chronic kidney disease (CKD) were 5.9, 31 and 7.8%, respectively. Cardiovascular events, defined as the occurrence of myocardial infarction, stroke or an invasive coronary procedure, occurred in 2.9% of patients. The highest age-adjusted mortality rates were observed among patients 51-55 years of age. Mortality rates were also higher among patients with CKD and patients with viremic hepatitis C virus ($p < 0.05$). CONCLUSIONS: Helping the aging HIV-positive population avoids premature morbidity and mortality from NICMs represents a key challenge to further improve patient outcomes. Belgium has an advanced system of HIV care and patient management; however, standardized data collection across ARCs is needed to improve knowledge sharing and to support future countrywide analyses.

Wyndham-Thomas, C., Delforge, M., Mulkay, J. P. and De Wit, S. "**Barriers to liver transplantation in HIV infected patients**." Acta Clin Belg **2013** 68(5): 349-355.

OBJECTIVES: Liver disease is one of the most frequent causes of non AIDS related deaths in HIV patients and transplantation has become a therapeutic option. In spite of this progress, no liver transplantation has ever been recorded for the patients of the Brussels Saint-Pierre HIV Cohort. The aim of this study is to identify the barriers to liver transplantation in HIV patients that arise in our practice. METHODS: All patients enrolled in the Brussels Saint-Pierre HIV

Cohort presenting a theoretical indication for liver transplantation, as recommended by the AASLD, between 01/01/2002 and 01/07/2010 were considered. The reasons for not retaining these patients as candidates for liver transplantation were classified as HIV or non-HIV related. RESULTS: Nineteen patients were identified. All patients presented an HBV and/or HCV co-infection. Indication for liver transplantation was based on first severe complication of cirrhosis for 15 patients, hepatocellular carcinoma fulfilling the Milan criteria for 2 and chronic liver failure for 2 others. Three patients could have been transplantation candidates but only one was enlisted and died prior to transplantation whilst alternative treatments were chosen for the remaining two. Among the non candidates, 5 couldn't be enlisted for HIV-related reasons, 3 for non HIV related reasons and 8 on multifactorial grounds; non adherence to treatment, alcohol abuse, psychiatric disease and hepatotoxicities playing key roles. Eleven patients died, all within 12 months of their first major complication of cirrhosis. CONCLUSIONS: The undeniable medical progress that liver transplantation represents for HIV-infected individuals is, in practise, limited; only a minority of patients with an indication of liver transplant will fulfill the necessary criteria for enlistment. General awareness of this issue and early referral are essential to optimize pre-transplant management and increase the number of HIV patients developing ESLD that will be able to benefit from this cure.

Platteau, T., Wouters, K., Apers, L., Avonts, D., Nostlinger, C., Sergeant, M. and Florence, E. "**Voluntary outreach counselling and testing for HIV and STI among men who have sex with men in Antwerp**." Acta Clin Belg **2012** 67(3): 172-176.

BACKGROUND: High risk settings for transmission of HIV and sexually transmitted infections (STI) offer an opportunity for screening of difficult to reach risk groups. METHODS: Free, anonymous counselling and testing for HIV, syphilis, Chlamydia and hepatitis B/C were offered to visitors in two selected gay venues in Antwerp, by a multidisciplinary team. Participants completed an anonymous questionnaire. The STI-test results were communicated by cell phone using standardised text messages. RESULTS: In total, 137 MSM were tested. Facilitators of risky sexual behaviour (alcohol and drug use) were reported by 34 and 21%, respectively. Four men (3%) were newly diagnosed with HIV; 25 men (18%) had an active, transmittable STI. Infected MSM were significantly less often registered with a fixed general practitioner (GP). CONCLUSIONS: Outreach testing in gay venues is a suitable method to detect MSM at risk for HIV/STI. Although the outreach approach is very labour intensive, it shows a high yield of new STI-diagnoses that are not detected in the regular health system.

Defraye, A., Van Beckhoven, D. and Sasse, A. "**Surveillance of sexually transmitted infections among persons living with HIV**." Int J Public Health **2011** 56(2): 169-174.

OBJECTIVES: Surveillance of sexually transmitted infections (STI) among HIV patients in AIDS Reference Centers aims at identifying risk groups and detecting specific STI emerging in this population. METHODS: Seven of the nine AIDS Reference Centers in Belgium participate in this surveillance. The reported STI include Chlamydia, gonorrhea, syphilis, Lymphogranuloma venereum, hepatitis B virus and newly acquired hepatitis C in men who have sex with men (MSM). RESULTS: In 2008, 252 HIV patients (250 men, 2 women) were reported with a new STI episode. Sexual orientation was known for 245 men: 241 were MSM, 4 were heterosexual men. In total, 279 new STI episodes were reported. More than half of the diagnoses were syphilis. In 78% of the syphilis cases, the motive of the consultation was not related to an STI complaint. CONCLUSIONS: The results underline the importance of regular STI screening among HIV-positive persons, and show a particular sexual health problem among MSM. We estimate that the proportion of HIV-positive MSM acquiring an STI in 2008 was 8.8%.

Health-care workers

Hambach, R., Acke, S., Francois, G., Alen, Y., Droste, J. and van Sprundel, M. "**[Work related health risks among dentist's assistants in Flanders, Belgium]**." Ned Tijdschr Tandheelkd **2011** 118(7-8): 371-375.

The aim of this research project was to learn more about work-related health risks among dental assistants in Flanders, Belgium. Forty-seven dental assistants completed an extensive questionnaire concerning ionized radiation, protection against infection and exposure to

chemicals such as mercury, disinfectants and acrylates. Collective and personal means of protection, musculoskeletal disorders and work-related stress were also evaluated. Pain in the lower back, neck pain and shoulder pain were reported by, respectively, 15%, 17% and 22% of the respondents. Eczema resulting from skin irritation or contact-allergy was reported by 13%. Twenty-three percent of the assistants did not consistently make use ofa radiation badge; 80% wore a mouth mask and 33% wore protective glasses; and 82% was vaccinated against hepatitis B. Almost 10% reported verbal or physical aggression by patients. The mean stress score was 3.95 on a scale from 0 to 10. The results may contribute to the formulation of a number of recommendations for the improvement of the health of dental assistants.

MSM

Apers, L., Vanden Berghe, W., De Wit, S., Kabeya, K., Callens, S., Buyze, J., Kenyon, C., Florence, E. and Buve, A. "**Risk factors for HCV acquisition among HIV-positive MSM in Belgium**." J Acquir Immune Defic Syndr **2015** 68(5): 585-593.

OBJECTIVE: To better understand risk factors for the sexual transmission of hepatitis C viral (HCV) infection among men who have sex with men (MSM). DESIGN: Case-control study among HIV-infected MSM, attending AIDS Reference Centers in Belgium. METHODS: Cases were HIV-infected MSM who were diagnosed with HCV between January 2010 and December 2013. For each case, 2 controls were randomly selected among the HIV-positive MSM who tested negative for HCV around the same time as the cases were identified. Consenting participants were interviewed with a questionnaire on risk factors. Medical records were abstracted to document past episodes of sexually transmitted infections (STIs). Associations between HCV infection and risk factors were explored using bivariate analysis followed by multiple logistic regression analysis. RESULTS: A total of 52 cases and 90 controls were recruited. In multivariate analysis, douching before anal intercourse [adjusted odds ratio (AOR) = 9.84, 95% CI: 2.26 to 42.78], fisting (AOR = 3.54, 95% CI: 1.31 to 9.57), having intercourse with HIV-positive men (AOR = 5.51, 95% CI: 1.87 to 16.20), and a documented gonorrhoea or chlamydial infection in the year before inclusion in the study (AOR = 4.50, 95% CI: 1.11 to 18.31) were independently associated with incident HCV infection. CONCLUSIONS: Our study confirmed fisting and suffering from other STIs as risk factors for HCV and suggested an increased risk of HCV associated with serosorting. Furthermore, we identified anal douching as being associated with HCV infection. The role that douching plays in the acquisition of HCV infection and other STIs requires further research, as well as the effect of serosorting on STI transmission.

Apers, L., Koole, O., Bottieau, E., Vandenbruaene, M., Ophoff, D., Van Esbroeck, M., Crucitti, T. and Florence, E. "**Incidence of HCV and sexually transmitted diseases among hiv positive msm in antwerp, belgium, 2001-2011**." Acta Clin Belg **2013** 68(6): 421-426

Recurrent Sexually Transmitted Infections (STIs) are an indication of unsafe sexual practices and may be associated with HCV-infection among HIV-positive men who have sex with men. In a retrospective study we analysed the laboratory data of 99 HIV-positive MSM who acquired HCV during the observation period (cases) and 176 HIV-positive MSM who remained HCV negative during the observation period (controls), all followed at the HIV/STI-clinic in Antwerp, Belgium. All laboratory confirmed STI-episodes were recorded since the date of first consultation at our clinic, until the date of HCV-diagnosis of the cases. The HCV incidence varied between 0.24 (2001) and 1.36 (2011) new cases per hundred person-years, with a peak of 2.93 new cases per hundred person-years in 2009. The number of STI-episodes per person-year follow-up was significantly higher for the cases as compared to the controls for syphilis, non-LGV and LGV Chlamydia infections ($p < 0.005$). When considering the incidence of STIs that occurred 1 year prior to HCV conversion, all laboratory confirmed STIs remained more frequent among cases, but only the difference in syphilis incidence was statistically significant ($p < 0.01$). Recurrent STIs among HIV positive MSM should be considered as a behavioural and biological risk factor for acquiring HCV and should lead to intensified screening for HCV and counselling of the patient.

Platteau, T., Wouters, K., Apers, L., Avonts, D., Nostlinger, C., Sergeant, M. and Florence, E. "**Voluntary outreach counselling and testing for HIV and STI among men who have sex with men in Antwerp**." Acta Clin Belg **2012** 67(3): 172-176.

BACKGROUND: High risk settings for transmission of HIV and sexually transmitted infections (STI) offer an opportunity for screening of difficult to reach risk groups. METHODS: Free, anonymous counselling and testing for HIV, syphilis, Chlamydia and hepatitis B/C were offered to visitors in two selected gay venues in Antwerp, by a multidisciplinary team. Participants completed an anonymous questionnaire. The STI-test results were communicated by cell phone using standardised text messages. RESULTS: In total, 137 MSM were tested. Facilitators of risky sexual behaviour (alcohol and drug use) were reported by 34 and 21%, respectively. Four men (3%) were newly diagnosed with HIV; 25 men (18%) had an active, transmittable STI. Infected MSM were significantly less often registered with a fixed general practitioner (GP). CONCLUSIONS: Outreach testing in gay venues is a suitable method to detect MSM at risk for HIV/STI. Although the outreach approach is very labour intensive, it shows a high yield of new STI-diagnoses that are not detected in the regular health system.

De Ryck, I., Berghe, V. W., Antonneau, C. and Colebunders, R. "**Awareness of hepatitis C infection among men who have sex with men in Flanders, Belgium**." Acta Clin Belg **2011** 66(1): 46-48.

BACKGROUND: Over the past decade an increasing incidence of hepatitis C (HCV) has been observed in different countries among HIV-positive men who have sex with men (MSM). We conducted an online survey in the Dutch speaking part of Belgium among MSM to assess awareness of transmission routes and prevention measures for HCV. METHODS: A 37 question online survey was conducted via two well known websites in Belgium for MSM. RESULTS: Out of 333 responders, only 57% of men self reporting high-risk sexual behaviour considered themselves at risk for HCV. Only 48.2% knew there is no protective vaccine against HCV. Forty eight (16.6%) men were convinced they were protected for HCV by a vaccine. One third of men considered personal hygiene as an efficient way of HCV prevention. Over half of the responders never received any information about HCV, but almost all would find it useful. CONCLUSIONS: The online survey among MSM in Flanders, Belgium suggests that awareness of transmission routes and prevention measures for HCV is low and that there is an urgent need for more information.

Bottieau, E., Apers, L., Van Esbroeck, M., Vandenbruaene, M. and Florence, E. "**Hepatitis C virus infection in HIV-infected men who have sex with men: sustained rising incidence in Antwerp, Belgium, 2001-2009**." Euro Surveill **2010** 15(39): 19673.

During the last decade, outbreaks of acute hepatitis C virus (HCV) infection have been reported among human immunodeficiency virus (HIV)-infected men who have sex with men (MSM) in several European countries. To study this emerging infection in MSM in Antwerp, Belgium, we reviewed all cases of newly acquired HCV infection in HIV-positive MSM followed from 2001 to 2009 at the HIV/sexually transmitted infection (STI)reference clinic of the Institute of Tropical Medicine in Antwerp. Newly acquired HCV infection was considered as certain or probable according to local definitions. During the study period, 69 episodes of newly acquired HCV infection (40 certain and 29 probable) were diagnosed in 67 HIV-infected MSM. In only 10 episodes (14%) were the patients symptomatic. The annual incidence of HCV infection in our population of HIV-infected MSM rose steadily from 0.2% in 2001 to 1.51% in 2008, and then peaked to 2.9% in 2009. For 60 episodes (87%), another STI (mainly syphilis and lymphogranuloma venereum) had been diagnosed within the six months before the diagnosis of HCV infection. All but one patient with available genotyping (n=54) were found to be infected with the difficult to-treat HCV genotypes 1 or 4. Our results therefore demonstrate the rising incidence of HCV infection in HIV-positive MSM in Antwerp, since 2001, which reached an alarming level in 2009. Targeted awareness campaigns and routine screening are urgently needed to limit further HCV spread and its expected long-term consequences.

Prisoners

Michel, L., Lions, C., Van Malderen, S., Schiltz, J., Vanderplasschen, W., Holm, K., Kolind, T., Nava, F., Weltzien, N., Moser, A., et al. "**Insufficient access to harm reduction measures in prisons in 5**

countries (PRIDE Europe): a shared European public health concern." BMC Public Health **2015** 15: 1093.

BACKGROUND: Prisoners constitute a high-risk population, particularly for infectious diseases. The aim of this study was to estimate the level of infectious risk in the prisons of five different European countries by measuring to what extent the prison system adheres to WHO/UNODC recommendations. METHODS: Following the methodology used in a previous French survey, a postal/electronic questionnaire was sent to all prisons in Austria, Belgium, Denmark and Italy to collect data on the availability of several recommended HIV-HCV prevention interventions and HBV vaccination for prisoners. A score was built to compare adherence to WHO/UNODC recommendations (considered a proxy of environmental infectious risk) in those 4 countries. It ranged from 0 (no adherence) to 12 (full adherence). A second score (0 to 9) was built to include data from a previous French survey, thereby creating a 5-country comparison. RESULTS: A majority of prisons answered in Austria (100 %), France (66 %) and Denmark (58 %), half in Belgium (50 %) and few in Italy (17 %), representing 100, 74, 89, 47 and 23 % coverage of the prison populations, respectively. Availability of prevention measures was low, with median adherence scores ranging from 3.5 to 4.5 at the national level. These results were confirmed when using the second score which included France in the inter-country comparison. Overall, the adherence score was inversely associated with prison overpopulation rates (p = 0.08). CONCLUSIONS: Using a score of adherence to WHO/UNODC recommendations, the estimated environmental infectious risk remains extremely high in the prisons of the 5 European countries assessed. Public health strategies should be adjusted to comply with the principle of equivalence of care and prevention with the general community.

PWID

Fraser, H., Martin, N. K., Brummer-Korvenkontio, H., Carrieri, P., Dalgard, O., Dillon, J., Goldberg, D., Hutchinson, S., Jauffret-Roustide, M., Kaberg, M., et al. "**Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe**"." J Hepatol **2017**.

BACKGROUND: Prevention of hepatitis C virus (HCV) transmission among people who inject drugs (PWID) is critical to eliminating HCV in Europe. We estimate impact of current and scaled-up HCV treatment with and without scaling-up opioid substitution therapy (OST) and needle and syringe programmes (NSP) across Europe over the next 10 years. METHODS: We collected data on PWID HCV treatment rates, PWID prevalence, HCV prevalence, OST and NSP coverage from 11 European settings. We parameterized a HCV transmission model to setting-specific data that projects chronic HCV prevalence and incidence among PWID. RESULTS: At baseline, chronic HCV prevalence varied from <25% (Slovenia/Czech Republic) to >55% (Finland/Sweden), and <2% (Amsterdam/Hamburg/Norway/Denmark/Sweden) to 5% (Slovenia/Czech Republic) of chronically infected PWID were treated annually. Current treatment rates using new direct acting antivirals (DAAs) may achieve observable reductions in chronic prevalence (38-63%) in 10 years in Czech Republic, Slovenia and Amsterdam. Doubling HCV-treatment rates will reduce prevalence in other sites (12-24%, Belgium/Denmark/Hamburg/Norway/Scotland) but is unlikely to reduce prevalence in Sweden and Finland. Scaling-up OST and NSP to 80% coverage with current treatment rates using DAAs could achieve observable reductions in HCV prevalence (18-79%) in all sites. Using DAAs, Slovenia and Amsterdam are projected to reduce incidence to 2 per 100pyrs or less in 10 years. Moderate to substantial increases in current treatment rates are required to achieve the same impact elsewhere, from 1.4-3 times (Czech Republic/France), 5-17 times (France/Scotland/Hamburg/Norway/Denmark/Belgium/Sweden), to 200 times (Finland). Scaling-up OST and NSP coverage to 80% in all sites reduces treatment scale-up needed by 20-80%. CONCLUSIONS: Scale-up of HCV treatment and other interventions is needed in most settings to minimise HCV transmission among PWID in Europe. Lay summary Measuring the amount of HCV in the population of people who inject drugs is uncertain. To reduce HCV infection to minimal levels in Europe will require scale-up of both HCV treatment and other interventions that reduce injecting risk (especially opioid substitution treatment and provision of sterile injecting equipment).

Marshall, A. D., Cunningham, E. B., Nielsen, S., Aghemo, A., Alho, H., Backmund, M., Bruggmann, P., Dalgard, O., Seguin-Devaux, C., Flisiak, R., et al. "**Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe**." Lancet Gastroenterol Hepatol **2017**.

All-oral direct-acting antiviral drugs (DAAs) for hepatitis C virus, which have response rates of 95% or more, represent a major clinical advance. However, the high list price of DAAs has led many governments to restrict their reimbursement. We reviewed the availability of, and national criteria for, interferon-free DAA reimbursement among countries in the European Union and European Economic Area, and Switzerland. Reimbursement documentation was reviewed between Nov 18, 2016, and Aug 1, 2017. Primary outcomes were fibrosis stage, drug or alcohol use, prescriber type, and HIV co-infection restrictions. Among the 35 European countries and jurisdictions included, the most commonly reimbursed DAA was ombitasvir, paritaprevir, and ritonavir, with dasabuvir, and with or without ribavirin (33 [94%] countries and jurisdictions). 16 (46%) countries and jurisdictions required patients to have fibrosis at stage F2 or higher, 29 (83%) had no listed restrictions based on drug or alcohol use, 33 (94%) required a specialist prescriber, and 34 (97%) had no additional restrictions for people co-infected with HIV and hepatitis C virus. These findings have implications for meeting WHO targets, with evidence of some countries not following the 2016 hepatitis C virus treatment guidelines by the European Association for the Study of Liver.

Bielen, R., Moreno, C., Van Vlierberghe, H., Bourgeois, S., Mulkay, J. P., Vanwolleghem, T., Verlinden, W., Brixko, C., Decaestecker, J., De Galocsy, C., et al. "**Belgian experience with direct acting antivirals in people who inject drugs**." Drug Alcohol Depend **2017** 177: 214-220.

BACKGROUND AND AIM: Hepatitis C viral infection (HCV) has become a curable disease due to the development of direct acting antivirals (DAA). The WHO has set a target to eliminate HCV completely. Therefore, people who inject drugs (PWID) also need to be treated. In this study, we compared the real-life uptake and outcome of DAA treatment for HCV in PWID and non-PWID. METHODS: We performed a nation-wide, retrospective cohort study in 15 hospitals. All patients who were treated with simeprevir-sofosbuvir, daclatasvir-sofosbuvir, or ombitasvir/paritaprevir ritonavir-dasabuvir between December 2013 and November 2015 were included. RESULTS: The study population consisted of 579 patients: 115 PWID (19.9%) and 464 non-PWID (80.1%). Of the PWID 18 were active PWID (15.6%), 35 still received opiate substitution therapy (OST) (30.4%) and 62 were former PWID without OST (53.9%). PWID were more infected with genotype 1a and 3 (p=0.001). There were equal rates of side-effects (44.7% vs. 46.6%; p=0.847), similar rates of treatment completion (95.7% vs 98.1%; p=0.244) and SVR (93.0% vs 94.8%; p=0.430) between PWID and non-PWID, respectively. CONCLUSION: PWID, especially active users, are underserved for DAA treatment in real life in Belgium. Reimbursement criteria based on fibrosis stage make it difficult to treat PWID. Treatment adherence is similar in PWID and the general population, even in patients with active abuse. DAA were safe and effective in PWID despite the higher prevalence of difficult-to-treat genotypes. Based on these data more efforts to treat PWID are needed and policy changes are necessary to reach the WHO targets.

Mathei, C., Bourgeois, S., Blach, S., Brixko, C., Mulkay, J. P., Razavi, H. and Robaeys, G. "**Mitigating the burden of hepatitis C virus among people who inject drugs in Belgium**." Acta Gastroenterol Belg **2016** 79(2): 227-232.

BACKGROUD AND AIMS: In 2010, there were an estimated 10 100 PWID in Belgium and 43% (34%-57%) were HCV infected. Understanding HCV transmission dynamics in high-risk populations and assessing the potential impact of improved HCV treatment strategies requires robust epidemiological data and mathematical modeling. METHODS: CV transmission was modeled using cohorts to track HCV incidence and prevalence among active PWID in the general PWID population, OST and NSP. Model assumptions were derived from published literature and expert consensus. The relative impact of increasing the number of PWID treated with new oral DAAs was considered. RESULTS: If the current transmission paradigm continues, there will be 2645 HCV-infected PWID in 2030. Annually treating 30 (1% of 2015 population) or 120 (4% of 2015 population) HCV-infected PWID with oral DAAs will result in 5% and 25% reductions, respectively, in HCV-infected PWID by 2030. Treating 370 PWID annually (12.5% of 2015 population) will result in a > 90% reduction by 2030. CONCLUSION: Treating a small number of

PWID can result in substantial reduction in HCV prevalence in this population ; however, high levels of treatment are necessary to reduce the viral pool and thus the risk of secondary infections. This analysis supports implementation of a screening and treatment strategy among PWID when combined with an expansion of harm reduction programs.

Arain, A., De Sousa, J., Corten, K., Verrando, R., Thijs, H., Mathei, C., Buntinx, F. and Robaeys, G. "**Pilot Study: Combining Formal and Peer Education with FibroScan to Increase HCV Screening and Treatment in Persons who use Drugs**." J Subst Abuse Treat **2016** 67: 44-49.

BACKGROUND: Treatment uptake for hepatitis C virus (HCV) infection remains low in persons who inject drugs (PWID), due to lack of knowledge and low perceived need for treatment. Therefore, we conducted a pilot study to assess the influence on knowledge and willingness for HCV screening and treatment among persons who use drugs (PWUD) by combining formal and peer education with FibroScan measurement. METHODS: Clients of the Center for Alcohol and other Drug problems (CAD) in Limburg (Belgium) were randomized into a control group, which received the standard of care, and an intervention group, which received an innovative combination of formal and peer education followed by FibroScan. Knowledge of HCV infection and willingness for screening and treatment were evaluated at baseline, after intervention and 1 and 3months after intervention by means of questionnaires. RESULTS: Baseline knowledge was similar for the control (n=27) and the intervention group (n=25) (58 vs. 59%; p=0.67). Immediately after the information session, knowledge increased to 86% (p<0.001) in the intervention group. After 3months, knowledge decreased significantly (69%; p=0.01). No significant changes in knowledge were found in the control group. Baseline willingness for treatment was 81% in both the control and intervention groups, but after 1 month decreased in the control group (44%) and remained stable in the intervention group (75%). Differences in actual screening uptake between the control and intervention group were not significant (7% vs. 20%). Four percent of the intervention group and no one in the control group started treatment. CONCLUSION: The small number of subjects should be considered when interpreting the results of this study. In brief, the single information session significantly improved HCV knowledge among PWUD, but did not result in a higher uptake for screening and treatment. This could signify that there are other important reasons, besides lack of knowledge, not to undergo screening or start treatment. The fact that knowledge decreased after 3months indicates that it would be beneficial to repeat the information session regularly.

Arain, A., Bourgeois, S., de Galocsy, C., Henrion, J., Deltenre, P., d'Heygere, F., George, C., Bastens, B., Van Overbeke, L., Verrando, R., et al. "**Belgian experience with triple therapy with boceprevir and telaprevir in genotype 1 infected patients who inject drugs**." J Med Virol **2016** 88(1): 94-99.

No data have been reported yet on treatment outcome in persons who inject drugs (PWID) infected with hepatitis C virus treated with boceprevir or telaprevir in combination with peginterferon (Peg IFN) and ribavirin (RBV). Additionally, there are concerns about the safety of boceprevir and telaprevir in some subgroups of patients with hepatitis C (HCV). In a cohort of HCV patients infected with genotype 1 in Belgium, treatment outcome of patients infected due to IV drug use was analyzed and compared with patients who have no history of substance use. The study population consisted of 179 patients: 78 PWID and 101 controls treated with boceprevir (n = 79) or telaprevir (n = 100) additional to Peg IFN and RBV; 53 (30%) had advanced disease (F3, F4) and 79 (44%) had an antiviral therapy previously. There were no significant differences in the baseline characteristics between both groups, except that PWID patients were more frequently infected with genotype 1a (67% vs 21%), were younger and were predominantly male. Psychiatric complaints during follow-up occurred more frequently in the PWID patients: 24% versus 11% (P = .02). Treatment failure for other reasons than absence of viral response was 70% and 64% in PWID and non-PWID respectively. The sustained viral response (SVR) rates were similar in both groups (71% in PWID vs 72% in non-PWID); with a non-inferiority test with -5% margin there is a difference of -1% (95% CI [-15%, 13%]) and P = 0.30. There are no reasons to exclude PWID from treatment with boceprevir, telaprevir and novel antiviral therapies.

Robaeys, G., Nevens, F., Starkel, P., Colle, I., Van Eyken, P., Bruckers, L., Van Ranst, M. and

Buntinx, F. "**Previous intravenous substance use and outcome of liver transplantation in patients with chronic hepatitis C infection**." Transplant Proc **2009** 41(2): 589-594.

BACKGROUND: End-stage liver disease due to hepatitis C viral (HCV) infection is the most common reason for liver transplantation. One of the major risk factors for infection with HCV is intravenous drug use (IVDU). The pretransplantation characteristics and outcome of liver transplantation in patients with chronic hepatitis C (CHC) infected after IVDU are poorly known. METHODS: We performed a retrospective cohort study in patients with CHC who underwent liver transplantation between 1998 and 2002 in Belgium. Seven patients with and 60 patients without a history of IVDU were compared. RESULTS: Patients with CHC infected after IVDU were primarily men, significantly younger, and affected more by genotype 2 or 3. There was no relapse in substance use. No patients required a second transplantation or developed surgical complications. Progression to fibrosis in the posttransplantation period seemed to be slower. Graft and patient survival, and compliance were similar in both groups. CONCLUSIONS: Compared with patients in the non-IVDU group, patients with CHC infected after IVDU in complete remission have the same compliance, and patient and graft survival after liver transplantation. Therefore, patients with IVDU should not be excluded for liver transplantation because of HCV-induced cirrhosis.

Sutton, A. J., Hope, V. D., Mathei, C., Mravcik, V., Sebakova, H., Vallejo, F., Suligoi, B., Brugal, M. T., Ncube, F., Wiessing, L., et al. "**A comparison between the force of infection estimates for blood-borne viruses in injecting drug user populations across the European Union: a modelling study**." J Viral Hepat **2008** 15(11): 809-816.

A number of studies have been conducted in injecting drug user (IDU) populations in Europe, in which the prevalence of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) was measured together with demographic and epidemiological information such as age and the age at first injection. A measure of the risk of becoming infected is the force of infection (FOI), defined as the per capita rate at which susceptible individuals acquire infection. The objective of this study was to estimate the FOI and its heterogeneity for HBV, HCV and HIV (where available) for IDU populations in a number of countries in Europe. Data were obtained from five countries: Belgium, the United Kingdom, Spain and Italy, and the Czech Republic, which provided two data sets. The model describes the prevalence of infection as a function of the FOI that may vary over time or duration of IDU. In addition to this, if two or more infections were being considered then a parameter describing the potential heterogeneity of the FOI within the IDU population was also estimated. The results here add to the growing evidence that new initiates to injecting are at an increased risk of blood-borne viral infection compared with more experienced IDUs. In addition, there is evidence of individual heterogeneity of FOI estimates within the overall IDU populations. This suggests that different proportions of individuals in each population are at increased risk of infection compared with the rest of the population. Future interventions should identify and target these individuals. Moreover, changes over time in individual heterogeneity estimates of IDU populations may provide an indicator for measuring intervention impacts.

Micalessi, M. I., Gerard, C., Ameye, L., Plasschaert, S., Brochier, B. and Vranckx, R. "**Distribution of hepatitis C virus genotypes among injecting drug users in contact with treatment centers in Belgium, 2004-2005**." J Med Virol **2008** 80(4): 640-645.

The aim of this study was to determine the current prevalence of HCV genotypes in injecting drug users recruited at treatment centers all over Belgium, and to analyze if the distribution of genotypes was correlated with demographic characteristics, at-risk behaviors, and co-infection with other viruses. Therefore 147 anti-HCV-positive serum samples were selected for subsequent HCV RNA detection and genotyping. HCV RNA could be detected in 98 (67%) of the 147 serum samples. Genotype 1 (38%) and 3 (49%) were the most common genotypes followed by genotype 4 (9%) and genotype 2 (2%). One mixed infection (1%) was detected. The subtype could be determined in 80 cases: genotype 3a was the most prevalent (49%), followed by genotype 1a (16%) and genotype 1b (15%). No significant difference was found between the distribution of genotypes and the location of treatment centers, at-risk behaviors and co-infection with other viruses. Nevertheless, a slight variation over time could be identified (P = 0.06): one in two genotype 3 drug users started with their injecting drug use in the last 10 years

(33% in the period 1995-1999 and 21% in the period > or =2000) compared to only one in four genotype 1 drug users (20% in the period 1995-1999 and 9% in the period > or =2000).

Mathei, C., Van Dooren, S., Lemey, P., Van Damme, P., Buntinx, F. and Vandamme, A. M. "**The epidemic history of hepatitis C among injecting drug users in Flanders, Belgium**." J Viral Hepat **2008** 15(6): 399-408.

We employed recently developed statistical methods to explore the epidemic behaviour of hepatitis C subtype 1a and subtype 3a among injecting drug users (IDUs) in Flanders, Belgium, using new gene sequence data sampled among two geographically distinct populations of IDUs. First the extent of hepatitis C transmission across regions/countries was studied through calculation of association indices. It was shown that viral exchange had occurred between both populations in Flanders as well as across international borders. Furthermore, evidence was found suggestive of subtypes 1a and 3a predominantly circulating in subpopulations of Flemish IDUs, exhibiting different degrees of travelling/migration behaviour. Secondly, through coalescent-based analysis the viral epidemic history of the hepatitis C subtype 1a and 3a epidemics was inferred. Evidence was found for different dynamic forces driving both epidemics. Moreover, results suggested that the hepatitis C subtype 3a epidemic has reached a steady state, while the hepatitis C 1a epidemic has not, which therefore might become the predominant subtype among IDUs.

Others

Van Kesteren, L. and Wojciechowski, M. "**International adoption from Ethiopia: An overview of the health status at arrival in Belgium**." Acta Clin Belg **2016**: 1-6.

BACKGROUND: Ethiopia is a densely populated country with a fast growing economy. Still socioeconomic and health issues render many children parentless. One thousand and twenty eight Ethiopian children have been adopted in Belgium from September 2005 to September 2015. Little has been published about their health status at arrival. METHODS: Three hundred and fifteen children adopted from Ethiopia were clinically evaluated at the Institute of Tropical Medicine in Antwerp from 1 January 2008 until 31 December 2014. Epidemiological and medical data were collected and analysed retrospectively. RESULTS: Data about 164 boys and 151 girls with a mean age of three years were analysed. Twenty per cent was adequately vaccinated, for 66.7% of children these data were absent. About 8.6% of the children were wasted/thin, 28.9% stunted. Skin abnormalities were seen in 40.3%, especially Tinea capitis. No children tested positive for HIV, syphilis or hepatitis C. Four children had an acute or chronic hepatitis B (HBV) infection, eight children had a cured HBV infection. Two children tested positive for malaria. Active pulmonary tuberculosis was found in six children. Sixty-two per cent had one or more intestinal parasite. Giardia lamblia (41.9%) and Blastocystis hominis (27.0%) were most frequently isolated. There is a statistically relevant association between the number of intestinal parasites and age at presentation. In this group eosinophilia had a sensitivity of 30.2%, a specificity of 79.1% for intestinal parasites and a positive likelihood ratio of 1.44 with a negative likelihood ratio of 0.88. CONCLUSION: Apart from the high prevalence of stunting and intestinal parasites important medical problems were infrequent. A systematic clinical examination and screening for infectious diseases remain important to ensure a healthy start of a new life in Belgium.

Presentation related references

Prevention and control of viral hepatitis in IDU/prisoners - Belgium

Provided by speaker: Cathy Matheï

Presentation related references
Prevention and control of viral hepatitis in sex workers
Provided by speaker: Heleen Van Mieghem

1. RIVM Nederland - Landelijke Coördinatie Infectieziektebestrijding –richtlijn Hepatitis B [NL]
2. Up-to-date : Hepatitis B vaccination and diagnosis
3. CDC, 2015 STD Treatment Guidelines (June 4, 2015), Viral hepatitis A and B 2015 Sexually transmitted diseases treatment guidelines

Presentation related references
Migrants: hepatitis B and C in Chinese population in Antwerp
Provided by speaker: Erwin Ho

1.3.5 Control – treatment viral hepatitis (session 7)

Hepatitis B

Hulstaert, F., Schwierz, C., Nevens, F., Thiry, N., Gamil, M., Colle, I., Van de Sande, S. and Horsmans, Y. "**Should chronic hepatitis B be treated as early as possible?**" Int J Technol Assess Health Care **2013** 29(1): 35-41.

OBJECTIVES: We studied the cost-effectiveness of tenofovir and entecavir in e antigen positive (CHBe+) and negative (CHBe-) chronic hepatitis B. METHODS: Using a multicenter survey including 544 patients we measured patient quality of life and attributable costs by clinical disease stage. Natural disease progression was studied in 278 patients in a single center. A Markov model was constructed to follow hypothetical cohorts of treated and untreated 40-year-old CHBe+ and CHBe- patients and 50-year-old patients with compensated cirrhosis. RESULTS: We did not find an improvement in quality of life when viral load was reduced under treatment. Transition rates to liver cirrhosis were found to be age-dependent. Assuming equal effectiveness, tenofovir dominates the entecavir strategy because of its lower price in Belgium. The incremental cost-effectiveness ratio (ICER) of tenofovir after 20 years is more favorable for treating Caucasian cirrhotic patients (mean ICER euro29,000/quality-adjusted life-year [QALY]) compared with treating non-cirrhotic patients (mean ICER euro110,000 and 131,000/QALY for CHB e+ and e-, respectively). Within the non-cirrhotic patients the ICER decreases with increasing cohort starting age from 30 to 50 years. CONCLUSIONS: Results of long-term models for tenofovir or entecavir treatment of CHB need to be interpreted with caution as long-term trials with hard end points are lacking. Especially the effect on HCC remains highly uncertain. Based on cost-effectiveness

considerations such antiviral treatment should be targeted at patients with cirrhosis or at risk of rapid progression to this disease stage.

Hepatitis C

Rob, B., Moreno, C., Van Vlierberghe, H., Bourgeois, S., Mulkay, J. P., Vanwolleghem, T., Verlinden, W., Brixco, C., Decaestecker, J., De Galocsy, C., et al. "**The risk of early occurrence and recurrence of hepatocellular carcinoma in hepatitis C infected patients treated with direct acting antivirals with and without Pegylated Interferon: A Belgian experience**." J Viral Hepat **2017**.

Recently, concerns were raised of high rates of HCC recurrence in patients treated with direct acting antivirals (DAA) for hepatitis C infection. We investigated the HCC occurrence and recurrence rates within six months after treatment with DAA with or without Pegylated Interferon (PEG-IFN) in real life. This is a retrospective, multicenter cohort trial, executed in 15 hospitals distributed across Belgium. Populations were matched based on fibrosis score (Metavir F3-F4). Patients with a Child-Pugh score >/= B were excluded. In total, 567 patients were included, of whom 77 were treated with PEG-IFN+DAA between 2008 and 2013 and 490 with DAA without PEG-IFN between 2013 and 2015. Patients treated with PEG-IFN+DAA (53+/-9y) were younger than patients treated with DAA without PEG-IFN (59+/-12y) (p=0.001). 47% of patients treated with PEG-IFN+DAA were in the F4 stage versus 67% of patients treated with DAA without PEG-IFN (p=0.001). Screening was inadequate in 20% of both patient groups (p=0.664). The early occurrence rate of HCC was 1.7% and 1.1% in patients treated with DAA with and without PEG-IFN respectively (p=0.540). The early recurrence rate was 0% in patients treated with PEG-IFN+DAA, and 15.0% in patients treated with DAA without PEG-IFN (p=0.857). There is no difference in early occurrence of new HCC between patients treated with DAA with and without PEG-IFN. We did observe a high early recurrence rate of HCC in patients treated with DAA without PEG-IFN. However, these patients were at baseline more at risk for HCC. Finally, in 20% screening for HCC was inadequate.

Degre, D., Serste, T., Lasser, L., Delwaide, J., Starkel, P., Laleman, W., Langlet, P., Reynaert, H., Bourgeois, S., Vanwolleghem, T., et al. "**Sofosbuvir in Combination with Simeprevir +/- Ribavirin in Genotype 4 Hepatitis C Patients with Advanced Fibrosis or Cirrhosis: A Real-World Experience from Belgium**." PLoS One **2017** 12(1): e0170933.

INTRODUCTION: Hepatitis C virus (HCV) is a major global health issue and successful treatment has been associated with a reduction of risk of all-cause mortality. Advancements have been made in HCV treatment through the use of interferon-free regimens. Most trials have been conducted in HCV genotype (GT) 1 and data for interferon-free regimens in GT4 patients are limited. The aim of this study was to evaluate the safety and efficacy of sofosbuvir plus simeprevir in a real-world cohort of HCV GT4 patients with advanced fibrosis. PATIENTS AND METHODS: Eighty-seven GT4 treatment-naive or -Interferon (IFN) ribavirin (RBV) experienced patients treated with sofosbuvir and simeprevir +/- ribavirin (RBV) were enrolled in this cohort study (41% severe fibrosis, 59% cirrhosis). RESULTS: Patients were 51.7% male, 78.2% IFN/RBV treatment-experienced, and 37.9% received RBV treatment. The overall sustained virologic response at least 12 weeks after treatment (SVR12) rate was 87.4% while patients treated with and without RBV had rates of 87.9% and 87% (p = 0.593), respectively, and patients with advanced fibrosis (F3) and patients with cirrhosis had SVR12 rates of 94.4% and 82.4% (p = 0.087), respectively. SVR12 rates in treatment-naive patients and in IFN/RBV -experienced patients were 78.9% and 89.7% (p = 0.191), respectively. Treatment failure occurred most commonly in patients with cirrhosis and severe disease. The treatment was well tolerated and no patient died or discontinued treatment due to adverse events. CONCLUSIONS: Sofosbuvir in combination with simeprevir +/- ribavirin in GT 4 HCV patients with advanced fibrosis achieved high SVR12 rates and was well tolerated. RBV did not appear to increase the rate of SVR12.

Mulkay, J. P., Bourgeois, S., Lasser, L., De Galocsy, C., Tomasovic, S., Horsmans, Y. and Van Vlierberghe, H. "**Characteristics, treatment, and virologic responses of chronic hepatitis C patients treated with peginterferon alfa-2a and ribavirin in belgium: a sub-analysis of the**

PROPHESYS study." Acta Gastroenterol Belg **2014** 77(1): 30-40.

BACKGROUND AND STUDY AIMS: PROPHESYS was a prospective, international cohort study of monoinfected, treatment-naive chronic hepatitis C patients treated with a combination of peginterferon alfa-2a or alfa-2b and ribavirin.It included worldwide 7,163 patients from 19 countries (including 384 patients from Belgium alone) and demonstrated that sustained virologic response rates in the real world were similar to those achieved in well-controlled clinical trials. The objective of this sub-analysis was to present an overview of the baseline characteristics, anti-hepatitis C drug treatment, and virologic responses of the patients treated in Belgium, infected with HCV genotype 1, 2, 3, or 4, and administered pegin-terferon alfa-2a. Moreover, the impact of ribavirin dosage on the response to treatment was studied. PATIENTS AND METHODS: 356 patients were included in this sub-analysis. All variables were summarized using descriptive statistics. RESULTS: Compared to the published data of the whole study population (1), the Belgian data presented some significant differences in terms of genotype distribution and response to treatment (e.g. lower prevalence of HCV genotype 1 infection, lower virologic response rates in HCV genotype 2 patients). Deviations from existing recommendations were identified (e.g. higher dose of ribavirin in HCV genotype 2 or 3 patients). Patients who received less than 80% of the target dose of ribavirin experienced a significantly weaker response to treatment. CONCLUSION: This sub-analysis provided an interesting profile of the Belgian experience in the treatment of chronic hepatitis C.

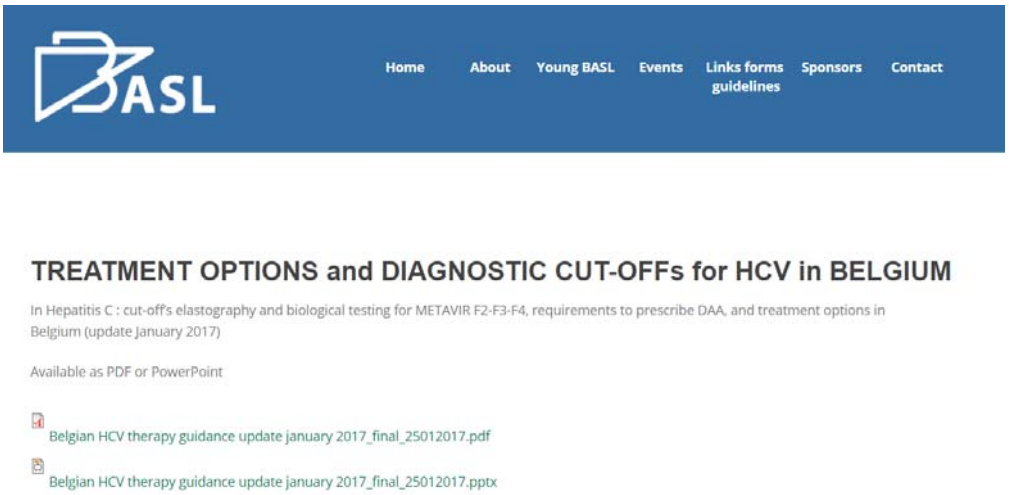
Bourgeois, S., Deltenre, P., Delwaide, J., Henrion, J., Adler, M., Langlet, P., Mulkay, J. P., Nevens, F., Brixko, C. and Moreno, C. "**A non-interventional phase IV Belgian survey to assess the antiviral effectiveness of pegylated interferon-alpha-2b and ribavirin treatment according to the stage of liver fibrosis in previously untreated patients with genotype 1/4/5/6 chronic hepatitis C (PRACTICE)**." Acta Gastroenterol Belg **2014** 77(4): 393-400.

BACKGROUND AND STUDY AIMS: This was an observational, non-interventional, multicenter, phase IV study, in patients with genotype 1/4/5/6 chronic hepatitis C (CHC). The primary objectives were to evaluate SVR in patients with no or minimal fibrosis (METAVIR F0-F1) versus well established fibrosis (F2-F4), and to estimate response on Weeks 12, 24 and 48 on treatment in previously untreated patients with genotypes 1/4/5/6 CHC. PATIENTS AND METHODS: 538 patients treated with pegylated interferon alfa 2b 1.5 mcg/kg in combination with ribavirin 800-1200 mg/day were enrolled in 55 sites in Belgium and Luxembourg, 505 being considered for the analysis. 40% of the patients were female and 60% male, the average age was 47.5 years, 10.5% were 65 or older. RESULTS: SVR was observed in 35% of the patients, EVR in 68%, of which pEVR in 33% and cEVR in 35%. SVR was observed in 43% of the low fibrosis group (F0, F1) and 30% of the high fibrosis group (F2, F3, F4) (p = 0.005). SVR rates were 34% for genotype 1, 37% for genotype 4, and 47% for genotype 5 (NS). Multivariate analysis showed that EVR and baseline METAVIR score are independent prognostic factors for SVR. CONCLUSIONS: This trial confirms that fibrosis stage and early viral response are the most important key-factors to predict sustained response, suggesting that the earlier patients are treated, the better the outcome. Non-invasive techniques enable us to closely monitor progression of fibrosis, allowing a better selection of patients for antiviral treatment in the DAA-era.

Degre, D., Colle, I., Van Vlierberghe, H. and Moreno, C. "**Boceprevir-based triple therapy for belgian liver transplant patients infected with hepatitis C virus: a preliminary experience**." Liver Transpl **2013** 19(6): 669-670.

Presentation related references
BASL Treatment guidelines for viral hepatitis B/C
Provided by speaker: Anja Geerts (BASL)

http://www.basl.be/treatmentoptionsanddiagnosticcutoffshcvbelgium



1.3.6 National hepatitis plan - policies (session 8)

Moreno, C. and Domngang, D. "**[Management of chronic hepatitis C in 2016]**." Rev Med Brux **2016** 37(4): 283-288.

Chronic hepatitis C virus infection is a major public health problem. It is estimated that 15 to 35 % of infected patients will develop cirrhosis after a period of 30 years. Fibrosis stage must be evaluated in all hepatitis-C-infected patients, even in patients with normal serum transaminases. Non-invasive methods for the evaluation of liver fibrosis have been developed, mainly serum markers and transient elastography or Fibroscan'N cent. The goal of therapy is to achieve a sustained virological response, defined by hepatitis C RNA undetectable in serum 12 weeks after the end of therapy. This indicates viral eradication. Treatment of chronic hepatitis C is a real revolution. New therapies consist in direct acting antivirals. These treatments offer high chance of viral eradication (> 90 %), and are very well tolerated. In Belgium, at the moment, reimbursement of new antiviral therapies is limited to patients with advanced fibrosis or cirrhosis. Those reimbursement criteria would change in a very near future, allowing more patients to be treated. Hepatitis C viral elimination is possible in the next 15 years at a population level in Belgium, but this implies a significant improvement in screening and access to therapy.

Vandijck, D. and Starkel, P. "**Innovative strategies for hepatitis C in Belgium integrating treatment efficacy, public disease burden, and healthcare costs**." Acta Gastroenterol Belg **2014** 77(2): 274-276.

Vandijck, D., Moreno, C., Starkel, P., Van Damme, P., Van Vlierberghe, H., Hindman, S. J., Razavi, H. and Laleman, W. "**Current and future health and economic impact of hepatitis C in Belgium**." Acta Gastroenterol Belg **2014** 77(2): 285-290.

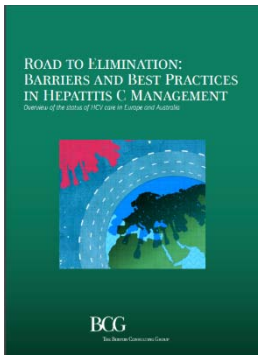
BACKGROUND AND STUDY AIMS: Chronic hepatitis C virus (HCV) infection is a serious global health problem affecting 150 million individuals worldwide. Although infection rates are decreasing, an aging population with progressing disease is expected to result in increased burden of advanced stage disease with high associated costs. This analysis describes the current and projected future economic impact of HCV sequelae in Belgium. METHODS: A previously described and validated model was populated with Belgian inputs and calibrated to project the current and future health and economic burden of HCV. Monte Carlo and sensitivity analyses were run to quantify uncertainty. All estimates exclude the cost of antiviral therapy. RESULTS: Costs associated with HCV were projected to peak in 2026 at Euro126M (Euro30M-Euro257M),

while decompensated cirrhosis and hepatocellular carcinoma costs were projected to increase until 2031 and 2034. The projected 2014-2030 cumulative cost of HCV under current conditions was Euro1,850M. Scenarios to reduce the burden of HCV could result in Euro70M-Euro400M in cumulative cost savings. Starting treatment (1,000 patients) in 2015 could result in Euro150M cost savings. The lifetime cost of HCV increases with life expectancy, with highest future costs projected among young females with early stage disease. CONCLUSIONS: The economic burden of HCV and advanced stage disease were projected to further increase. Cost reductions are possible with timely interventions aimed at minimizing the health burden of advanced stage disease.

De, G. K., Delwaide, J. and Michielsen, P. "**The Costs-Effectiveness Of Sofosbuvir Verse Standard Of Care (Soc) In Chronic Hepatitis C From A Belgian Reimbursement Perspective**." Value Health **2014** 17(7): A371.

Orlent, H., Deltenre, P., Francque, S., Laleman, W., Moreno, C., Bourgeois, S., Colle, I., Delwaide, J., De Maeght, S., Mulkay, J. P., et al. "**Update of the Belgian Association for the Study of the Liver guidelines for the treatment of chronic hepatitis C genotype 1 with protease inhibitors**." Acta Gastroenterol Belg **2012** 75(2): 245-259.

Boston consulting group (BCG) – Road to Elimination: Barriers and Best Practices in hepatitis C manangement
Overview of the status of HCV care in Europe and Australia.



Presentation related references
National Hepatitis plan - Belgium
Provided by speaker: Jean-Pierre Mulkay

Bourgeois, S., Blach, S., Blach, C., Laleman, W., Mathei, C., Mulkay, J. P., Ravazi, H., Robaeys, G., Starkel, P., Van Damme, P., et al. "**Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium**." Acta Gastroenterol Belg **2016** 79(2): 222-226.

BACKGROUD: The World Health Organization (WHO) released updated guidelines for the screening, care and treatment of patients with chronic hepatitis C virus (HCV) infection. METHODS: A previously described HCV disease burden model was used to develop a "WHO scenario" to achieve the WHO recommendations of a 90% reduction in incidence and 65% reduction in liver-related deaths. After determining the steps necessary to achieve this goal, the impact of realistic constraints was modeled. RESULTS: In 2015, there were 66.200 viremic infections, with 43% diagnosed and 1.350 treated. In order to reduce new infections, treatment must be extended to >/= F0 patients, including people who inject drugs and other individuals at risk of transmitting HCV. -Additionally, diagnosis and treatment of 3.030 and 4.060 patients, respectively, would be required. The largest attenuation of the WHO scenario would occur if no new cases were diagnosed after 2018 (300% more viremic infections by 2030). Limiting treatment to >/= F2 patients or treating fewer patients (3.000) would result in 220% or 140% more viremic cases, respectively, compared with the WHO scenario. CONCLUSION: Achieving the WHO guidelines in Belgium requires a coordinated effort to scale up treatment and prevention efforts and to allow treatment access to patients of all fibrosis stages. A scale-up of treatment, however, requires patients to be both diagnosed and linked to care, suggesting a need for increased awareness and expanded screening efforts. Finally, prevention of new HCV infections requires a comprehensive understanding of the population at risk of transmitting HCV.

Presentation related references

Do or don't screen – screening in hospital emergency service

Provided by speaker:* *Rob Bielen

2. Luxembourg

2.1 General Background

Wikipedia: Luxembourg officially the Grand Duchy of Luxembourg, is a landlocked country in western Europe. It is bordered by Belgium to the west and north, Germany to the east, and France to the south. Its capital, Luxembourg City, is, together with Brussels and Strasbourg, one of the three official capitals of the European Union and the seat of the European Court of Justice, the highest juridical authority in the EU. Its culture, people and languages are highly intertwined with its neighbours, making it essentially a mixture of French and Germanic cultures. This is emphasised by the three official languages, Luxembourgish, French, and German. With an area of 2,586 square kilometres (998 sq mi), it is one of the smallest sovereign states in Europe.

World Factbook

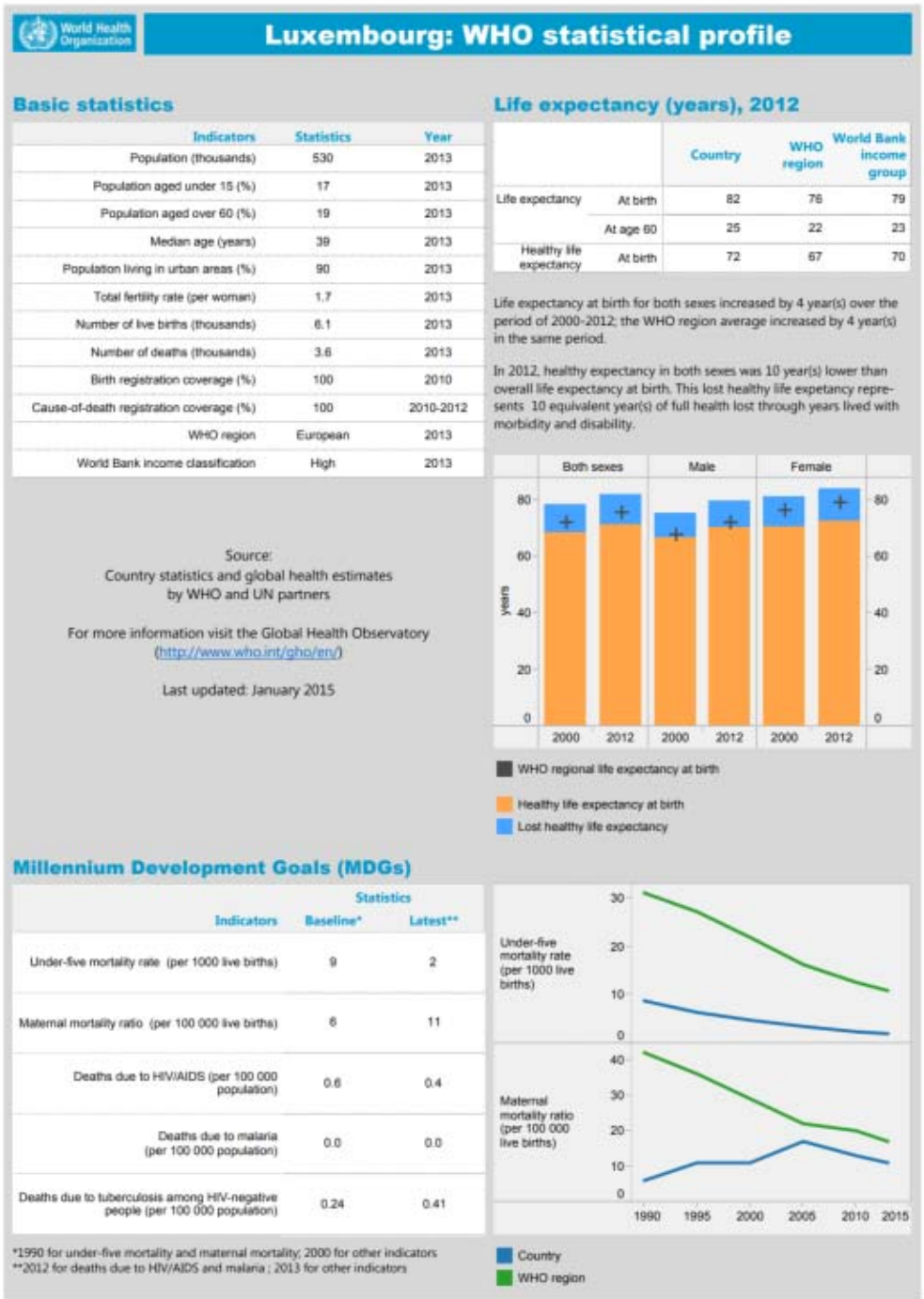
https://www.cia.gov/library/publications/the-world-factbook/geos/kv.html

	Demographics data
Population	594,130 (July 2017 est.)
GDP (PPP) per capita	$104,000 (2016 est.)
GDP	$59.47 billion (2016 est.)
Unemployment rate	6.4% (2016 est.)
Population growth	2% (2017 est.)
Birth rate:	11.5 births/1,000 population (2017 est.)
Death rate:	7.3 deaths/1,000 population (2017 est.)
Net migration rate	15.5 migrant(s)/1,000 population (2017 est.)
Health expenditures	6.6% of GDP (2014)
Physicians density:	2.92 physicians/1,000 population (2015)
Life expectancy at birth	82.3 years

2.2 Hepatitis

2.2.1 WHO Data

http://www.who.int/gho/countries/lux.pdf



World Health Organization

Luxembourg: WHO statistical profile

Basic statistics

Indicators	Statistics	Year
Population (thousands)	530	2013
Population aged under 15 (%)	17	2013
Population aged over 60 (%)	19	2013
Median age (years)	39	2013
Population living in urban areas (%)	90	2013
Total fertility rate (per woman)	1.7	2013
Number of live births (thousands)	6.1	2013
Number of deaths (thousands)	3.6	2013
Birth registration coverage (%)	100	2010
Cause-of-death registration coverage (%)	100	2010-2012
WHO region	European	2013
World Bank income classification	High	2013

Source:
Country statistics and global health estimates
by WHO and UN partners

For more information visit the Global Health Observatory
(http://www.who.int/gho/en/)

Last updated: January 2015

Life expectancy (years), 2012

		Country	WHO region	World Bank income group
Life expectancy	At birth	82	76	79
	At age 60	25	22	23
Healthy life expectancy	At birth	72	67	70

Life expectancy at birth for both sexes increased by 4 year(s) over the period of 2000-2012; the WHO region average increased by 4 year(s) in the same period.

In 2012, healthy expectancy in both sexes was 10 year(s) lower than overall life expectancy at birth. This lost healthy life expetancy represents 10 equivalent year(s) of full health lost through years lived with morbidity and disability.

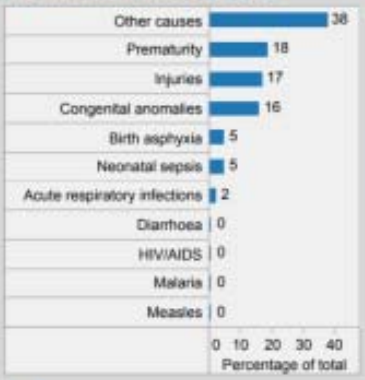
Millennium Development Goals (MDGs)

Indicators	Statistics Baseline*	Statistics Latest**
Under-five mortality rate (per 1000 live births)	9	2
Maternal mortality ratio (per 100 000 live births)	6	11
Deaths due to HIV/AIDS (per 100 000 population)	0.6	0.4
Deaths due to malaria (per 100 000 population)	0.0	0.0
Deaths due to tuberculosis among HIV-negative people (per 100 000 population)	0.24	0.41

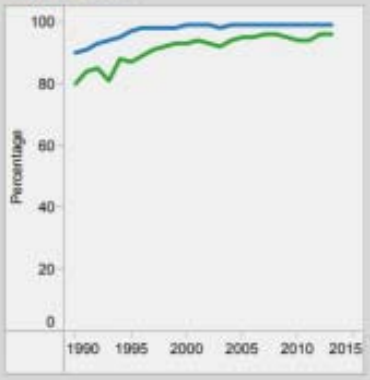
*1990 for under-five mortality and maternal mortality; 2000 for other indicators
**2012 for deaths due to HIV/AIDS and malaria ; 2013 for other indicators

Luxembourg: WHO statistical profile

Distribution of causes of deaths in children under-5, 2013



DTP3 immunization among 1-year-olds



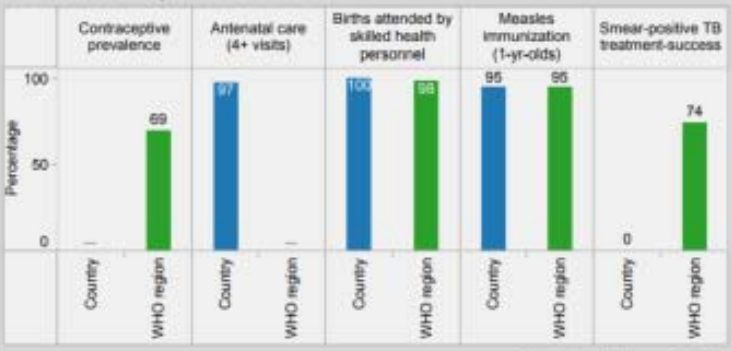
Children aged under-5 stunted

Country
WHO region

Source: Country statistics and global health estimates by WHO and UN partners
For more information visit the Global Health Observatory (http://www.who.int/gho/en//)
Last updated: January 2015

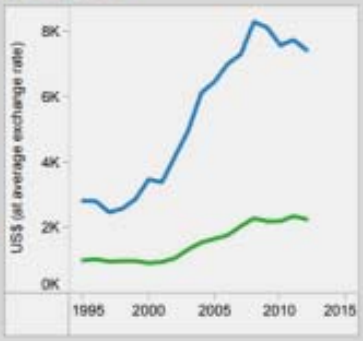
Utilisation of health services*

*Data refer to the latest year available from 2007.

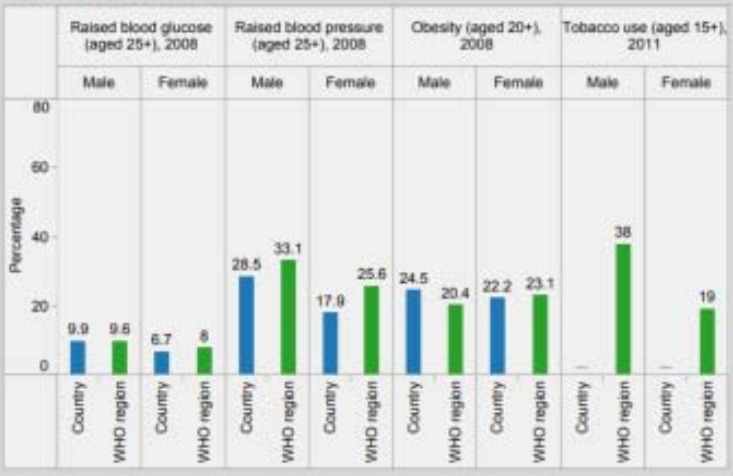


.. Data not available or applicable

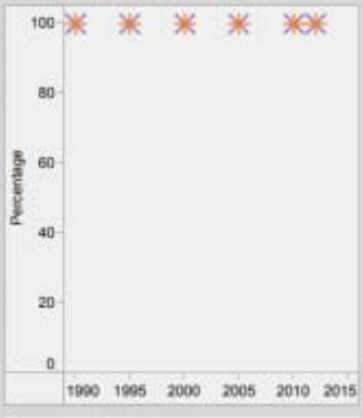
Per capita total expenditure on health



Adult risk factors



Population using improved water and sanitation

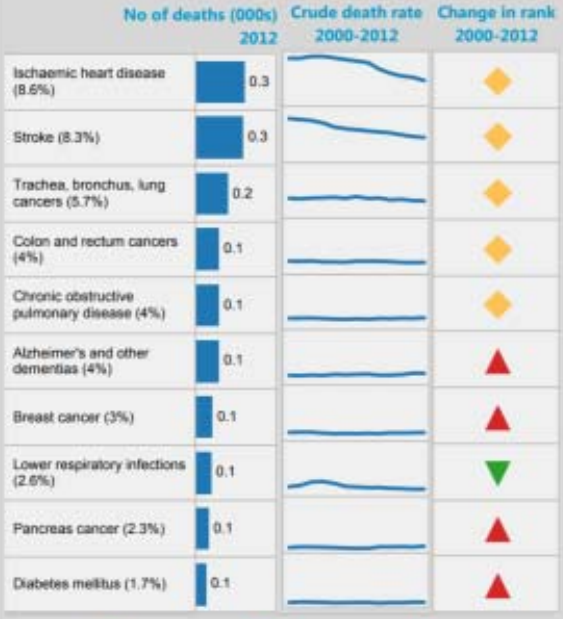


+ Improved drinking-water sources
× Improved sanitation facilities

Luxembourg: WHO statistical profile

Top 10 causes of death

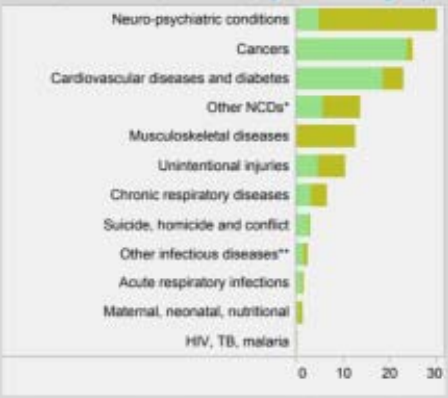
Ischaemic heart disease was the leading cause of death, killing 0.3 thousand people in 2012



Burden of disease, 2012

Disability-adjusted life years (DALYs) are the sum of years of life lost due to premature mortality (YLL) and years of healthy life lost due to disability (YLD).

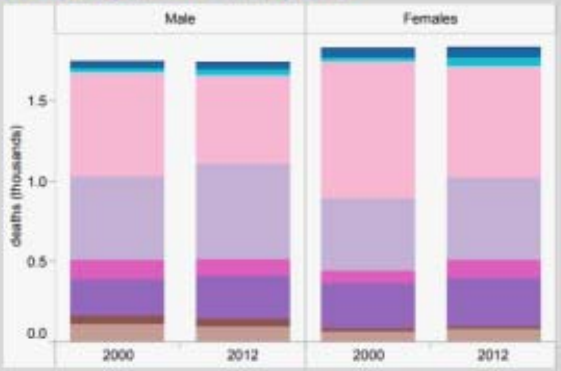
DALYs, YLL and YLD (thousands) by broad cause group



*Other noncommunicable diseases (NCDs) including non-malignant neoplasms; endocrine, blood and immune disorders; sense organ, digestive, genitourinary, and skin diseases; oral conditions; and congenital anomalies.

** Infectious diseases other than acute respiratory diseases, HIV, TB and malaria.

Deaths by broad cause group



Causes

- HIV, TB, malaria
- Acute respiratory infections
- Other infectious diseases
- Maternal, neonatal, nutritional
- Cardiovascular diseases and diabetes
- Cancers
- Chronic respiratory diseases
- Other NCDs
- Suicide, homicide and conflict
- Unintentional injuries

Probability of dying, 2012

Probability of dying between relevant exact ages, for a person experiencing the 2012 age-specific mortality risks throughout their life.

Before age 15, all causes	Male	1%
	Female	1%
Before age 70, all causes	Male	29%
	Female	19%
Between ages 15 and 49, from maternal causes	Female	0%
Between ages 30 and 70, from 4 major noncommunicable diseases (NCDs)~	Both sexes	11%

~Cancers, cardiovascular diseases, chronic respiratory diseases and diabetes

Source: Country statistics and global health estimates by WHO and UN partners
For more information visit the Global Health Observatory (http://who.int/gho/mortality_burden_disease/en/)
Last updated: January 2015

WHO CISID database info (http://data.euro.who.int/cisid/?TabID=399572)

Hepatitis A

6012 - Hepatitis A - Incidence (cases per 100 000 population)											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Luxembourg	0.64	0.21	0.62	1.01	0.39						

Hepatitis B

6180 - Hepatitis B,chronic - Incidence (cases per 100 000 population)											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Luxembourg				3.82							

9008 - Hepatitis B - Number of cases											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Luxembourg			21		16						

Hepatitis C

6015 - Hepatitis C - Incidence (cases per 100 000 population)											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Luxembourg	2.57		11.92	11.27	14.39						

6014 - Hepatitis C - Number of cases											
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Luxembourg	12		58	56	73						

Immunization coverage

Source: http://www.who.int/immunization/monitoring_surveillance/data/en/

	Country	Immunization coverage %	2017	2016	2015	2014	2013	2012	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000	1999	1998
BEL	Belgium	HepB3	97	98	98	98	98	97	97	97	98	94	94	77	64	64	60	60	60		31	2
LUX	Luxembour	HepB3	94	94	94	94	94	95	95	95	94	87	95	95		49	95					49

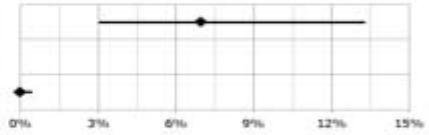
2.2.2 ECDC Data

3.19 Luxembourg

HbsAg prevalence

Author (year of publication)	Population	Sampling period	Risk of bias score	Sample size	Sampling method	Sampling description	Age range
Removille et al. (2011)	Prisoners	2005	4	115	Convenience	Multi-centre study in the two prisons. Population of problem drug users (not all PWID)	N/R
Council of Europe	First-time blood donors	2011	N/A	907	N/A	N/A	N/A

Author (year of publication)	Sampling period	Estimate (95% CI)	Sample size	Forest plot of estimates and 95% CI
Prisoners				
Removille et al. (2011)	2005	7.0% (3.0-13.3)	115	
First-time blood donors				
Council of Europe	2011	0.0% (0.0–0.4)	907	



Anti-HCV prevalence

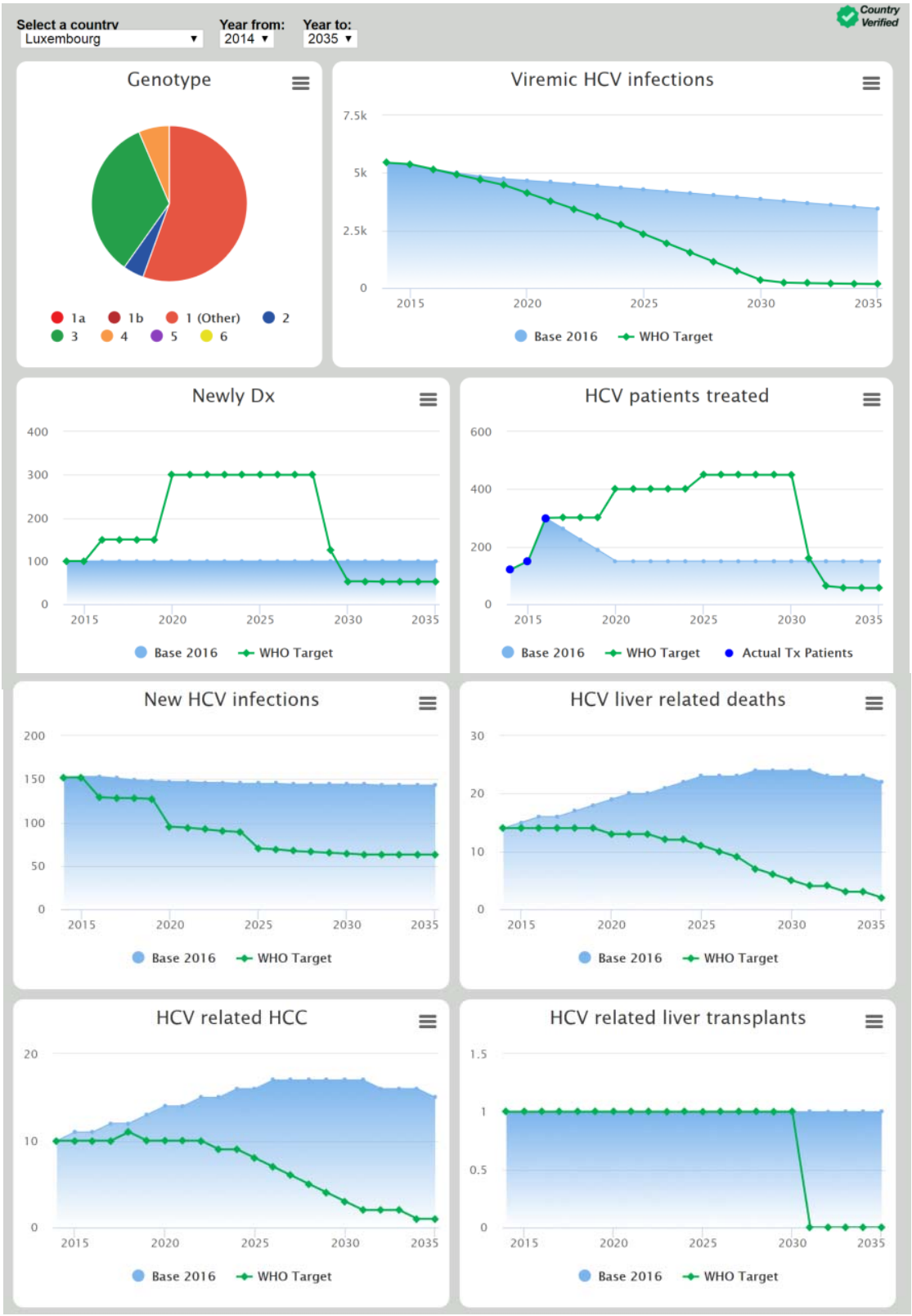
Author (year of publication)	Population	Sampling period	Risk of bias score	Sample size	Sampling method	Sampling description	Age range
Removille et al. (2011)	Prisoners	2005	4	124	Convenience	Multi-centre study in the two prisons. Population of problem drug users (not all PWID)	N/R
Council of Europe	First-time blood donors	2011	N/A	907	N/A	N/A	N/A

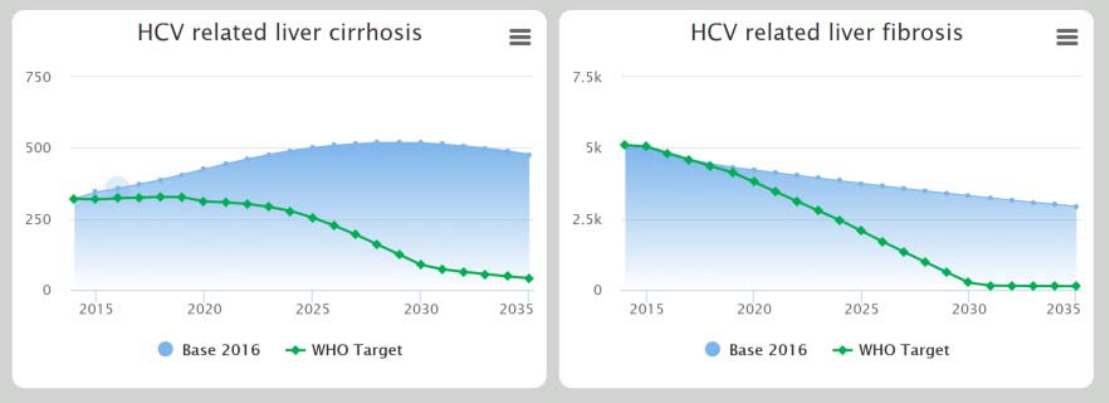
Author (year of publication)	Sampling period	Estimate (95% CI)	Sample size	Forest plot of estimates and 95% CI
Prisoners				
Removille et al. (2011)	2005	86.3% (79.0-91.8)	124	
First-time blood donors				
Council of Europe	2011	0.22% (0.03–0.79)	907	

Source: ECDC
Systematic review on hepatitis Band C prevalence in the EU/EEA 2016.
https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/systematic-review-hepatitis-B-C-prevalence.pdf

2.2.3 Centre of Disease analysis – Polaris Observatory

http://polarisobservatory.org/polaris_view/hepC.htm




HCV related liver cirrhosis
750
500
250
0
2015
2020
2025
2030
2035
Base 2016
WHO Target
HCV related liver fibrosis
7.5k
5k
2.5k
0
2015
2020
2025
2030
2035
Base 2016
WHO Target

2.3 Presentation related publications - Luxembourg

2.3.1 Surveillance, epidemiology of viral hepatitis in Luxembourg (session 3)

Kafatos, G., Andrews, N., McConway, K. J., Anastassopoulou, C., Barbara, C., De Ory, F., Johansen, K., Mossong, J., Prosenc, K., Vranckx, R., et al. "**Estimating seroprevalence of vaccine-preventable infections: is it worth standardizing the serological outcomes to adjust for different assays and laboratories?**" Epidemiol Infect **2015** 143(11): 2269-2278.

The aim of the European Sero-Epidemiology Network 2 (ESEN2) project was to estimate age-specific seroprevalence for a number of vaccine-preventable diseases in Europe. To achieve this serosurveys were collected by 22 national laboratories. To adjust for a variety of laboratory methods and assays, all quantitative results were transformed to a reference laboratory's units and were then classified as positive or negative to obtain age-specific seroprevalence. The aim of this study was to assess the value of standardization by comparing the crude and standardized seroprevalence estimates. Seroprevalence was estimated for measles, mumps, rubella, diphtheria, varicella zoster and hepatitis A virus (HAV) and compared before and after serological results had been standardized. The results showed that if no such adjustment had taken place, seroprevalence would have differed by an average of 3.2% (95% bootstrap interval 2.9-3.6) although this percentage varied substantially by antigen. These differences were as high as 16% for some serosurveys (HAV) which means that standardization could have a considerable impact on seroprevalence estimates and should be considered when comparing serosurveys performed in different laboratories using different assay methods.

Roman, F., Hawotte, K., Struck, D., Ternes, A. M., Servais, J. Y., Arendt, V., Hoffman, P., Hemmer, R., Staub, T., Seguin-Devaux, C., et al. "**Hepatitis C virus genotypes distribution and transmission risk factors in Luxembourg from 1991 to 2006**." World J Gastroenterol **2008** 14(8): 1237-1243.

AIM: To analyze the Hepatitis C virus (HCV) genotype distribution and transmission risk factors in a population of unselected patients in Luxembourg. METHODS: Epidemiological information (gender, age and transmission risks) were collected from 802 patients newly diagnosed for hepatitis C and living in Luxembourg, among whom 228 patients referred from prison. Genotyping using 5'noncoding (5'NC) sequencing was performed. We compared categorical data using the Fisher's exact F-test and odds ratios (OR) were calculated for evaluating association of HCV genotype and risk factors. RESULTS: The sex ratio was predominantly male (2.2) and individuals aged less than 40 years represented 49.6% of the population. Genotype 1 was predominant (53.4%) followed by genotype 3 (33%). Among risk factors, intravenous drug usage (IVDU) was the most frequently reported (71.4%) followed by medical-related transmission (17.6%) including haemophilia, transfusion recipients and other nosocomial reasons. Genotype 3 was significantly associated to IVDU (OR = 4.84, P < 0.0001) whereas genotype 1 was significantly associated with a medical procedure (OR = 2.42, P < 0.001). The HCV genotype distribution from inmate patients differed significantly from the rest of the population (Chi-square test with four degrees of freedom, P < 0.0001) with a higher frequency of genotype 3 (46.5% vs 27.5%) and a lower frequency of genotype 1 and 4 (44.7% vs 56.8% and 5.3% vs 9.6%, respectively). IVDU was nearly exclusively reported as a risk factor in prison. CONCLUSION: We report the first description of the HCV genotype distribution in Luxembourg. The repartition is similar to other European countries, with one of the highest European prevalence rates of genotype 3 (33%). Since serology screening became available in 1991, IVDU remains the most common way of HCV transmission in Luxembourg.

Presentation related references

Overview of surveillance and epidemiology of hepatitis in Luxembourg

Provided by speaker: ***Carole Devaux***

Polaris Observatory, H. C. V. C. "**Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study**." Lancet Gastroenterol Hepatol **2017** 2(3): 161-176.

BACKGROUND: The 69th World Health Assembly approved the Global Health Sector Strategy to eliminate hepatitis C virus (HCV) infection by 2030, which can become a reality with the recent launch of direct acting antiviral therapies. Reliable disease burden estimates are required for national strategies. This analysis estimates the global prevalence of viraemic HCV at the end of 2015, an update of-and expansion on-the 2014 analysis, which reported 80 million (95% CI 64-103) viraemic infections in 2013. METHODS: We developed country-level disease burden models following a systematic review of HCV prevalence (number of studies, n=6754) and genotype (n=11 342) studies published after 2013. A Delphi process was used to gain country expert consensus and validate inputs. Published estimates alone were used for countries where expert panel meetings could not be scheduled. Global prevalence was estimated using regional averages for countries without data. FINDINGS: Models were built for 100 countries, 59 of which were approved by country experts, with the remaining 41 estimated using published data alone. The remaining countries had insufficient data to create a model. The global prevalence of viraemic HCV is estimated to be 1.0% (95% uncertainty interval 0.8-1.1) in 2015, corresponding to 71.1 million (62.5-79.4) viraemic infections. Genotypes 1 and 3 were the most common cause of infections (44% and 25%, respectively). INTERPRETATION: The global estimate of viraemic infections is lower than previous estimates, largely due to more recent (lower) prevalence estimates in Africa. Additionally, increased mortality due to liver-related causes and an ageing population may have contributed to a reduction in infections. FUNDING: John C Martin Foundation.

Hatzakis, A., Chulanov, V., Gadano, A. C., Bergin, C., Ben-Ari, Z., Mossong, J., Schreter, I., Baatarkhuu, O., Acharya, S., Aho, I., et al. "**The present and future disease burden of hepatitis C virus (HCV) infections with today's treatment paradigm - volume 2**." J Viral Hepat **2015** 22 Suppl 1: 26-45.

Morbidity and mortality attributable to chronic hepatitis C virus (HCV) infection are increasing in many countries as the infected population ages. Models were developed for 15 countries to quantify and characterize the viremic population, as well as estimate the number of new infections and HCV related deaths from 2013 to 2030. Expert consensus was used to determine current treatment levels and outcomes in each country. In most countries, viremic prevalence has already peaked. In every country studied, prevalence begins to decline before 2030, when current treatment levels were held constant. In contrast, cases of advanced liver disease and liver related deaths will continue to increase through 2030 in most countries. The current treatment paradigm is inadequate if large reductions in HCV related morbidity and mortality are to be achieved.

Saraswat, V., Norris, S., de Knegt, R. J., Sanchez Avila, J. F., Sonderup, M., Zuckerman, E., Arkkila, P., Stedman, C., Acharya, S., Aho, I., et al. "**Historical epidemiology of hepatitis C virus (HCV) in select countries - volume 2**." J Viral Hepat **2015** 22 Suppl 1: 6-25.

Chronic hepatitis C virus (HCV) infection is a leading cause of liver related morbidity and mortality. In many countries, there is a lack of comprehensive epidemiological data that are crucial in implementing disease control measures as new treatment options become available. Published literature, unpublished data and expert consensus were used to determine key parameters, including prevalence, viremia, genotype and the number of patients diagnosed and treated. In this study of 15 countries, viremic prevalence ranged from 0.13% in the Netherlands to 2.91% in Russia. The largest viremic populations were in India (8 666 000 cases) and Russia (4 162 000 cases). In most countries, males had a higher rate of infections, likely due to higher rates of injection drug use (IDU). Estimates characterizing the infected population are critical to focus screening and treatment efforts as new therapeutic options become available.

Gane, E., Kershenobich, D., Seguin-Devaux, C., Kristian, P., Aho, I., Dalgard, O., Shestakova, I., Nymadawa, P., Blach, S., Acharya, S., et al. "**Strategies to manage hepatitis C virus (HCV) infection disease burden - volume 2**." J Viral Hepat **2015** 22 Suppl 1: 46-73.

The hepatitis C virus (HCV) epidemic was forecasted through 2030 for 15 countries, and the relative impact of two scenarios was considered: (i) increased treatment efficacy while holding the treated population constant and (ii) increased treatment efficacy and increased annual treated population. Increasing levels of diagnosis and treatment, in combination with improved treatment efficacy, were critical for achieving substantial reductions in disease burden. In most countries, the annual treated population had to increase several fold to achieve the largest reductions in HCV-related morbidity and mortality. This suggests that increased capacity for screening and treatment will be critical in many countries. Birth cohort screening is a helpful tool for maximizing resources. In most of the studied countries, the majority of patients were born between 1945 and 1985.

Roman, F., Hawotte, K., Struck, D., Ternes, A. M., Servais, J. Y., Arendt, V., Hoffman, P., Hemmer, R., Staub, T., Seguin-Devaux, C., et al. "**Hepatitis C virus genotypes distribution and transmission risk factors in Luxembourg from 1991 to 2006**." World J Gastroenterol **2008** 14(8): 1237-1243.

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2.3.2 Viral hepatitis Burden of disease (session 4)

Mossong, J., Bill, S., Hawotte, K., Gilson, G., Knolle, U., Weber, J., Roskams, T. and Arendt, V. "**Predicting significant fibrosis in hepatitis C patients in Luxembourg using serological markers**." Bull Soc Sci Med Grand Duche Luxemb **2011** (1): 19-30.

OBJECTIVE: The aim of our study was to assess the diagnostic performance of various serological markers and scores for predicting significant fibrosis retrospectively in a population of patients referring to our hospital for liver biopsy and chronic hepatitis C. MATERIALS AND METHODS: Stored serum obtained from 186 patients were tested for a number of biological markers putatively associated with liver fibrosis. Fibrotest and Forns scores were compared with liver fibrosis pathology scored according to the METAVIR system by multiple logistic regression.

RESULTS: The prevalence of significant fibrosis was 44%. Aspartate amino transferase (AST) and gamma-glutamyltransferase (GGT) were most correlated with METAVIR staging, followed by platelet counts and alpha2-macroglobulin. The negative predictive value was 77% and 83% and the positive predictive value was 100% and 84% for the Forns score and the Fibrotest, respectively. In multivariate analysis AST, GGT and alpha2-macroglobulin had independent predictive power. CONCLUSIONS: The accuracy of serological markers in predicting significant fibrosis is limited, because approximately two thirds of patients lie into an indeterminate "grey zone". Serological markers might be useful for patients reluctant to undergo liver biopsy but current predictive scoring systems are too inaccurate to replace biopsies in a routine manner.

Presentation related references

Chronic viral hepatitis and liver disease in Luxembourg

Provided by speaker: ***Carole Devaux***

2.3.3 Prevention of viral hepatitis in Luxembourg (session 5)

Presentation related references

Vaccination program in Luxembourg

Provided by speaker: ***Françoise Berthet***

2.3.4 Viral hepatitis in different risk groups in Luxembourg (seesion 6)

Origer, A. and Schmit, J. C. "**Prevalence of hepatitis B and C and HIV infections among problem drug users in Luxembourg: self-report versus serological evidence**." J Epidemiol Community Health **2012** 66(1): 64-68.EMCDDA Focal point, CRP-Sante (Public Health Research Centre), Villa Louvigny, Allee Marconi L-2021, Luxembourg. alain.origer@ms.etat.lu

BACKGROUND: To determine the seroprevalence of hepatitis B (HBV), hepatitis C (HCV) and HIV infections in problem drug users (PDU) in Luxembourg. To measure the validity of self-reported test results provided by study participants as well as obtained through the national drug-monitoring system (RELIS). METHODS: In a cross-sectional multisite study, data were collected by voluntary, anonymous and assisted questionnaires and serological detection of antibodies and antigens. Out of 1169 contacts, 397 participants were recruited within in and out-of-treatment settings (84.2% injecting drug users; IDU). RESULTS: The prevalence of antibodies to HIV was 8/272 (2.9%; 95% CI 0.9% to 4.9%), to HCV 245/343 (71.4%; 66.6% to 76.2%), and 67/310 (21.6%; 17.1% to 26.2%) to total HBV antibodies and surface antigen (for IDU 5/202, 218/268 and 59/239, respectively). Specificity of study self-reports was very high for HBV and perfect for HCV and HIV. Sensitivity was 0.224, 0.798 and 0.800, respectively. Kappa scores provided degrees of agreement between serological tests and study self-reports of 0.89 for HIV, 0.65 for HCV and 0.25 for HBV. In contrast to simultaneous cross-sectional self-reports, secondary self-reported data

(RELIS) showed high agreement for HIV and HBV infections and provided a good proxy for estimation of HCV seroprevalence. CONCLUSION: HIV testing routines in PDU should be completed at least by HBV and HCV detection given the poor validity of cross-sectional self-reports on hepatitis infections. HIV and hepatitis prevalence estimations in PDU gain by relying on multisite/setting data collection. Research should further investigate the validity of HIV and hepatitis self-reports from routine drug-monitoring systems versus cross-sectional surveys.

Removille, N., Origer, A., Couffignal, S., Vaillant, M., Schmit, J. C. and Lair, M. L. **"A hepatitis A, B, C and HIV prevalence and risk factor study in ever injecting and non-injecting drug users in Luxembourg associated with HAV and HBV immunisations**." BMC Public Health **2011** 11: 351.Centre de Recherche Public de la Sante, Luxembourg. nathalie.removille@crp-sante.lu

BACKGROUND: In Luxembourg, viral hepatitis and HIV infection data in problem drug users (PDUs) are primarily based on self-reporting. Our study aimed to determine the prevalence of HAV, HBV, HCV and HIV infections in ever injecting (IDUs) and non-injecting drug users (nIDUs) including inherent risk factors analysis for IDUs. Secondary objectives were immunisation against HAV and HBV, referral to care and treatment facilities as well as reduction in risk behaviour. METHODS: A nationwide, cross-sectional multi-site survey, involving 5 in-, 8 out-treatment and 2 prison centres, included both an assisted questionnaire (n = 368) and serological detection of HIV and Hepatitis A, B, C (n = 334). A response rate of 31% resulted in the participation of 310 IDUs and 58 nIDUs. Risk factors such as drug use, sexual behaviour, imprisonment, protection and health knowledge (HAV, HBV status and immunisations, HCV, HIV), piercing/tattoo and use of social and medical services were studied by means of chi2 and logistic models. RESULTS: Seroprevalence results for IDUs were 81.3% (218/268, 95%CI=[76.6; 86.0]) for HCV, 29.1% (74/254, 95%CI=[25.5;34.7]) for HBV (acute/chronic infection or past cured infection), 2.5% (5/202, 95%CI=[0.3; 4.6]) for HIV-1 and 57.1% (108/189, 95%CI=[50.0; 64.1]) for HAV (cured infections or past vaccinations). Seroprevalence results for nIDUs were 19.1% (9/47, 95%CI=[7.9;30.3]) for HCV, 8.9% (4/45, 95%CI=[0.6;17.2]) for HBV (acute/chronic infection or past cured infection), 4.8% (2/42, 95%CI=[-1.7;11.3]) for HIV-1 and 65.9% (27/41, 95%CI=[51.4;80.4]) for HAV. Prisoners showed the highest rates for all infections. Age, imprisonment and setting of recruitment were statistically associated with HCV seropositivity. Age, speedball career and nationality were significantly associated with HBV seropositivity. Only 56% of the participants in outpatient centres collected their serology results and 43 doses of vaccine against HAV and/or HBV were administered. CONCLUSIONS: Despite the existing national risk-reduction strategies implemented since 1993, high prevalence of HCV and HBV infections in injecting drug users is observed. Our study showed that implementing risk-prevention strategies, including immunisation remains difficult with PDUs. Improvement should be looked for by the provision of field healthcare structures providing tests with immediate results, advice, immunisation or treatment if appropriate.

Strock, P., Mossong, J., Hawotte, K. and Arendt, V. **"Access to treatment of hepatitis C in prison inmates**." Dig Dis Sci **2009** 54(6): 1325-1330.Hepatogastroenterology, Service d'Hepato-Gastroenterologie, Centre Hospitalier de Luxembourg, Luxembourg-City, Luxembourg. strock.paul@chl.lu

We conducted a prospective study to investigate access to treatment in hepatitis C in 268 prisoners. Hepatitis C positivity had been known for 182 prisoners previously and 19 reported previous attempts to treat (10%). In comparison, during our study, 86/268 prisoners (32%) started therapy (P < 0.0001). They represented 41% of 211 prisoners with a positive viral load. In the genotype 2 or 3 group, 46 prisoners (50%) started therapy versus 40 prisoners (33%) with other genotypes (P = 0.01). This difference was due to prisoners waiting for liver biopsy. On an intention to treat basis, 45 prisoners (52%) achieved sustained virological response 6 months after the end of therapy. We conclude that a stay in prison is an effective opportunity to treat a group of hepatitis C patients which otherwise have very limited access to therapy.

Presentation related references

Prevention and control of viral hepatitis in IDU/prisoners - Luxembourg

Provided by speaker: ***Patrick Hoffmann***

Strock, P., Mossong, J., Hawotte, K. and Arendt, V. "**Access to treatment of hepatitis C in prison inmates.**" Dig Dis Sci 2009 54(6): 1325-1330.

We conducted a prospective study to investigate access to treatment in hepatitis C in 268 prisoners. Hepatitis C positivity had been known for 182 prisoners previously and 19 reported previous attempts to treat (10%). In comparison, during our study, 86/268 prisoners (32%) started therapy (P < 0.0001). They represented 41% of 211 prisoners with a positive viral load. In the genotype 2 or 3 group, 46 prisoners (50%) started therapy versus 40 prisoners (33%) with other genotypes (P = 0.01). This difference was due to prisoners waiting for liver biopsy. On an intention to treat basis, 45 prisoners (52%) achieved sustained virological response 6 months after the end of therapy. We conclude that a stay in prison is an effective opportunity to treat a group of hepatitis C patients which otherwise have very limited access to therapy.

Carole Devaux et al. **High recurrence rate of Hepatitis C infection after treatment in prison inmates in Luxembourg**, 2017

2.3.5 Treatment of viral hepatitis in Luxembourg (session 7)

Hermans, L. E., Svicher, V., Pas, S. D., Salpini, R., Alvarez, M., Ben Ari, Z., Boland, G., Bruzzone, B., Coppola, N., Seguin-Devaux, C., et al. "**Combined Analysis of the Prevalence of Drug-Resistant Hepatitis B Virus in Antiviral Therapy-Experienced Patients in Europe (CAPRE).**" J Infect Dis **2016** 213(1): 39-48.

BACKGROUND: European guidelines recommend treatment of chronic hepatitis B virus infection (CHB) with the nucleos(t)ide analogs (NAs) entecavir or tenofovir. However, many European CHB patients have been exposed to other NAs, which are associated with therapy failure and resistance. The CAPRE study was performed to gain insight in prevalence and characteristics of NA resistance in Europe. METHODS: A survey was performed on genotypic resistance testing results acquired during routine monitoring of CHB patients with detectable serum hepatitis B virus DNA in European tertiary referral centers. RESULTS: Data from 1568 patients were included. The majority (73.8%) were exposed to lamivudine monotherapy. Drug-resistant strains were detected in 52.7%. The most frequently encountered primary mutation was M204V/I (48.7%), followed by A181T/V (3.8%) and N236T (2.6%). In patients exposed to entecavir (n = 102), full resistance was present in 35.3%. Independent risk factors for resistance were age, viral load, and lamivudine exposure (P < .001). CONCLUSIONS: These findings support resistance testing in cases of apparent NA therapy failure. This survey highlights the impact of exposure to lamivudine and adefovir on development of drug resistance and cross-resistance. Continued use of these NAs needs to be reconsidered at a pan-European level.

Presentation related references

Luxembourg Treatment guidelines for viral hepatitis B/C *Provided by speaker:* ***provided by speaker: Victor Arendt***

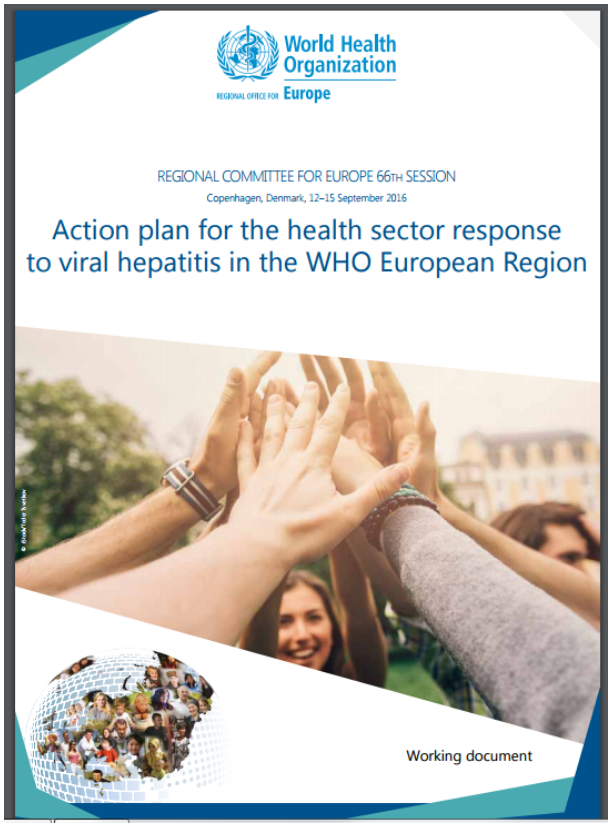
2.3.6 Luxembourg's national hepatitis plan – policies (session 8)

Presentation related references

Luxembourg Treatment guidelines for viral hepatitis B/C *Provided by speaker:* ***provided by speaker: Victor Arendt - Patrick Hoffmann***

3. WHO Euro Action plan for the health sector response to viral hepatitis

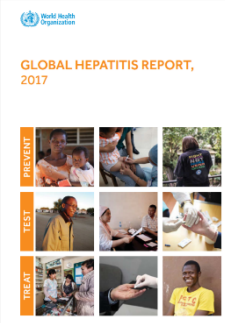
EUR/RC66/R10 Action plan for the health sector response to viral hepatitis in the WHO European Region



At the Sixty-sixth Session of the WHO Regional Committee for Europe (RC66), the 53 Members States of the WHO European Region have unanimously adopted the first ever "Action plan for the health sector response to Viral Hepatitis in the WHO European Region", and endorsed the EUR/RC66/R10. Many Member States and WHO partners have voiced their support through strong statements of support at RC66

http://www.euro.who.int/__data/assets/pdf_file/0008/315917/66wd10e_HepatitisActionPlan_160555.pdf?ua=1

Global hepatitis report, 201



In May 2016, the World Health Assembly endorsed the *Global Health Sector Strategy (GHSS) on viral hepatitis 2016–2021*. The GHSS calls for the elimination of viral hepatitis as a public health threat by 2030 (reducing new infections by 90% and mortality by 65%).

This WHO *Global hepatitis report* describes, for the first time, the global and regional estimates on viral hepatitis in 2015, setting the baseline for tracking progress in implementing the new global strategy.
The report focuses on hepatitis B and C, which are responsible for 96% of all hepatitis mortality. It presents data along the five strategic directions (strategic information, interventions, equity, financing and innovation) – key pillars of the GHSS to facilitate monitoring of progress in countries, regions and globally, and to measure the impact of interventions on reducing new infections and saving lives between 2015 and 2030.

Global report

Presentation related references

Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium - The disease burden of hepatitis C in Belgium: an update of a realistic disease control strategy,

Provided by speaker: Peter Stärkel

1. European Union HCV Collaborators. Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study. Lancet Gastroenterol Hepatol. 2017 May;2(5):325-336

2. **Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study**. Lancet Gastroenterol Hepatol. 2017 Mar;2(3):161-176 (see page 54)

3. Bourgeois S, Blach S, Blach C, Laleman W, Matheï C, Mulkay JP, Ravazi H, Robaeys G, Stärkel P, Van Damme P, Van Vlierberghe H, Vandijck D, Vandijck C. **Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium**. Acta Gastroenterol Belg. 2016;79(2):222-6 BACKGROUND: The World Health Organization (WHO) released updated guidelines for the screening, care and treatment of patients with chronic hepatitis C virus (HCV) infection. METHODS: A previously described HCV disease burden model was used to develop a "WHO scenario" to achieve the WHO recommendations of a 90% reduction in incidence and 65% reduction in liver-related deaths. After determining the steps necessary to achieve this goal, the impact of realistic constraints was modeled. RESULTS: In 2015, there were 66.200 viremic infections, with 43% diagnosed and 1.350 treated. In order to reduce new infections, treatment must be extended to >/= F0 patients, including people who inject drugs and other individuals at risk of transmitting HCV. - Additionally, diagnosis and treatment of 3.030 and 4.060 patients, respectively, would be required. The largest attenuation of the WHO scenario would occur if no new cases were diagnosed after 2018 (300% more viremic infections by 2030). Limiting treatment to >/= F2 patients or treating fewer patients (3.000) would result in 220% or 140% more viremic cases, respectively, compared with the WHO scenario. CONCLUSION: Achieving the WHO guidelines in Belgium requires a coordinated effort to scale up treatment and prevention efforts and to allow treatment access to patients of all fibrosis stages. A scale-up of treatment, however, requires patients to be both diagnosed and linked to care, suggesting a need for increased awareness and expanded screening efforts. Finally, prevention of new HCV infections requires a comprehensive understanding of the population at risk of transmitting HCV.

4. Stärkel P, Vandijck D, Laleman W, Van Damme P, Moreno C, Blach S, Razavi H, Van Vlierberghe H. **The Disease Burden of Hepatitis C in Belgium : An update of a realistic disease control strategy**. Acta Gastroenterol Belg. 2015;78(2):228-32 BACKGROUND: This manuscript serves as an update to position papers published in

2014 based on the available Belgian hepatitis C virus (HCV) epidemiological data. METHODS: Building on the current standard of care (2015 : 900 >/= F3 patients treated with 70-85% SVR), four new scenarios were developed to achieve the goals of near viral elimination and prevention of HCV associated morbidity and mortality by 2026 and 2031. Increases in treatment efficacy were assumed in 2016 (90% SVR) and 2017 (95% SVR). RESULTS: Scenario 1: Treating 6,670 patients annually by 2018 (>/= F0 beginning in 2017) and diagnosing 3,790 patients annually by 2020, a 90% reduction in viremic cases and advanced outcomes was observed by 2026. Scenario 2: Treating 4,300 patients annually by 2018 (>/= F0 beginning in 2020) without increasing the number diagnosed, a 90% reduction in viremic cases and 85%-95% reduction in advanced outcomes was observed by 2031. Scenario 3: Treating 5,000 >/= F2 patients annually by 2018, and diagnosing 3,620 patients annually by 2020, a 90% reduction in advanced outcomes and 50% reduction in viremic cases was observed by 2026. Scenario 4: Treating 3,100 >/= F2 patients annually by 2018 without increasing the number diagnosed, a 90%-95% reduction in advanced outcomes and 55% reduction in viremic cases was observed by 2031. CONCLUSIONS: Scenario 2 would provide the most favorable balance of outcomes (90% reduction in viremic prevalence and advanced outcomes) and realistic requirements for implementation (gradual increase in treatment, delayed incorporation of patients with no/mild fibrosis).

5. Starkel, P., Vandijck, D., Laleman, W., Van Damme, P., Moreno, C., Hindman, S., Razavi, H. and Van Vlierberghe, H. "**The disease burden of hepatitis C in Belgium: development of a realistic disease control strategy.**" Acta Gastroenterol Belg **2014** 77(2): 280-284.
BACKGROUND: Novel direct antiviral agents (DAAs) will become available soon with higher sustained viral response (SVR), fewer side-effects and higher compliance. Our aim was to evaluate different realistic strategies to control the projected increase in HCV-related disease burden in Belgium. METHODS: Based on literature review, expert opinions and historical assumptions, HCV-disease progression and mortality in Belgium was modeled to 2030. Strategies exploring the impact of increased treatment, treatment delay, and treatment restrictions were developed. RESULTS: Although the overall HCV prevalence is decreasing in Belgium, the burden of advanced stage HCV, including cirrhosis and hepatocellular carcinoma (HCC), is expected to increase under current treatment and cure rates. By increasing SVR to 90% from 2016 onward and the number of treated cases (from 710 to 2,050), in 2030 the cases with cirrhosis, decompensated cirrhosis and HCC would be significantly lower than in 2013. This strategy was found most efficient when applied to F2-F4 cases. To obtain comparable outcomes with F0-F4 cases, 3,490 patients should be treated. A two year delayed access to the DAAs increased HCV related morbidity and mortality by 15% relative to our strategy. CONCLUSIONS: Considering the evolving burden of HCV disease and the need for efficacious usage of healthcare resources, primary application of new DAAs in Belgium should focus on patients with significant and advanced fibrosis (F2-F4), providing these new drugs without delay upon availability and increasing access to therapy.

6. Bruggmann P, Berg T, Øvrehus AL, Moreno C, Brandão Mello CE, Roudot-Thoraval F, Marinho RT, Sherman M, Ryder SD, Sperl J, Akarca U, Balık I, Bihl F, Bilodeau M, Blasco AJ, Buti M, Calinas F, Calleja JL, Cheinquer H, Christensen PB, Clausen M, Coelho HS, Cornberg M, Cramp ME, Dore GJ, Doss W, Duberg AS, El-Sayed MH, Ergör G, Esmat G, Estes C, Falconer K, Félix J, Ferraz ML, Ferreira PR, Frankova S, García-Samaniego J, Gerstoft J, Giria JA, Gonçales FL Jr, Gower E, Gschwantler M, Guimarães Pessôa M, Hézode C, Hofer H, Husa P, Idilman R, Kåberg M, Kaita KD, Kautz A, Kaymakoglu S, Krajden M, Krarup H, Laleman W, Lavanchy D, Lázaro P, Marotta P, Mauss S, Mendes Correa MC, Müllhaupt B, Myers RP, Negro F, Nemecek V, Örmeci N, Parkes J, Peltekian KM, Ramji A, Razavi H, Reis N, Roberts SK, Rosenberg WM, Sarmento-Castro R, Sarrazin C, Semela D, Shiha GE, Sievert W, Stärkel P, Stauber RE, Thompson AJ, Urbanek P, van Thiel I, Van Vlierberghe H, Vandijck D, Vogel W, Waked I, Wedemeyer H, Weis N, Wiegand J, Yosry A, Zekry A, Van Damme P, Aleman S, Hindman SJ. Historical epidemiology of hepatitis C virus (HCV) in selected countries. J Viral Hepat. 2014; 21 Suppl 1:5-33

Chronic infection with hepatitis C virus (HCV) is a leading indicator for liver disease. New treatment options are becoming available, and there is a need to characterize the epidemiology and disease burden of HCV. Data for prevalence, viremia, genotype, diagnosis and treatment were obtained through literature searches and expert consensus for 16 countries. For some countries, data from centralized registries were used to estimate diagnosis and treatment rates. Data for the number of liver transplants and the proportion attributable to HCV were obtained from centralized databases. Viremic prevalence estimates varied widely between countries, ranging from 0.3% in Austria, England and Germany to 8.5% in Egypt. The largest viremic populations were in Egypt, with 6,358,000 cases in 2008 and Brazil with 2,106,000 cases in 2007. The age distribution of cases differed between countries. In most countries, prevalence rates were higher among males, reflecting higher rates of injection drug use. Diagnosis, treatment and transplant levels also differed considerably between countries. Reliable estimates characterizing HCV-infected populations are critical for addressing HCV-related morbidity and mortality. There is a need to quantify the burden of chronic HCV infection at the national level.

4. Bibliography of the Speakers

List of publications achieved via speaker's form, when this form was not available a Pubmed MEDLINE search was performed on Name of the speaker in [Author]-field. If more than 10 references were available only the most recent articles are shown.
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JEAN-CLAUDE SCHMIT , *Ministry of Health Luxembourg, Directorate of Health*
From speaker's form:

1. Ruiz-Castell M, Kandala NB, Kuemmerle A, Schritz A, Barre J, Delagardelle C, Krippler S, Schmit JC, Stranges S. **Hypertension burden in Luxembourg: Individual risk factors and geographic variations, 2013 to 2015 European Health Examination Survey**. *Medicine (Baltimore)* 2016,**95**:e4758.
2. Hofstra LM, Sauvageot N, Albert J, Alexiev I, Garcia F, Struck D, ..., Schmit JC, et al.. **Transmission of HIV Drug Resistance and the Predicted Effect on Current First-line Regimens in Europe**. *Clin Infect Dis* 2016,**62**:655-663.
3. Hofstra LM, Sauvageot N, Albert J, Alexiev I, Garcia F, Struck D, ..., Schmit JC, et al.. **Transmission of HIV Drug Resistance and the Predicted Effect on Current First-line Regimens in Europe**. *Clin Infect Dis* 2016,**62**:655-663.
4. Chevigne A, Delhalle S, Counson M, Beaupain N, Rybicki A, Verschueren C, Staub T, Schmit JC, Seguin-Devaux C, Deroo S. **Isolation of an HIV-1 neutralizing peptide mimicking the CXCR4 and CCR5 surface from the heavy-chain complementary determining region 3 repertoire of a viremic controller**. *AIDS* 2016,**30**:377-382.
5. Magiorkinis G, Angelis K, Mamais I, Katzourakis A, Hatzakis A, Albert J, Lawyer G, Hamouda O, Struck D, Vercauteren J, Wensing A, Alexiev I, Asjo B, Balotta C, Gomes P, Camacho RJ, Coughlan S, Griskevicius A, Grossman Z, Horban A, Kostrikis LG, Lepej SJ, Liitsola K, Linka M, Nielsen C, Otelea D, Paredes R, Poljak M, Puchhammer-Stockl E, Schmit JC, Sonnerborg A, Stanekova D, Stanojevic M, Stylianou DC, Boucher CAB, program S, Nikolopoulos G, Vasylyeva T, Friedman SR, van de Vijver D, Angarano G, Chaix ML, de Luca A, Korn K, Loveday C, Soriano V, Yerly S, Zazzi M, Vandamme AM, Paraskevis D. **The global spread of HIV-1 subtype B epidemic**. *Infect Genet Evol* 2016,**46**:169-179.
6. Santos da Silva E, Mulinge M, Lemaire M, Masquelier C, Beraud C, Rybicki A, Servais JY, Iserentant G, Schmit JC, Seguin-Devaux C, Perez Bercoff D. **The Envelope Cytoplasmic Tail of HIV-1 Subtype C Contributes to Poor Replication Capacity through Low Viral Infectivity and Cell-to-Cell Transmission**. *PLoS One* 2016,**11**:e0161596.
7. Struck D, Roman F, De Landtsheer S, Servais JY, Lambert C, Masquelier C, Venard V, Ruelle J, Nijhuis M, Schmit JC, Seguin-Devaux C. **Near Full-Length Characterization and Population Dynamics of the Human Immunodeficiency Virus Type I Circulating Recombinant Form 42 (CRF42_BF) in Luxembourg**. *AIDS Res Hum Retroviruses* 2015,**31**:554-558.
8. Angelis K, Albert J, Mamais I, Magiorkinis G, Hatzakis A, Hamouda O, Struck D, Vercauteren J, Wensing AM, Alexiev I, Asjo B, Balotta C, Camacho RJ, Coughlan S, Griskevicius A, Grossman Z, Horban A, Kostrikis LG, Lepej S, Liitsola K, Linka M, Nielsen C, Otelea D, Paredes R, Poljak M, Puchhammer-Stockl E, Schmit JC, Sonnerborg A,

Stanekova D, Stanojevic M, Boucher CA, Kaplan L, Vandamme AM, Paraskevis D. **Global Dispersal Pattern of HIV Type 1 Subtype CRF01_AE: A Genetic Trace of Human Mobility Related to Heterosexual Sexual Activities Centralized in Southeast Asia**. *J Infect Dis* 2015,**211**:1735-1744.

9. Swartz JE, Vandekerckhove L, Ammerlaan H, de Vries AC, Begovac J, Bierman WF, Boucher CA, van der Ende ME, Grossman Z, Kaiser R, Levy I, Mudrikova T, Paredes R, Perez-Bercoff D, Pronk M, Richter C, Schmit JC, Vercauteren J, Zazzi M, Zidovec Lepej S, De Luca A, Wensing AM, European Society for translational Antiviral R. **Efficacy of tenofovir and efavirenz in combination with lamivudine or emtricitabine in antiretroviral-naive patients in Europe**. *J Antimicrob Chemother* 2015,**70**:1850-1857.
10. Origer A, Schmit JC. **Prevalence of hepatitis B and C and HIV infections among problem drug users in Luxembourg: self-report versus serological evidence**. *J Epidemiol Community Health* 2012,**66**:64-68.

STEVEN VAN GUCHT *Scientific Institute of Public Health (WIV-ISP), Belgium*

From speaker's form:

1. Aspinall EJ, Couturier E, Faber M, Said B, Ijaz S, Tavoschi L, Takkinen J, Adlhoch C, Country experts. **Hepatitis E virus infection in Europe: surveillance and descriptive epidemiology of confirmed cases, 2005 to 2015**. Euro Surveill. 2017 Jun 29;22(26). pii: 30561. doi: 10.2807/1560-7917.ES.2017.22.26.30561.
2. Cattoir L, Van Hoecke F, Van Maerken T, Nys E, Ryckaert I, De Boulle M, Geerts A, Verhelst X, Colle I, Hutse V, Suin V, Wautier M, Van Gucht S, Van Vlierberghe H, Padalko E. 2017. Hepatitis E virus serology and PCR: does the methodology matter? Arch Virol. 2017 May 18. doi: 10.1007/s00705-017-3395-0.
3. Baylis SA, Blümel J, Mizusawa S, Matsubayashi K, Sakata H, Okada Y, Nübling CM, Hanschmann KM; HEV Collaborative Study Group. 2013. World Health Organization International **Standard to harmonize assays for detection of hepatitis E virus RNA**. Emerg Infect Dis. May;19(5):729-35. doi: 10.3201/eid1905.121845.
4. Halleux D, Kanaan N, Kabamba B, Thomas I, Hassoun Z. 2012. **Hepatitis E virus: an underdiagnosed cause of chronic hepatitis in renal transplant recipients**. Transpl Infect Dis. 2012 Feb;14(1):99-102. doi: 10.1111/j.1399-3062.2011.00677.x. Epub 2011 Sep 28. Review.
5. Baylis SA, Hanschmann KM, Blümel J, Nübling CM; HEV Collaborative Study Group. **Standardization of hepatitis E virus (HEV) nucleic acid amplification technique-based assays: an initial study to evaluate a panel of HEV strains and investigate laboratory performance**.J Clin Microbiol. 2011 Apr;49(4):1234-9. Epub 2011 Feb 9.
6. Jahfari S, de Vries A, Rijks JM, Van Gucht S, Vennema H, Sprong H, Rockx B**. Tick-Borne Encephalitis Virus in Ticks and Roe Deer, the Netherlands.** Emerg Infect Dis. 2017 Jun;23(6):1028-1030. doi: 10.3201/eid2306.161247.
7. Terryn S, Francart A, Rommelaere H, Stortelers C, Van Gucht S. 2016. **Post-exposure Treatment with Anti-rabies VHH and Vaccine Significantly Improves Protection of Mice from Lethal Rabies Infection.** PLoS Negl Trop Dis. 2016 Aug 2;10(8):e0004902. doi: 10.1371/journal.pntd.0004902. eCollection 2016 Aug.
8. Terryn S., Francart A., Lamoral S., Hultberg A., Rommelaere H., Wittelsberger A., Callewaert F., Stohr T., Meerschaert K., Ottevaere I., Stortelers C., Vanlandschoot P., Kalai M., Van Gucht S. 2014. **Protective effect of different anti-rabies virus VHH constructs against rabies disease in mice**. PLoS One. 2014 Oct 7;9(10):e109367. doi: 10.1371/journal.pone.0109367. eCollection 2014.
9. Florence Nazé, Vanessa Suin, Sophie Lamoral, Aurélie Francart, Bernard Brochier, Stefan Roels, Mast J., Michael Kalai and Steven Van Gucht. 2012. **Infectivity of rabies virus-**

exposed macrophages. Microbes and Infection, Nov 14. doi:pii: S1286-4579(12)00272-9. 10.1016/j.micinf.2012.10.018.

10. Hultberg A, Temperton NJ, Rosseels V, Koenders M, Gonzalez-Pajuelo M, Schepens B, Ibañez LI, Vanlandschoot P, Schillemans J, Saunders M, Weiss RA, Saelens X, Melero JA, Verrips CT, Van Gucht S, de Haard HJ. **Llama-derived single domain antibodies to build multivalent, superpotent and broadened neutralizing anti-viral molecules**. PLoS One. 2011 Apr 1;6(4):e17665.

GAËTAN MUYLDERMANS *Scientific Institute of Public Health (WIV-ISP), Belgium*

From speaker's form:

1. Muyldermans G, Ducoffre G, Leroy M, Dupont Y, Quolin S. **Surveillance of Infectious Diseases by the Sentinel Laboratory Network in Belgium: 30 Years of Continuous Improvement**. *PLoS One* 2016,**11**:e0160429.
2. Berger N, Muyldermans G, Dupont Y, Quoilin S. **Assessing the sensitivity and representativeness of the Belgian Sentinel Network of Laboratories using test reimbursement data**. *Arch Public Health* 2016,**74**:29.
3. Muyldermans G, Sasse A. **HIV-1 resistance and trend analysis in newly diagnosed patients in Belgium**. *Acta Clin Belg* 2014,**69**:1-7.
4. Requena-Méndez A, Albajar-Viñas P, Angheben A, Chiodini P, Gascón J, Muñoz J; Chagas Disease COHEMI Working Group**. Health policies to control Chagas disease transmission in European countries.** PLoS Negl Trop Dis. 2014 Oct 30;8(10).
5. Muyldermans G, Litzroth A, Ducoffre G, Quoilin S. **Correction: Establishment and reinforcement of the National Reference Centers for Human Microbiology in Belgium**. *Arch Public Health* 2013,**71**:8.
6. Muyldermans G, Litzroth A, Ducoffre G, Quoilin S. **Establishment and reinforcement of the national reference centers for human microbiology in Belgium**. *Arch Public Health* 2012,**70**:16.
7. Muyldermans G, Ducoffre G, Thomas I, Clement F, De Laere E, Glupczynski Y, Hougardy N, Lagrou K, Léonard PE, Meex C, Pierard D, Raymaekers M, Reynders M, Stalpaert M, Verstrepen W, Quoilin S. (2010**). Confirmation diagnosis of Influenza A(H1N1)2009 by Belgian sentinel laboratories during the epidemic phase**. Archives of Public Health. 68: 76-82
8. Quoilin S, Thomas I, Gérard C, Brochier B, Bots J, Lokietek S, Robesyn E, Wuillaume F, Muyldermans G. (2010). **Case finding of Influenza A(H1N1)2009 in Belgium in the early pandemic.** Archives of Public Health. 68:53-61
9. Van Marck H, Dierynck I, Kraus G, Hallenberger S, Pattery T, Muyldermans G, Geeraert L, Borozdina L, Bonesteel R, Aston C, Shaw E, Chen Q, Martinez C, Koka V, Lee J, Chi E, de Bethune MP, Hertogs K. **The impact of individual human immunodeficiency virus type 1 protease mutations on drug susceptibility is highly influenced by complex interactions with the background protease sequence**. *J Virol* 2009,**83**:9512-

CAROLE DEVAUX *Luxembourg Institute of Health, Luxembourg*

From speaker's form:

1. Marshall AD, Cunningham EB, Nielsen S, Aghemo A, Alho H, Backmund M, Bruggmann P, Dalgard O, Seguin-Devaux C, et al International Network on Hepatitis in Substance Users. **Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe**. Lancet Gastroenterol Hepatol. 2017 Oct 3.
2. Amand M, Iserentant G, Poli A, Sleiman M, Fievez V, Sanchez IP, Sauvageot N, Michel T, Aouali N, Janji B, Trujillo-Vargas CM, Seguin-Devaux C*, Zimmer J*.**Human CD56dimCD16dim cells as an individualized Natural Killer cell subset**. Front Immunol. 2017;8:699.

- Shared last authorship

3. Pressiat C, Amorissani-Folquet M, Yonaba C, Treluyer JM, Dahourou DL, Eboua F, Blanche S, Mea-Assande V, Bouazza N, Foissac F, Malateste K, Ouedraogo S, Lui G, Leroy V, Hirt D, MONOD Study Group. **Pharmacokinetics of Efavirenz in 2-3 years old children: a high dose of 25 mg/kg per day..** Antimicrob Agents Chemother. 2017;61(7).
4. Amani-Bosse C, Dahourou DL, Malateste K, Amorissani-Folquet M, Coulibaly M, Dattez S, Emieme A, Barry M, Rouzioux C, N'Gbeche S, Yonaba C, Timite-Konan M, Mea V, Ouedraogo S, Blanche S, Meda N, Seguin-Devaux C, Leroy V. **Virological response and resistances over 12 months among HIV-infected children less than two years receiving first-line lopinavir/ritonavir-based antiretroviral therapy in Cote d'Ivoire and Burkina Faso: the MONOD ANRS 12206 cohort**. J Int AIDS Soc. 2017;20(1):1-13.
5. Dahourou DL, Amorissani-Folquet M, Malateste K, Amani-Bosse C, Coulibaly M, Seguin-Devaux C, Toni T, Ouedraogo R, Blanche S, Yonaba C, Eboua F, Lepage P, Avit D, Ouedraogo S, Van de Perre P, N'Gbeche S, Kalmogho A, Salamon R, Meda N, Timite-Konan M, Leroy V, MONOD Study Group.**Efavirenz-based simplification after successful early lopinavir-boosted-ritonavir-based therapy in HIV-infected children in Burkina Faso and Cote d'Ivoire: the MONOD ANRS 12206 non-inferiority randomised trial.** BMC Med. 2017;15(1):85.
6. The Polaris Observatory HCV Collaborators. **Hepatitis C virus prevalence and level of intervention required to achieve the WHO targets for elimination in the European Union by 2030: a modelling study**.. Lancet Gastroenterol Hepatol. 2017;2(5):325-336.
7. The Polaris Observatory HCV Collaborators. **Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study**.. Lancet Gastroenterol Hepatol. 2017;2(3):161-176.
8. Santos da Silva E, Mulinge M, Lemaire M, Masquelier C, Beraud C, Rybicki A, Servais JY, Iserentant G, Schmit JC, Seguin-Devaux C, Perez Bercoff D. **The envelope cytoplasmic tail of HIV-1 Subtype C contributes to poor replication capacity through low viral infectivity and cell-to-cell transmission.** PLoS One. 2016;11(9):e0161596
9. Templer SP, Seiverth B, Baum P, Stevens W, Seguin-Devaux C, Carmona S. **Improved Sensitivity of a Dual-Target HIV-1 Qualitative Test for Plasma and Dried Blood Spots**. J Clin Microbiol. 2016. 54(7):1877-82.
10. Kartashev V, Döring M, Nieto L, Coletta E, Kaiser R, Sierra S, Euresist HCV group **New Findings in HCV Genotype Distribution in selected West European, Russian and Israeli Regions.** J Clin Virol. 2016. 81:82-89.

PIERRE DELTENRE *Centre hospitalier universitaire Vaudois (Switzerland)*
From speaker's form:

1. Deltenre P, Corouge M, Canva V, Castel H, Wartel F, Dharancy S, Louvet A, Lazrek M, Moreno C, Henrion J, Mathurin P. **Usefulness of viral kinetics for early prediction of a sustained virological response in HCV-1 non-responders re-treated with pegylated interferon and ribavirin**. J Hepatol 2011; 55: 989-95.
2. Deltenre P, Louvet A, Lemoine M, Mourad A, Fartoux L, Moreno C, Henrion J, Mathurin P, **Serfaty L. Impact of insulin resistance on sustained response in HCV patients treated with pegylated interferon and ribavirin: a meta-analysis**. J Hepatol 2011; 55: 1187-94.

3. Deltenre P, Moreno C, Tran A, Castel H, El Nady M, Canva V, Louvet A, Colin M, Provot F, Glowacki F, Dharancy S, Stanke F, Henrion J, Noel C, Mathurin P. **Antiviral therapy in hemodialyzed HCV patients: efficacy, tolerance and treatment strategy.** Aliment Pharmacol Ther 2011; 34: 354-61.
4. Schreiber J, Moreno C, Garcia Garcia B, Louvet A, Trepo E, Henrion J, Thabut D, Mathurin P, Deltenre P**. Meta-analysis: the impact of IL28B polymorphisms on rapid and sustained virological response in HCV-2 and -3 patients**. Aliment Pharmacol Ther 2012;36:353-62.
5. Deuffic-Burban S, Deltenre P, Buti M, Stroffolini T, Parkes J, Mühlberger N, Siebert U, Moreno C, Hatzakis A, Rosenberg W, Zeuzem S, Mathurin P. **Predicted effects of treatment for HCV infection vary among European countries**. Gastroenterology 2012;143:974-85.
6. de Vos M, De Vroey B, Garcia Garcia B, Roy C, Kidd F, Henrion J, Deltenre P. **The role of proton pump inhibitors in the occurrence and prognosis of spontaneous bacterial peritonitis in cirrhotic patients with ascites.** Liv Int 2013;33:1316-23.
7. Trépo E, Nahon P, Bontempi G, Valenti L, Falleti E, Nischalke HD, Hamza S, Corradini SG, Burza MA, Guyot E, Donati B, Spengler U, Hillon P, Toniutto P, Henrion J, Franchimont D, Devière J, Mathurin P, Moreno C, Romeo S, Deltenre P. **Association between PNPLA3 (rs738409 C>G) variant and hepatocellular carcinoma: evidence from a meta-analysis of individual participant** data. Hepatology 2014;59:2170-77.
8. Marot A, Trépo E, Doerig C, Moreno C, Moradpour D, Deltenre P. **Systematic review with meta-analysis: self-expanding metal stents in patients with cirrhosis and severe or refractory esophageal variceal bleeding.** Aliment Pharmacol Ther 2015;42:1250-60.
9. Vandenbulcke H, Moreno C, Colle I, Knebel JF, Francque S, Sersté T, George C, de Galocsy C, Laleman W, Delwaide J, Orlent H, Lasser L, Trépo E, Van Vlierberghe H, Michielsen P, van Gossum M, de Vos M, Marot A, Doerig C, Adler M, Henrion J, Deltenre P**. Alcohol intake increases the risk of hepatocellular carcinoma in patients with HCV-related compensated cirrhosis: a prospective study.** J Hepatol 2016;65:543-61.
10. Marot A, Trépo E, Doerig C, Schoepfer A, Moreno C, Deltenre P. **Liver stiffness and platelet count for identifying patients with compensated liver disease at low risk of variceal bleeding**. Liv Int 2017;37:707-13.

GEERT TOP *Agency for Care and Health, Flanders, Belgium*

From speaker's form:

1. Maertens K, Braeckman T, Top G, Van Damme P, Leuridan E. **Maternal pertussis and influenza immunization coverage and attitude of health care workers towards these recommendations in Flanders, Belgium**. *Vaccine* 2016,**34**:5785-5791.
2. Lefevere E, Theeten H, Hens N, De Smet F, Top G, Van Damme P. **From non school-based, co-payment to school-based, free Human Papillomavirus vaccination in Flanders (Belgium): a retrospective cohort study describing vaccination coverage, age-specific coverage and socio-economic inequalities**. *Vaccine* 2015,**33**:5188-5195.
3. Braeckman T, Lernout T, Top G, Paeps A, Roelants M, Hoppenbrouwers K, Van Damme P, Theeten H. **Assessing vaccination coverage in infants, survey studies versus the Flemish immunisation register: achieving the best of both worlds**. *Vaccine* 2014,**32**:345-349.
4. Braeye T, Sabbe M, Hutse V, Flipse W, Godderis L, Top G. **Obstacles in measles elimination: an in-depth description of a measles outbreak in Ghent, Belgium,**

spring 2011. *Arch Public Health* 2013,**71**:17.

5. Robesyn E, De Schrijver K, Wollants E, Top G, Verbeeck J, Van Ranst M. **An outbreak of hepatitis A associated with the consumption of raw beef**. *J Clin Virol* 2009,**44**:207-210.
6. Lernout T, Kissling E, Hutse V, De Schrijver K, Top G. **An outbreak of measles in orthodox Jewish communities in Antwerp, Belgium, 2007-2008: different reasons for accumulation of susceptibles**. *Euro Surveill* 2009,**14**.
7. Lernout T, Kissling E, Hutse V, Top G. **Clusters of measles cases in Jewish orthodox communities in Antwerp, epidemiologically linked to the United Kingdom: a preliminary report**. *Euro Surveill* 2007,**12**:E071115 071113.
8. De Schrijver K, Boeckx H, Top G, Mertens A, De Mol P. **Cholera among Belgian travellers in Turkey in 2005**. *Travel Med Infect Dis* 2007,**5**:236-238.
9. Quoilin S, Hutse V, Vandenberghe H, Claeys F, Verhaegen E, De Cock L, Van Loock F, Top G, Van Damme P, Vranckx R, Van Oyen H. **A population-based prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium**. *Eur J Epidemiol* 2007,**22**:195-202.
10. .De Schrijver K, Boeckx H, Top G, Mertens A, De Mol P. **Cholera in Belgian tourists after travel to Turkey**. *Euro Surveill* 2005,**10**:E051013 051012.

INGRID MORALES *Office de la Naissance et de l'Enfance (ONE), Belgium*

FRANÇOISE BERTHET *Direction de la Santé, Division de la Médecine curative, Luxembourg*

From Pubmed [Berthet, F.(Author)]:

1. Galanakis E, D'Ancona F, Jansen A, Lopalco PL. VENICE. **The issue of mandatory vaccination for healthcare workers in Europe**. *Expert Rev Vaccines* 2014,**13**:277-283.
2. Nohynek H, Wichmann O, F DA. **National Advisory Groups and their role in immunization policy-making processes in European countries**. *Clin Microbiol Infect* 2013,**19**:1096-1105.
3. Mereckiene J, Cotter S, Weber JT, Nicoll A, D'Ancona F, Lopalco PL, Johansen K, Wasley AM, Jorgensen P, Levy-Bruhl D, Giambi C, Stefanoff P, Dematte L, O'Flanagan D. VENICE Nationale gatekeepers.**Influenza A(H1N1)pdm09 vaccination policies and coverage in Europe**. *Euro Surveill* 2012,**17**.
4. Haverkate M, D'Ancona F, Giambi C, Johansen K, Lopalco PL, Cozza V, Appelgren E. VENICE **Mandatory and recommended vaccination in the EU, Iceland and Norway: results of the VENICE 2010 survey on the ways of implementing national vaccination programmes**. *Euro Surveill* 2012,**17**.
5. Dorleans F, Giambi C, Dematte L, Cotter S, Stefanoff P, Mereckiene J, O'Flanagan D, Lopalco PL, D'Ancona F, Levy-Bruhl D. VENICE 2 project gatekeepers group **The current state of introduction of human papillomavirus vaccination into national immunisation schedules in Europe: first results of the VENICE2 2010 survey**. *Euro Surveill* 2010,**15**.
6. Billiau AD, Loop M, Le PQ, Berthet F, Philippet P, Kasran A, Wouters CH. **Etanercept improves linear growth and bone mass acquisition in MTX-resistant polyarticular-course juvenile idiopathic arthritis**. *Rheumatology (Oxford)* 2010,**49**:1550-1558.
7. Aspesberro F, Siebler T, Van Nieuwenhuyse JP, Panosetti E, Berthet F. **Lemierre syndrome in a 5-month-old male infant: Case report and review of the pediatric literature**. *Pediatr Crit Care Med* 2008,**9**:e35-37.

THOMAS VANWOLLEGHEM *University Hospital Antwerp, Belgium*

From speaker's form:

1. Wranke A, Pinheiro Borzacov LM, Parana R, Lobato C, Hamid S, Ceausu E, Dalekos GN, Rizzetto M, Turcanu A, Niro GA, Lubna F, Abbas M, Ingiliz P, Buti M, Ferenci P, Vanwolleghem T, Hayden T, Dashdorj N, Motoc A, Cornberg M, Abbas Z, Yurdaydin C, Manns MP, Wedemeyer H, Hardtke S; Hepatitis Delta International Network**. Clinical and virological heterogeneity of hepatitis delta in different regions world-wide: The Hepatitis Delta International Network (HDIN).** Liver Int. 2017 Sep 29. doi: 10.1111/liv.13604
2. van de Garde MDB, Pas SD, van Oord GW, Gama L, Choi Y, de Man RA, Boonstra A, Vanwolleghem T. **Interferon-alpha treatment rapidly clears Hepatitis E virus infection in humanize**d mice. Sci Rep. 2017 Aug 15;7(1):8267.
3. Hou J, Brouwer WP, Kreefft K, Gama L, Price SL, Janssen HLA, French PJ, Vanwolleghem T, Boonstra A. **Unique intrahepatic transcriptomics profiles discriminate the clinical phases o**f a chronic HBV infection. PLoS One. 2017 Jun 29;12(6):e0179920.
4. Chi H, Wong D, Peng J, Cao J, Van Hees S, Vanwolleghem T, Qi X, Chen L, Feld JJ, de Knegt RJ, Hansen BE, Janssen HLA. **Durability of Response After Hepatitis B Surface Antigen Seroclearance During Nucleos(t)ide Analogue Treatment in a Multiethnic Cohort of Chronic Hepatitis B Patients: Results After Treatment Cessation.** Clin Infect Dis. 2017 Aug 15;65(4):680-683.
5. Vanwolleghem T, Boonstra A. **Focus on the liver: Host-virus interactions in HBV.** J Hepatol. 2017 May;66(5):884-885. IF: 10.590
6. van de Garde MD, Movita D, van der Heide M, Herschke F, De Jonghe S, Gama L, Boonstra A, Vanwolleghem T. **Liver Monocytes and Kupffer Cells Remain Transcriptionally Distinct during Chronic Viral Infection**. PLoS One. 2016 Nov 3;11(11):e0166094. IF: 3.057
7. Verlinden W, Francque S, Michielsen P, Vanwolleghem T**. Successful antiviral treatment of chronic hepatitis C leads to a rapid decline of liver stiffness without an early effect on spleen stiffness.** Hepatology. 2016 Nov;64(5):1809-1810.
8. van de Garde MD, Pas SD, van der Net G, de Man RA, Osterhaus AD, Haagmans BL, Boonstra A, Vanwolleghem T. **Hepatitis E virus genotype three infection of human liver chimeric mice as a model for chronic HEV infection**. J Virol. 2016 Apr 14;90(9):4394-401
9. Vanwolleghem T, Hou J, van Oord G, Andeweg AC, Osterhaus AD, Pas SD, Janssen HL, Boonstra A. **Re-evaluation of hepatitis B virus clinical phases by systems biology identifies unappreciated roles for the innate immune response and B cells.** Hepatology. 2015 Jul;62(1):87-100.
10. Movita D, van de Garde MD, Biesta P, Kreefft K, Haagmans B, Zuniga E, Herschke F, De Jonghe S, Janssen HL, Gama L, Boonstra A, Vanwolleghem T. **Inflammatory monocytes recruited to the liver within 24 hours after virus-induced inflammation resemble Kupffer cells but are functionally distinct**. J Virol. 2015 May;89:4809-17.

NAÏMA HAMMAMI *Scientific Institute of Public Health (WIV-ISP, Belgium*

From speaker's form:

1. Zingg W, Hopkins S, Suetens C et al. and the ECDC PPS study group**. Health-care-associated infections in neonates, children, and adolescents: an analysis of paediatric data from the European Centre for Disease Prevention and Control point- prevalence survey.** Lancet Infect Dis 2017. 2017 (16) 30517-5. http://dx.doi.org/10.1016/S1473-3099(16)30517-5
2. Valencia C, Hammami N, Blot S, Vincent JL, Lambert ML, et al. **Poor adherence to guidelines for preventing central line-associated bloodstream infections**

(CLABSI): results of a worldwide survey. Antimicrobial Resistance and Infection Control 2016; 5:49 DOI: 10.1186/s13756-016-0139-y

3. Hammami N, Mertens K, Overholser R, Goetgebeur E, Catry B, Lambert M. **Validation of a sampling method to collect exposure data for central line-associated bloodstream infections.** Infection Control and Hospital Epidemiology 2016; 1(5):1-6. https://www.researchgate.net/profile/Naima_Hammami/publication/290432395_Validation_of_a_Sampling
4. Hammami N, Catry B, Lambert ML. **Septicémies associées aux cathéters veineux centraux dans les hôpitaux Belges: données de surveillance 2000-2014**. Noso-Info 2015;19(3). http://www.nosoinfo.be/nosoinfos/septicemies-associees-aux-catheters-veineux-centraux-dans-les-hopitaux-belges-donnees-de-surveillance-2000-2014/?ref=r315
5. Lambert ML, Hammami N, Goossens H et al. **The Belgian policy of funding antimicrobial stewardship in hospitals and trends of selected quality indicators for antimicrobial use, 1999-2010: a longitudinal study.** BMJ Open 2015;5(2):e006916. http://bmjopen.bmj.com/cgi/content/full/bmjopen-2014-006916?ijkey=cmCL2QPPv3zgzjZ&keytype=ref
6. 03/2013: Poster presentation during International Forum on Quality and Safety healthcare organised by IHI/BMJ in London: "**Improving usefulness of data collection systems at hospital level: the example of Belgian national surveillance of hospital acquired bloodstream infections"**
7. Hammami N, Nöstlinger C, Hoerée T, Lefèvre P, Jonckheer T, and Kolsteren P. **Integrating adherence to highly active antiretroviral treatment into children's daily life: a qualitative study.** Pediatrics 2004; 114 (5): pp. e591 – e597. http://pediatrics.aappublications.org/cgi/content/full/114/5/e591

CATHY MATHEÏ *KU Leuven, Public Health & Primary Care,Belgium*

From Pubmed [Matheï, C..(Author)]:

1. Thapa S, Bista N, Hannes K, Buve A, Vermandere M, Mathei C. **Vulnerability of wives of Nepalese labor migrants to HIV infection: Integrating quantitative and qualitative evidence**. *Women Health* 2016,**56**:745-766.
2. Bourgeois S, Blach S, Blach C, Laleman W, Mathei C, Mulkay JP, Ravazi H, Robaeys G, Starkel P, Van Damme P, Van Vlierberghe H, Vandijck D, Vandijck C. **Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium**. *Acta Gastroenterol Belg* 2016,**79**:222-226.
3. Mathei C, Bourgeois S, Blach S, Brixko C, Mulkay JP, Razavi H, Robaeys G. **Mitigating the burden of hepatitis C virus among people who inject drugs in Belgium**. *Acta Gastroenterol Belg* 2016,**79**:227-232.
4. Thapa S, Pathak S, Leppin A, Buve A, Hannes K, Kandel G, Mathei C. **Factors Associated With Condom Use for HIV Prevention Among Nepalese Labor Migrant Couples**. *AIDS Educ Prev* 2016,**28**:180-190.
5. Thapa S, Hannes K, Cargo M, Buve A, Mathei C. **Effect of stigma reduction intervention strategies on HIV test uptake in low- and middle-income countries: a realist review protocol**. *Syst Rev* 2015,**4**:142.
6. Robaeys G, Van Vlierberghe H, Mathei C, Van Ranst M, Bruckers L, Buntinx F. **Similar compliance and effect of treatment in chronic hepatitis C resulting from intravenous drug use in comparison with other infection causes**. *Eur J Gastroenterol Hepatol* 2006,**18**:159-166.
7. Mathei C, Robaeys G, Van Ranst M, Van Damme P, Buntinx F. **The epidemiology of hepatitis C among injecting drug users in Belgium**. *Acta Gastroenterol Belg* 2005,**68**:50-54.

8. Robaeys G, Buntinx F, Bottieau E, Bourgeois S, Brenard R, Colle I, De Bie J, Mathei C, Mulkay JP, Van Damme P, Van Ranst M, Verrando R, Michielsen P, Bourgeois N, Brenard R, de Galocsy C, Delwaide J, Henrion J, Horsmans Y, Michielsen P, Reynaert H, Robaeys G, Sprengers D. **Guidelines for the management of chronic hepatitis C in patients infected after substance use**. *Acta Gastroenterol Belg* 2005,**68**:38-45.
9. Robaeys G, Mathei C, Van Ranst M, Buntinx F. **Substance use in Belgium : prevalence and management**. *Acta Gastroenterol Belg* 2005,**68**:46-49.
10. Verrando R, Robaeys G, Mathei C, Buntinx F. **Methadone and buprenorphine maintenance therapies for patients with hepatitis C virus infected after intravenous drug use**. *Acta Gastroenterol Belg* 2005,**68**:81-85.

PATRICK HOFFMANN *Luxembourg Health Directorate*
From speaker's form:

1. Marshall AD et al**. Restrictions for reimbursement of interferon-free direct-acting antiviral drugs for HCV infection in Europe, 2017,** Lancet Gastroenterol Hepatol **2017**, http://dx.doi.org/10.1016/S2468-1253(17)30284-4

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No publication available

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From Pubmed [Ho,E..(Author)]:

1. Verhulst SL, Vekemans K, Ho E, Aerts L, Jacobs S, De Backer LA, Dhanapala H, Perera P, De Backer WA, Desager KN., **Is wheezing associated with decreased sleep quality in Sri Lankan children?** A questionnaire study. Pediatr Pulmonol. 2007 Jul;42(7):579-83.
2. Ho E, Coveliers J, Amsel BJ, Stockman B, Walpot J, Ieven M, Rodrigus I**. A case of endocarditis due to Aerococcus urinae**. J Heart Valve Dis. 2010 Mar;19(2):264-6.
3. Michielsen P, Ho E. **Viral hepatitis B and hepatocellular carcinoma.** Acta Gastroenterol Belg. 2011 Mar;74(1):4-8.
4. Michielsen P, Ho E, Francque S. **Does antiviral therapy reduce the risk of hepatocellular carcinoma in patients with chronic hepatitis C**? Minerva Gastroenterol Dietol 2012;58:65-79
5. Ho E, Deltenre P, Nkuize M, Delwaide J, Colle I, Michielsen P; Belgian Association for the Study of the Liver**. Coinfection of hepatitis B and hepatitis delta virus in Belgium: a multicenter BASL study. Prospective epidemiology and comparison with HBV mono-infection. J Med Virol. 2013 Sep;85(9):1513-7.**
6. Piet Cools; Erwin Ho, MD; Katleen Vranckx, PhD; Petra Schelstraete, MD, PhD; Bettina Wurth, MD; Hilde Franckx, MD; Greet Ieven, PhD; Leen Van Simaey; Sabine Van daele, MD, PhD; Stijn Verhulst, MD, PhD; Frans De Baets, MD, PhD; Mario Vaneechoutte, PhD. **Epidemic Achromobacter xylosoxidans strain among Belgian cystic fibrosis patients and review of literature.** BMC Microbiol. 2016 Jun 24;16(1):122. doi: 10.1186/s12866-016-0736-1.

ANJA GEERTS *University Hospital Ghent, Belgium*
From Pubmed [Geerts, A.(Author)]:

1. Detry O, Van Deynse D, Van Vlierberghe H, Pirenne J. Belgian Transplantation Society (BTS) **Organ Procurement and Transplantation in Belgium**. *Transplantation* 2017,**101**:1953-1955.

2. Raevens S, Geerts A, Paridaens A, Lefere S, Verhelst X, Hoorens A, Van Dorpe J, Maes T, Bracke KR, Casteleyn C, Jonckx B, Horvatits T, Fuhrmann V, Van Vlierberghe H, Van Steenkiste C, Devisscher L, Colle I. **Placental growth factor inhibition targets pulmonary angiogenesis and represents a novel therapy for hepatopulmonary syndrome in mice**. *Hepatology* 2017.
3. Cattoir L, Van Hoecke F, Van Maerken T, Nys E, Ryckaert I, De Boulle M, Geerts A, Verhelst X, Colle I, Hutse V, Suin V, Wautier M, Van Gucht S, Van Vlierberghe H, Padalko E. **Hepatitis E virus serology and PCR: does the methodology matter?** *Arch Virol* 2017.
4. Paridaens A, Raevens S, Colle I, Bogaerts E, Vandewynckel YP, Verhelst X, Hoorens A, van Grunsven LA, Van Vlierberghe H, Geerts A, Devisscher L. **Combination of tauroursodeoxycholic acid and N-acetylcysteine exceeds standard treatment for acetaminophen intoxication**. *Liver Int* 2017,**37**:748-756.
5. Verhelst X, Vanderschaeghe D, Castera L, Raes T, Geerts A, Francoz C, Colman R, Durand F, Callewaert N, Van Vlierberghe H. **A Glycomics-Based Test Predicts the Development of Hepatocellular Carcinoma in Cirrhosis**. *Clin Cancer Res* 2017,**23**:2750-2758.
6. Lefere S, Hoorens A, Raevens S, Troisi R, Verhelst X, Van Vlierberghe H, Geerts A. **Refractory subacute steatohepatitis after biliopancreatic diversion**. *Hepatology* 2017,**66**:289-291.
7. Paridaens A, Raevens S, Devisscher L, Bogaerts E, Verhelst X, Hoorens A, Van Vlierberghe H, van Grunsven LA, Geerts A, Colle I. **Modulation of the Unfolded Protein Response by Tauroursodeoxycholic Acid Counteracts Apoptotic Cell Death and Fibrosis in a Mouse Model for Secondary Biliary Liver Fibrosis**. *Int J Mol Sci* 2017,**18**.
8. Degre D, Serste T, Lasser L, Delwaide J, Starkel P, Laleman W, Langlet P, Reynaert H, Bourgeois S, Vanwolleghem T, Negrin Dastis S, Gustot T, Geerts A, Van Steenkiste C, de Galocsy C, Lepida A, Orlent H, Moreno C. **Sofosbuvir in Combination with Simeprevir +/- Ribavirin in Genotype 4 Hepatitis C Patients with Advanced Fibrosis or Cirrhosis: A Real-World Experience from Belgium**. *PLoS One* 2017,**12**:e0170933.
9. Devisscher L, Vieri M, Logue SE, Panse J, Geerts A, van Vlierberghe H, Chevet E, Gorman AM, Samali A, Kharabi Masouleh B. **Targeting the angio-proteostasis network: Combining the forces against cancer**. *Pharmacol Ther* 2016,**167**:1-12.
10. Onghena L, Develtere W, Poppe C, Geerts A, Troisi R, Vanlander A, Berrevoet F, Rogiers X, Van Vlierberghe H, Verhelst X. **Quality of life after liver transplantation: State of the art**. *World J Hepatol* 2016,**8**:749-756.

VICTOR ARENDT *Centre hospitalier de Luxembourg,*
From Pubmed [Arendt, V.(Author)]:

1. Mukeba-Tshialala D, Nachega JB, Mutombo-Tshingwali M, Arendt V, Gilson G, Moutschen M. **[Obesity, high blood pressure, hypercholesterolaemia, and untreated diabetes in HIV-infected and HIV-uninfected adults in Mbuji-Mayi (Democratic Republic of Congo)]**. *Bull Soc Pathol Exot* 2017.
2. Dahourou DL, Amorissani-Folquet M, Coulibaly M, Avit-Edi D, Meda N, Timite-Konan M, Arendt V, Ye D, Amani-Bosse C, Salamon R, Lepage P, Leroy V, Monod Anrs 12206 Study G. **Missed opportunities of inclusion in a cohort of HIV-infected children to initiate antiretroviral treatment before the age of two in West Africa, 2011 to 2013**. *J Int AIDS Soc* 2016,**19**:20601.
3. Hofstra LM, Sauvageot N, Albert J, Alexiev I, Garcia F, Struck D, ...Arendt V, ...et al.. **Transmission of HIV Drug Resistance and the Predicted Effect on Current First-**

line Regimens in Europe. *Clin Infect Dis* 2016,**62**:655-663.

4. Gane E, Kershenobich D, Seguin-Devaux C, Kristian P, Aho I, Dalgard O, ... Arendt V, et al.. **Strategies to manage hepatitis C virus (HCV) infection disease burden - volume 2**. *J Viral Hepat* 2015,**22 Suppl 1**:46-73.
5. Hatzakis A, Chulanov V, Gadano AC, Bergin C, Ben-Ari Z, Mossong J, ..., Arendt V,.... et al. . **The present and future disease burden of hepatitis C virus (HCV) infections with today's treatment paradigm - volume 2**. *J Viral Hepat* 2015,**22 Suppl 1**:26-45.
6. Saraswat V, Norris S, de Knegt RJ, Sanchez Avila JF, Sonderup M, Zuckerman E, ... Arendt V, ...et al. **Historical epidemiology of hepatitis C virus (HCV) in select countries - volume 2**. *J Viral Hepat* 2015,**22 Suppl 1**:6-25.
7. Zheng Y, Lambert C, Arendt V, Seguin-Devaux C. **Virological and immunological outcomes of elvitegravir-based regimen in a treatment-naive HIV-2-infected patient**. *AIDS* 2014,**28**:2329-2331.
8. Radloff R, Gras A, Zanger UM, Masquelier C, Arumugam K, Karasi JC, Arendt V, Seguin-Devaux C, Klein K. **Novel CYP2B6 enzyme variants in a Rwandese population: functional characterization and assessment of in silico prediction tools**. *Hum Mutat* 2013,**34**:725-734.
9. Baatz F, Struck D, Lemaire M, De Landtsheer S, Servais JY, Arendt V, Schmit JC, Perez Bercoff D. **Rescue of HIV-1 long-time archived X4 strains to escape maraviroc**. *Antiviral Res* 2011,**92**:488-492.
10. Zachariah R, Van Damme W, Arendt V, Schmit JC, Harries AD. **The HIV/AIDS epidemic in sub-Saharan Africa: thinking ahead on programmatic tasks and related operational research**. *J Int AIDS Soc* 2011,**14 Suppl 1**:S7.

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From Pubmed [Mulkay, JP.(Author)]:

1. Bielen R, Moreno C, Van Vlierberghe H, Bourgeois S, Mulkay JP, Vanwolleghem T, Verlinden W, Brixko C, Decaestecker J, De Galocsy C, Janssens F, Cool M, Van Overbeke L, Van Steenkiste C, D'heygere F, Cools W, Nevens F, Robaeys G.
2. **Belgian experience with direct acting antivirals in people who inject drugs.** Drug Alcohol Depend. 2017 Aug 1;177:214-220. doi: 10.1016/j.drugalcdep.2017.04.003. Epub 2017 May 30.
3. Bielen R, Moreno C, Van Vlierberghe H, Bourgeois S, Mulkay JP, Vanwolleghem T, Verlinden W, Brixco C, Decaestecker J, de Galocsy C, Janssens F, Van Overbeke L, Van Steenkiste C, D'Heygere F, Cool M, Wuyckens K, Nevens F, Robaeys G The risk of early occurrence and recurrence of hepatocellular carcinoma in hepatitis C-infected patients treated with direct-acting antivirals with and without pegylated interferon: A Belgian experience. J Viral Hepat. 2017 Nov;24(11):976-981. doi: 10.1111/jvh.12726. Epub 2017 Aug 3.
4. Bruyneel M, Sersté T, Libert W, van den Broecke S, Ameye L, Dachy B, Mulkay JP, Moreno C, Gustot T **Improvement of sleep architecture parameters in cirrhotic patients with recurrent hepatic encephalopathy with the use of rifaximin.** *Eur J Gastroenterol Hepatol* 2017,**29**:302-308
5. Matheï C, Bourgeois S, Blach S, Brixko C, Mulkay JP, Razavi H, Robaeys G**.Mitigating the burden of hepatitis C virus among people who inject drugs in Belgium.** Acta Gastroenterol Belg. 2016 Apr-Jun;79(2):227-32.
6. Bourgeois S, Blach S, Blach C, Laleman W, Matheï C, Mulkay JP, Ravazi H, Robaeys G, Stärkel P, Van Damme P, Van Vlierberghe H, Vandijck D, Vandijck C.. **Achieving WHO recommendations for Hepatitis C Virus Elimination in Belgium.**Acta Gastroenterol Belg. 2016 Apr-Jun;79(2):222-6.

7. Nkuize M, Sersté T, Buset M, Mulkay JP**.Combination ledipasvir-sofosbuvir for the treatment of chronic hepatitis C virus infection: a review and clinical perspective.** Ther Clin Risk Manag. 2016 Jun 3;12:861-72.
8. Nkuize M, Mulkay JP, Moreno C, Lasser L, Michielsen P, de Galocsy C, Scheen R, Assene C, Delwaide J**. Ethnic epidemiological profiles and antiviral therapy among patients infected with hepatitis C virus genotype 4: a multicenter study from Belgium.** Acta Gastroenterol Belg. 2015 Dec;78(4):365-72.
9. Bourgeois S, Deltenre P, Delwaide J, Henrion J, Adler M, Langlet P, Mulkay JP, Nevens F, Brixko C, Moreno C. **A non-interventional phase IV Belgian survey to assess the antiviral effectiveness of pegylated interferon-alpha-2b and ribavirin treatment according to the stage of liver fibrosis in previously untreated patients with genotype 1/4/5/6 chronic hepatitis C (PRACTICE).**Acta Gastroenterol Belg. 2014 Dec;77(4):393-400.
10. Mulkay JP, Bourgeois S, Lasser L, De Galocsy C, Tomasovic S, Horsmans Y, Van Vlierberghe H; Belgian PROPHESYS investigators **Characteristics, treatment, and virologic responses of chronic hepatitis C patients treated with peginterferon alfa-2a and ribavirin in belgium: a sub-analysis of the PROPHESYS study.** Acta Gastroenterol Belg. 2014 Mar;77(1):30-40.
11. Nkuize M, Mulkay JP, Adler M, Lasser L, Michielsen P, de Galocsy C, Assene C, Delwaide **Response of Black African patients with hepatitis C virus genotype 4 to treatment with peg-interferon and ribavirin**. Acta Gastroenterol Belg. 2013 Sep;76(3):291-9.

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From Pubmed [Bielen, R.(Author)]:

1. Bielen R, Moreno C, Van Vlierberghe H, Bourgeois S, Mulkay JP, Vanwolleghem T, Verlinden W, Brixco C, Decaestecker J, de Galocsy C, Janssens F, Van Overbeke L, Van Steenkiste C, D'Heygere F, Cool M, Wuyckens K, Nevens F, Robaeys G. **The risk of early occurrence and recurrence of hepatocellular carcinoma in hepatitis C-infected patients treated with direct-acting antivirals with and without pegylated interferon: A Belgian experience**. *J Viral Hepat* 2017,**24**:976-981.
2. Bielen R, Moreno C, Van Vlierberghe H, Bourgeois S, Mulkay JP, Vanwolleghem T, Verlinden W, Brixko C, Decaestecker J, De Galocsy C, Janssens F, Cool M, Van Overbeke L, Van Steenkiste C, D'Heygere F, Cools W, Nevens F, Robaeys G. **Belgian experience with direct acting antivirals in people who inject drugs**. *Drug Alcohol Depend* 2017,**177**:214-220.
3. Robaeys G, Bielen R, Azar DG, Razavi H, Nevens F. **Global genotype distribution of hepatitis C viral infection among people who inject drugs**. *J Hepatol* 2016,**65**:1094-1103.

PETER STÄRKEL *Cliniques Universitaires Saint-Luc, Brussels, Belgium*

From speaker's form:

1. Sophie Leclercq, Christine De Saeger, Nathalie Delzenne, Philippe de Timary, Peter Starkel. **Role of Inflammatory Pathways, Blood Mononuclear Cells, and Gut-derived Bacterial Products in Alcohol Dependence**. Biol Psychiatry 2014; 76:725-33 (IF 2014: 10,255)
2. Leclercq S, Matamoros S, Cani PD, Neyrinck AM, Jamar F, Stärkel P, Windey K, Tremaroli V, Bäckhed F, Verbeke K, de Timary P, Delzenne NM**. Intestinal permeability, gut-bacterial dysbiosis, and behavioral markers of alcohol-dependence severity**. Proc Natl Acad Sci U S A. 2014; 111:E4485-93 (IF 2014: 9,674)
3. Wedemeyer H, Duberg AS, Buti M, Rosenberg WM, Frankova S, Esmat G, Örmeci N, Van Vlierberghe H, Gschwantler M, Akarca U, Aleman S, Balık I, Berg T, Bihl F, Bilodeau M, Blasco AJ, Brandão Mello CE, Bruggmann P, Calinas F, Calleja JL, Cheinquer H,

Christensen PB, Clausen M, Coelho HS, Cornberg M, Cramp ME, Dore GJ, Doss W, El-Sayed MH, Ergör G, Estes C, Falconer K, Félix J, Ferraz ML, Ferreira PR, García-Samaniego J, Gerstoft J, Giria JA, Gonçales FL Jr, Guimarães Pessôa M, Hézode C, Hindman SJ, Hofer H, Husa P, Idilman R, Kåberg M, Kaita KD, Kautz A, Kaymakoglu S, Krajden M, Krarup H, Laleman W, Lavanchy D, Lázaro P, Marinho RT, Marotta P, Mauss S, Mendes Correa MC, Moreno C, Müllhaupt B, Myers RP, Nemecek V, Øvrehus AL, Parkes J, Peltekian KM, Ramji A, Razavi H, Reis N, Roberts SK, Roudot-Thoraval F, Ryder SD, Sarmento-Castro R, Sarrazin C, Semela D, Sherman M, Shiha GE, Sperl J, Stärkel P, Stauber RE, Thompson AJ, Urbanek P, Van Damme P, van Thiel I, Vandijck D, Vogel W, Waked I, Weis N, Wiegand J, Yosry A, Zekry A, Negro F, Sievert W, Gower E. **Strategies to manage hepatitis C virus (HCV) disease burden.** J Viral Hepat. 2014; 21 Suppl 1:60-89

4. Chen P, Stärkel P, Turner JR, Ho SB, Schnabl B. **Dysbiosis-induced intestinal inflammation activates tumor necrosis factor receptor I and mediates alcoholic liver disease in mice.** Hepatology. 2015; 61(3):883-94 (IF 2015: 11,71)
5. Delire B, Stärkel P. **The Ras/MAPK pathway and hepatocarcinoma: pathogenesis and therapeutic implications**. Eur J Clin Invest. 2015;45(6):609-23 (IF 2015: 2,687)
6. Stärkel P, Schnabl B. **Bidirectional Communication between Liver and Gut during Alcoholic Liver Disease**. Semin Liver Dis. 2016 Sep;36(4):331-339
7. Wang L, Fouts DE, Stärkel P, Hartmann P, Chen P, Llorente C, DePew J, Moncera K, Ho SB, Brenner DA, Hooper LV, Schnabl B **. Intestinal REG3 Lectins Protect against Alcoholic Steatohepatitis by Reducing Mucosa-Associated Microbiota and Preventing Bacterial Translocation.** Cell Host Microbe. 2016;19(2):227-39 (IF 2015: 12,55)
8. Leclercq S, de Timary P, Delzenne NM, Stärkel P. **The link between inflammation, bugs, the intestine and the brain in alcohol dependence**. Transl Psychiatry. 2017 Feb 28;7(2):e1048
9. Yang AM, Inamine T, Hochrath K, Chen P, Wang L, Llorente C, Bluemel S, Hartmann P, Xu J, Koyama Y, Kisseleva T, Torralba MG, Moncera K, Beeri K, Chen CS, Freese K, Hellerbrand C, Lee SM, Hoffman HM, Mehal WZ, Garcia-Tsao G, Mutlu EA, Keshavarzian A, Brown GD, Ho SB, Bataller R, Stärkel P, Fouts DE, Schnabl B. **Intestinal fungi contribute to development of alcoholic liver disease**. J Clin Invest. 2017 May 22. pii: 90562. doi: 10.1172/JCI90562
10. Lanthier N, Stärkel P. **Treatment of severe alcoholic hepatitis: past, present and future.** Eur J Clin Invest. 2017 May 18. doi: 10.1111/eci.12767

DAVID FITZSIMONS, *rapporteur*

1. Larson HJ, Van Damme P, FitzSimons D **A hepatitis-free future: strategy first, then pricing.** Lancet Infect Dis. 2016 Apr;16(4):399-400
2. FitzSimons D, Hendrickx G, Lernout T, Badur S, Vorsters A, Van Damme P. **Incentives and barriers regarding immunization against influenza and hepatitis of health care workers.** Vaccine 2014,32:4849-4854.
3. FitzSimons D, McMahon B, Hendrickx G, Vorsters A, Van Damme P. **Burden and prevention of viral hepatitis in the Arctic region, Copenhagen, Denmark, 22-23 March 2012**. Int J Circumpolar Health. 2013 Jul 17;72
4. Fitzsimons DW. **World Health Organization.** Acta Med Port. 2013 May-Jun;26(3):186-7.
5. FitzSimons D, Hendrickx G, Vorsters A, Van Damme P**. Identification and management of persons with chronic viral hepatitis in Europe**. European Gastroenterology & Hepatology 2012;8(1).

6. Fitzsimons D, Kojouharova M, Hallauer J, Hendrickx G, Vorsters A, Van Damme P. **Burden and prevention of viral hepatitis in Bulgaria**. *Vaccine* 2011,29:8471-8476.
7. FitzSimons D, Hendrickx G, Vorsters A, Van Damme P. **Hepatitis A and E: update on prevention and epidemiology**. *Vaccine*. 2010 Jan 8;28(3):583-8. Epub 2009 Nov 17.
8. FitzSimons DW. **Prevention and control of viral hepatitis: the role and impact of patient and advocacy groups in and outside Europe**. *Vaccine*. 2008 Oct 23;26(45):5669-74. Epub 2008 Aug 30.
9. FitzSimons D, François G, De Carli G, Shouval D, Prüss-Ustün A, Puro V, Williams I, Lavanchy D, De Schryver A, Kopka A, Ncube F, Ippolito G, Van Damme P. **Hepatitis B virus, hepatitis C virus and other blood-borne infections in healthcare workers: guidelines for prevention and management in industrialized countries**. *Occup Environ Med*. 2008 Jul;65(7):446-51.
10. FitzSimons D, Vorsters A, Hoppenbrouwers K, Van Damme P; **Viral Hepatitis Prevention Board (VHPB); European Union for School and University Health and Medicine (EUSUHM). Prevention and control of viral hepatitis through adolescent health programmes in Europe**. *Vaccine*. 2007 Dec 17;25(52):8651-9. Epub 2007 Oct 23.