BULGARIA

A.KEVORKYAN

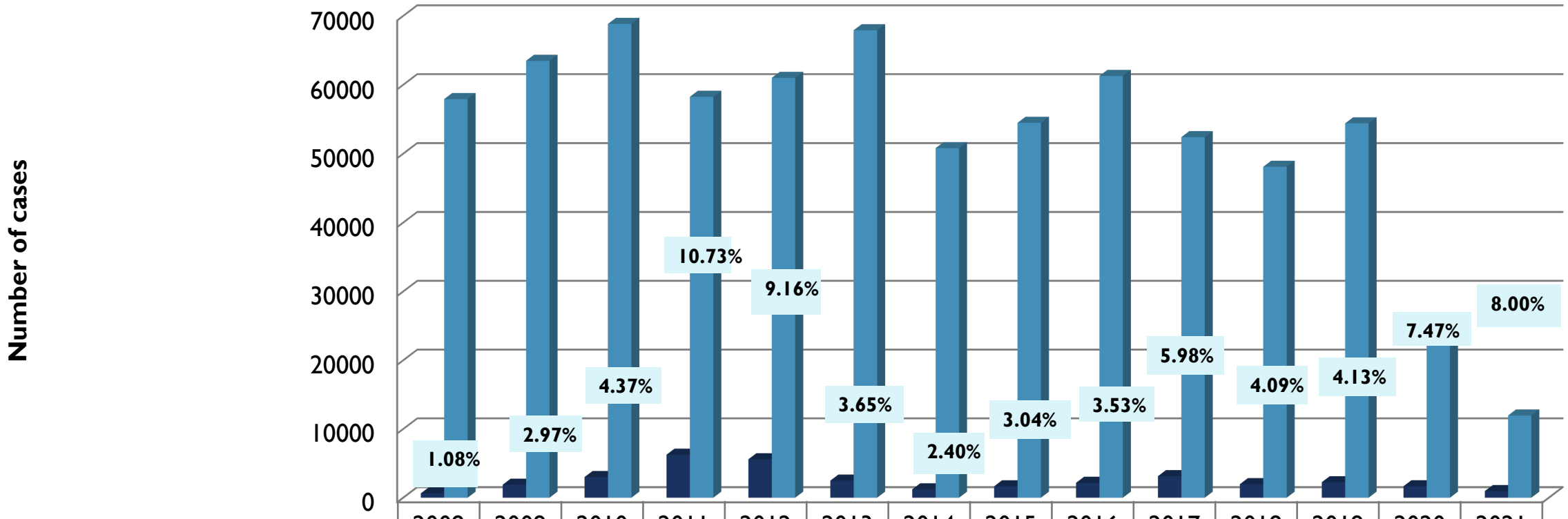
VHPB BALKAN MEETING

CURRENT SITUATION: EPIDEMIOLOGY, BURDEN OF DISEASE, SCREENING & PREVENTION

SEPARATE REGISTRATION OF VIRAL HEPATITIS IN BULGARIA

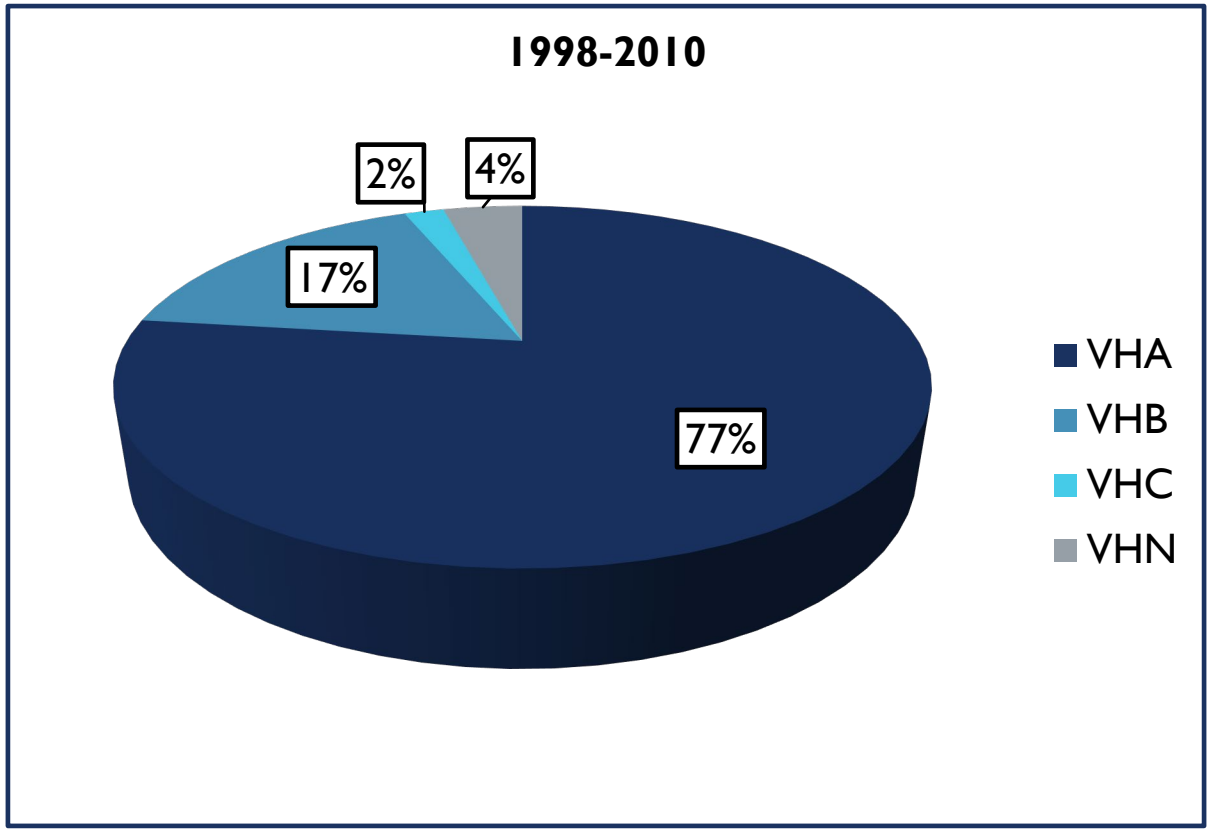
- 1983 – Viral hepatitis A and Viral hepatitis B
- 1997 – Viral hepatitis C
- 2019 - Viral hepatitis E (the first case was reported in 1995, Teoharov P. et al.)

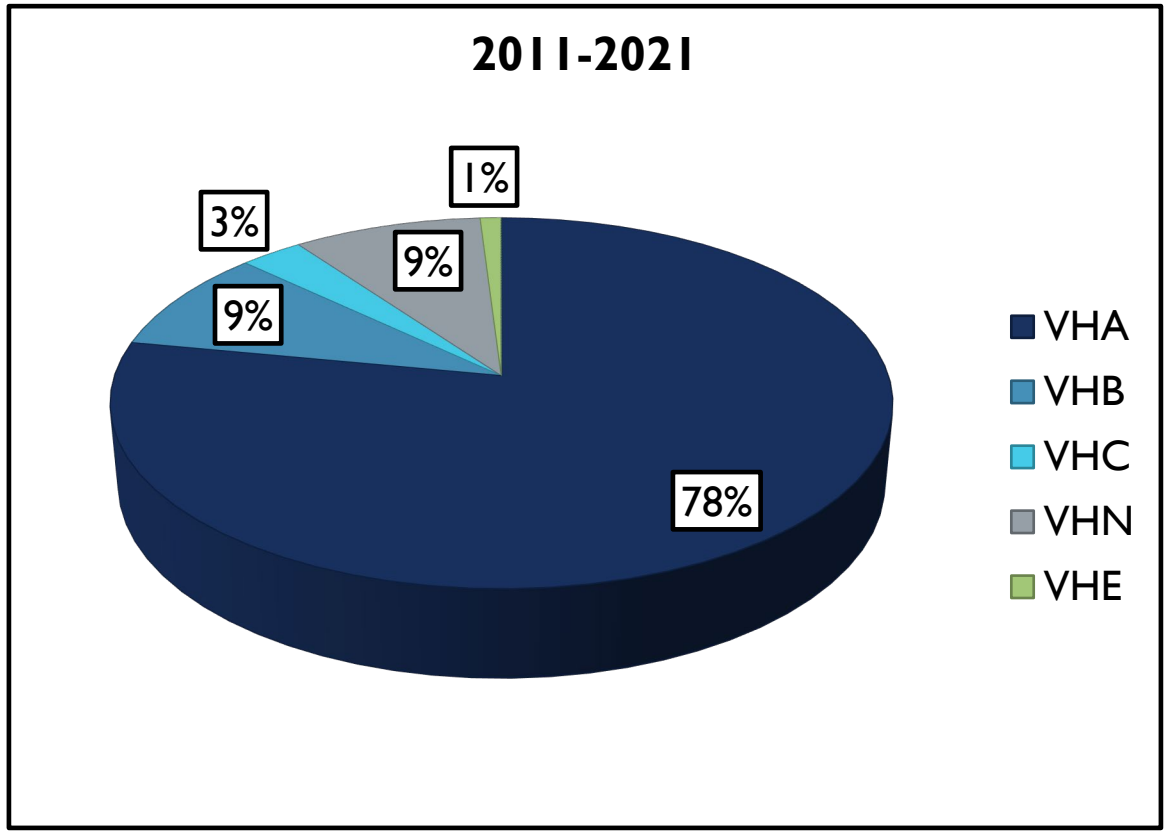
RELATIVE SHARE OF VIRAL HEPATITIS (%) IN THE STRUCTURE OF ACUTE INFECTIOUS DISEASES IN BULGARIA 2008-2021



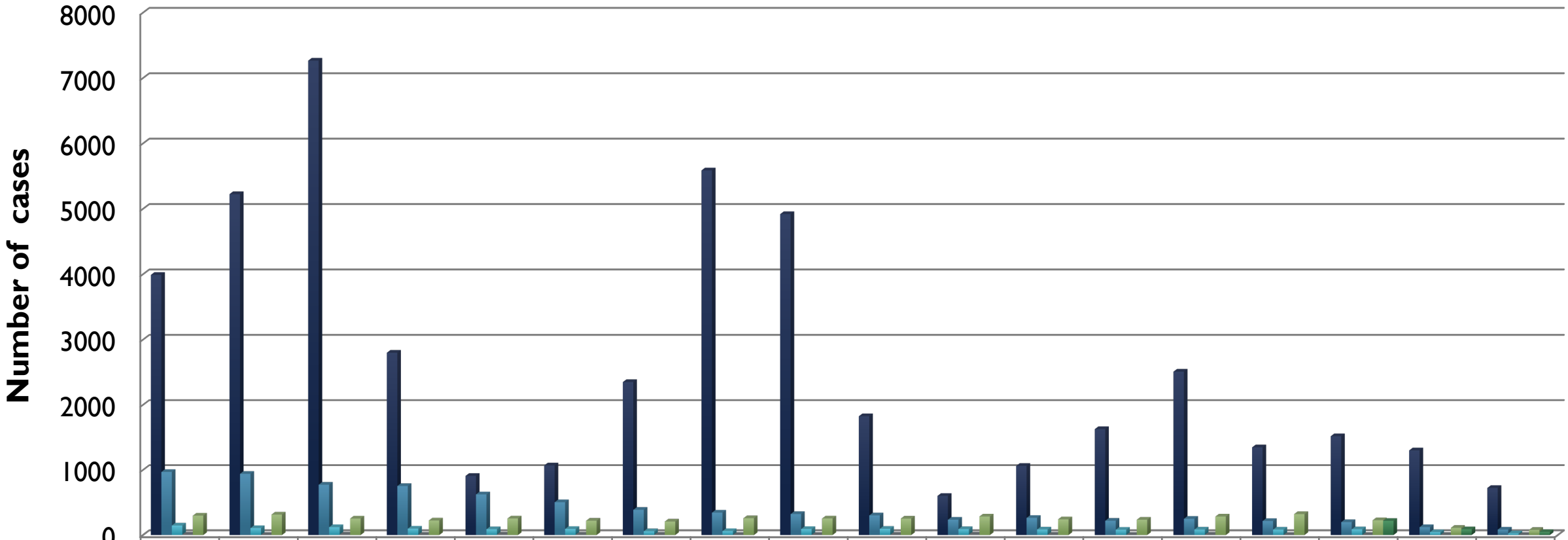
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Viral hepatitis (cases, n)	624	1887	3007	6253	5590	2479	1218	1656	2165	3132	1968	2249	1664	957
Communicable diseases (cases, n)	57.916	63.474	68.839	58.259	60.998	67.916	50.800	54.471	61.283	52.393	48.092	54.397	22.261	11.956

STRUCTURE OF THE VIRAL HEPATITIS IN BULGARIA IN TWO PERIODS: 1998-2010 AND 2011-2021



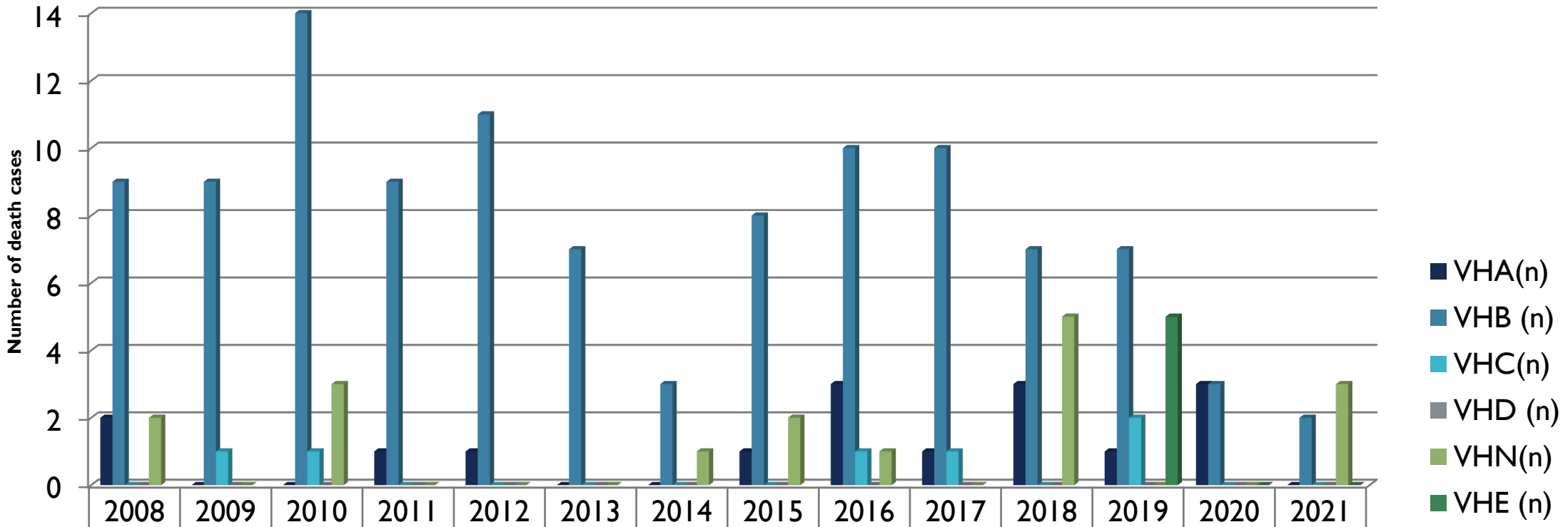


Viral hepatitis by type (number of cases) in Bulgaria (2004-2021)



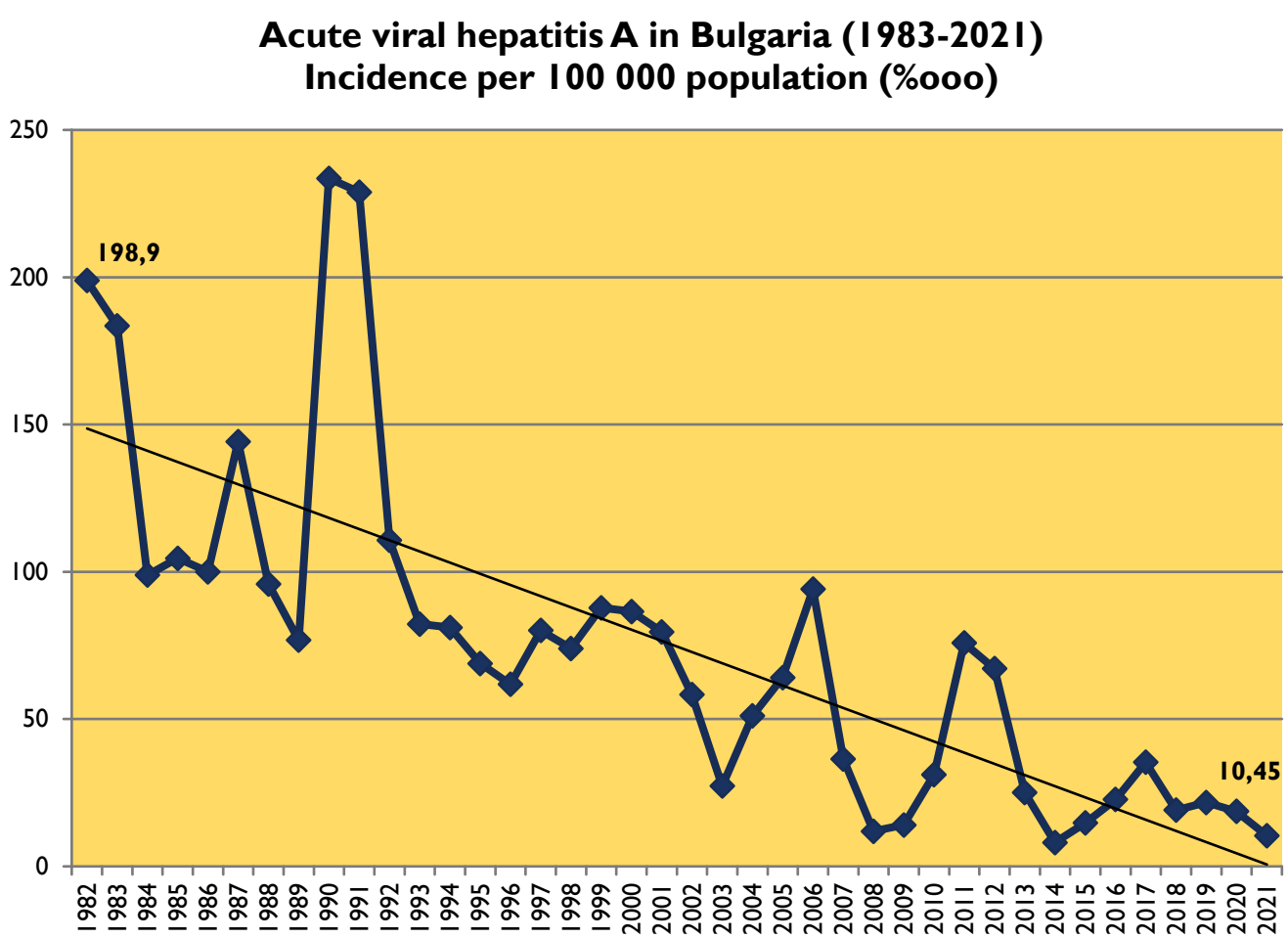
	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
VHA(n)	3990	5225	7266	2800	908	1069	2350	5588	4919	1825	601	1062	1627	2510	1347	1518	1300	723
VHB (n)	969	940	773	753	624	504	387	344	322	302	235	263	219	249	215	198	121	83
VHC(n)	146	106	121	98	89	93	58	60	92	95	90	85	81	84	83	88	44	25
VHD (n)	7	3	8	4	8	6	5	3	3	5	8	5	3	5	2	1	1	2
VHN(n)	298	314	253	223	254	220	207	258	254	252	284	241	235	284	321	227	110	78
VHE (n)																217	88	46

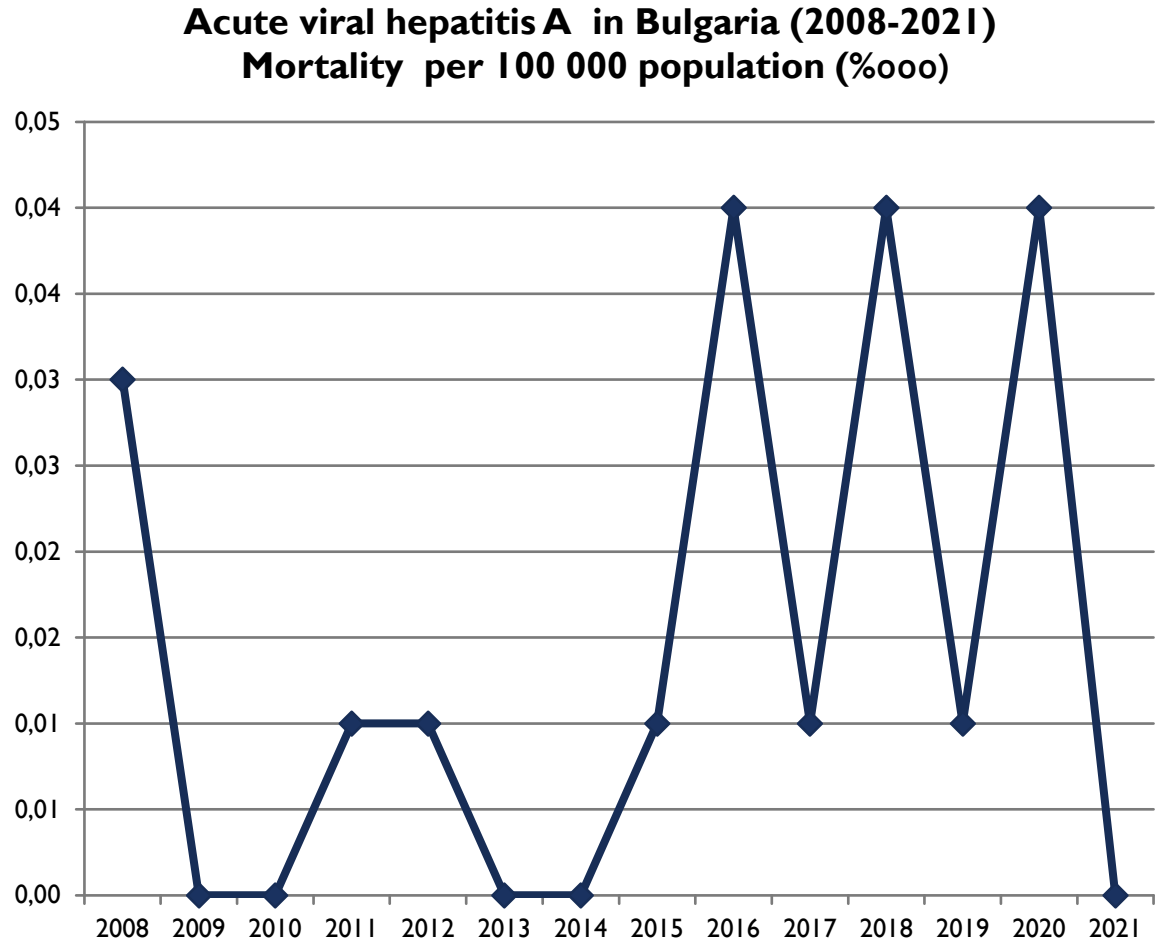
Viral hepatitis by type (death cases) in Bulgaria (2008-2021)



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
VHA(n)	2	0	0	1	1	0	0	1	3	1	3	1	3	0
VHB (n)	9	9	14	9	11	7	3	8	10	10	7	7	3	2
VHC(n)	0	1	1	0	0	0	0	0	1	1	0	2	0	0
VHD (n)	0	0	0	0	0	0	0	0	0	0	0	0	0	0
VHN(n)	2	0	3	0	0	0	1	2	1	0	5	0	0	3
VHE (n)												5	0	0

HEPATITIS A


Acute viral hepatitis A in Bulgaria (1983-2021)
Incidence per 100 000 population (%ooo)
250
200
150
100
50
0
198,9
10,45
1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021


Acute viral hepatitis A in Bulgaria (2008-2021)
Mortality per 100 000 population (%ooo)
0,05
0,04
0,04
0,03
0,03
0,02
0,02
0,01
0,01
0,00
2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021

EPIDEMIOLOGICAL STUDY OF HEPATITIS A INFECTION IN EASTERN BULGARIA

TSANKOVA GS, TODOROVA TT, ERMENLIEVA NM, POPOVA TK, TSANKOVA DT. FOLIA MEDICA 2017;59(1):63-69.

- 2879 reported cases of acute hepatitis A in the Eastern regions of Bulgaria over a 7-year period between 2008 and 2014 were retrospectively reviewed:

-the average incidence of HAV was higher in the south-eastern regions than in the north-eastern regions (55.30%000 vs 15.04%000 respectively, $p < 0.0001$).

-the most affected age group in all regions was the 5-9-year olds ($p < 0.0001$) and males were significantly more susceptible to HAV ($p = 0.02$).

-HAV incidence did not correlate with the following factors: total number of the population of the corresponding region, population density, Roma ethnic origin, proportion of population aged under 10 years and poverty rate;

- A relatively strong negative correlation with the available useful living space per person (-0.6) and with the number of children enrolled in daycare units (-0.7) ($p > 0.05$)

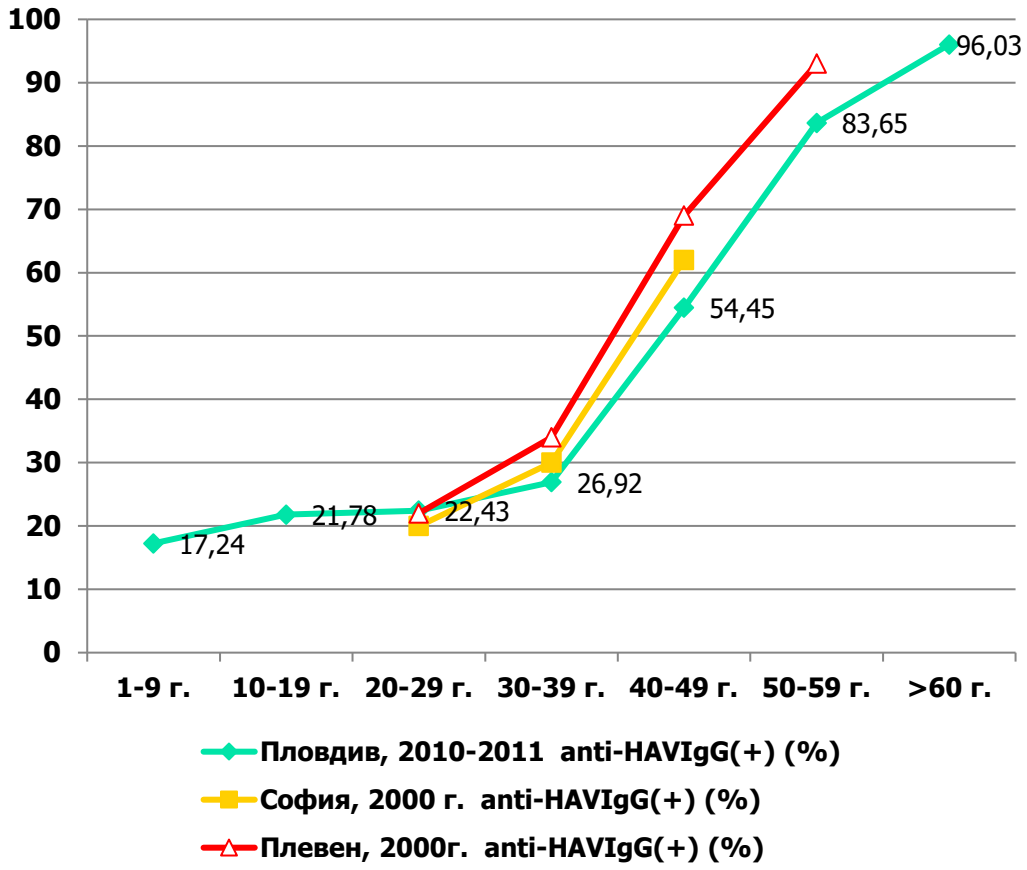
Table. Spearman's rank correlation coefficients between 7-year average HAV annual incidence and sociodemographic variables

Potential risk factors	Correlation coefficient
Total population number	0.1
Population density (per km^2)	0.1
Proportion of population of Roma ethnic origin (%)	0.3
Proportion of population aged <10 years (%)	0.3
Enrollment rate of children in day-care units (%)	-0.7
Useful floor area per person (m^2 per person)	-0.6
Poverty rate (%)	0.1

VIRAL HEPATITIS A (VHA) IN BULGARIA, 2021

- All reported cases (n=723) are laboratory confirmed;
- 691 (95,57%) were hospitalized;
- The distribution of patients by gender: men 57.81% (418 cases) vs. women 42.19% (305 cases);
- The disease was registered in all age groups, mostly within children (418 cases, 57.81%) with highest incidence rate among 5-9 years and 10-14 years, respectively 50.11‰ and 33.97‰, exceeding the average value for the country (10.45‰);
- Cases of VHA have been registered in 23 out of 28 regions of the country;
- No death cases of VHA were reported

PREVALENCE OF HEPATITIS A IN BULGARIA



- *Vatev NT, Atanasova MV, Stoilova YD, Chervenyakova TP, Troyancheva MG. Seroprevalence of hepatitis A viral infection in Plovdiv, Bulgaria. Folia Med (Plovdiv). 2009 Jan-Mar;51(1):70-3.*

-180 tested individuals, divided into 2 groups

-a mean anti-HAV seroprevalence of 68.33% with the highest value among subjects living in poor hygienic and sanitary conditions than those with normal ones (90.23% vs 44.83%)

- *Kevorkyan A, Raycheva R, Markova E, Presti ALo, Angeletti S, et al. (2015) Prevalence of Hepatitis A virus in Bulgaria. J Virol Antivir Res 4:2*

  presence of anti-HAV IgG,% (not vaccinated)

  - 561 individuals (20-84 years) from Sofia, 2000 – 44.06%

  - 420 individuals (20-84 years) from Pleven, 2000 -54.5%

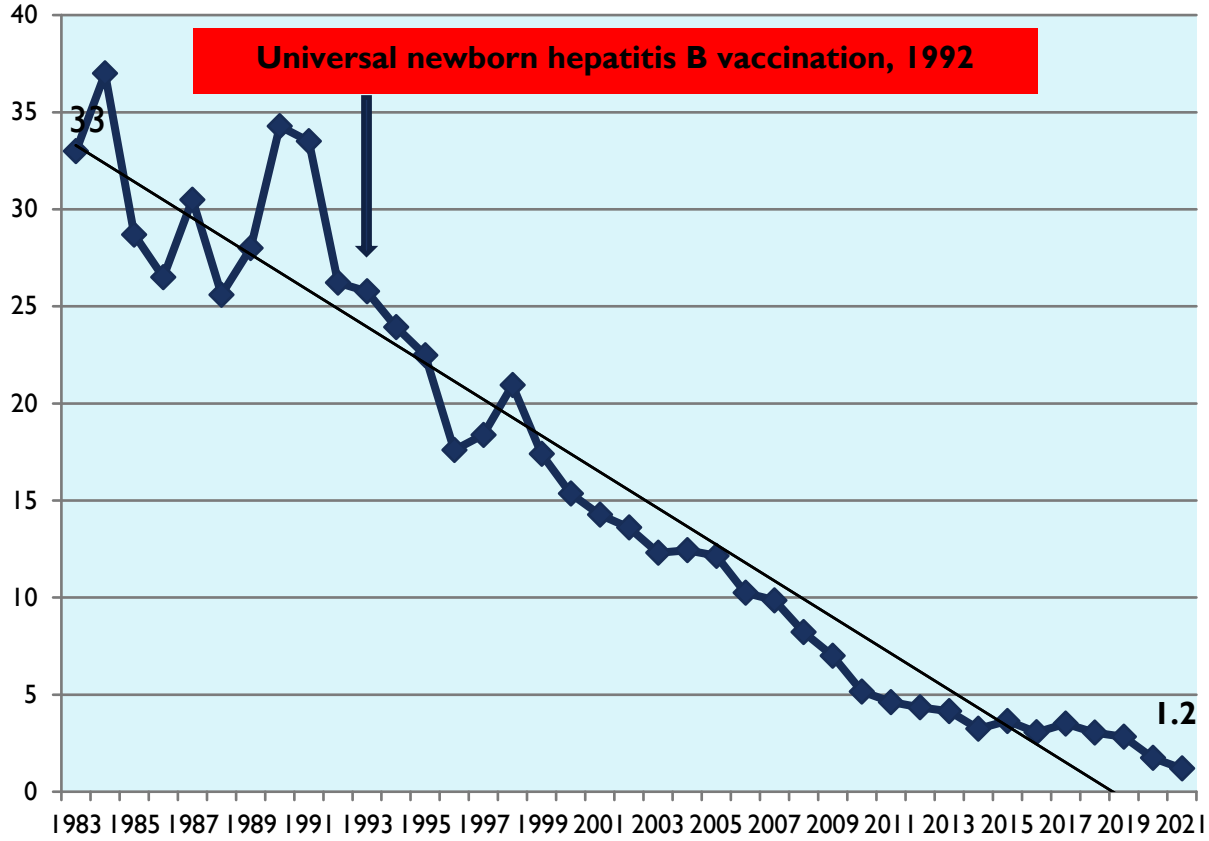
  - 705 individuals (1-84 years) from Plovdiv, 2010/11 – 46.5%

HEPATITIS A VIRUS GENOTYPES IN BULGARIA

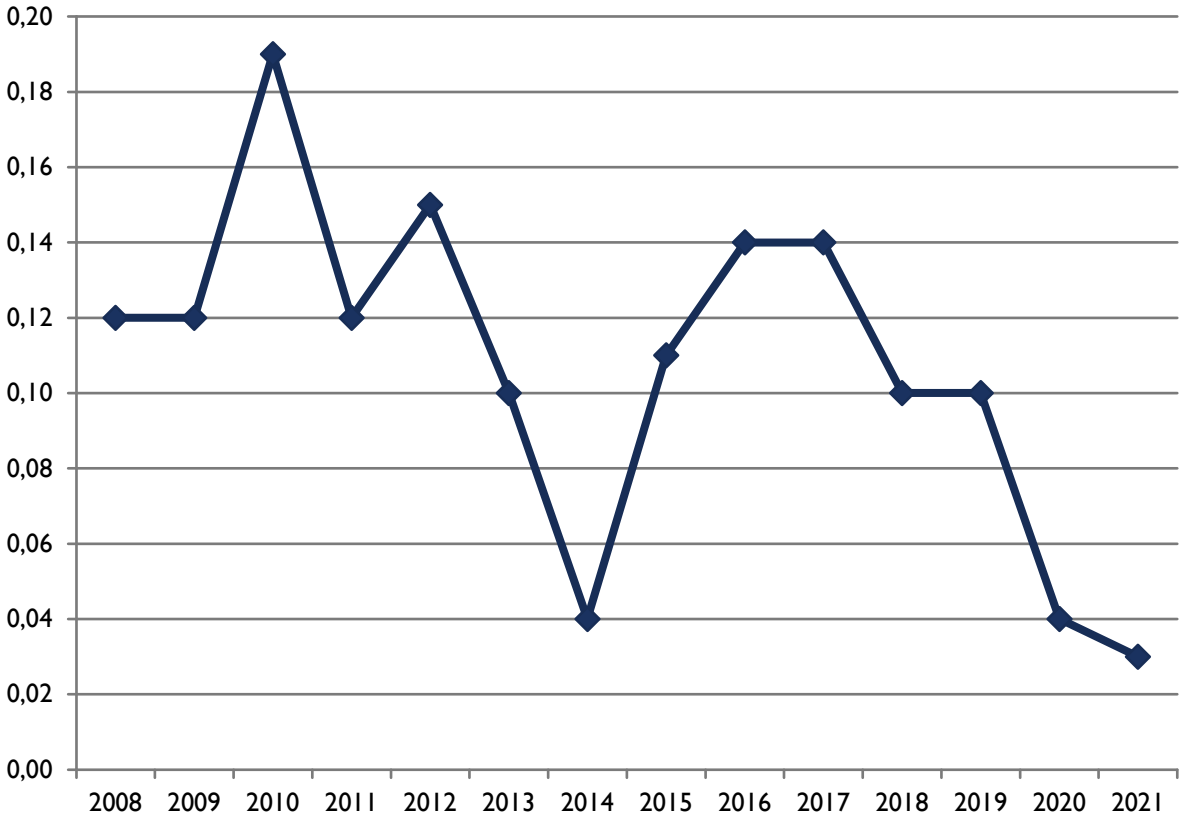
Article	Year of samples collection	Number of tested samples	Age groups of tested patients	Genotype
Bruni R, Taffon S, Equestre M, Cella E, Lo Presti A, Costantino A, Chionne P, Madonna E, Golkocheva-Markova E, Bankova D, Ciccozzi M, Teoharov P, Ciccaglione AR. Hepatitis A virus genotypes and strains from an endemic area of Europe, Bulgaria 2012-2014. BMC Infect Dis. 2017 Jul 14;17(1):497.	2012-2014	105	Children: 0–12-47.1% Teens: >12 to 19 -12.7% Adults: >19 -40.2%	74%- IA-sub-genotype 26% –IB-sub-genotype

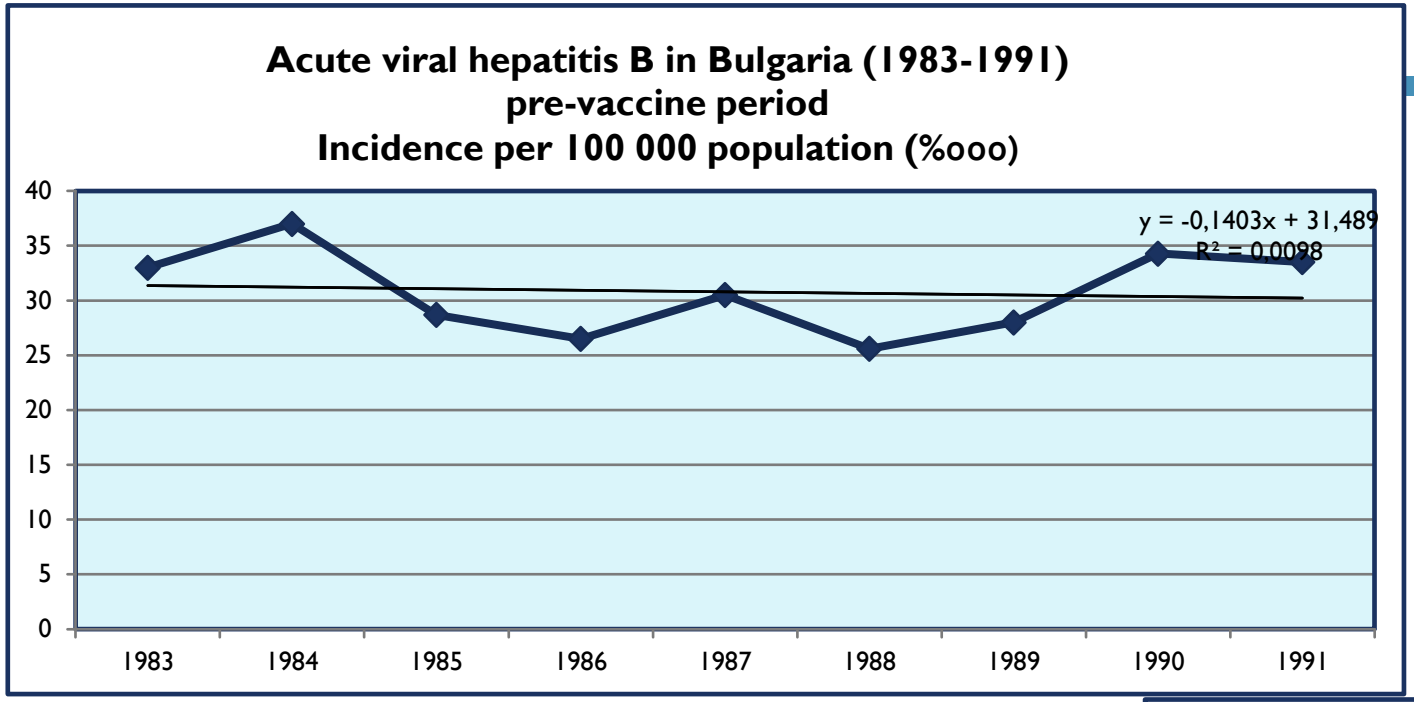
HEPATITIS B

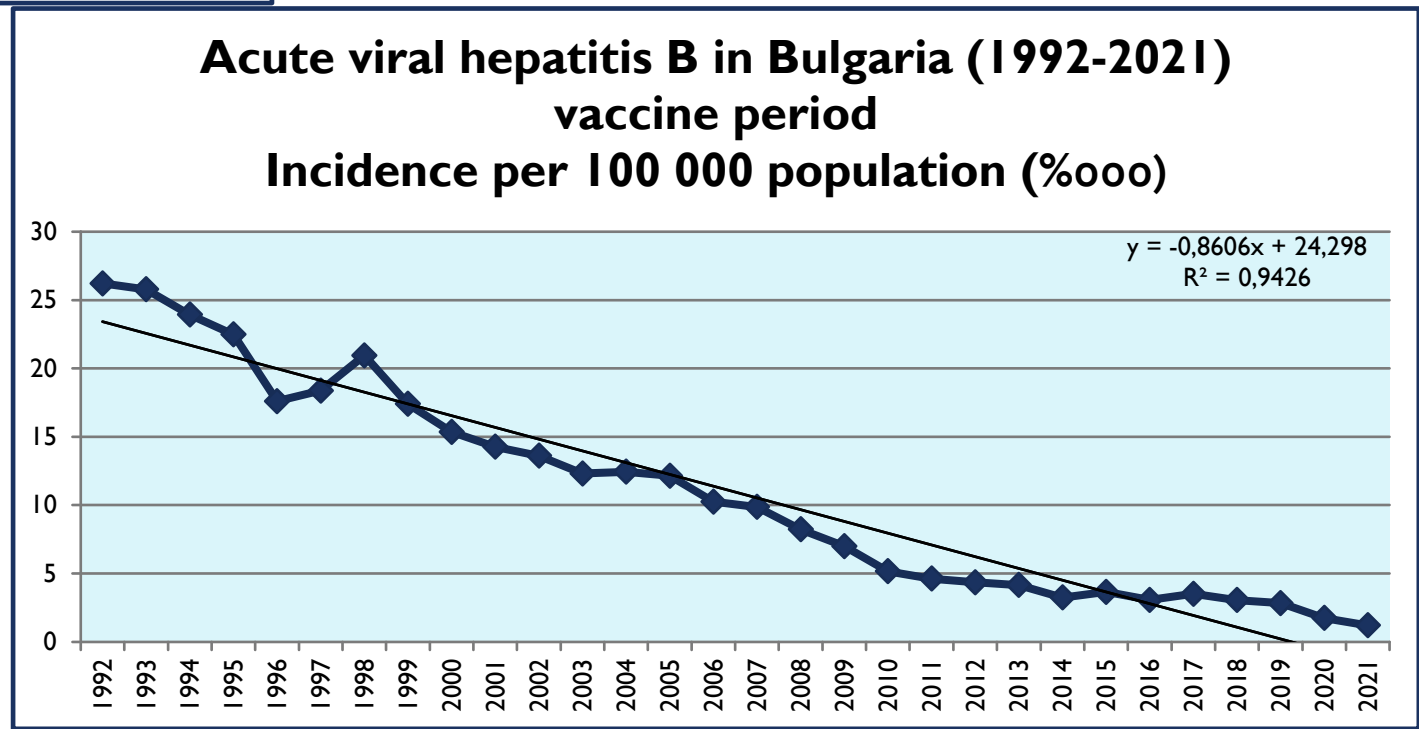
Acute viral hepatitis B in Bulgaria (1983-2021)
Incidence per 100 000 population (‰)



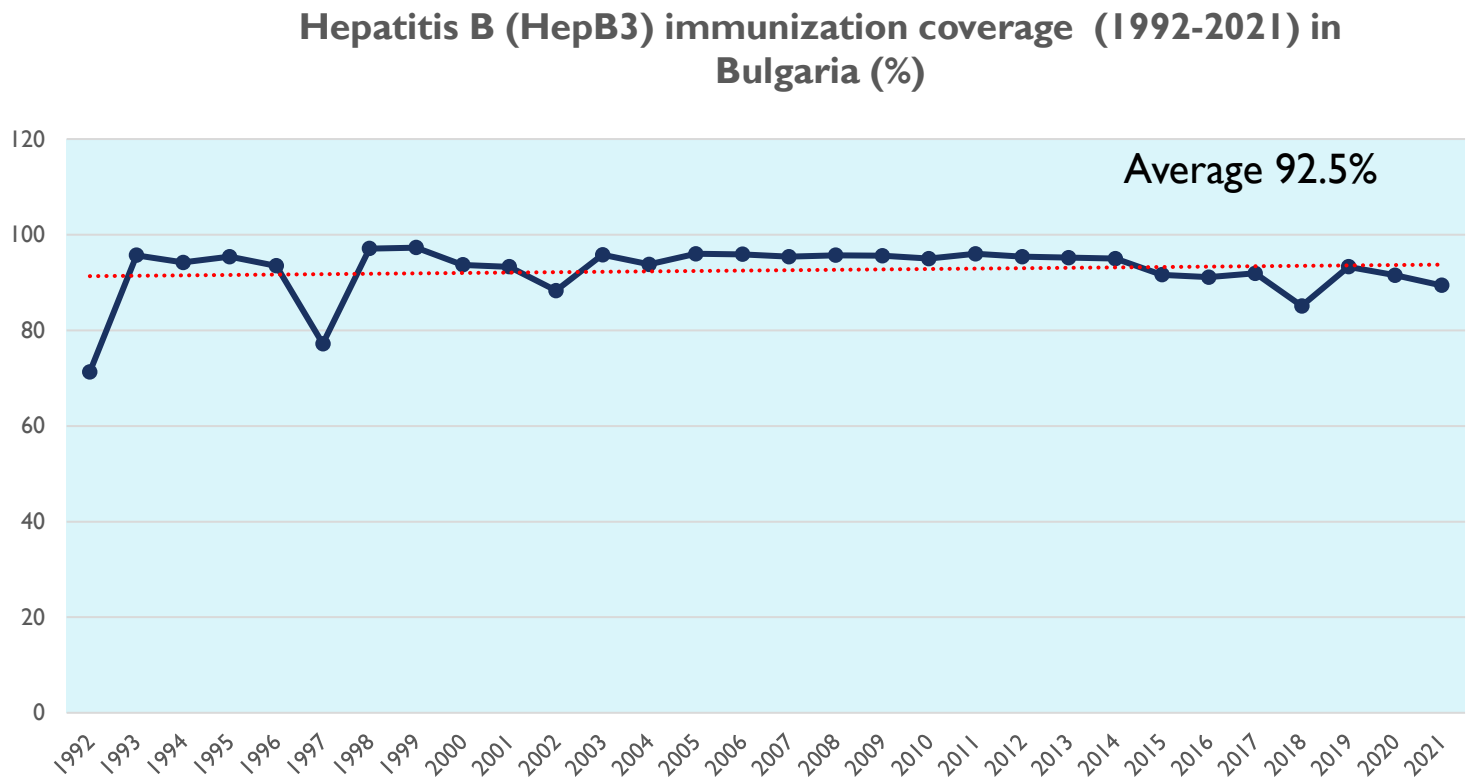
Acute viral hepatitis B in Bulgaria (2008-2021)
Mortality per 100 000 population (‰)




Acute viral hepatitis B in Bulgaria (1983-1991)
pre-vaccine period
Incidence per 100 000 population (‰)
y = -0,1403x + 31,489
R² = 0,0098
40
35
30
25
20
15
10
5
0
1983
1984
1985
1986
1987
1988
1989
1990
1991


Acute viral hepatitis B in Bulgaria (1992-2021)
vaccine period
Incidence per 100 000 population (‰)
y = -0,8606x + 24,298
R² = 0,9426
30
25
20
15
10
5
0
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021

	HepB3 immunization coverage (%),1992-2021
1992	71.3
1993	95.7
1994	94.2
1995	95.4
1996	93.5
1997	77.2
1998	97.1
1999	97.3
2000	93.7
2001	93.3
2002	88.3
2003	95.8
2004	93.8
2005	96
2006	95.9
2007	95.4
2008	95.7
2009	95.6
2010	95
2011	96
2012	95.4
2013	95.2
2014	95
2015	91.6
2016	91.1
2017	91.9
2018	85.1
2019	93.3
2020	91.5
2021	89.4



FACTORS OF INFLUENCE ON THE CURRENT EPIDEMIOLOGY OF **ACUTE VIRAL HEPATITIS B**

- **The main factor: universal hepatitis B vaccination of newborns since 1992**
- Additional factors:
- 1992-2000 - introduction of immunization of HCWs and medical students (state funded), since 2002 immunization of HCWs are paid by the employer *(Ordinance No. 4/14.10.2002 on the protection of workers from risks related to exposure to biological agents at work)*
- Improvement of specific lab diagnosis: quality and quantitative tests
- Screening of blood and blood products for HBsAg (since 1979); donated tissues & organs
- Standard precautions for all patient care applied in hospitals, BTC, labs, dentistry
- Use of disposable equipments (syringe+ needle and etc.)
- Training of medical personnel (*NCIPD, Medical universities, The Bulgarian Association for Prevention and Control of Nosocomial Infections – BULNOSO since 2003)*
- Introduction of medical standards *(Ordinance No. 3/ 8 May 2013 for approval of medical standard for prevention and control of nosocomial infections)*
- Informative campaigns and advertising activities organized by patient associations and pharmaceutical business

VIRAL HEPATITIS B (VHB) IN BULGARIA, 2021

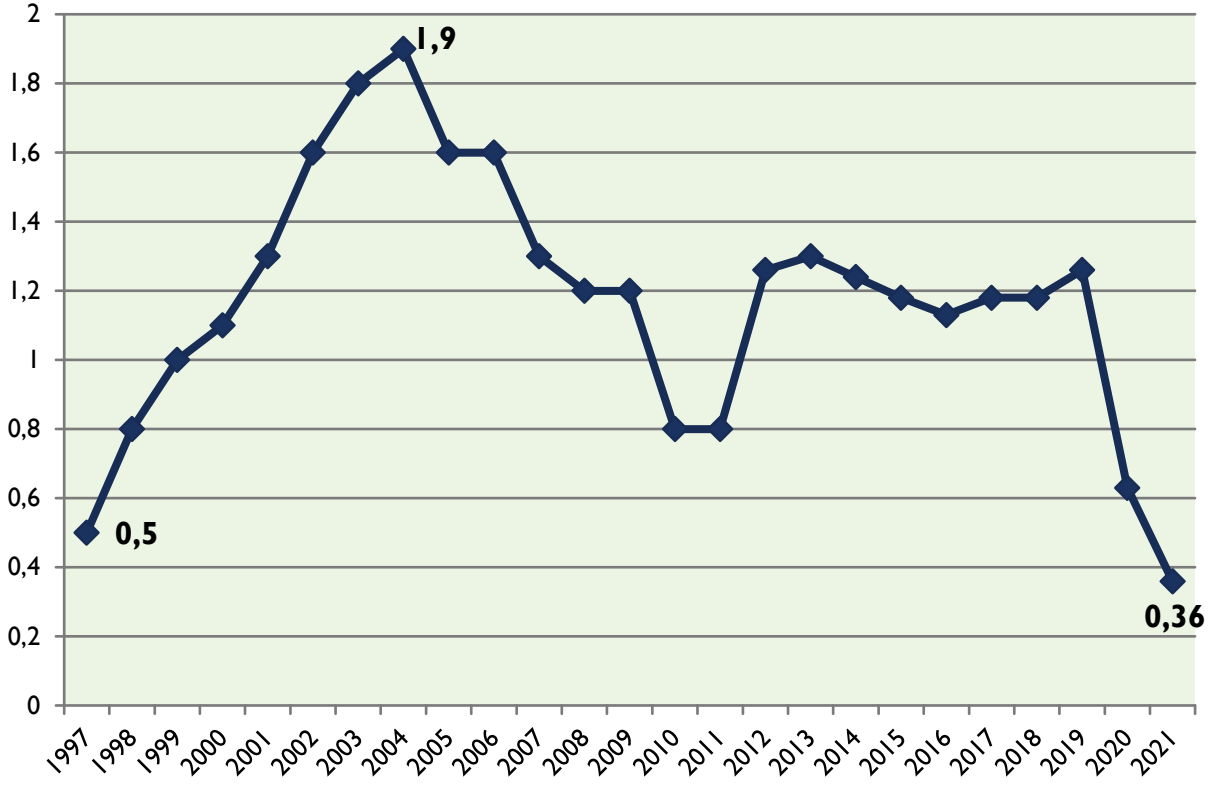
- All reported cases (n=83) are laboratory confirmed;
- 72 (86.75%) were hospitalized;
- The distribution of patients by gender: men **55 (66,27%)** vs. women 28 (33,73%);
- The disease was registered with highest incidence rate among 40-44 years and 30-34 years, respectively 2.30 ‰ and 2.11 ‰, exceeding the average value for the country (1.20 ‰);
- The incidence in the age groups 1-29 years who are subject to mass vaccination against hepatitis B decreases;
- Cases of VHB have been registered in 20 out of 28 regions of the country;
- Two death cases of VHB were reported (males in the age groups 40-44 and 60-64; mortality 0,03 ‰; lethality 2,41%).

HEPATITIS B VIRUS GENOTYPES IN BULGARIA

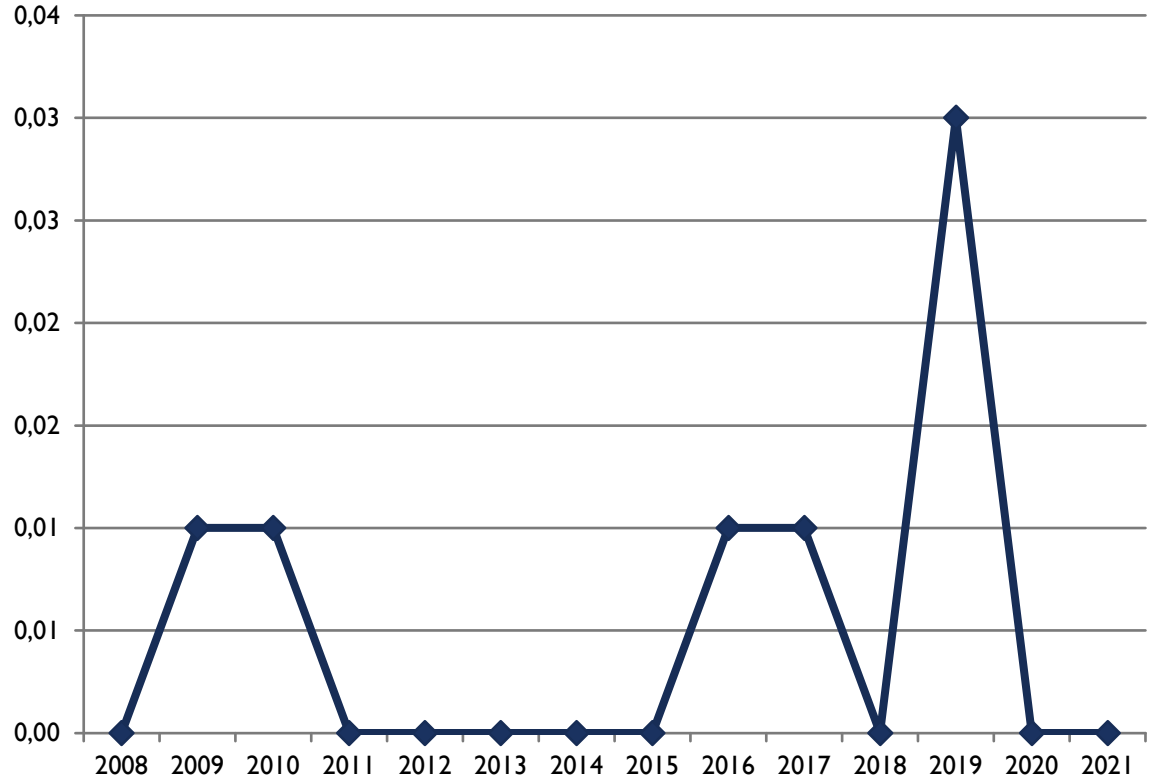
Article	Year of samples collection	Number of tested samples	The probable route of infection was as follows:	Genotype
Ciccozzi M, Babakir-Mina M, Lo Presti A, Salpini R, Cella E, Gabanelli E, Teoharov P, Kevorkyan A, Perno CF, Zehender G, Ciotti M. Molecular analysis of hepatitis B virus in Bulgaria. J Med Virol. 2013 Jan;85(1):49-54.	2009- 2010	46	-Heterosexual contact (19) -Nosocomial infection (10) -MSM (3) -Familiar contact (5) - Unknown (9)	D1 and A2 were the subgenotypes detected most frequently in the patients examined

HEPATITIS C

Viral hepatitis C in Bulgaria (1997-2021)
Incidence per 100 000 population (‰)



Viral hepatitis C in Bulgaria (2008-2021)
Mortality per 100 000 population (‰)



VIRAL HEPATITIS C (VHC) IN BULGARIA, 2021

- All reported cases (n=25) are laboratory confirmed;
- 19 (76%) were hospitalized;
- The distribution of patients by gender: men 13 vs. women 12;
- The disease was registered mainly among patients over 30 years (23 cases) with highest incidence - 1.29‰ in 55- 59 years of age; 2 cases among children were also registered;
- Cases of VHC have been registered in 14 out of 28 regions of the country;
- No death cases of VHC were reported.

HEPATITIS C VIRUS GENOTYPES IN BULGARIA

Article	Year of samples collection	Number of tested samples	Risk or demographic factors among tested individuals:	Genotype
Ganova-Raeva L, Dimitrova Z, Alexiev I, Punkova L, Sue A, Xia G-l, et al. (2019) HCV transmission in high-risk communities in Bulgaria. PLoS ONE 14(3): e0212350.	2014- 2015	125 cases of HIV/HCV coinfections from 15 different Bulgarian cities	- PWID (n = 96), - MSM (n = 10), - Incarceration (n = 28), - Blood transfusion (n= 4), - Sex Workers (n = 8), - No reported risk (n= 14)	**1a (54%),** 1b (20.8%), 2a (1.4%), **3a (22.3%)** 4a (1.4%), indicating ongoing transmission of many HCV strains of different genotypes
Zarina Brady & Zhivka Stoykova (2019) Hepatitis C virus genotype analysis in patients with chronic hepatitis in North Eastern Bulgaria, Journal of Drug Assessment, 8:1, 146-149,	March-October 2018	115 cases of chronic liver diseases in North Eastern Bulgaria	-58 males (50.43%) and 57 females (49.57%); -mean age of 51.4 years (17–87 years)	**1b (73%),** **1a (13.9%),** 3 (11,3%), 2 (0.9%), 4 (0.9%)
Massimo Ciccozzi, Gianni Zehender, Valeria Cento, Alessandra Lo Presti, Pavel Teoharov, Ivan Pavlov, Violeta Bogdanova, Carlo Federico Perno, Dr. Marco Ciotti. Molecular analysis of hepatitis C virus infection in Bulgarian injecting drug users. Journal of medical virology, 2011, 83(9):1565-1570		32 drug users infected chronically with hepatitis C and admitted at the National Center for Addictions	from 23 to 57 years	**3a -13 cases** 1a – 6 cases 1b – 1 case

DIMITROVA M, PAVLOV K, MITOV K, GENOV J AND PETROVA GI (2017).CHRONIC HEPATITIS C-RELATED CIRRHOSIS HOSPITALIZATION COST ANALYSIS IN BULGARIA. FRONT. MED. 4:125.

- A prospective, real life observational study of 297 patients with chronic HCV infection and cirrhosis monitored in the University Hospital "Queen Joanna-ISUL" for 3-year period (2012-2014)
- 76% of patients were male.
- 93% were diagnosed in grade Child-Pugh A and B. 97% reported complications, and almost all developed esophageal varices. During the 3 years observational period, patients did not change the critical clinical values for Child-Pugh status - the group was considered as homogenous.
- 847 hospitalizations were recorded with average length of stay 17 days.
- The mortality rate of 6.90% was extremely high.
- The total direct medical costs for the observed cohort of patients for 3-year period accounted for **1,290,533 BGN (€659,839)** with an average cost per patient 4,577 BGN (€2,340).
- Statistically significant correlation was observed between the total cost per patient from the different payers' perspective and the Child-Pugh cirrhosis score.

SERO-EPIDEMIOLOGICAL STUDIES

	HBsAg (year)	Anti-HCV (year)
General population	**-3.9%** in 1999-2000 *(INTEREG II EU programme)* **-3.9%** in 2010-2011 in Plovdiv region *(Kevorkyan A., et al. J Med Virol. ,2015)* **-2.9%** in 2016-2019 *in* Panagyurishte (out- and in-patients) *(Gotseva A., Наука Инфектология и паразитология, 2019)*	**-1.3%** in 1999-2000 *(Petrunov et al., 2002; Fitzsimons et al., 2011).* - **0.7%** in 2010-2011 in Plovdiv region *(Kevorkyan A., et al. J Med Virol. ,2015)* - **0.8%** [95% CI 0.2–3.1%] in 2018 in Stara Zagora region *(Sperle, I. et al. BMC Research Notes, 2020)*
Blood donors	**-2.72%***(V.Yordanova, et al., VHPB meeting, Sofia, 2011)*	**-0.36%** *(V.Yordanova, et al. VHPB meeting, Sofia, 2011)*
Pregnant women	-2.26% in 2009-2013 in Varna region *(Tsankova GS, et al. J Med Virol. 2016).*	
Risk Groups: - PWID - Prisoners - *HIV/AIDS, 2010-2015 (n=1158)* - Healthcare workers: *(n=324)* *(n=100)* - Bulgarian Mohammedans living in village of Ablaniza *(n=677)* - Military personnel *(n=411)*	-9.8% *(2012, NPPC of HIV and STI)* **- 11%** *(2012, NPPC of HIV and STI)* **-9.3%** *(I.Alexiev et al.Future viroly, 2020)* **-5%** (antiHBc- 20.7%, anti-HBs–63.4%) *(Gacheva N. et al, 2008)* **-4 %** *(Kevorkyan A. et al.Probl.Inf.Parasit.Dis, 2011)* **-7.7%** *(adults);* **0.7%** (adolescents) *(Krastev Z. et al. Journal of IMAB, 2011)* **- 5.8%** *(Gotseva A., Military medicine,2021)*	-78.6% *(2012, NPPC of HIV and STI)* - 26% *(2012, NPPC of HIV and STI)* **-23.2%** *(I.Alexiev et al.Future viroly, 2020)* **-0%** *(Gacheva N. et al, 2008)* **-0%** *(Kevorkyan A. et al.Probl.Inf.Parasit.Dis, 2011)* **-0%** *(Krastev Z. et al. Journal of IMAB, 2011)* **-0.7%** *(Gotseva A., Military medicine,2021)*

COUNTRY
VACCINATION PROGRAM

Hepatitis A	Y/N	population + Schedule	Since/period
Universal	No		
Risk group	No		

Hepatitis B	Y/N	population + Schedule	Since/period
Universal	Yes	➢ *At birth (within 24 hours) → 1 month → 6 months (Hepatitis B Recombinant DNA)* ➢ *At birth (within 24 hours) (Hepatitis B Recombinant DNA) - 2 months of age - 3 months of age - 4 months of age (DTaP/Hib/HepB/IPV)*	1992
Catch-up	No		
Risk Group	No		

VHPB

Hepatitis B vaccination (recommended)

(monovalent formulations)

- ***persons born before 1992;***
- ***HCWs;***
- ***persons with HIV infection;***
- ***patients who frequently require blood or blood products;***
- ***dialysis patients;***
- ***persons with chronic liver disease;***
- ***military /police officers;***
- ***PWID;***
- ***household and sexual contacts of persons with chronic HBV infection;***
- ***MSM;***
- ***persons with multiple sexual partners;***
- ***travelers to high endemic for hepatitis B countries.***

Hepatitis A vaccination (recommended)

- ***Adults and children over 12 months of age;***
- ***Patients with chronic liver diseases;***
- ***Persons undergoing frequent transfusions of blood and blood products;***
- ***PWID;***
- ***MSM;***
- ***Traveling to high endemic areas, especially when staying for more than three months;***
- ***Certain occupations:***

-personnel of laboratories working directly with hepatitis A virus;

-staff and patients of medical institutions and LTCF for mental disorders etc.;

- ***Limitation of epidemic outbreaks.***

COUNTRY
SCREENING

Recommended for following groups:	Hep B	Hep C
General population (40, 45, 50, 55 and 60 years)- prority area in the National Programme	Yes (new)	Yes(new)
Birth cohorts	No	No
Blood and organ donors	Yes	Yes
Pregnant women	Yes	Yes (new)
PWID	Yes	Yes
STI clinic patients	No	No
Haemodialysis patients	Yes	Yes
Health care workers	Yes (new)	Yes(new)
Men having sex with men	Yes	Yes
Prison population	Yes	Yes
Migrants	Yes	Yes
Others		

VHPB

COUNTRY
TREATMENT

National guidelines available	Y/N (year)
Hepatitis B	Yes (04.01. 2018)- the last edition
Hepatitis C	Yes (01.01. 2020) -the last edition
Other (specify)	

The treatment of diffrent types of viral hepatitis is included in the package of health activities guaranteed by the budget of the National Health Insurance Fund — both in terms of hospital treatment and dispensary monitoring.
The treatment of chronic hepatitis B and C is carried out in accordance with the requirements of Ordinance No. 15 of 2019 for the adoption of pharmaco-therapeutic guidelines for the treatment of gastroenterological diseases (Government Gazette, issue 95 of 2019).

COUNTRY TREATMENT

Drugs available for HCV treatment*	Y/N
PegInterferon	N
Ribavirin	Y
Boceprevir	N
Telaprevir	N
Simeprevir	N
Sofosbuvir	Y
Daclatasvir	N
Sofosbuvir/Ledipasvir	Y
Sofosbuvir/Velpatasvir	Y
Glecaprevir/Pibrentasvir	Y
Sofosbuvir/Velpatasvir/Voxilaprevir	Y
Other: Elbasvir/ Grazoprevir Glecaprevir/ Pibrentasvir Ombistavir/ Peritaprevir /Ritonavir	Y Y Y

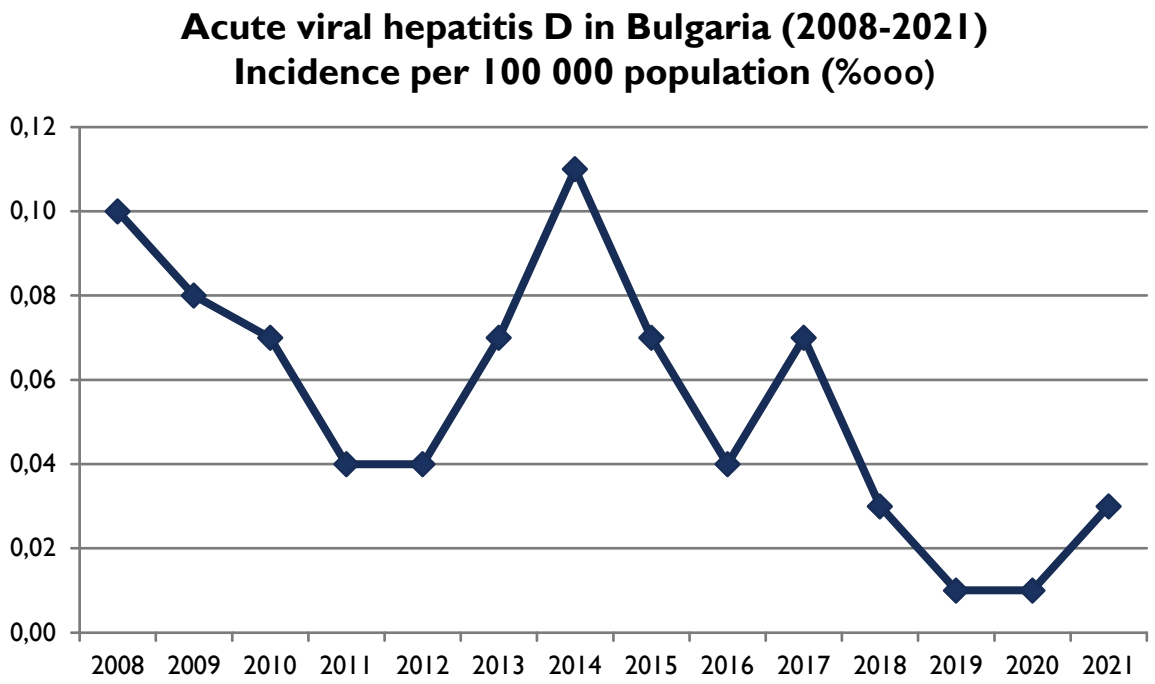
Drugs available for HBV treatment*	Y/N
Lamivudine	Y
Adefovir	N
Telbivudine	Y
Entacavir	Y
Tenofovir disoproxil fumarate (TDF)	Y
Tenofovir alafenamide (TAF)	N
Interferon Alfa-2a	Y

Number of patients treated (cumulative)-NHIF	
Hep B	14 392 (2016 -2021) (average 2 399 per year)
Hep C	5 518 (2016-2021) (average 920 per year)

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

VHPB

HEPATITIS D



*D. Tsaneva-Damyanova, Z. Stoykova, I. Ivanova, T. Kostadinova, L.Ivanova. **Hepatitis D virus in Bulgaria: virology, epidemiology and pathogenesis in chronic HBV carriers with liver dysfunction. Scripta Scientifica Medica, [S.l.], 2020, 52(3):12-18.***

- a retrospective study conducted between 2013-2019 at St. Marina University Hospital, Varna, Bulgaria.
- 391 patients with chronic liver disease using ELISA, PCR and HDV sequencing and genotyping.
- **16.6% (95% CI: 15.9% - 23.8%, n = 65) had an etiological association with HDV in ELISA.**
- HDV RNA positive results in 63 out of all 65 anti-HDV Ab (antibody) positive patients (96.9%).
- 38.1% (95% CI: 26.1% - 51.2%, n = 24), were on antiviral HBV/HDV therapy. For five of them, or 20.8% (95% CI: 7.1% - 42.2%, n = 5), **HDV genotype I was found.**

No death cases were recorded since 2008.

HEPATITIS E

- 1995- first cases of HEV infection were described *(Teoharov P et al., 1995)*
- 2008, 2009, 2010 and 2011 only sporadic cases were described *(Teoharov P., 2008; Popov G, 2009; Ruseva A, 2010, Popov G, et.al. 2011)*
- In the last decade, a lot of surveys were conducted (both among humans and animals) *(E. Golkocheva-Markova, C. Ismailova, T. Tenev, L. Nikolaeva-Glomb. Probl. Inf. Parasit. Dis.2021, Vol. 49, 3, 27-34).*
- In 2019 Hepatitis E was included in the list of communicable diseases *(ORDINANCE No 21 of 18 July 2005 on the procedure for registration, notification and reporting of CD (State Gazette, No62, 29.07.2005, Last update 31.05.2022)*

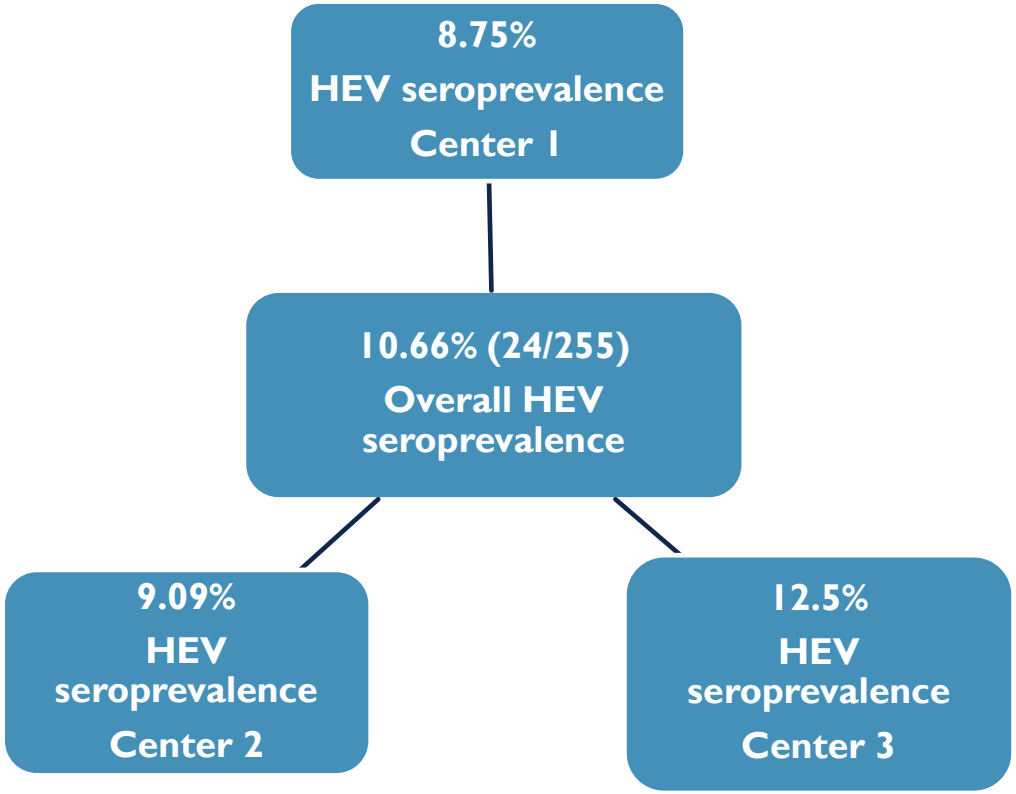
CHARACTERISTICS OF THE STUDIES REPORTING SEROLOGICAL PREVALENCE OF HEPATITIS E AMONG AVH PATIENTS AND GENERAL POPULATION / BLOOD DONORS

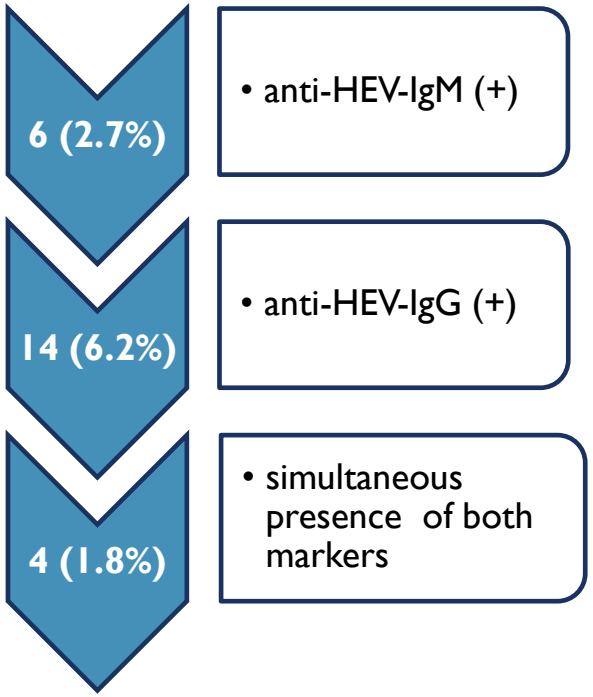
Total number of studied samples (N)	Anti-HEV IgM/ IgG positive samples (%)	co-infection/ comorbidities	reference
53 (non-A non-B AVH)	7,55	CMV; ch HBV	*Teoharov P, Tiholova M, Draganov P, Lilyanova V, Ivanova R, Varleva T, et al. First cases of hepatitis E virus infection in Bulgaria. Infectologia. 1995; 32 (3): 17–18. [in Bulgarian]*
32 (patients with AVH)	44*	NS	*Teoharov P., E. Markova, T. Cherveniakova, G. Goranova, A. Andonov. 11 National Congess of Clinical Microbiology and Infections, Sofia, 09–11 May, 2013*
806 (AVH were retrospectively evaluated)	2,48	HBV	*Baymakova M, Sakem B, Plochev K, Popov GT, Mihaylova-Garnizova R, Kovaleva V, Kundurdjiev T. Epidemiological characteristics and clinical manifestations of hepatitis E virus infection in Bulgaria: A report on 20 patients. Srp Arh Celok Lek. 2016; 144 (1-2): 63-68.*
325 (287 hospitalized with AVH and 38 outpatients with liver dysfunction)	13,2 / 20,9	NS	*Stoykova Zh, Ivanova L, Tsaneva-Damyanova D, Kostadinova Ts. Hepatitis E virus infection in Northeastern Bulgaria. Medical Review. 2017; 53 (3): 30-34. [in Bulgarian]*
741 (general population)	ND / 9,04	NS	*Teoharov P, Kevorkyan A, Raycheva R, Golkocheva-Markova E, Trandeva-Bankova D, Andonov A. Data on the prevalence of hepatitis E virus in Bulgaria. C. R. Acad. Bulg. Sci. 2014; 67(10): 1427-1432.*
896 (general population)	11,5 / 16,1	NS	*Mladenova-Dimitrova Z, Gotseva A, Velcheva D. Prevalence of hepatitis E in general population in Bulgaria. Obshta meditsina. 2020;22 (3): 16-22. [in Bulgarian]*
555 (blood donors from different districts)	NS / 21,7 to 28,8	NS	*Baymakova M., Terzieva K., Popov, R., Grancharova E., Kundurzhiev T., Pepovich, R., Tsachev I. Seroprevalence of Hepatitis E Virus Infection among Blood Donors in Bulgaria. Viruses. 2021; 13(3): 492.*

Legend: NS = not studied; CMV = cytomegalovirus; ch HBV = chronic HBV infection; HBV = hepatitis B virus; ND = not detected; * = anti-HEV positive.

CHARACTERISTICS OF THE STUDIES REPORTING SEROLOGICAL PREVALENCE OF HEPATITIS E AMONG SPECIFIC RISK GROUPS - HD PATIENTS

(KEVORKYAN A. ET AL. ECCMID, LISBON, 2022)





Median age of the patients – 64 years; Male (n=126; 56%); January- August 2020;South Bulgaria
All hemodialyzed are HEV RNA negative.
No association was found between eating habits, contact with animals, blood transfusions, travel abroad, duration of hemodyalisis > 5 years and HEV seropositivity.

CHARACTERISTICS OF THE STUDIES REPORTING SEROLOGICAL PREVALENCE OF HEPATITIS E AMONG SPECIFIC RISK GROUPS – HIV POSITIVE PATIENTS

- ***Golkocheva-Markova E, et al. Assessment of hepatitis E seropositivity among HIV-infected patients in Bulgaria. Braz J Infect Dis. 2022 Jan-Feb;26(1):102329. d:***

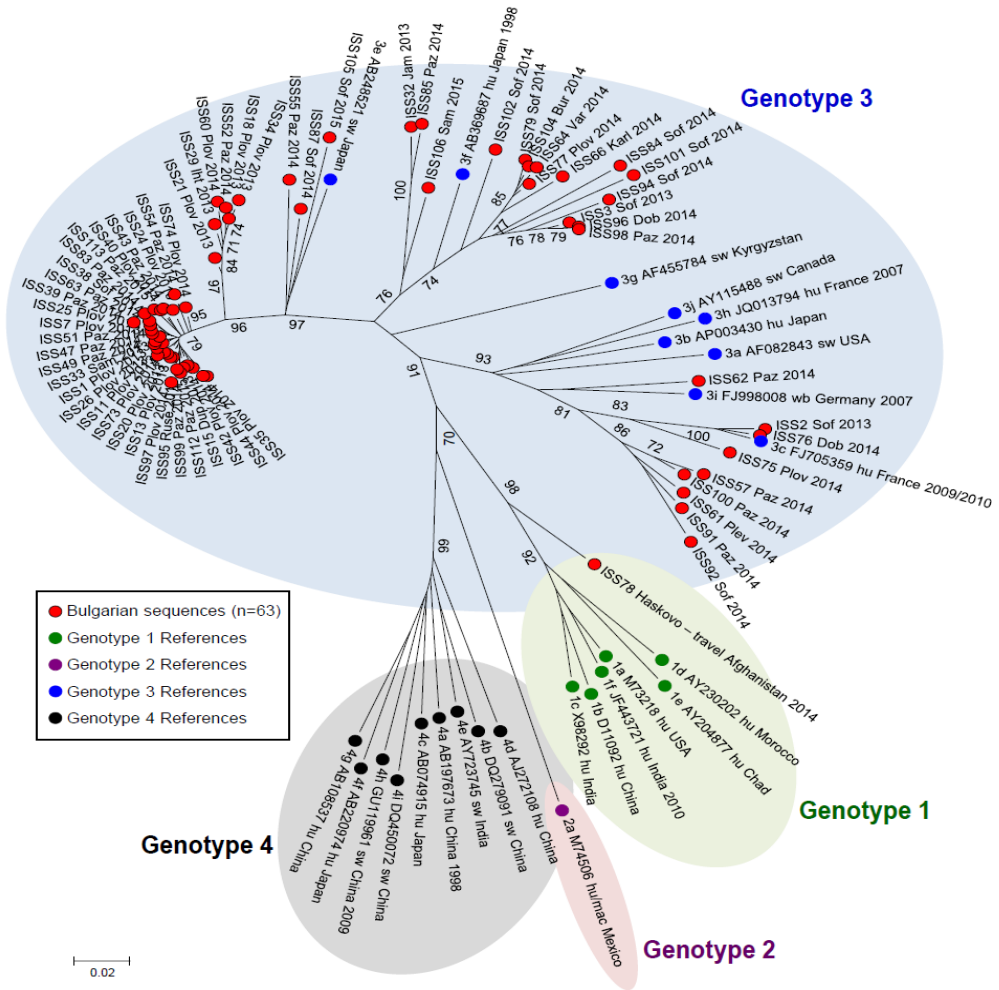
- a retrospective cohort study among 312 HIV-infected patients between December, 2019 and March, 2021;
- median age was 35 years (range 8 – 69) and male to female ratio of 5:1, 84.6% (264/312) men and 15.4% (48/312) women.
- The main transmission routes for HIV infection were: homosexual sex in 45.2%,heterosexual sex in 39.6%, IDU -14.5% and 0.7% was vertically infected.
- The median known duration of HIV seropositivity was less than one year. The longest period of HIV seropositivity was 15 years.

- HEV seroprevalence among HIV-infected patients was 10.9%.
- None of the tested samples were positive for HEV RNA.
- Regarding HBV and HCV coinfections, 12.2% of the HIV-infected patients was HBV infected (HBsAg and/or HBV DNA positive) and 15.4% was HCV infected (anti-HCV and/or HCV RNA positive).

STUDIES ASSESSING MOLECULAR-GENETIC CHARACTERISTICS OF HEV IN BULGARIA

Total number of studied samples (N)	Amplified genome region	Genotype	Sub-genotype	Reference
14	ORF1	3	e, f	1
103	ORF2	3; 1*	e, f, c	2

Legend: ORF – open reading frame; * HEV genotype 1 was imported for Bulgaria (from Afghanistan)



Reference:

1. Teoharov P, Kevorkyan A, Raycheva R, Golkocheva-Markova E, Trandeva-Bankova D, Andonov A. Data on the prevalence of hepatitis E virus in Bulgaria. C. R. Acad. Bulg. Sci. 2014; 67(10): 1427-1432.

2. Bruni R, Villano U, Equestre M, Chionne P, Madonna E, Trandeva-Bankova D, Peleva-Pishmisheva M, Tenev T, Cella E, Ciccozzi M, Pisani G, Golkocheva-Markova E, Ciccaglione AR. Hepatitis E virus genotypes and subgenotypes causing acute hepatitis, Bulgaria, 2013-2015. PLoS One. 2018; 13 (6): e0198045.

CHARACTERISTICS OF THE STUDIES REPORTING HEV SEROPREVALENCE AMONG DOMESTIC AND WILD ANIMALS.

Animal species (age in months)	Total number of studied samples	Number of covered pig farms/ slaughterhouses	anti-HEV antibodies positive samples (%)	Reference
Pig (1-6)	85	5	40	*Pishmisheva M, Baymakova M, Golkocheva-Markova E, Kundurzhiev T, Pepovich R, Popov GT., Tsachev I. First serological study of hepatitis E virus infection in pigs in Bulgaria. C. R. Acad. Bulg. Sci. 2018; 71(7): 1001–1008.*
EBS	171	NA	82,5	*Tsachev I, Baymakova M, Pepovich R., Palova N, Marutsov P, Gospodinova K, Kundurzhiev T, Ciccozzi M. High seroprevalence of hepatitis E virus infection among East Balkan Swine (Sus scrofa) in Bulgaria: preliminary results. Pathogens. 2020; 9 (11): 911.*
Pig, **Wild boar**	433 32	19 NA	60 12,5	*Takova K, Koynarski T, Minkov I, Ivanova Z, Toneva V, Zahmanova G. Increasing Hepatitis E Virus Seroprevalence in Domestic Pigs and Wild Boar in Bulgaria. Animals (Basel). 2020; 10 (9): 1521.*

Legend: NA = not applicable; EBS = East Balkan swine

THANK YOU FOR YOUR ATTENTION!