International VHPB Roundtable

Prevention and control of Viral Hepatitis in the Russian Federation: lessons learnt and the way forward

Control of hepatitis A through routine vaccination: experience of the Tyva Republic

Anna Saryglar,
Chief Doctor of Communicable Disease Hospital,
Kyzyl, Republic of Tyva

Moscow, 25-26 October, 2018

Content of Lecture

- **Full HAV vaccination course:**
  recommendations and challenges to inactivated vaccines (IAV)
- **Global single-dose IAV vaccination experience**
- **SD Havrix vaccination of children in Tyva**
- **Summary and recommendations**

WHO Guidelines (2012 г.)

- **Immunoprotection**
  - Positive/quality test on AB to HAV confirms immunity available (10-33 ME/ml)
- **Vaccines interchangeability**
  - All HAV IAV are fungible
  - Cross immunization, substituting one vaccine for another, is effective and safe (Havrix, Avaxim, Vaqta, combinations)

World Health Organization. Position paper on hepatitis A vaccines. WER 2012;87(28-29):261-76.
World Health Organization. The immunological basis for immunization series: module 18 - hepatitis A. Geneva, 2010

Full (double-dose) vaccination

- **The vaccines are permitted with a double-dose schedule, with first injection at 1 year of age or older, and a 6 months to 4-5 years' interval between the first (primary) and second (revaccination) doses.**

- **The second dose, injected in healthy vaccinated humans up to 6 months after the first shot, maintained the excellent humoral immune response to evidence the lasting induced cellular immunity (over 20 years).**

World Health Organization. Position paper on hepatitis A vaccines. WER 2012;87(28-29):261-76.
World Health Organization. The immunological basis for immunization series: module 18 - hepatitis A. Geneva, 2010

Single-dose vaccination

- **The National immunisation calendars may provide for a single-dose HAV IAV vaccination. This is comparable in efficacy, less expensive and easy to use versus the classical double-dose schedule.**

- **The primary immunization course preserves HAV AB for over 10 years (4-11 years) whereas the immunological memory protects much longer than the AB preservation period.**

- **The longest interval between primary and re-vaccination doses was 10.67 years.**

- **The anamnestic response to the revaccination dose (post-vaccination AGT) did not depend on the timing elapsed after primary injection.**

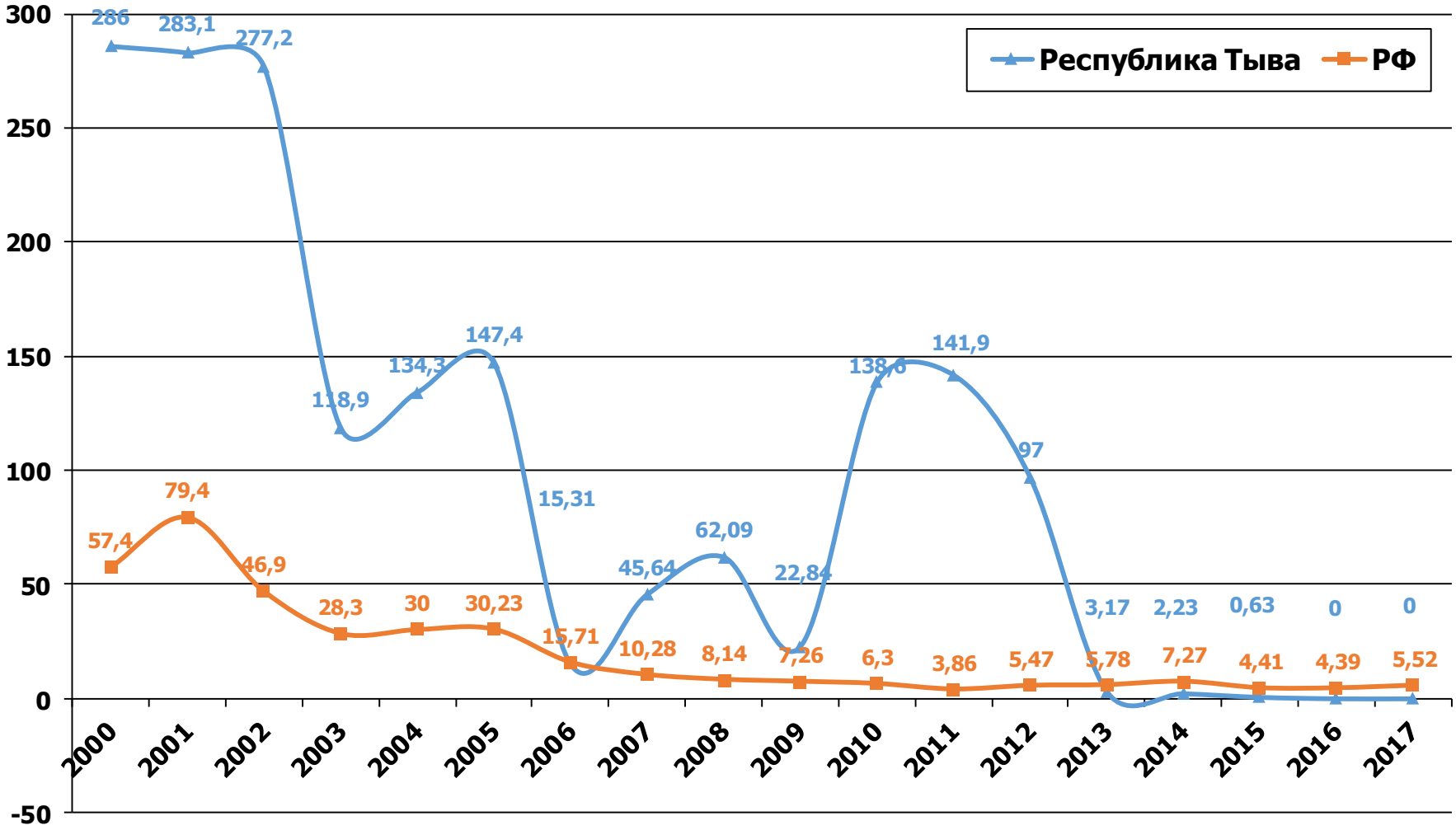
World Health Organization. Position paper on hepatitis A vaccines. WER 2012;87(28-29):261-76.
World Health Organization. The immunological basis for immunization series: module 18 - hepatitis A. Geneva, 2010

Republic of Tyva

RT is located in Southern Siberia.
Kyzyl-to-Moscow Distance - 4 668 км
Total area – 170,500 sq. km
(Switzerland – 7,580,000 – 41,284 sq. km)

Population (01.01. 2018) – 320 379 человек
Population density – 1.84 /sq. km

HAV incidence/100 000 in the Russian Federation in 2000-2012



RT districts

High incidence: - 2001-2006

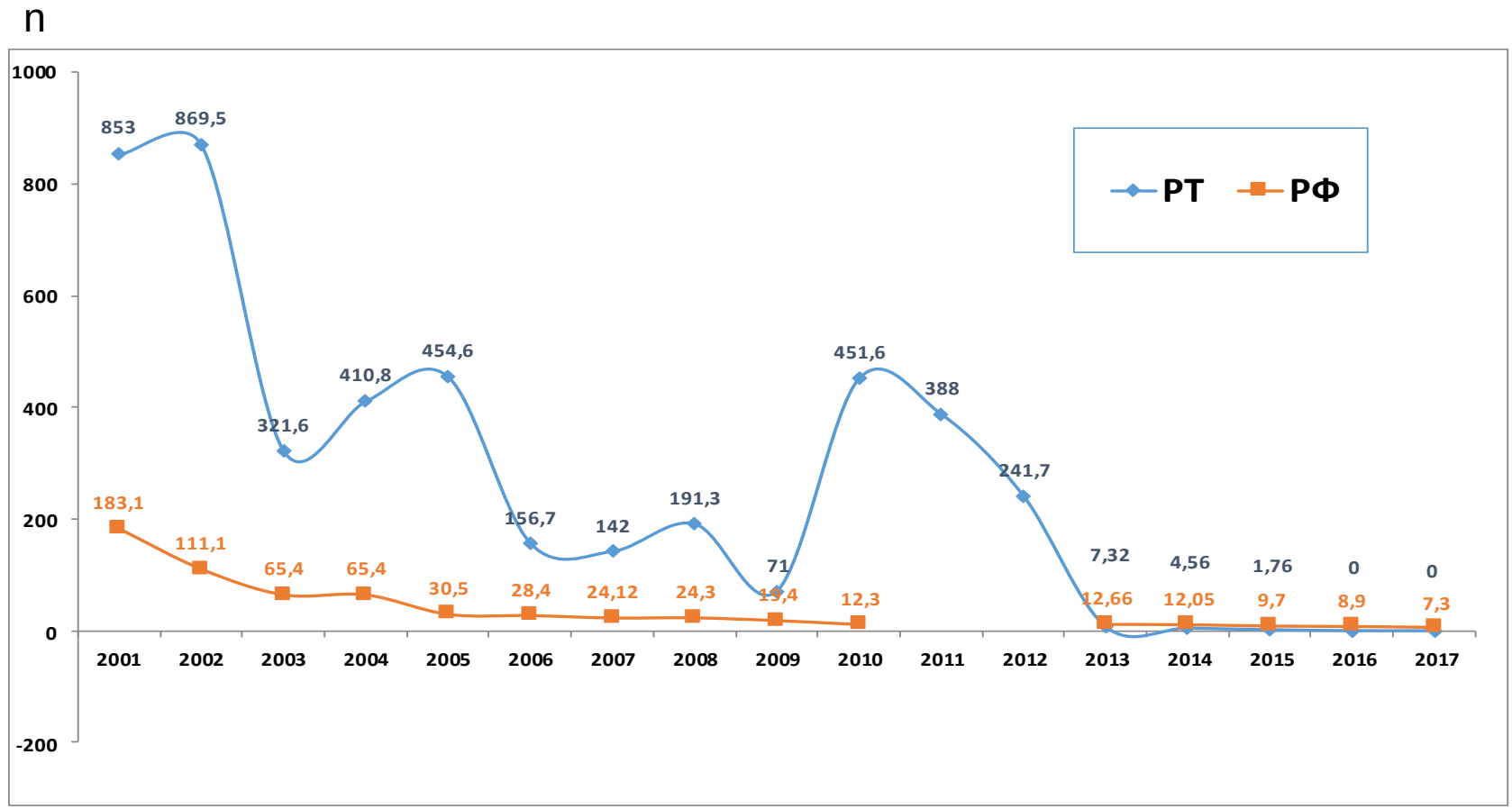
- 2007-2010

1 - Бай-Тайгинский район
2 - Барун-Хемчикский район
3 - Сут-Хольский район
4 - Дзун-Хемчинский район
5 - Чаа-Хольский район
6 - Улуг-Хемский район
7 - Пий-Хемский район
8 - Тоджинский район
9 - Кызылский район
10 - г. Кызыл
11 - Чеди-Хольский район
12 - Тандинский район
13 - Каа-Хемский район
14 - Монгун-Тайгинский район
15 - Овюрский район
16 - Тес-Хемский район
17 - Эрзинский район

HAV outbreaks in RT

Years	n outbreaks	n children infected	n water samples for HAV antigen testing	n positive test results
2001	8	57	No data	No data
2002	3	27	56	7 (12,5%)
2003	3	21	10	4 (40%)
2004	2	114	147	93 (63,3%)
2005	1	38	136	8
2006	0	0	185	17
2007	1	32	264	2
2008	3	115	137	0
2009	3	54	96	0
2010	12	395	184	0
2011	6	160	234	1
2012	2	19	99	4
2013	0	8	159	0
2014	0	5	197	0
2015	0	2	117	0
2016	0	0	192	0
2017	0	0	207	0
Total	44	1047		

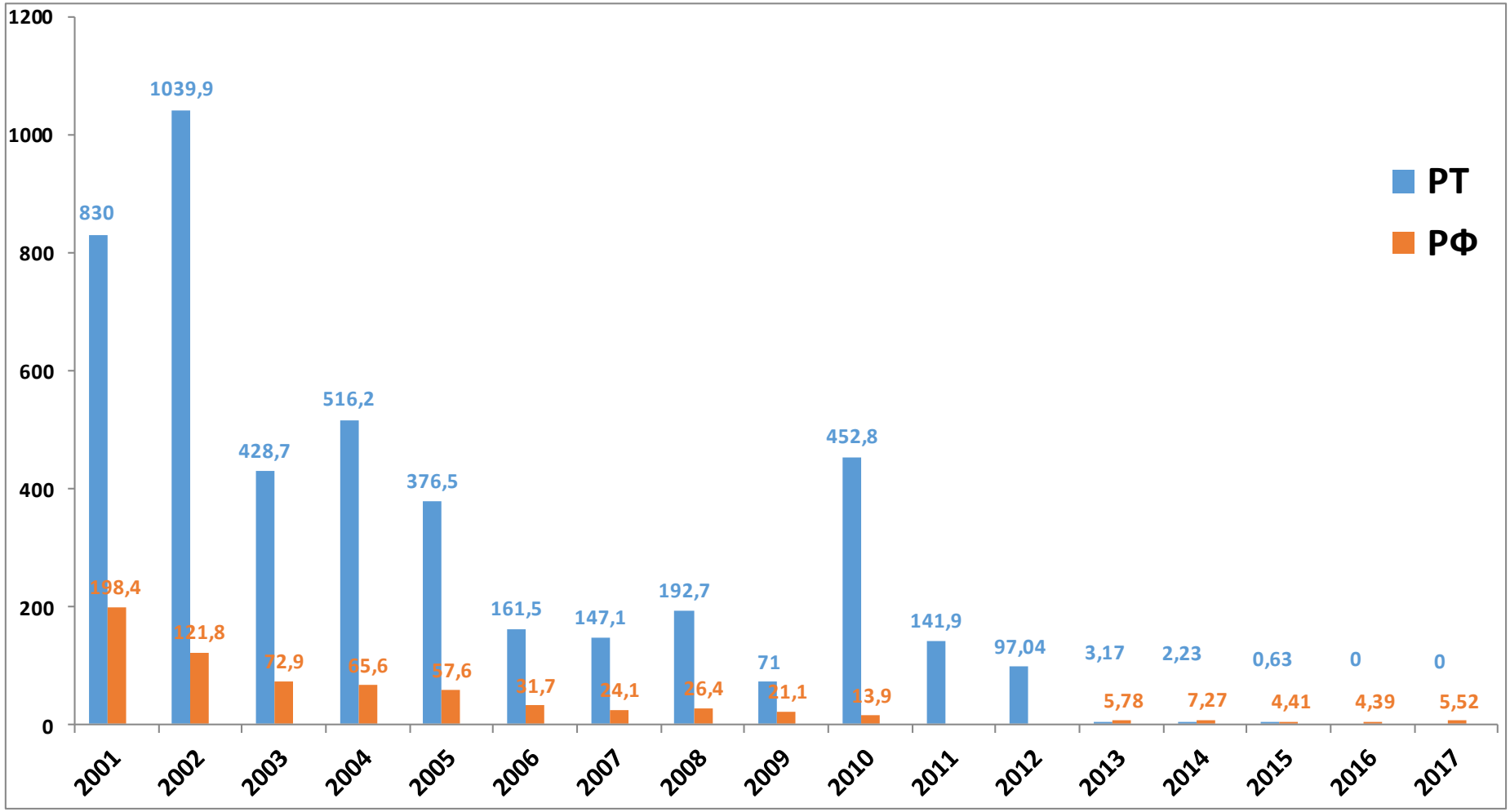
HAV incidence/100 000 children in 2001-2017



Source: Federal Consumer Protection and Human Wellbeing Service RF

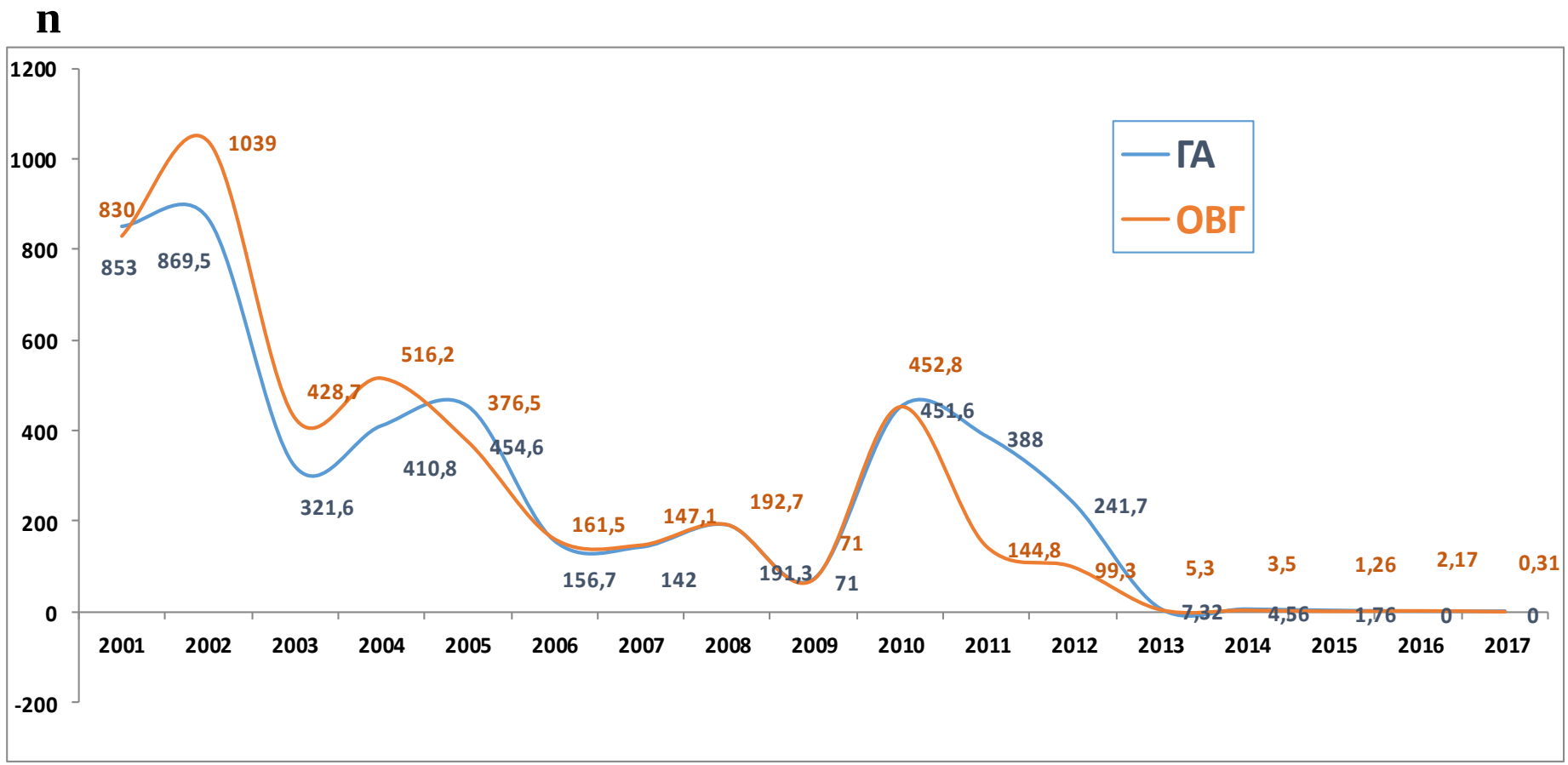
Acute VH incidence/100 000 children in RT versus RF in 2001-2017

n



Source: Federal Consumer Protection and Human Wellbeing Service RF

HAV incidence/100 000 children in acute VH incidence in RT versus RF in 2001-2017



Source: RT Consumer Protection and Human Wellbeing Service

Ministry of Health and Social Development RT released on July 18, 2018 the decree on mass HAV immunization of children and adolescents.

MH RT and RT Consumer Protection and Human Wellbeing Service issued in 2013 Decree 282/240 of July 25, 2013 on approval of the RT immunization calendar.

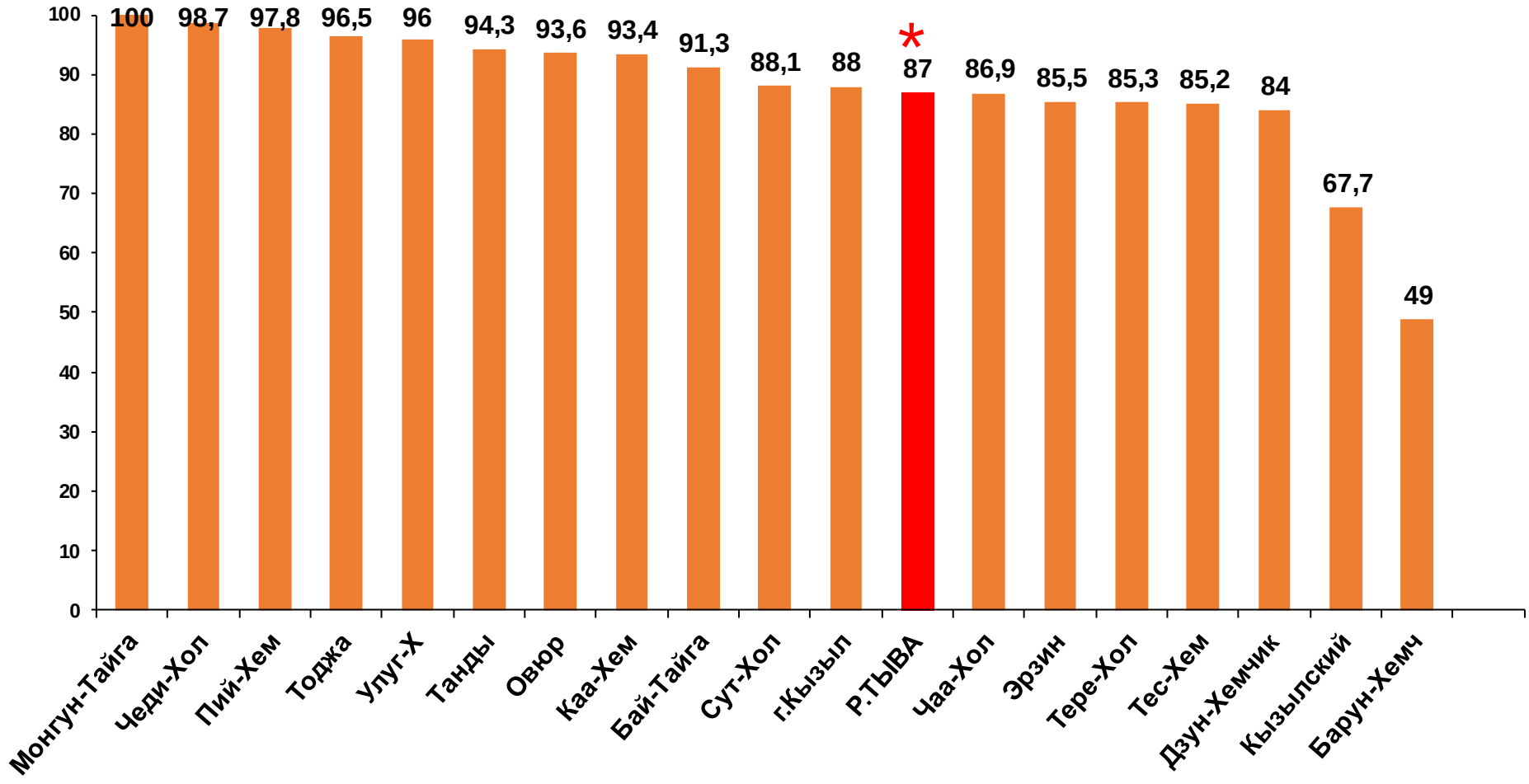
Government RT approved in January 2013 a resolution on HAV routine immunization of children.

Single-dose HAV IAV immunogenicity test

Design of study

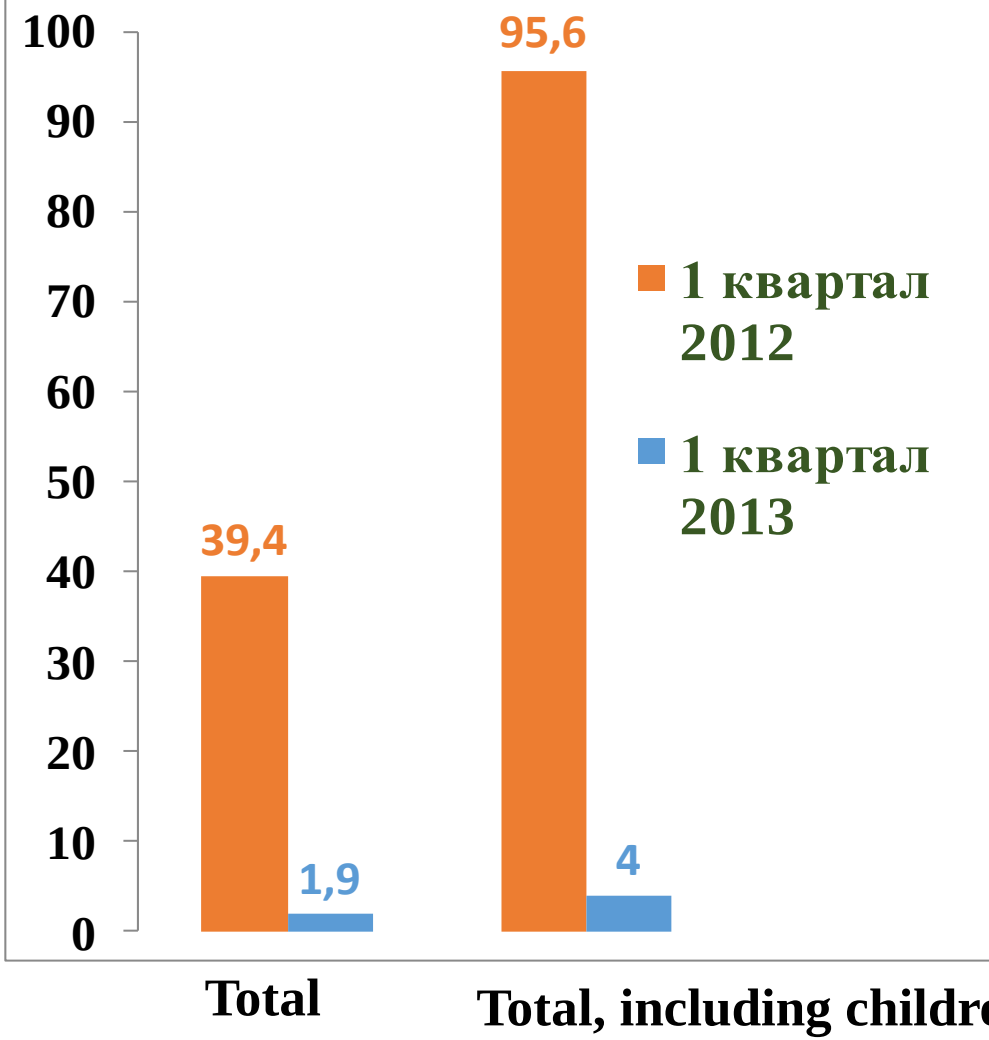
- **387** children blood-sampled in RT, aged 3-8 (mean **6.5 years**)
- 720 children Havrix-immunized in 2012. Anti-HAV tested in blood using DS-IFA-HAV-G-RECOMB (Diagnostic Systems Co.; Elecsys anti-HAV (Roche)

Single-dose HAV immunization coverage of children, aged 3-8, across RT districts (31.12.2012)



*Immunisation coverage of children, aged 3-8 – 87%

HAV incidence/100 000 in RT



87% children, aged 3-8, immunized simultaneously in RT (09.12.-12.12.).

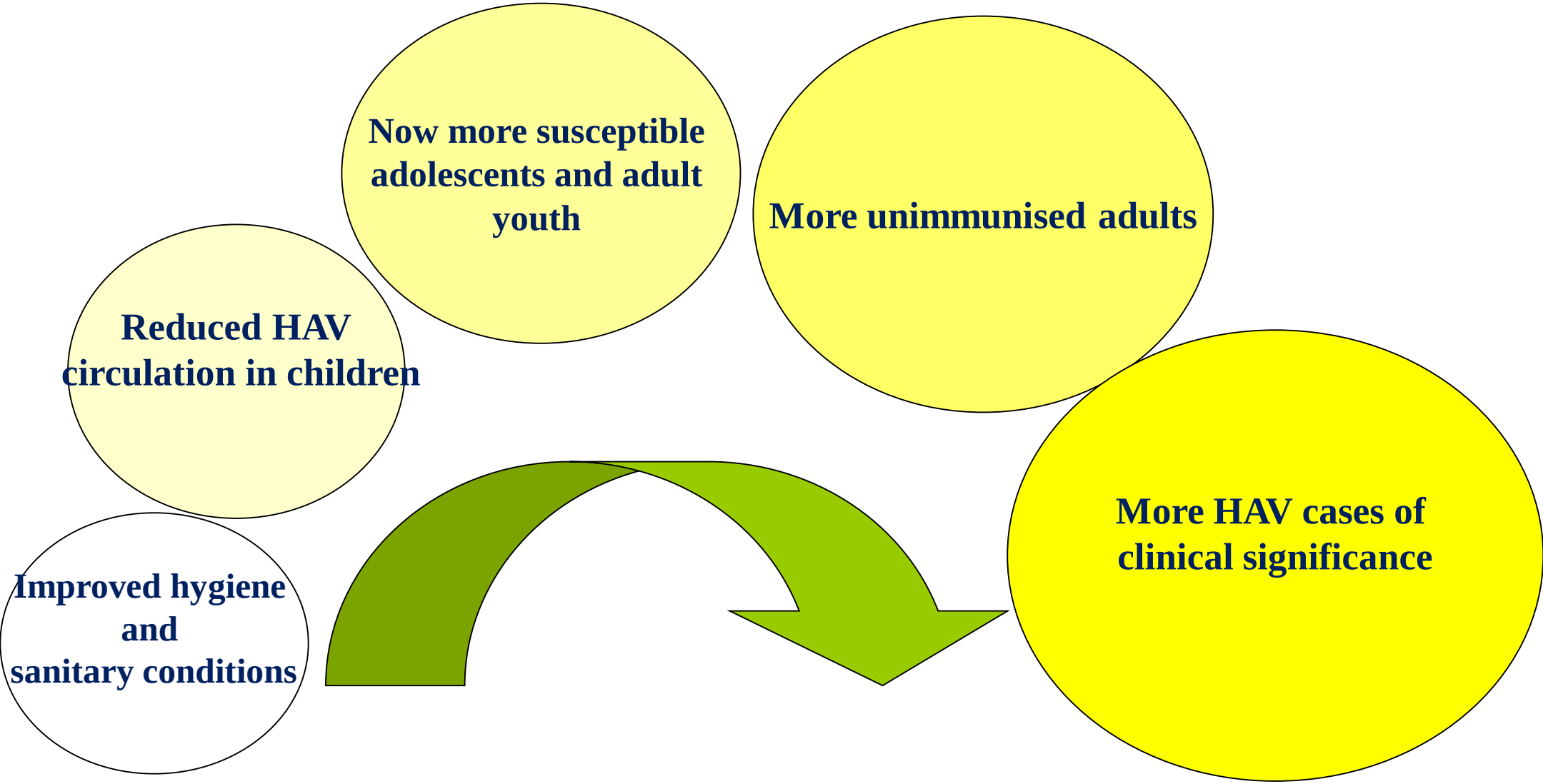
HAV incidence comparative analysis (Q1 2012 versus Q1 2013, i.e. 3 months after immunization) revealed a 20-fold reduction in HAV incidence in RT, with

24-fold for children.

4 unimmunized children fell ill.

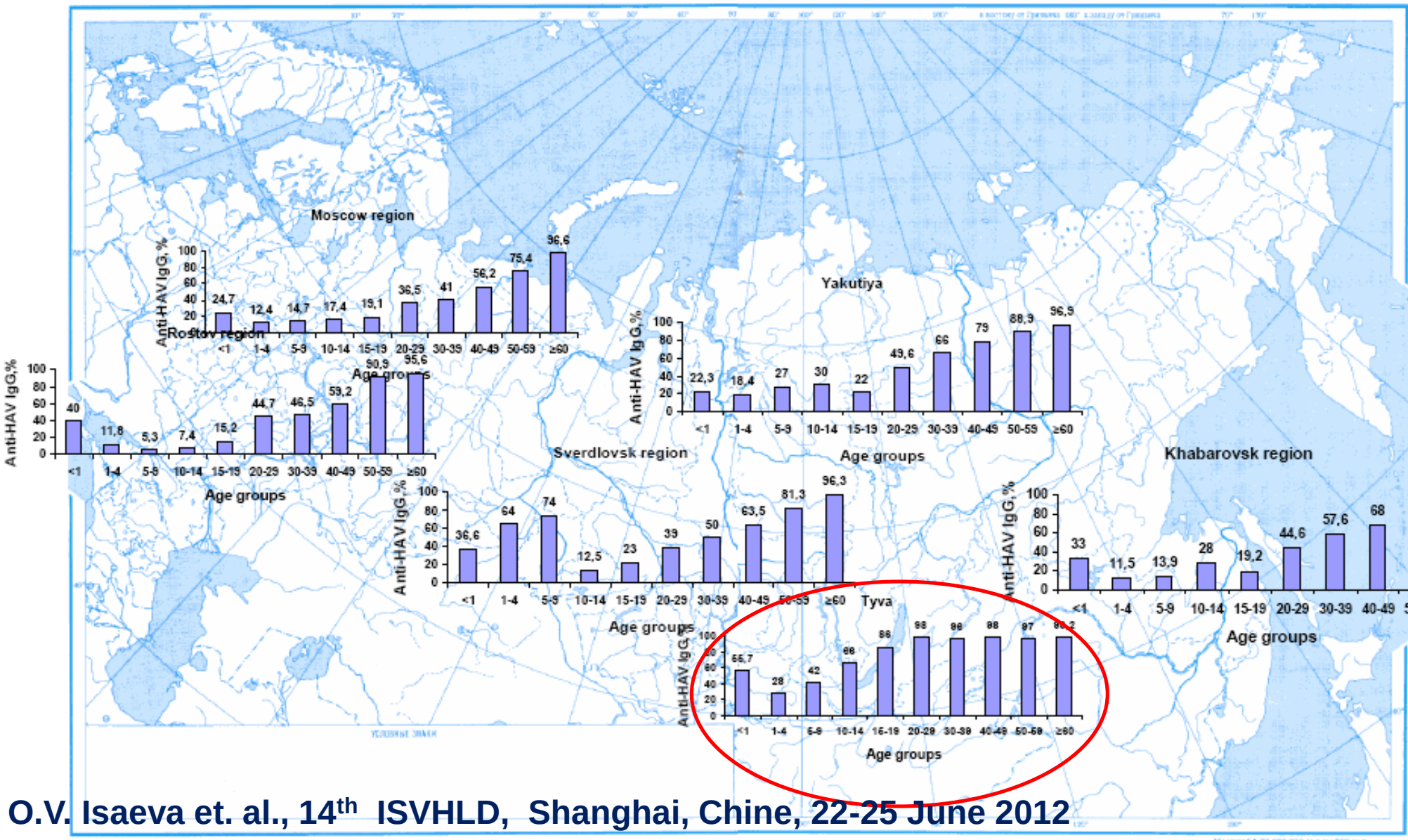
Clearly, mass immunization has no alternative.

HAV: changing epidemiology



Van Herck & Van Damme, *Expert Rev Vaccines* 2005; 4: 459–71.
WHO, Hepatitis A, WHO/CDS/CSR/EDC/2000.7

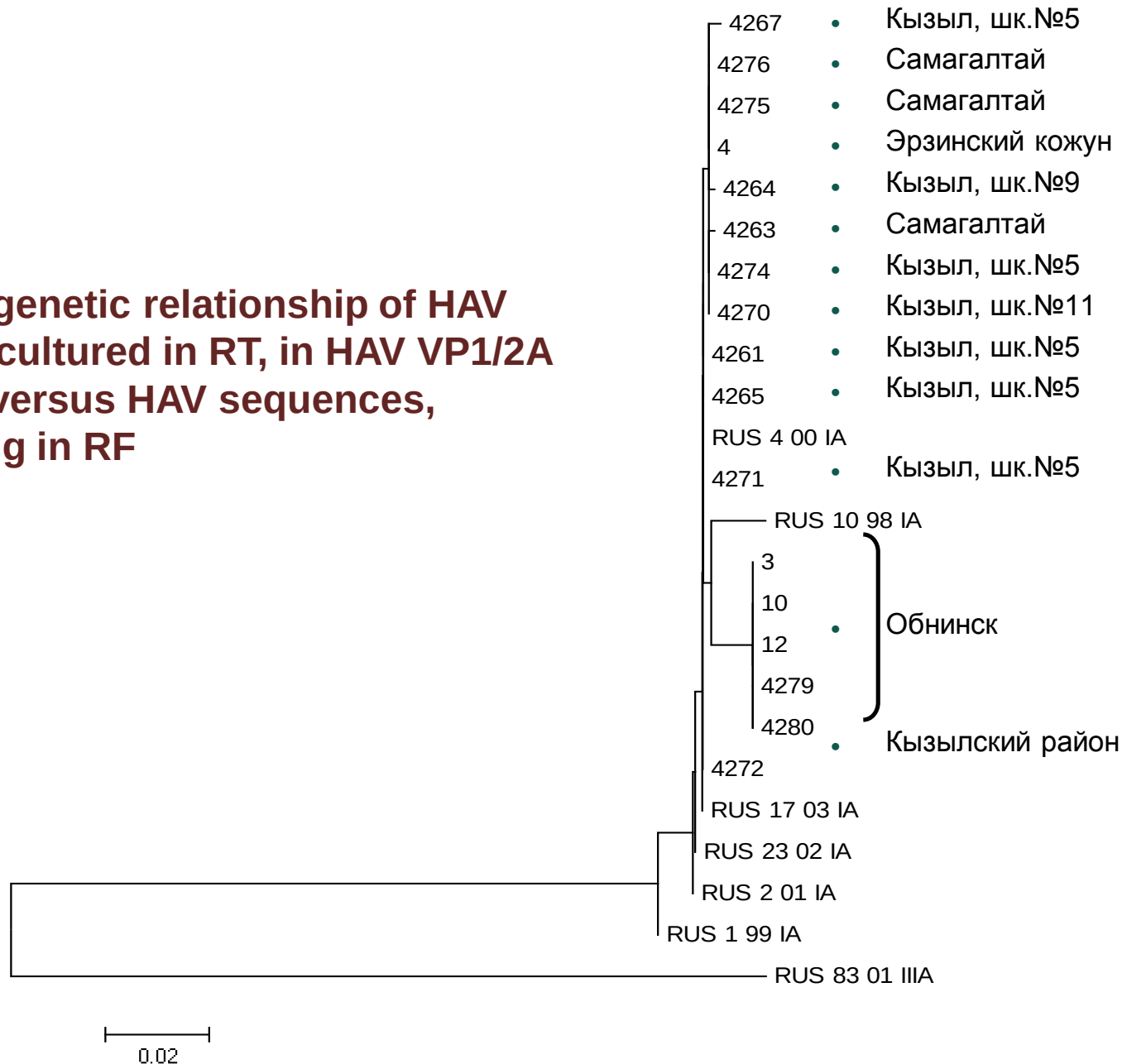
Anti-HAV incidence rate among notionally healthy population in RF (n=6074)



O.V. Isaeva et. al., 14th ISVHLD, Shanghai, Chine, 22-25 June 2012

Phylogenetic analysis

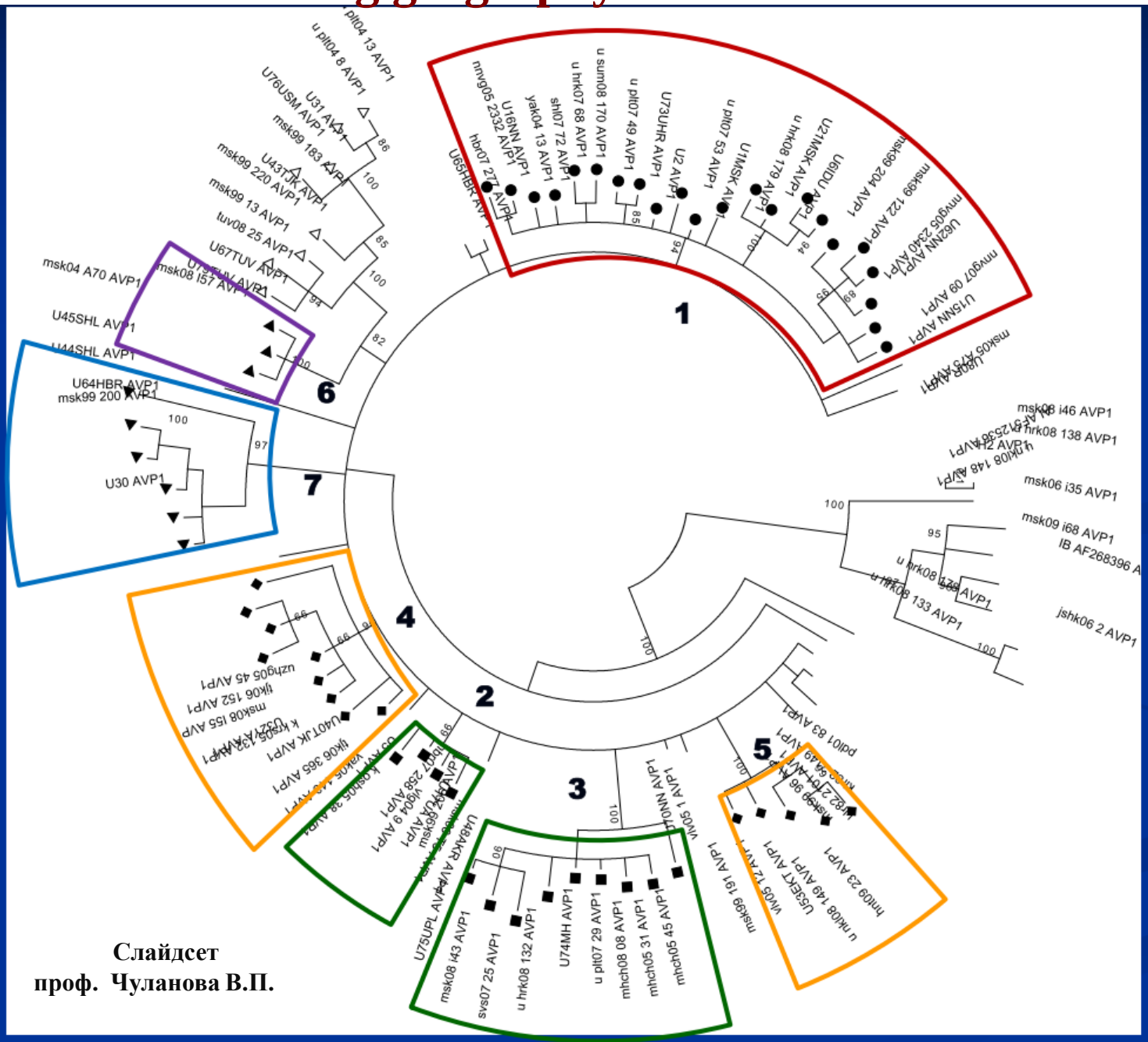
Phylogenetic relationship of HAV isolates, cultured in RT, in HAV VP1/2A genome versus HAV sequences, circulating in RF



Ia

Слайдсет
проф. Чуланова В.П.

HAV IA clustering geography



Слайдсет
проф. Чуланова В.П.

Филогенетические кластеры ВГА субтипа IA

1 – кластер штаммов европейской части РФ;

2, 3 – южные кластеры;

4, 5 – среднеазиатские кластеры;

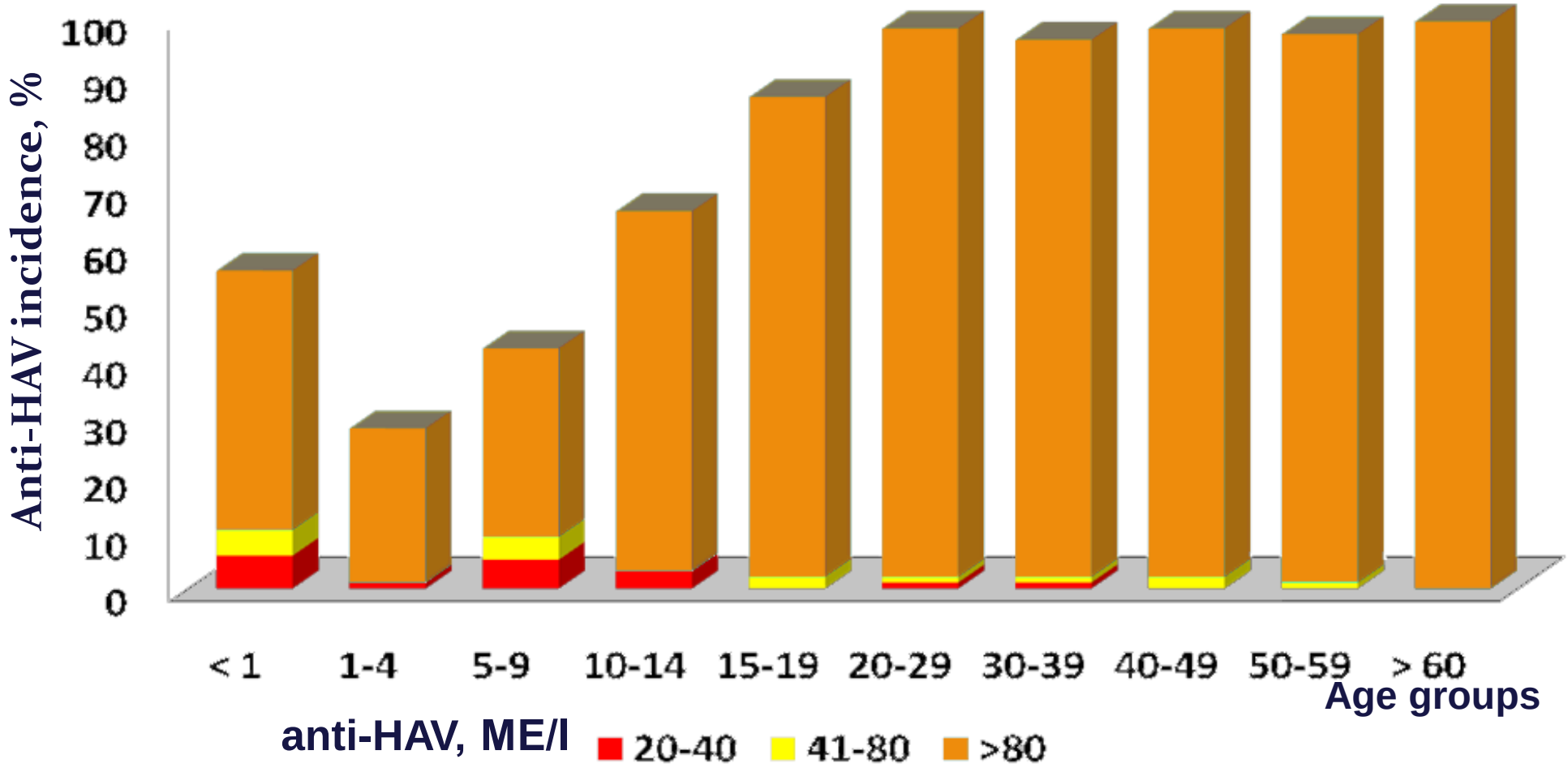
6 – тувинский кластер;

7 – дальневосточный кластер;

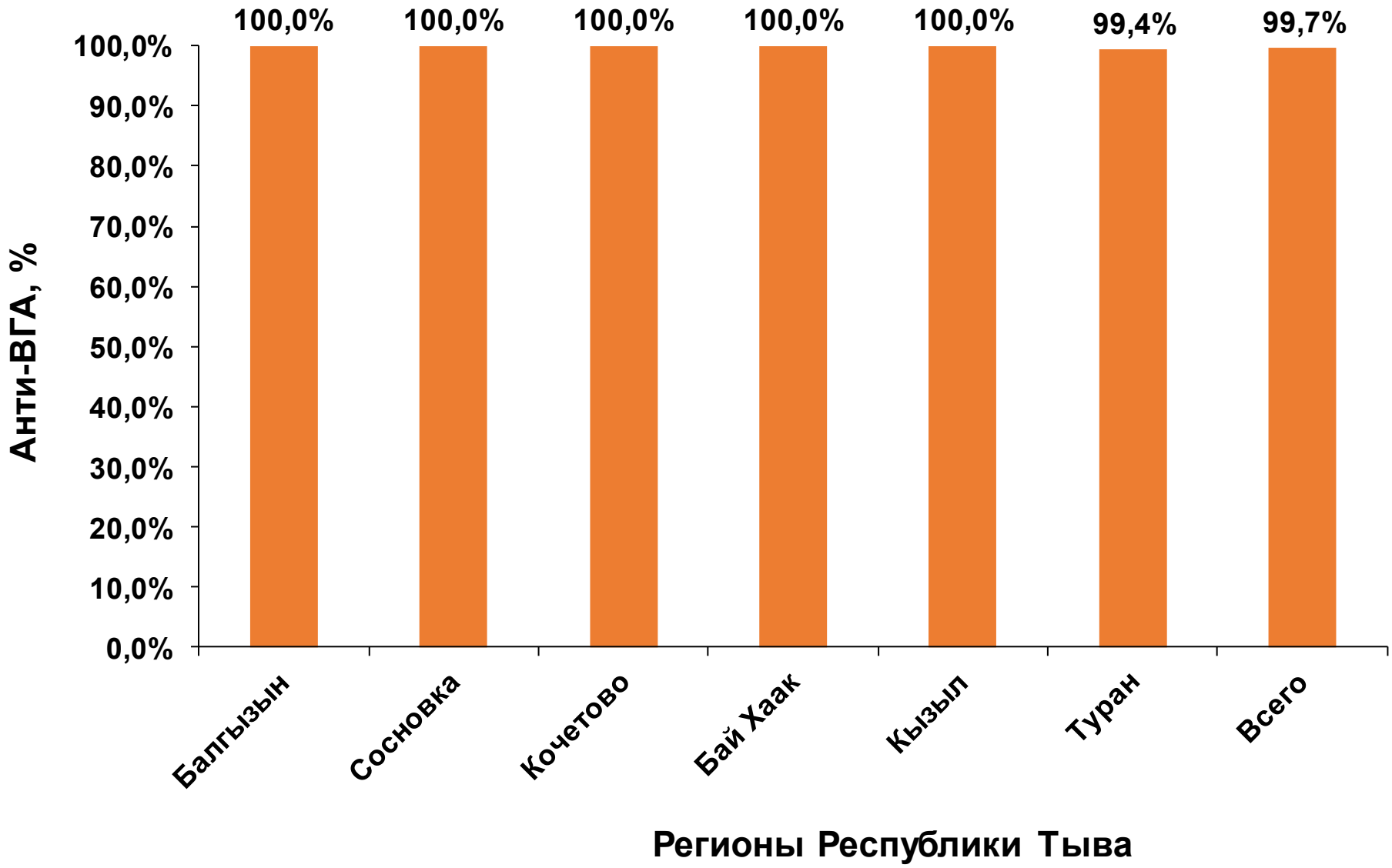
Область генома ВГА VP1/2A,
длина 411 нт, байесовский стат. метод,
модель GTR+I

Expeditions to RT

Anti-HAV incidence among notionally healthy community in RT (n = 1011; 2008)



Anti-HAV IgG incidence one month after single-dose Havrix immunization of 720 children across RT districts



Immunisation is the most effective HAV control method

even as a single-dose injection

The multi-year epidemiological monitoring should be continued in Argentina, and a similar experience to be gathered in other regions with a HAV transient endemnicity

The HAV single-dose mass immunization in average-endemnicity regions will help cut down short-term costs in the health sector and use most rationally local budgets to ensure health protection for some years ahead, while the complete booster-dose immunization course will secure a decades-long immunity in the immunized.

Mechnikov Vaccine and Sera Institute, Moscow

Михайлов М.И., Кожанова Т.В., Кюрегян К.К., Исаева О.В., Попова О.Е., Клушкина В.В., Лопатухина М.В., Замятина Н.А., Ильченко Л.Ю.

Kyzyl Communicable Disease Hospital, Republic of Tyva

Сарыглар А.А., Ооржак Н.Д., Я.Н. Сонам-Баир, Сарыг-Хаа О.Н., А.Б. Ооржак, М.К. Монгуш


Thank you!