
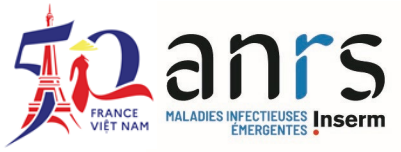

ANRS|MIE Scientific Days in Vietnam

Towards ending epidemics

15th to 16th of November, 2023

The status and challenges of viral hepatitis control in Vietnam

Prof. PHAM Minh Khue MD. PhD.

Haiphong University of Medicine and Pharmacy - Vietnam

Introduction (1)

- Vietnam, population 97.3 million, is one of twenty countries reported to shoulder 75% of the world's burden of viral hepatitis
- Morbidity from viral hepatitis in Vietnam is largely driven by HBV, with most chronic infections acquired through mother-to-child transmission and horizontal transmission in early childhood
- Vietnam's MOH approximates the prevalence of chronic HBV infection to range from 8-25%
- Approximately one million Vietnamese (~1%) have HCV chronic active infection, while the most recent GBD modelling suggests this figure may be over 60% higher (1.66% [95% C.I 1.35 – 2.0])
- HDV also makes an important contribution to Vietnam's hepatitis burden. HDV is not currently screened for in Vietnam and is not included in national treatment guidelines

Introduction (2)

- In the last thirty years, Vietnam has undergone unprecedented change.
- Notable progress has been made in:
  - Access to HBV vaccination,
  - Blood donor screening,
  - Government subsidization of HBV and HCV therapy,
- Altering the shape and scope of the hepatitis epidemic and shifting public health priorities.

Estimating seroprevalence of Hepatitis B, C and D in Vietnam

Seroprevalence of Hepatitis B, C and D in Vietnam: A systematic review and meta-analysis

Barnaby Flower,[a,b,1] Duc Du Hong,[a,1] Hang Vu Thi Kim,[a] Khue Pham Minh,[c] Ronald B Geskus,[a,d] Jeremy Day,[a] and Graham S Cooke[b]*

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Summary

Background Vietnam has one of the greatest disease burdens from chronic viral hepatitis. Comprehensive prevalence data are essential to support its elimination as a public health threat.

Methods We searched Medline and Embase from 1990 to 2021 for seroprevalence data relating to Hepatitis B (HBV), C (HCV) and D (HDV) in Vietnam. We estimated pooled prevalence with a DerSimonian-Laird random-effects model and stratified study populations into i) low-risk ii) high-risk exposure and iii) liver disease. We further estimated prevalence by decade and region and rates of HIV-coinfection.

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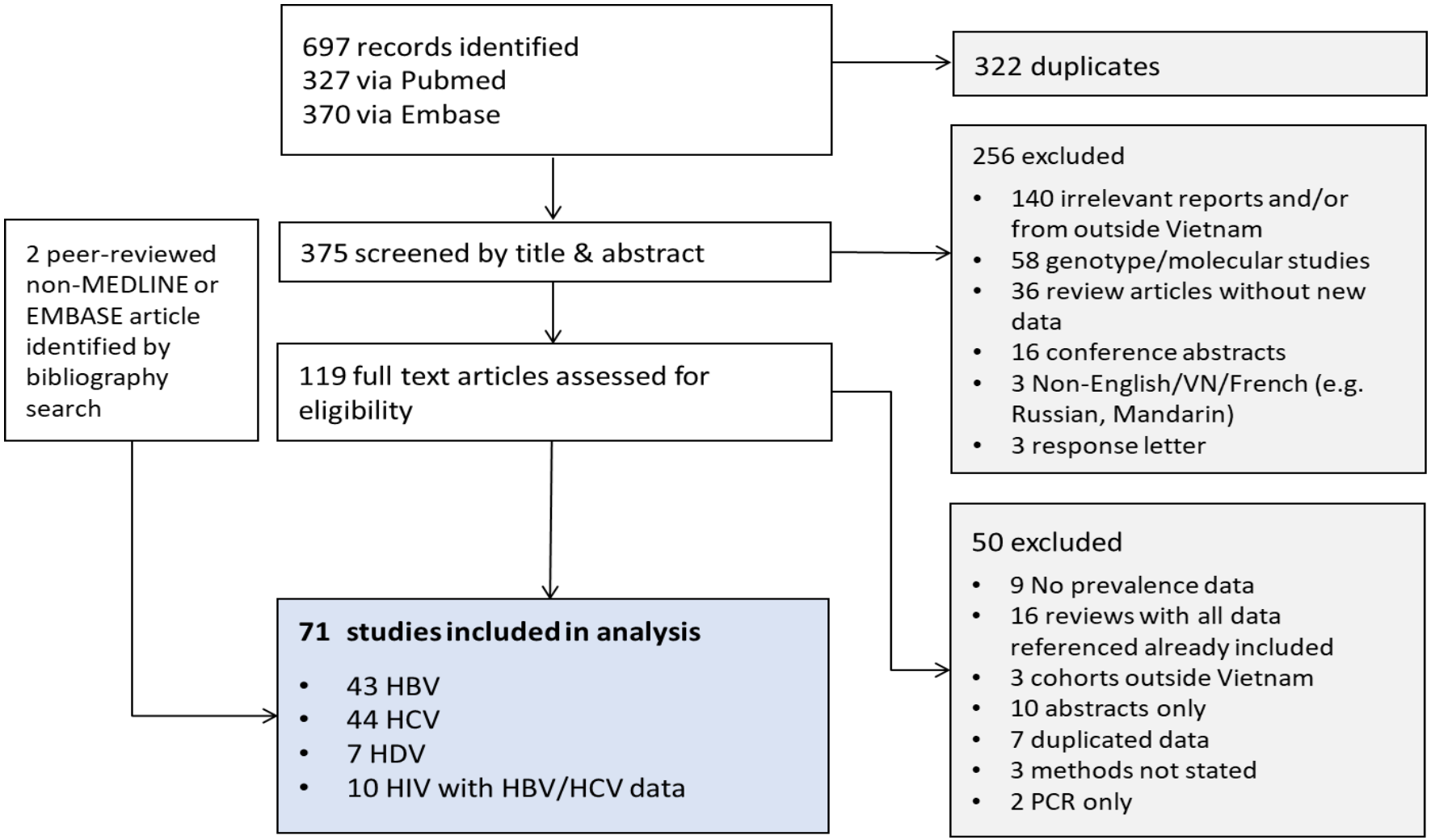
Study selection

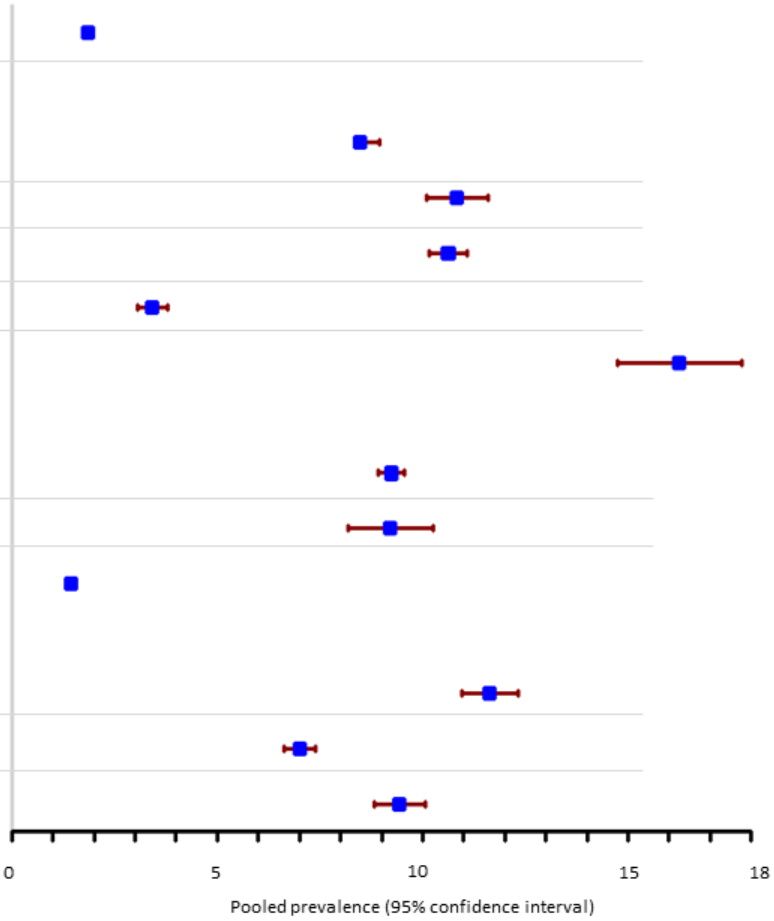


Seroprevalence of Hepatitis B and C among blood donors

- Overall infection rates:
  - HBsAg point prevalence: 1.86% (1.82 - 1.90),
  - HCV antibody: 0.18% (0.16 - 0.19)
  - HCV antigen: 0.31% (0.10 – 0.61).
- Pooled HBsAg prevalence :
  - 9% in cohorts from prior to 2011
  - 1.44% (1.41 – 1.48) in last decade
- Pooled HCV prevalence:
  - 7.6% [6.1 – 9.4]) when first discovered in the 1990s
  - 0.2% overall in studies since 2001

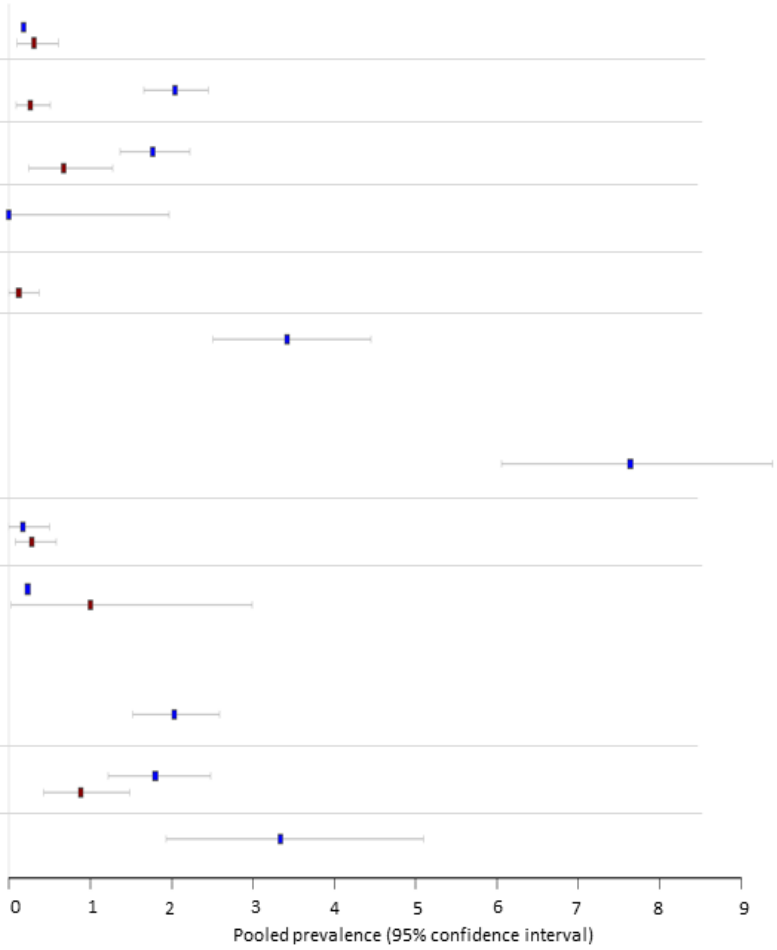
Estimated pooled seroprevalence of HBsAg in low-risk populations

	Studies	N	Pooled prevalence [95% C.I.]
Blood donors	**9**	**449,271**	**1.86 [1.82 – 1.90]**
Other low-risk cohorts			
Overall	**32**	**34,871**	**8.64 [8.34 – 8.94]**
Ante-natal	6	6781	10.83 [10.09 – 11.58]
Adults in general population	12	16,396	10.62 [10.15 – 11.09]
Children in general population	4	9358	3.42 [3.05 – 3.81]
Inpatients	9	2336	16.23 [14.74 – 17.77]
Blood donors by decade			
1990-2000	3	33,290	9.23 [8.92 – 9.54]
2001-2010	4	3076	9.20 [8.20 – 10.25]
2011-2020	2	412,905	1.44 [1.41 – 1.48]
Other low risk cohorts by decade			
1990-2000	13	8883	11.63 [10.96 – 12.32]
2001-2010	13	17,468	7.00 [6.62 – 7.39]
2011-2020	5	8520	9.42 [8.81 – 10.05]



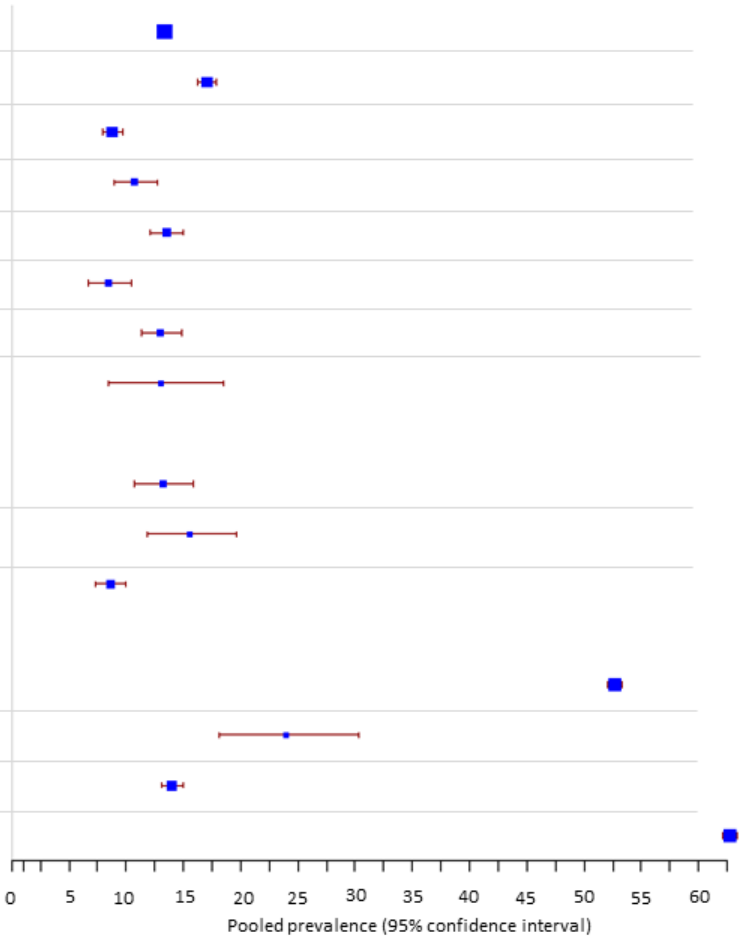
Estimated pooled seroprevalence of HCV in low-risk populations

	HCV antibody			HCV antigen		
	Studies	N	Pooled prevalence	Studies	N	Pooled prevalence
Blood donors	4	414,895	0.18 [0.16 – 0.19]	4	2616	0.31 [0.10 – 0.61]
Other low risk	15	5480	2.04 [1.66 – 2.45]	4	3516	0.26 [0.09 – 0.51]
Adults general population	7	3893	1.77 [1.37 – 2.22]	2	1350	0.67 [0.24 – 1.27]
Children gnrl. population	1	87	0.00 [0.00 – 1.97]	0		
Antenatal	0			2	2166	0.17 [0.00 – 0.37]
Inpatients	7	1500	3.42 [2.51 – 4.45]	0		
Blood donors by decade						
1990-2000	2	990	7.64 [6.06 – 9.39]	0		
2001-2010	1	1200	0.17 [0.00 – 0.50]	3	2416	0.28 [0.08 – 0.58]
2011-2020	1	412,705	0.23 [0.22 – 0.24]	1	200	1.00 [0.02 – 2.99]
Other low risk by decade						
1990-2000	10	3126	2.03 [1.52 – 2.59]	0		
2001-2010	4	1845	1.80 [1.22 – 2.48]	2	3416	0.88 [0.43 – 1.48]
2011-2020	1	509	3.34 [1.93 – 5.10]	0		



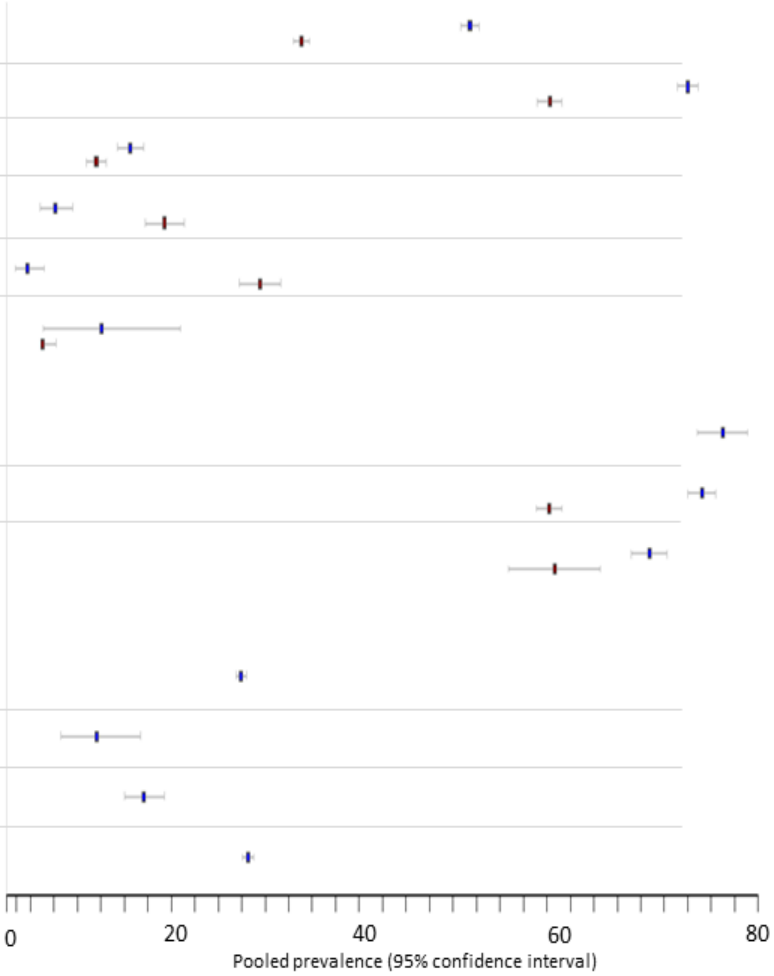
Estimated seroprevalence of HBV in high-risk populations

	Studies	N	Pooled prevalence [95% C.I.]
Overall	**49**	**17,401**	**13.32 [12.81 – 13.83]**
PWID	21	7740	17.07 [16.23 – 17.92]
CSW	9	3899	8.77 [7.89 – 9.70]
Dialysis	6	1110	10.76 [8.95 – 12.70]
MSM sexual health	7	2174	13.50 [12.09 – 14.98]
Multiple transfusions/surgery	4	902	8.47 [6.65 – 10.46]
Prisoners	1	1400	13.00 [11.29 – 14.81]
Infants of HBV infected mothers	1	176	13.07 [8.45 – 18.48]
High risk exposures by decade			
1990-2000	13	13	13.22 [10.77 – 15.88]
2001-2010	27	27	15.57 [11.88– 19.65]
2011-2020	9	9	8.63 [7.35 – 10.01]
Liver disease overall	**10**	**27,495**	**52.70 [52.10 – 53.29]**
Acute hepatitis	1	188	23.94 [18.09 – 30.32]
Chronic hepatitis	5	5151	14.04 [13.10 – 15.01]
Hepatocellular carcinoma	4	22,156	62.13 [62.13 – 63.41]

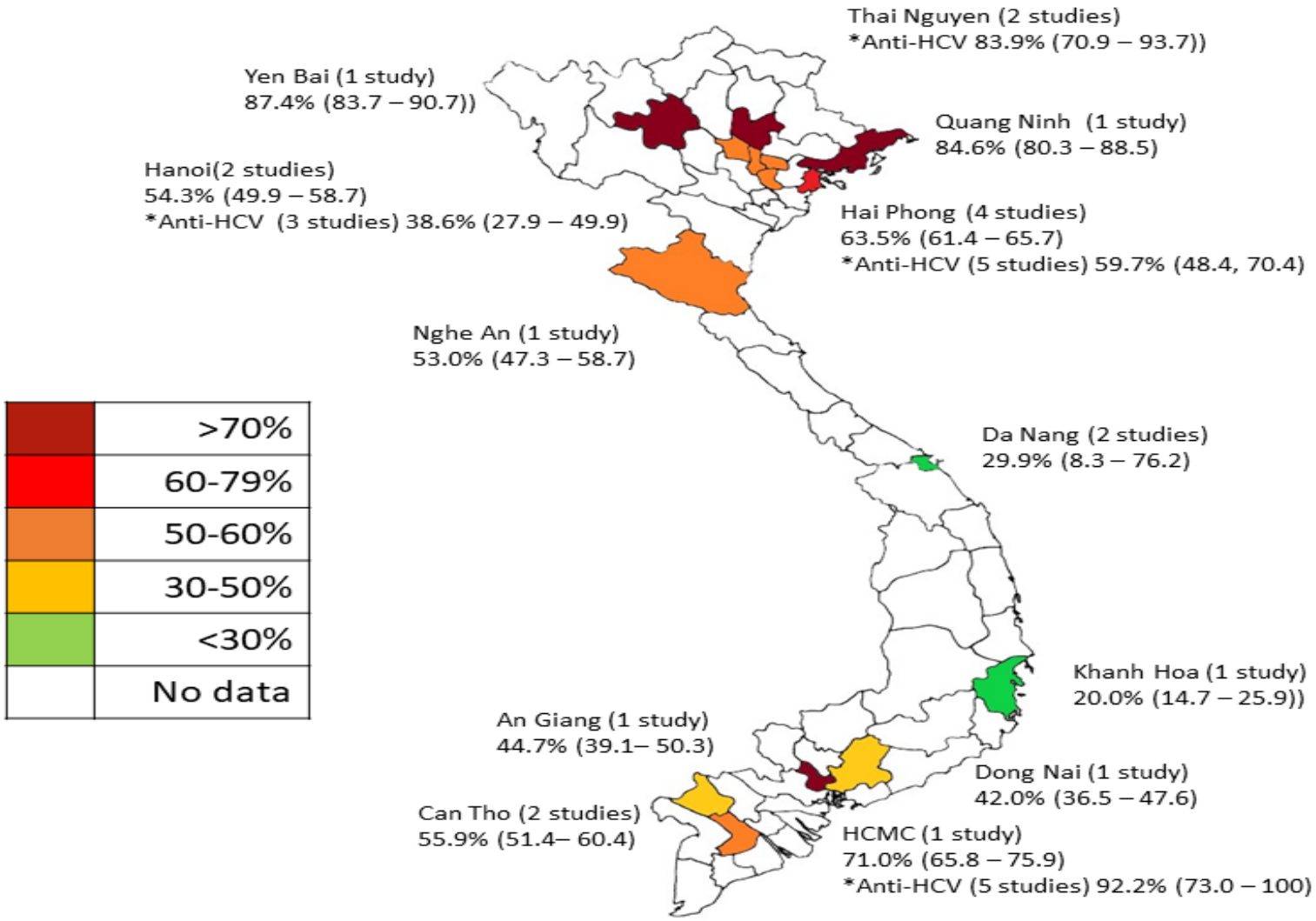


Estimated pooled seroprevalence of HCV in high-risk groups

	HCV antibody			HCV antigen		
	Studies	N	Pooled prevalence	Studies	N	Pooled prevalence
Overall	30	10,150	49.30 [48.32-50.28]	42	12,108	31.37 [30.54-32.20]
PWID	16	6666	72.51 [71.42-73.58]	17	5461	57.80 [56.48 -59.11]
CSW	6	2294	13.14 [11.78-14.57]	6	3066	9.51 [8.48-10.59]
Dialysis	4	713	5.18 [3.56-7.03]	9	1232	16.75 [14.70-18.91]
MSM	2	404	2.20 [0.91 – 3.94]	4	1520	26.91 [24.71-29.18]
Blood transfusion	2	73	10.09 [3.83-18.45]	6	529	3.76 [2.51 - 5.23]
PWID by decade						
1990-2000	6	1008	76.23 [73.52-78.84]	0		
2001-2010	6	3371	74.00 [72.50-75.47]	16	5072	57.76 [56.39-59.12]
2011-2020	4	2287	68.4 [66.51-70.33]	1	389	58.35 [53.41-63.21]
Liver disease						
Overall	8	22,986	24.94 [24.38-25.51]	0		
Acute hepatitis	1	188	9.57 [5.74-14.23]	0		
Chronic hepatitis	5	1065	14.58 [12.5-16.8]	0		
HCC	2	21,733	25.69 [25.11-26.28]	0		

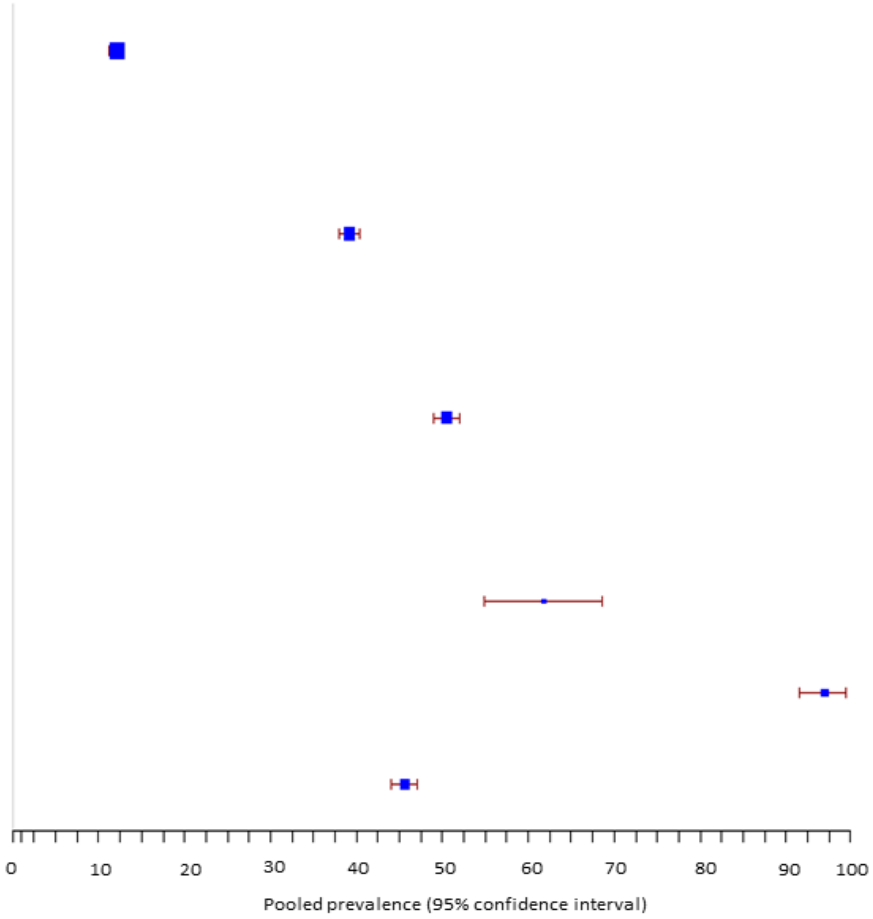


HCV antigen prevalence (and antibody where available) in PWID by region



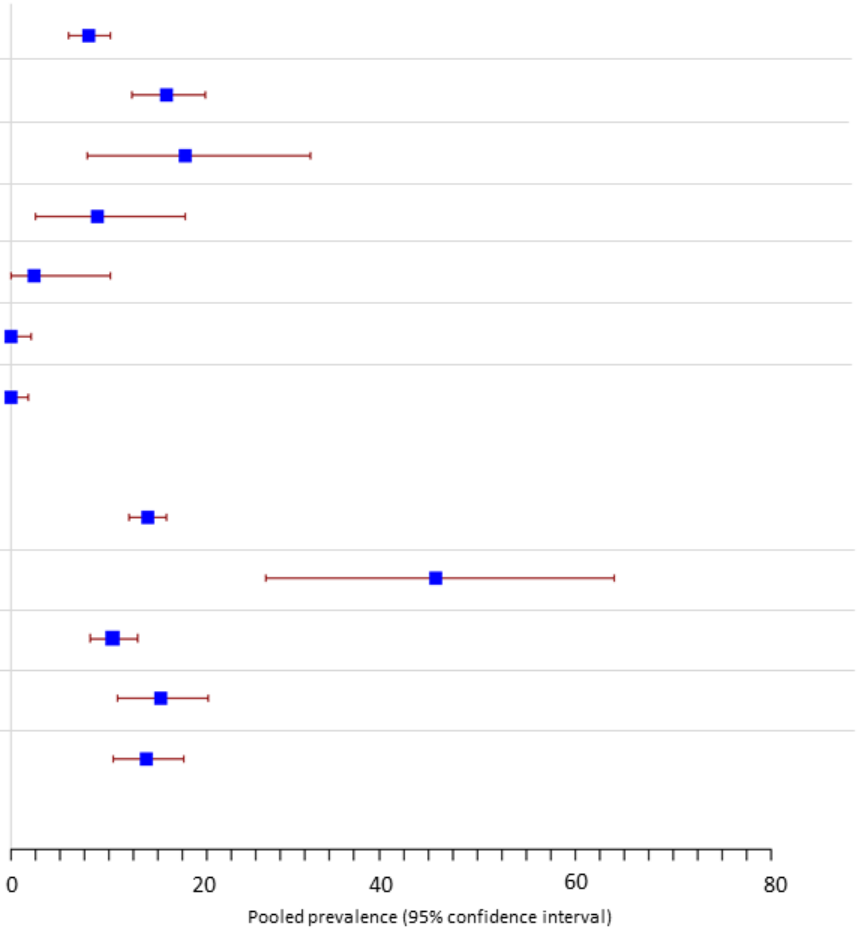
Estimated pooled prevalence of i) HBsAg and ii) HCV antibody in HIV positive cohorts and iii) HIV co-infection in HCV-antibody positive cohorts

	Studies	N	Pooled prevalence [95% C.I.]
HBsAg in HIV positive	12	5815	12.11 [11.27 – 12.97]
HCV Ab in HIV positive	13	7055	39.18 [38.04 – 40.33]
HIV in HCV Ab positives			
Overall	27	4676	50.52 [49.06 – 51.98]
By group			
CSW	8	206	61.85 [54.88 – 68.59]
MSM sexual health	4	345	94.51 [91.57 – 96.93]
PWID	15	4123	45.59 [44.06 – 47.12]



Estimated pooled prevalence of HDV antibody and HDV RNA in HBsAg positive cohorts

	Studies	N	Pooled prevalence [95% C.I.]
HDV antibody			
Overall	12	708	7.93 [5.92 – 10.17]
PWID	6	378	15.89 [12.29 – 19.84]
Military	1	45	17.78 [7.78 – 30.49]
CSW	1	57	8.77 [2.57 – 17.75]
Dialysis	1	41	2.44 [0.0 – 10.17]
Liver disease	1	80	0.00 [0.00 – 2.14]
Low risk	1	107	0.00 [0.00 – 1.76]
HDV RNA			
Overall	12	1267	13.90 [12.03 – 15.88]
Acute hepatitis	1	30	43.33 [25.96 – 61.54]
Mild liver disease	4	618	10.37 [8.05 – 12.95]
Cirrhosis	3	252	15.23 [10.90 – 20.08]
Hepatocellular carcinoma	3	367	13.87 [10.46 – 17.65]



Challenges

- The Vietnamese government has made considerable efforts over the last 5 years by releasing national guidelines for the management of CHB and C
  - Providing care and treatment, TDF or entecavir to HBV-infected patients.
  - CHB (CHC partly) covered by the Vietnamese Health Insurance System.
- Vietnam is not on track to achieve the WHO elimination goals over the next decade:
  - less than 5% of infected people are currently aware of their HBV infection,
  - 1.34% of HBV-infected people in need of treatment are on antiviral therapy.
  - HBV infection has been long neglected in Vietnam.
  - Lack of knowledge, attitude and practice in HBV prevention and management in general population and healthcare workers in Vietnam

VHC is a major public health issue

- Liver cancer is the 4th cause of death, predominantly related to hepatitis B virus but also for 25% of cases to HCV infection.
- The first national recommendations for HCV care were issued in 2014 and an updated version has just been published in September 2016
- In this new version, oral short-duration regimens using DAAs are preferred and Peg-Interferon based treatments are only mentioned as an alternative.
- Biology, medical imagery and drugs partially covered by Health Insurance since 2015
- In 2018: DAA added in drugs list covered by Health Insurance
- 3 months IFN-free treatments remain expensive (i.e., SOF/LED ≈ 1,000 USD)

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Article

Knowledge, Attitudes and Practices toward Hepatitis B Virus Infection among Students of Medicine in Vietnam

Thi Thuy Linh Nguyen [1], Thi Thanh Hang Pham [2], Samuel So [2], Thi Hai Van Hoang [3], Thi To Uyen Nguyen [4], Thanh Binh Ngo [5], Minh Phuong Nguyen [6], Quang Hung Thai [7], Ngoc Khoi Nguyen [8], Thi Quynh Anh Le Ho [9], Quang Phuc Tran [1] and Minh Khue Pham [1,*]

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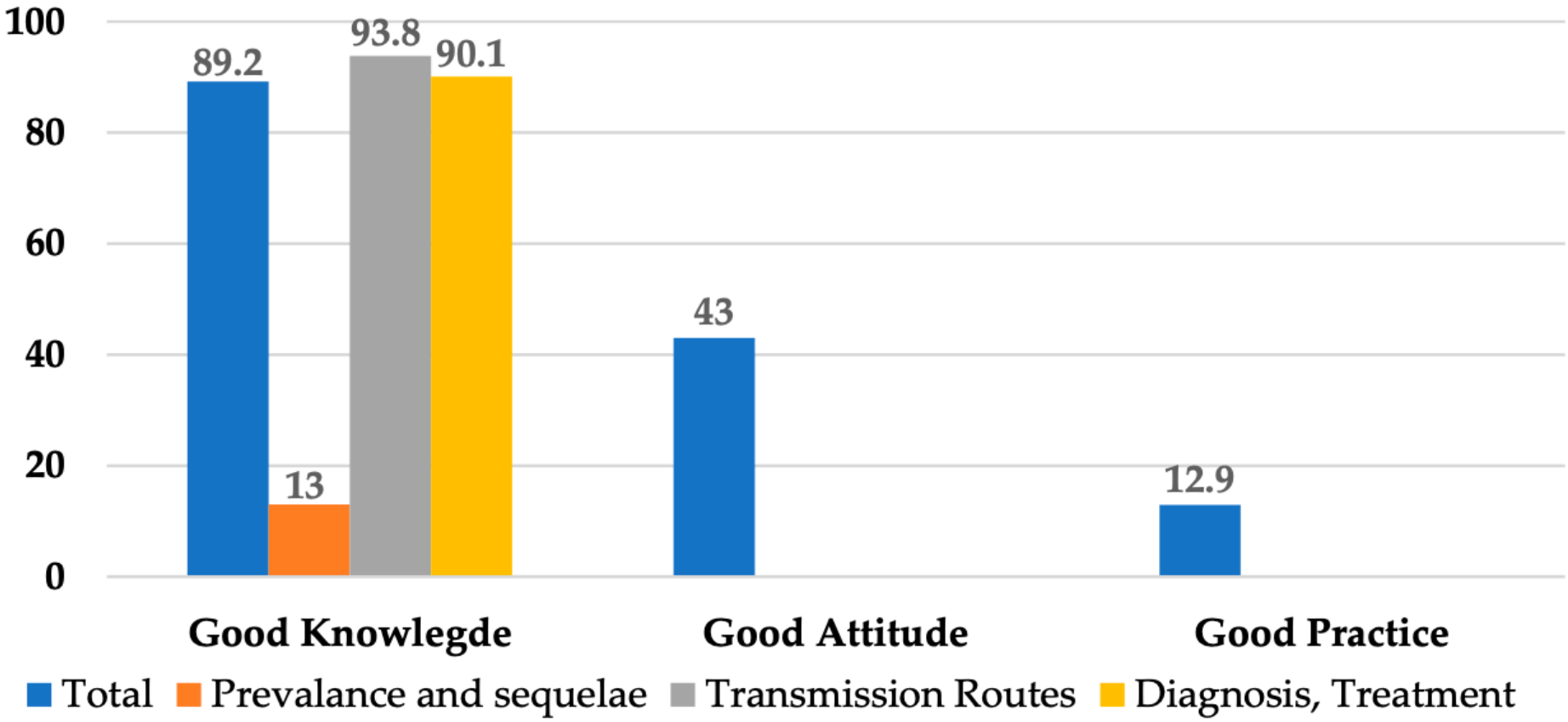
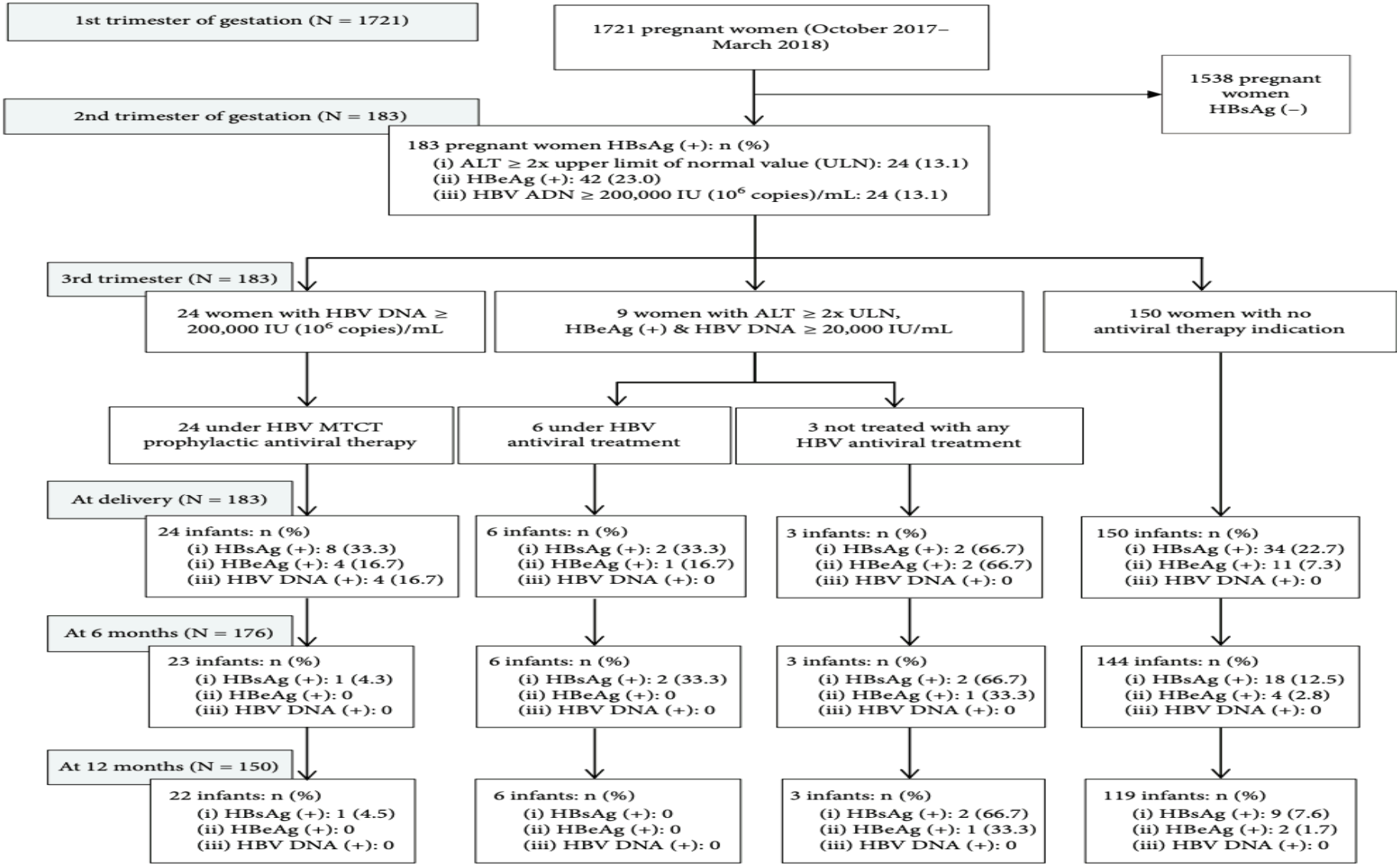
Knowledge, Attitudes and Practices toward Hepatitis B Virus Infection among Students of Medicine in Vietnam (N=2000)



Nguyen TTL, Pham TTH, So S, Hoang THV, Nguyen TTU, Ngo TB, Nguyen MP, Thai QH, Nguyen NK, Le Ho TQA, Tran QP, Pham MK. Knowledge, Attitudes and Practices toward Hepatitis B Virus Infection among Students of Medicine in Vietnam. Int J Environ Res Public Health. 2021 Jul 2;18(13):7081. doi: 10.3390/ijerph18137081. PMID: 34281017; PMCID: PMC8296898.



(Khue PM et al, 2020)

Factors associated with infant's HBV infection at 12-month follow-up (N = 150)

Infant's characteristics		Infant with positive HBsAg, *n* (%)	Crude OR[a], OR [95% CI]	Adjusted OR[b], OR [95% CI]	*p* value[c]
Mother's HBeAg status at delivery	HBeAg (-)	2 (1.7)	Ref.	Ref.	<0.001
	HBeAg (+)	10 (34.5)	31.3 [6.4-154.1]	65.8 [7.3-594.1]	
Mother's HBV DNA level at delivery	<200,000 IU/mL (10^6 copies/mL)	11 (7.6)	Ref.		
	≥200,000 IU/mL (10^6 copies/mL)	1 (16.7)	2.4 [0.3-22.6]		
Mother's HBV peripartum antiviral therapy	Yes	1 (3.4)	Ref.		
	No	11 (9.1)	2.8 [0.3-22.6]		
Having any family members infected with HBV[d]	No	7 (5.5)	Ref.	Ref.	0.119
	Yes	5 (21.7)	4.8 [1.4-16.6]	4.0 [0.7-23.4]	
Mode of delivery	Vaginal	8 (8.0)	Ref.		
	Caesarean	4 (8.0)	1.0 [0.3-3.5]		
Infant's sex	Female	7 (9.7)	Ref.		
	Male	5 (6.4)	1.6 [0.5-5.2]		
Infant's HBV birth dose vaccination	Yes	11 (7.4)	Ref.	Ref.	0.057
	No	1 (50.0)	12.5 [0.7-212.9]	36.1 [0.9-1459.5]	
Infant's HBIG immunization	Yes	7 (5.7)	Ref.	Ref.	0.181
	No	5 (18.5)	3.8 [1.1-12.9]	3.4 [0.6-19.9]	
Infant's scheduled HBV vaccination	Completed	10 (7.0)	Ref.	Ref.	0.593
	Uncompleted	2 (25.0)	4.4 [0.8-24.7]	2.1 [0.1-31.2]	
Infant feeding (during 12 months of age)	Breast-fed only	4 (8.5)	Ref.		
	Bottle-fed (and/or other food)	3 (5.8)	0.7 [0.1-3.1]		
	Mixed (breast-fed+bottle-fed and/or other food)	5 (9.8)	1.2 [0.3-4.6]		

[a]Univariate analysis; [b]multiple logistic regression; [c]likelihood-ratio test; [d]including infant's father HBV infection status. OR: odds ratio; CI: confidence interval. $\alpha < 0.05$.

Characteristics of mother-infant pairs whose infants are HBV infected (N = 12)

No.	Mothers' characteristics						Infants' characteristics						
	Maternal HBeAg status at 7th month of gestation	HBV DNA level at 7th month of gestation*	Antiviral treatment	Maternal HBeAg status at delivery	HBV DNA level at delivery*	Family member infected with HBV†	Mode of delivery	Infant's sex	BDV‡	HBIG#	Completed HBV vaccine schedule	Infant feeding	Infant HBeAg status at 12 months of age
1	Positive	1,174,000	Yes	Positive	82,400	No	Caesarean	Female	Yes	Yes	Yes	Mixed	Negative
2	Positive	47,600	No	Positive	1,756,000	Yes	Caesarean	Female	Yes	Yes	Yes	Breast-fed	Positive
3	Positive	30,000	No	Positive	24,600	No	Vaginal	Female	Yes	No	Yes	Breast-fed	Negative
4	Positive	420	No	Positive	Undetectable	Yes	Caesarean	Male	Yes	Yes	No	Mixed	Negative
5	Negative	Undetectable	No	Positive	402	No	Vaginal	Female	Yes	No	Yes	Mixed	Negative
6	Positive	Undetectable	No	Positive	Undetectable	No	Vaginal	Male	Yes	Yes	Yes	Breast-fed	Negative
7	Negative	Undetectable	No	Positive	Undetectable	Yes	Vaginal	Female	Yes	No	No	Mixed	Negative
8	Positive	Undetectable	No	Positive	Undetectable	No	Vaginal	Male	Yes	No	Yes	Mixed	Positive
9	Negative	Undetectable	No	Positive	Undetectable	No	Vaginal	Male	Yes	Yes	Yes	Bottle-fed	Negative
10	Positive	Undetectable	No	Positive	Undetectable	No	Vaginal	Female	Yes	Yes	Yes	Breast-fed	Negative
11	Negative	Undetectable	No	Negative	Undetectable	Yes	Vaginal	Female	No	No	Yes	Bottle-fed	Negative
12	Negative	Undetectable	No	Negative	Undetectable	Yes	Caesarean	Male	Yes	Yes	Yes	Bottle-fed	Negative

*Test results in IU/mL or undetectable (under limit of detection); †having any family member known being HBV infected (including husband/partner); ‡BDV: birth dose vaccination; #HBIG: hepatitis B immunoglobulin immunization.

Clinical Infectious Diseases

MAJOR ARTICLE

Assessment and Simplification of Treatment Eligibility Among Patients With Chronic Hepatitis B Infection in Vietnam

Vinh Vu Hai,[1,a] Yusuke Shimakawa,[2,a] Jin Kim,[3] Hai Do Ngoc,[4] Quang Le Minh,[5] Didier Laureillard,[6,7] and Maud Lemoine[3]

[1]Infectious and Tropical Diseases Department, Viet Tiep Hospital, Hai Phong, Vietnam, [2]Unité d'Epidémiologie des Maladies Emergentes, Institut Pasteur, Paris, France, [3]Department of Metabolism, Digestion and Reproduction, Division of Digestive Diseases Section of Hepatology, Imperial College London, London, United Kingdom, [4]Point of Care Laboratory, Viet Tiep Hospital, Hai Phong, Vietnam, [5]Hospital Management Department, Viet Tiep Hospital, Hai Phong, Vietnam, [6]Pathogenesis and Control of Chronic Infections, Inserm U1058, Etablissement Français du Sang, University of Montpellier, Montpellier, France, and [7]Infectious and Tropical Diseases Department, Caremeau University Hospital, Nîmes, France

(See the Editorial Commentary by Vinikoor on pages e1078–9.)

Performance of the Simplified Criteria to Select Patients Eligible for Antiviral Therapy in Reference to the Vietnamese National Guidelines at a Single Time Point (n = 400)

	TREAT-B			
AUROC	0.89 (0.87–0.92)			
Cutoff	≥1	≥2	≥3	4
True positive	167	165	124	43
False negative	0	2	43	124
True negative	22	134	206	233
False positive	211	99	27	0
Sensitivity (%)	100 (97.8–100)	98.8 (95.7–99.9)	74.3 (66.9–80.7)	25.7 (19.3–33.1)
Specificity (%)	9.4 (6.0–13.9)	57.5 (50.9–63.9)	88.4 (83.6–92.2)	100 (98.4–100)

The values in parentheses are the 95% confidence intervals.

Abbreviations: AUROC, area under the receiver operating characteristic; TREAT-B, Treatment Eligibility in Africa for the Hepatitis B Virus.

Performance of the Simplified Criteria to Select Patients Eligible for Antiviral Therapy in Reference to the Vietnamese National Guidelines in a Subgroup of Patients With 2 ALT Measurements Over 6 Months (n = 89)

	TREAT-B				Simplified WHO Criteria Without HBV DNA
AUROC	0.87 (0.80–0.94)				0.63 (0.55–0.71)
P value (compared with TREAT-B)	N/A				<.001
Cutoff	≥1	≥2	≥3	4	N/A
True positive	59	56	45	17	59
False negative	0	3	14	42	0
True negative	3	14	26	30	8
False positive	27	16	4	0	22
Sensitivity (%)	100 (93.9–100)	94.9 (85.9–98.9)	76.3 (63.4–86.4)	28.8 (17.8–42.1)	100 (93.9–100)
Specificity (%)	10.0 (2.1–26.5)	46.7 (28.3–65.7)	86.7 (69.3–96.2)	100 (88.4–100)	26.7 (12.3–45.9)

The values in parentheses are the 95% confidence intervals.

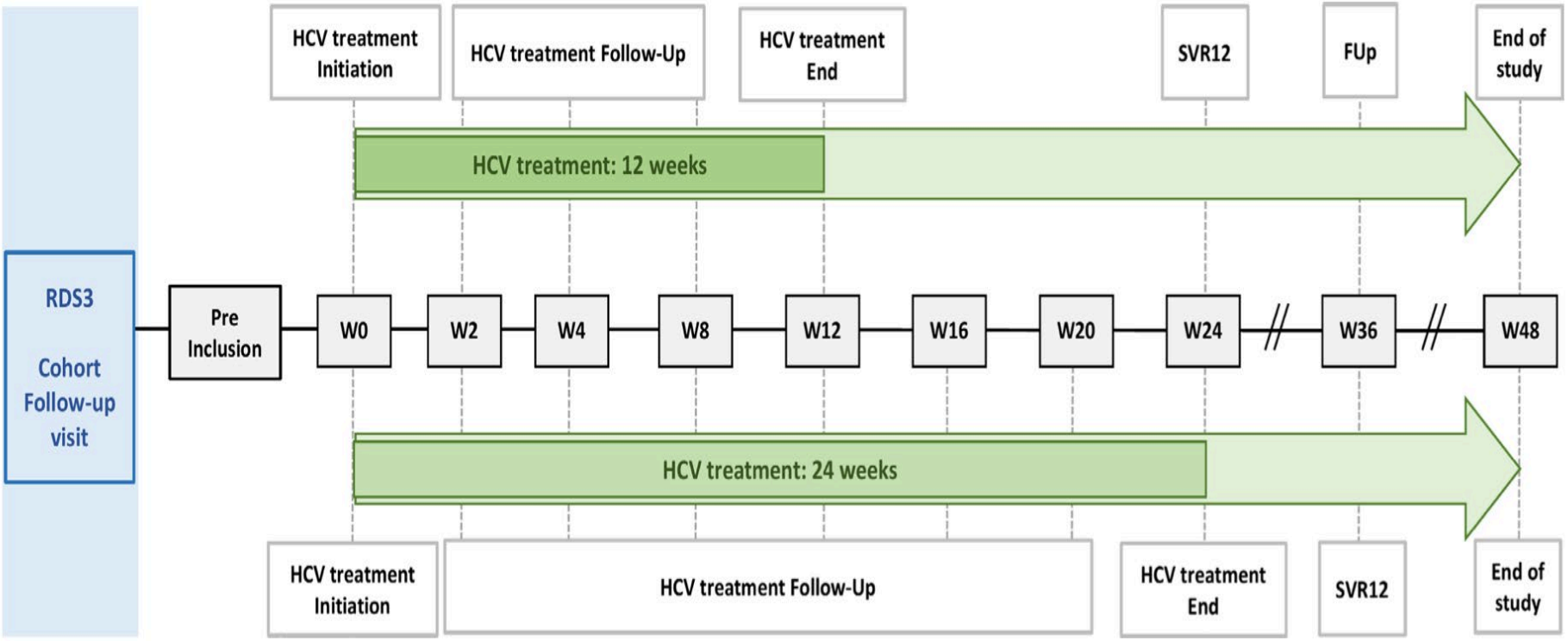
(Vu Hai V, Shimakawa Y, Kim J, Do Ngoc H, Le Minh Q, Laureillard D, Lemoine M. Assessment and Simplification of Treatment Eligibility Among Patients With Chronic Hepatitis B Infection in Vietnam. Clin Infect Dis. 2021 Sep 7;73(5):e1072-e1077. doi: 10.1093/cid/ciaa1814. PMID: 33331880.)

BMJ Open

Towards HCV elimination among people who inject drugs in Hai Phong, Vietnam: study protocol for an effectiveness-implementation trial evaluating an integrated model of HCV care (DRIVE-C: DRug use & Infections in ViEtnam–hepatitis C)

Delphine Rapoud ,[1] Catherine Quillet,[1] Khue Pham Minh,[2] Vinh Vu Hai,[3] Binh Nguyen Thanh,[2] Thanh Nham Thi Tuyet,[4] Hong Tran Thi,[2] Jean-Pierre Molès,[1] Roselyne Vallo,[1] Laurent Michel,[5] Jonathan Feelemyer,[6] Laurence Weiss,[7] Maud Lemoine,[8] Peter Vickerman,[9] Hannah Fraser,[9] Huong Duong Thi,[2] Oanh Khuat Thi Hai,[4] Don Des Jarlais,[6] Nicolas Nagot,[1] Didier Laureillard,[10] On behalf of the DRIVE-C Study Group

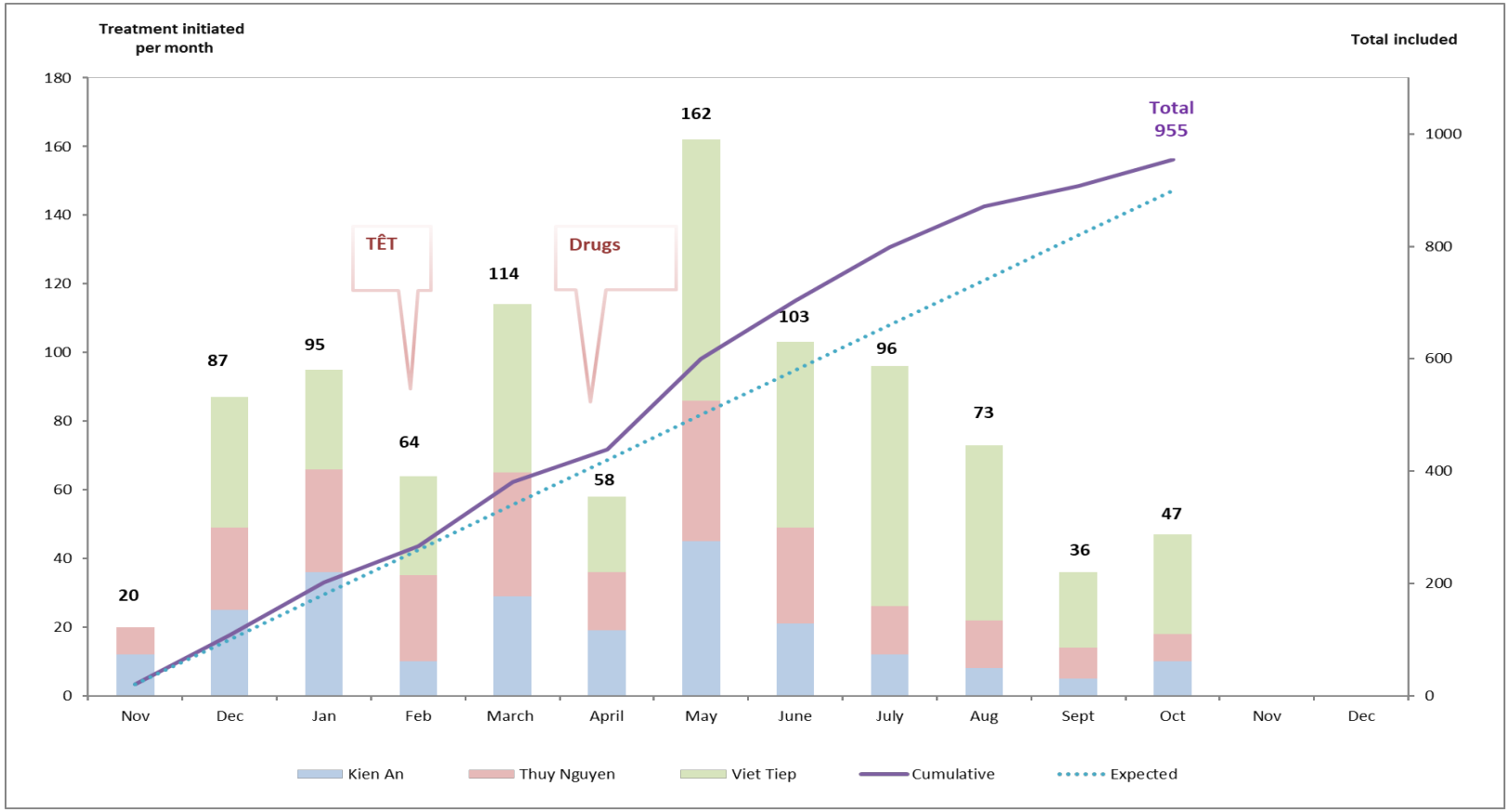
Patient visit schedule flowchart



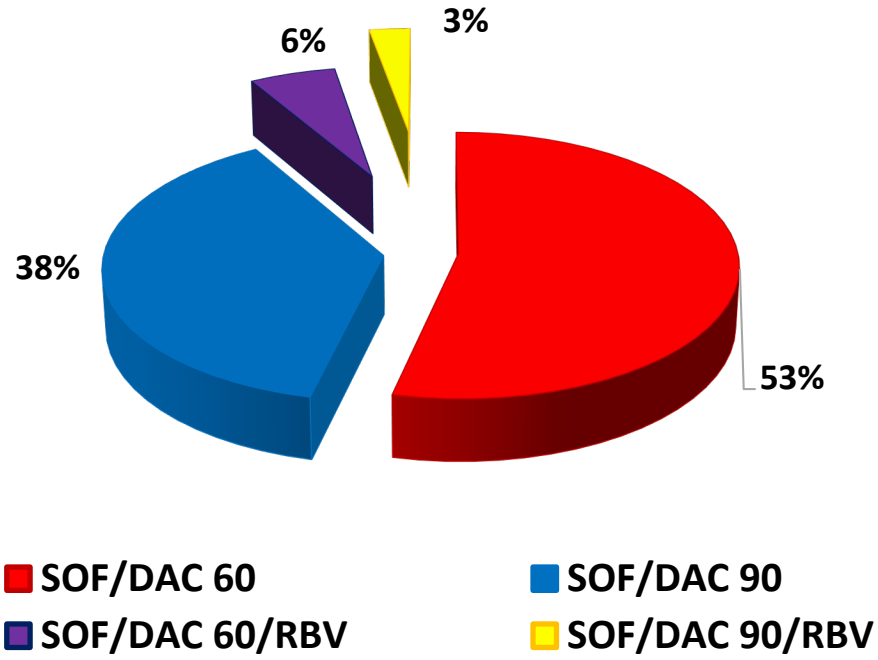
HCV, hepatitis C virus; FUp, follow-up; RDS, respondent-driven sampling; W0, week 0; SVR12, sustained virological response at post-treatment week 12

Study Progress: Treatment initiations

- Among 1017 patients pre-included: 7 deaths before inclusion, 12 exclusion, 5 refused to participate, 6 in closed settings, 32 on-going
- Inclusions started on 22/11/2019 ➔ 955 (30/10/2019)



HCV treatment



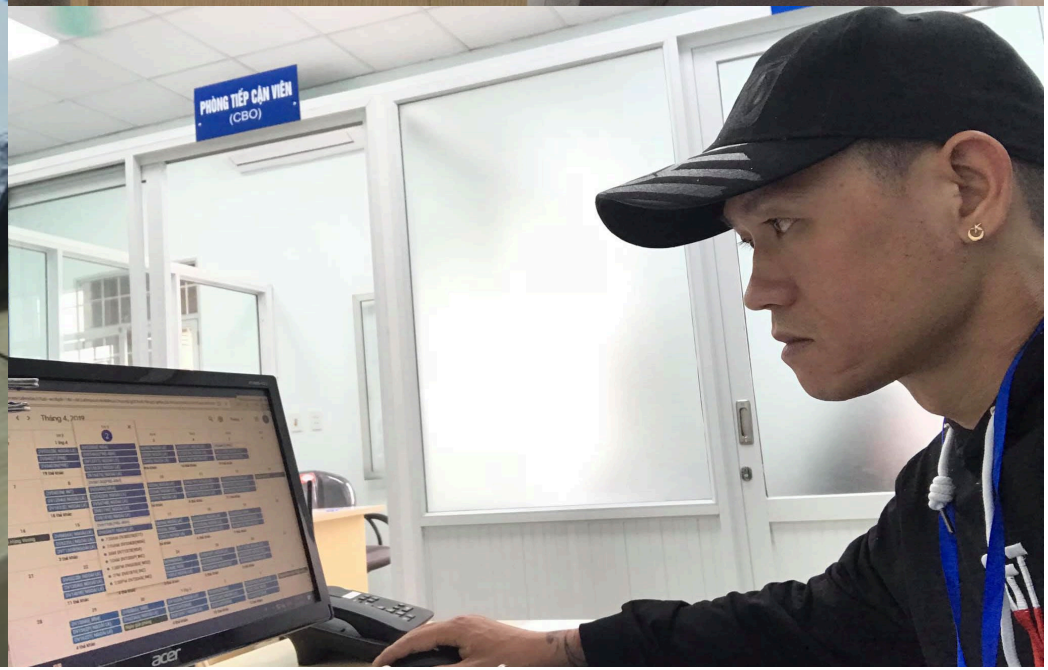
- Treatment completed: 788 patients
- SVR12 : 477 patients ➔ **≈ 96% cured in overall, 98% ITT participants**
- End of study: 23 patients ➔ **1 with RNA detectable (≈ 96% success)**

CBO activities
Preliminary phase

CBO activities: field CBOs
Linking to care, supports for adherence & education

CBO activities: clinic CBOs

Study process, interview, adherence support and tracking



Conclusion

- Viral hepatitis is a major public health issue in Vietnam
- Vietnam is not on track to achieve the WHO elimination goals over the next decade
- Lack of knowledge, attitude, and practice in HBV prevention and management in the general population and healthcare workers in Vietnam
- Innovative interventions are needed. Implementing immediate training programs for healthcare workers and educating the general population have the ability to improve access to care and prevention.