Fifteen years of HBV transmission risk reduction by different NAT methods used in Poland

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HBV epidemiology in Poland (XXth century)

Sterilization od medical instruments,
Single use of medical equipment,
Immunization risk groups, EPI, 14 year old in 2000-2011

HBsAg screening in Blood Donors *1995-2004 HBsAg prevalence 0,35%*

> DNA HBV screening from 2005

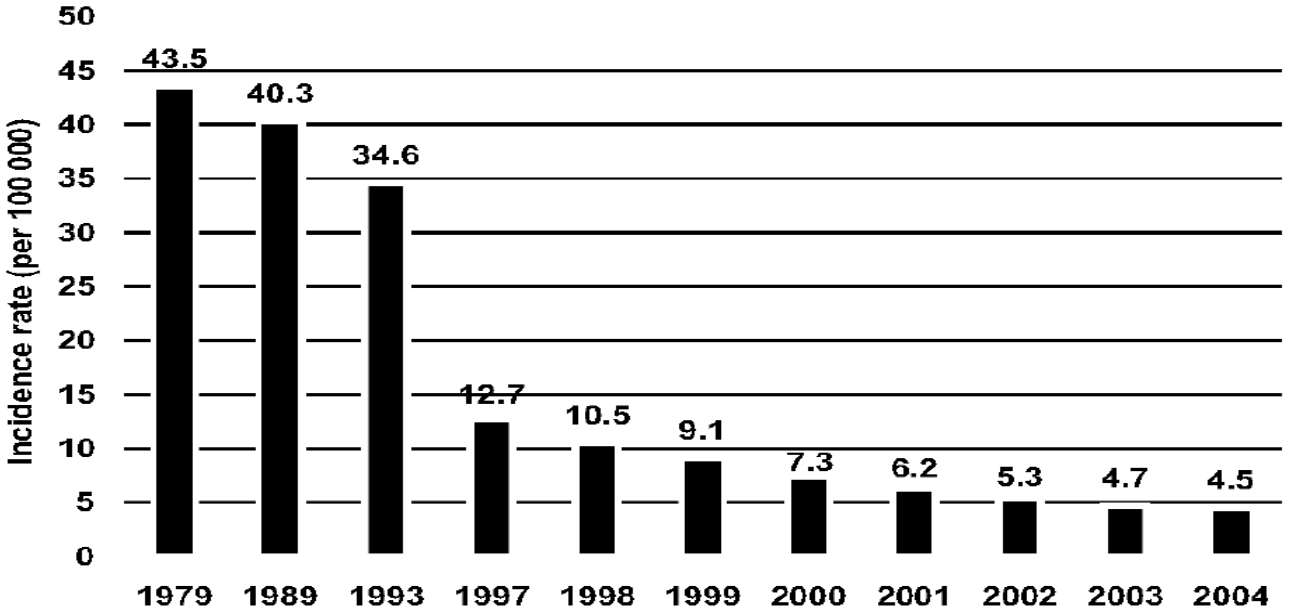
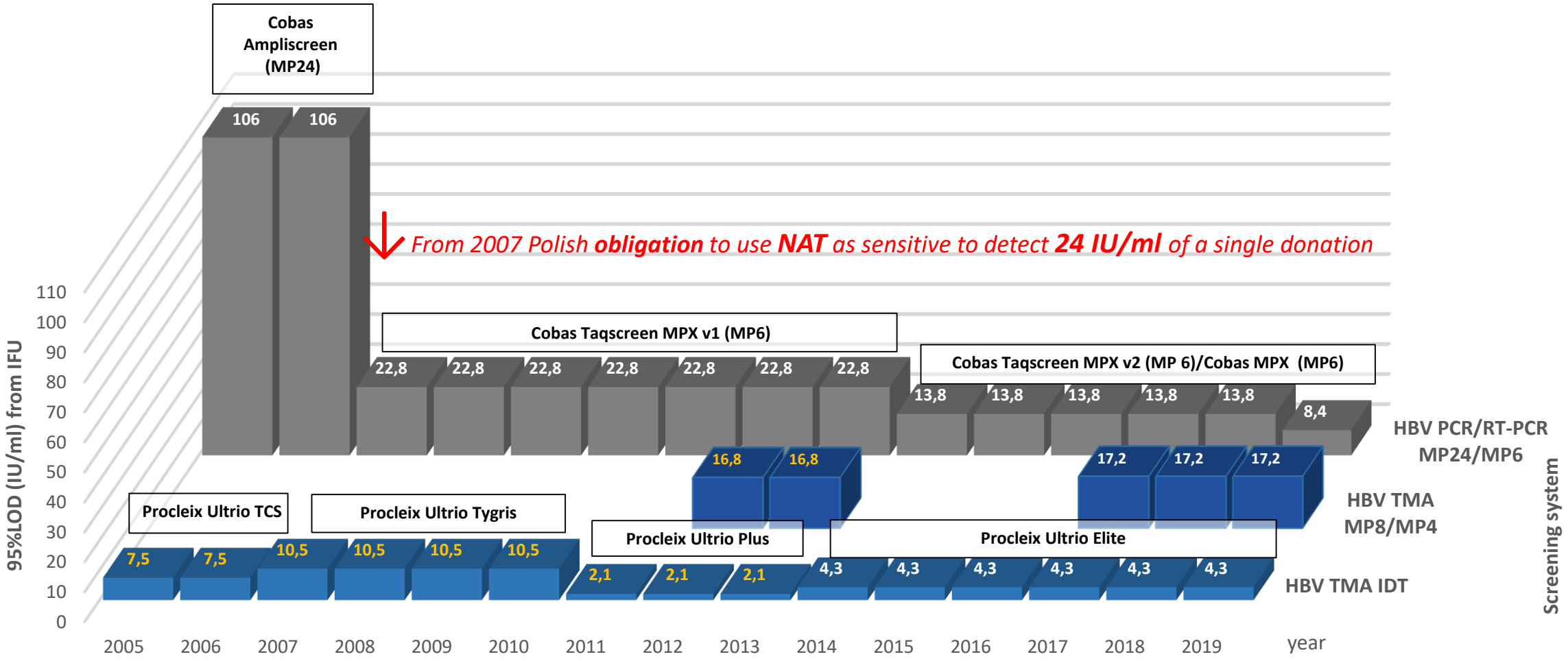


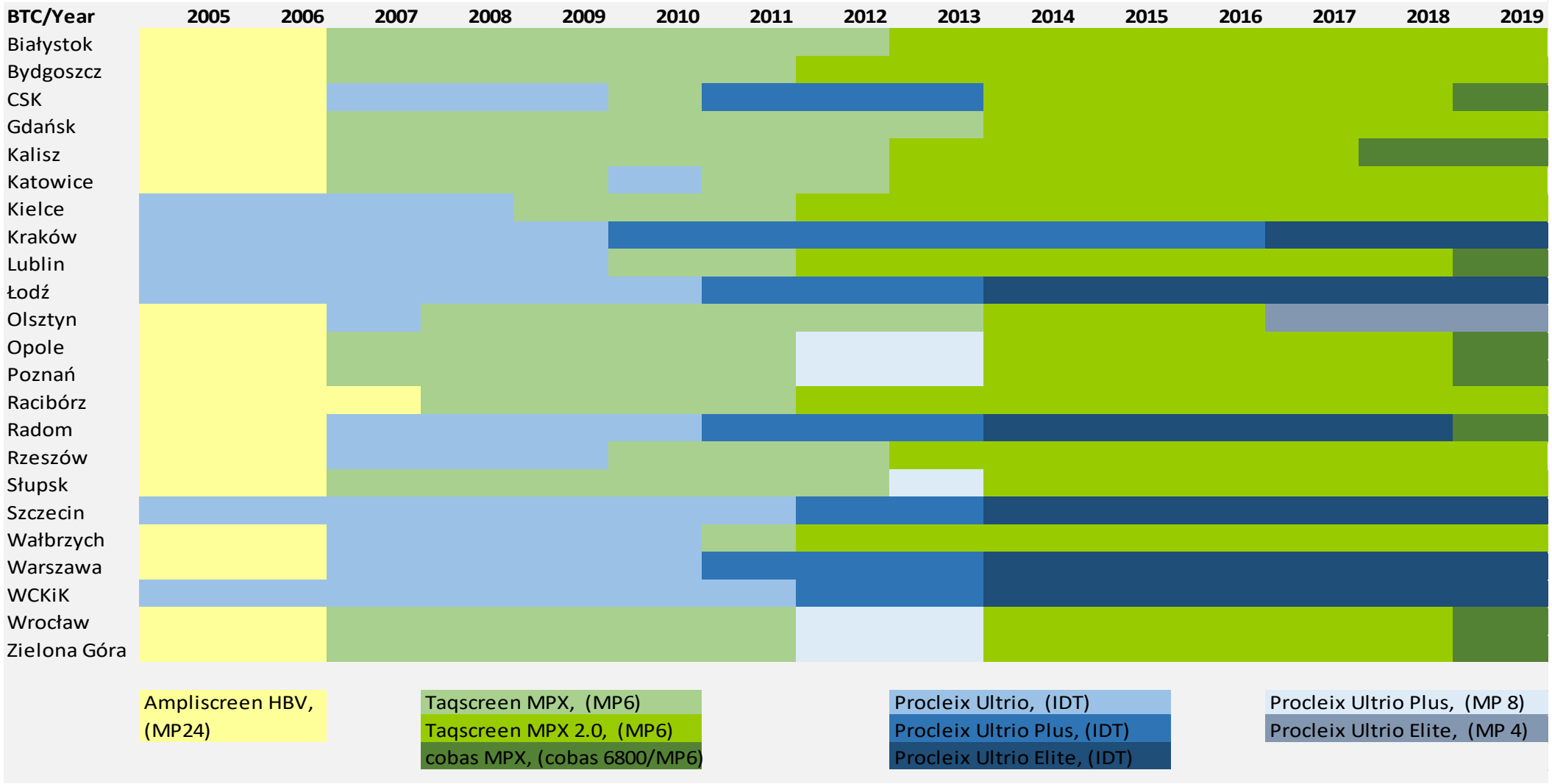
Fig. 1. Incidence of hepatitis B infection in Poland, 1979–2004 (modified and updated from Magdzik, 2000).

NAT methods and strategies in Poland (2005-2019)

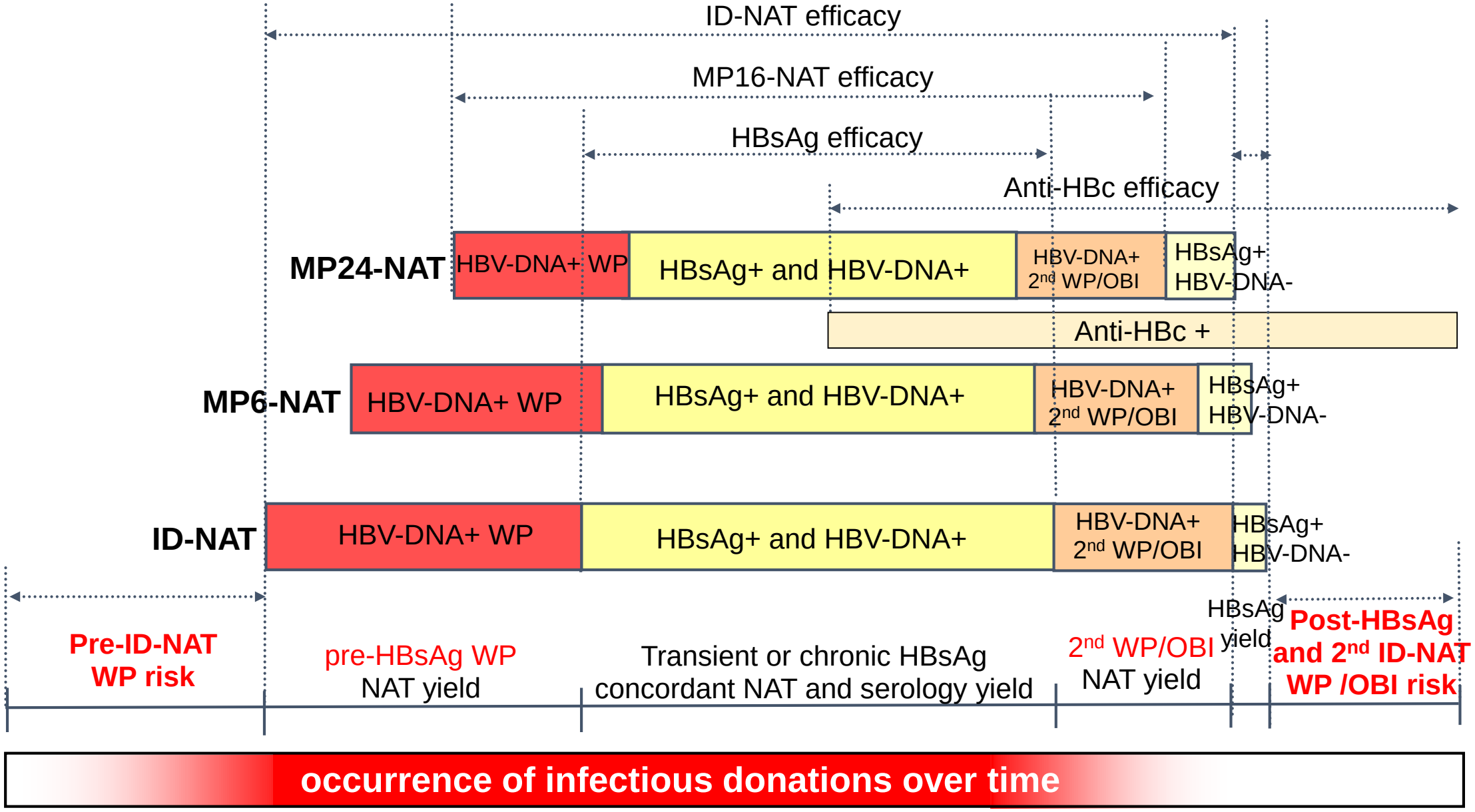


Ultrio had variable sensitivity and average 95% LOD on multiple HBV samples was verified as 73 IU/ml by Vermeulen et al.
Ultrio Plus verified as 4,6 IU/mL by Grabarczyk et al. and Grifols company later corrected 95% LOD in IFU

Change of NAT methods and strategies in Polish 23 BTCs (2005-2019)



Efficacy of HBV screening assays

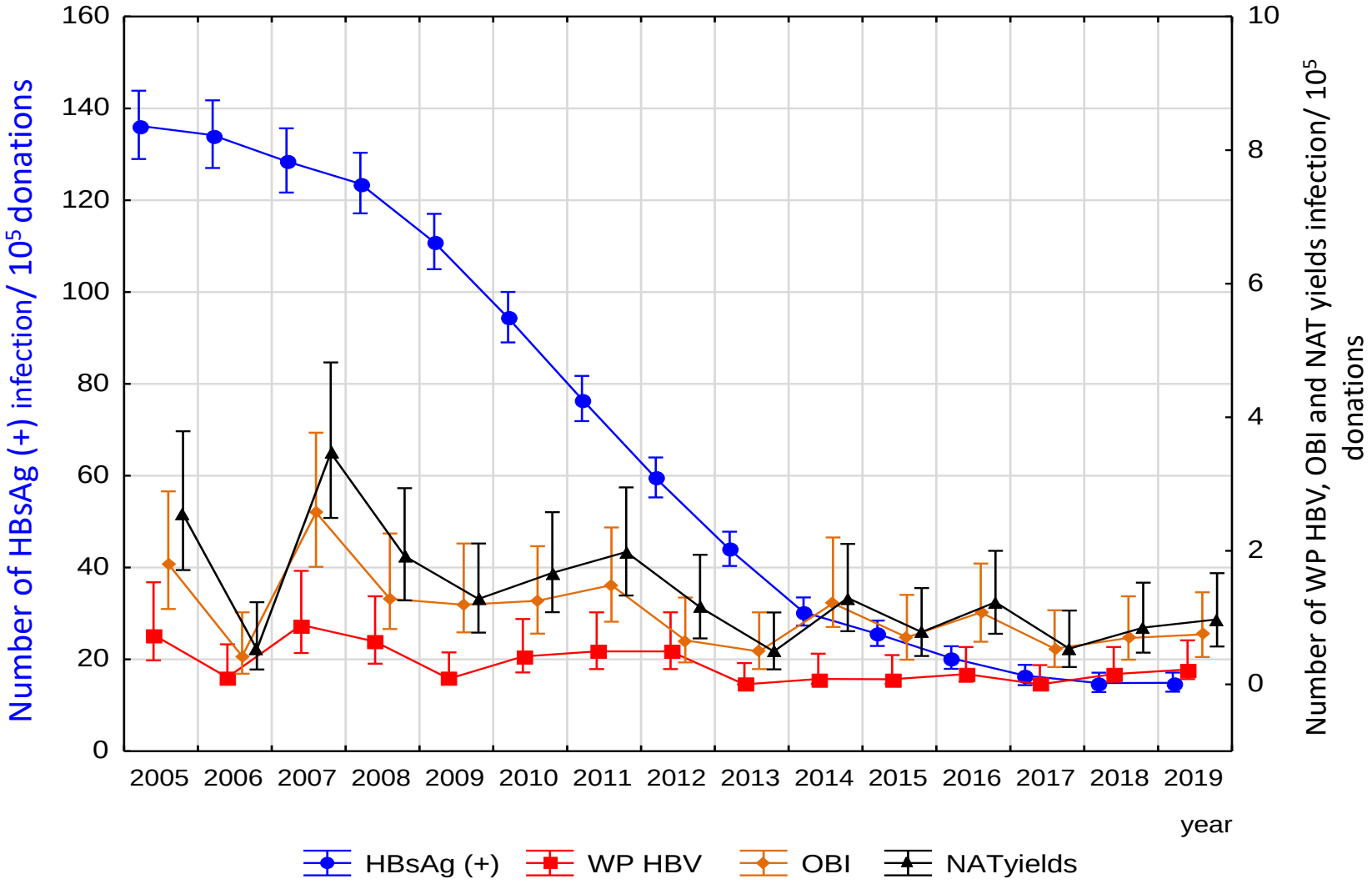


HBV infections detected by different test systems in all donations (2005-2019)

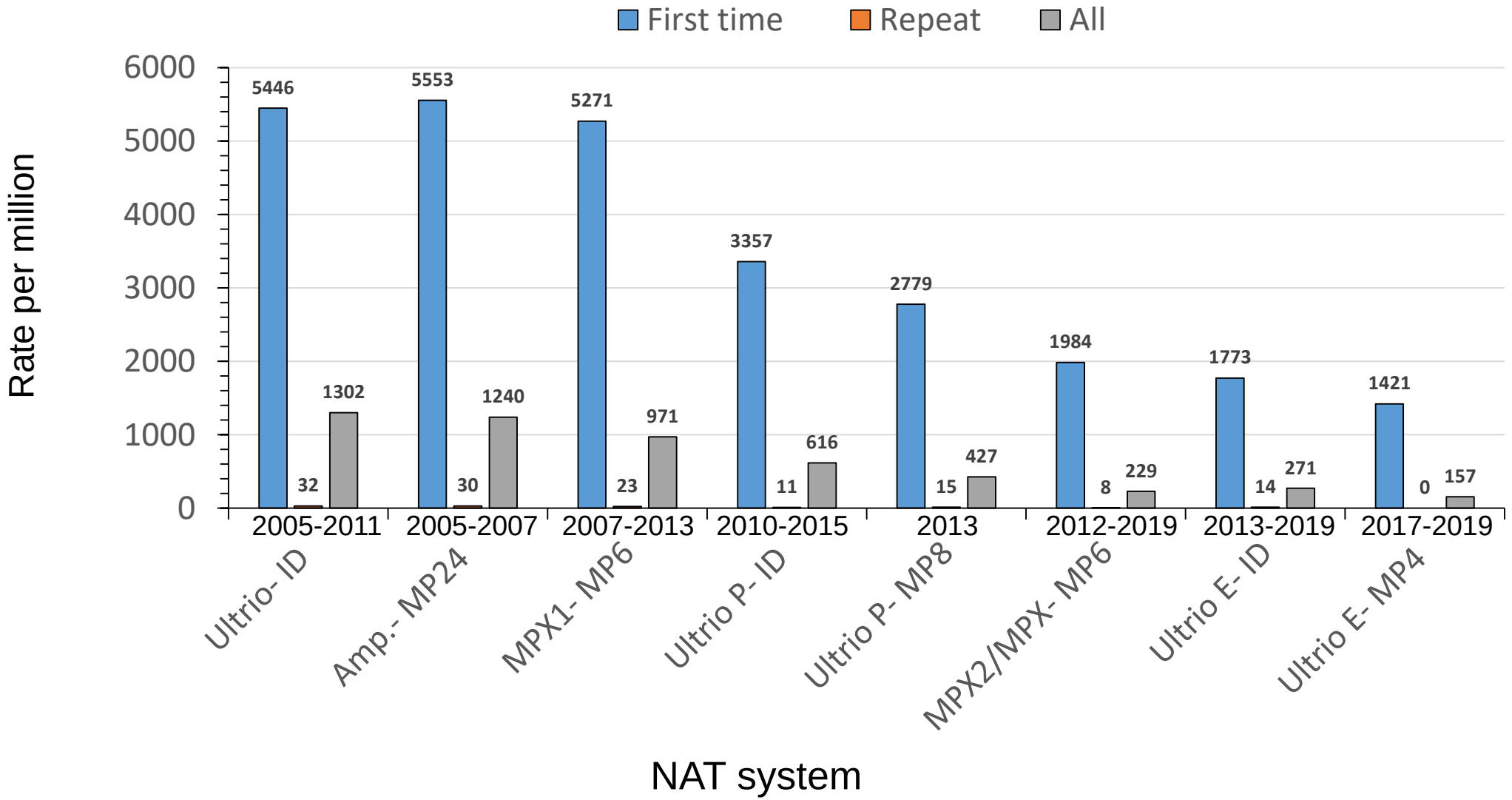
All donations - number HBV infections									
Assay **NAT - Format** **LOD* IU/ml** **Period**	**Ultrio** **ID** *7,5-10,5^* **2005-2011**	**Ampliscreen** **MP24** *106* **2005-2007**	**cobas** **MPX1** **MP6** *22,8* **2007-2013**	**Ultrio Plus** **ID** *2,1#* **2010-2015**	**Ultrio Plus** **MP8** *16,8* **2013**	**cobas** **MPX2/MPX** **MP6** *13,8/8,4* **2012-2019**	**Ultrio Elite** **ID** *4,3* **2013-2019**	**Ultrio Elite** **MP4** *17,2* **2017-2019**	**All NAT Assays** *2,1# - 106* **2005-2019**
All donations	2.262.854	1.426.157	3.639.201	1.480.734	227.429	6.012.089	2.027.013	133.614	17.209.091
WP	10	2	13	8	0	2	5	0	40
HBsAg+	2896	1762	3466	894	95	1335	519	20	10.987
OBI + 2nd WP	41	5	54	10	2	42	25	1	180
All HBV	2947	1769	3533	912	97	1379	549	21	11207
All donations - HBV infection rate per million									
WP	4,42	1,40	3,57	5,40	0,00	0,33	2,47	0,00	2,32
HBsAg+	1279,8	1235,5	952,4	603,8	417,7	222,1	256,0	149,7	638,4
OBI + 2nd WP	18,12	3,51	14,84	6,75	8,79	6,99	12,33	7,48	10,46
All HBV	1302,3	1240,4	970,8	615,9	426,5	229,4	270,8	157,2	651,2

*95% LOD from IFU,
^ verified as 73 IU/ml by Vermeulen et al., # verified as 4,6 by Grabarczyk et al. and Grifols company with change of 95% LOD in IFU

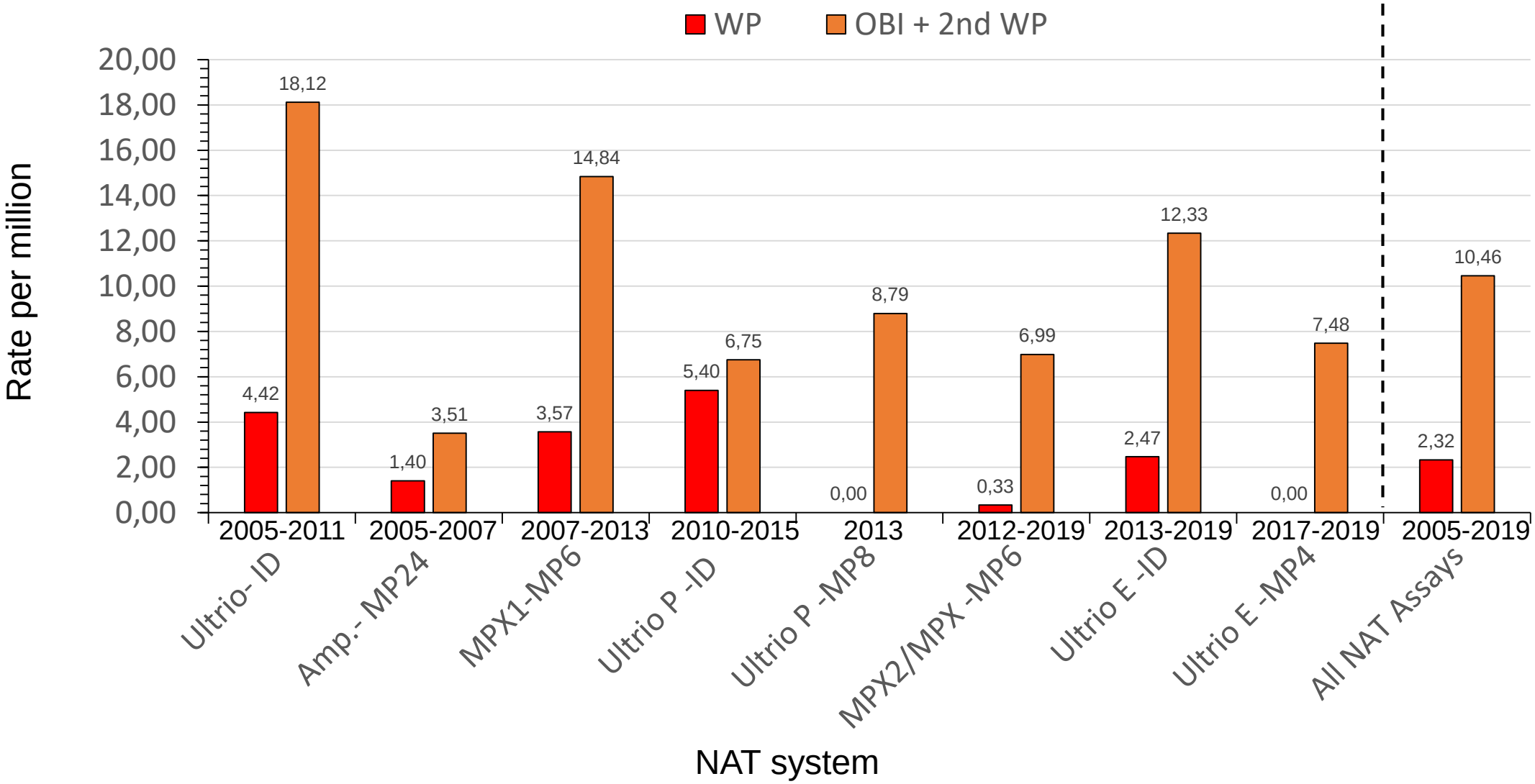
Annual HBV infection rates per 100,000 donations in Poland 2005-2019



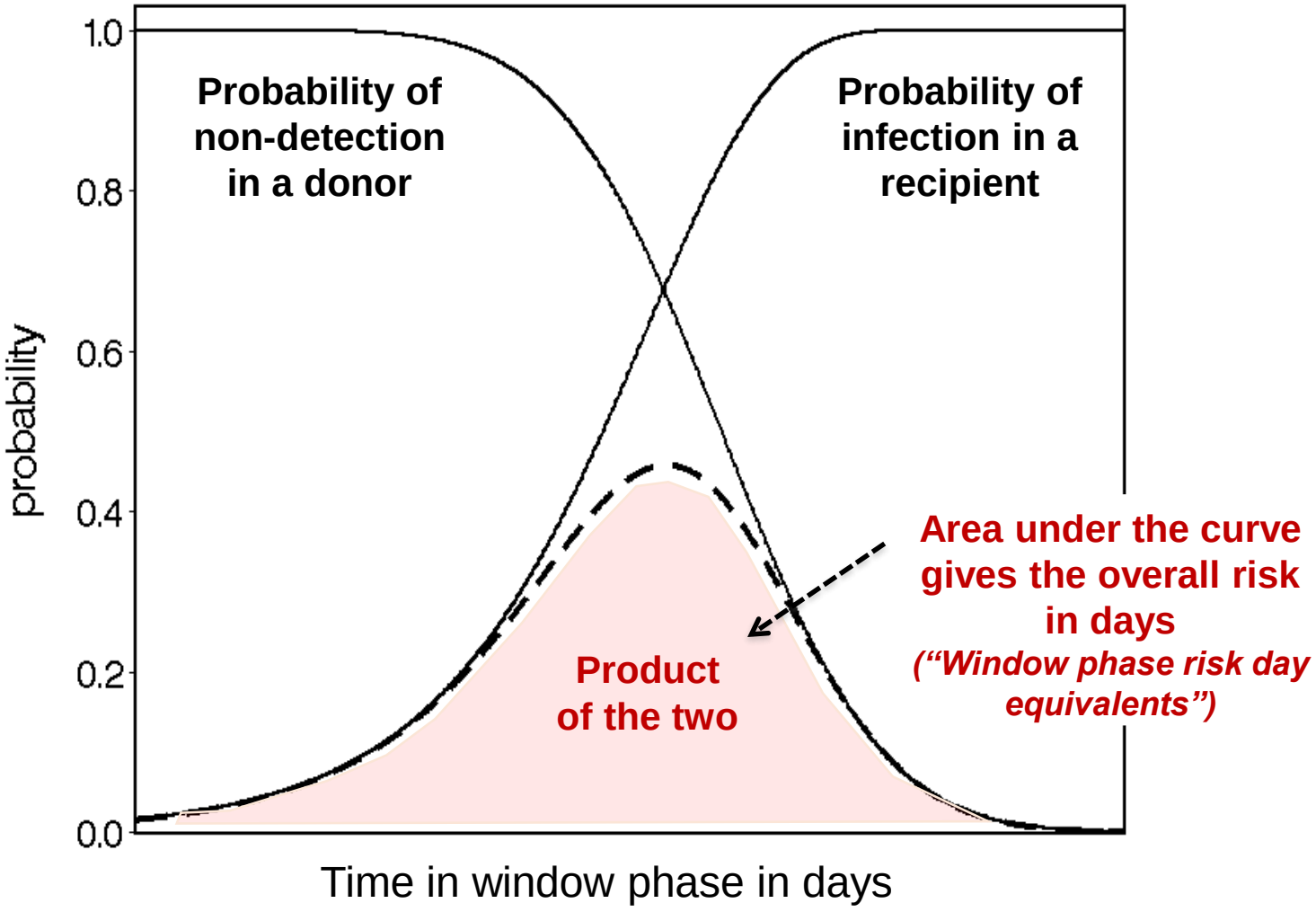
HBV infection rates per million donations in different test systems



WP and OBI rates per million donations in different test systems



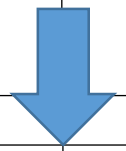
Probability of infectivity during the Window Period



Weusten J et al, Transfusion 2011;51:203-15

LODs in copies/mL used in Weusten WP and OBI risk models

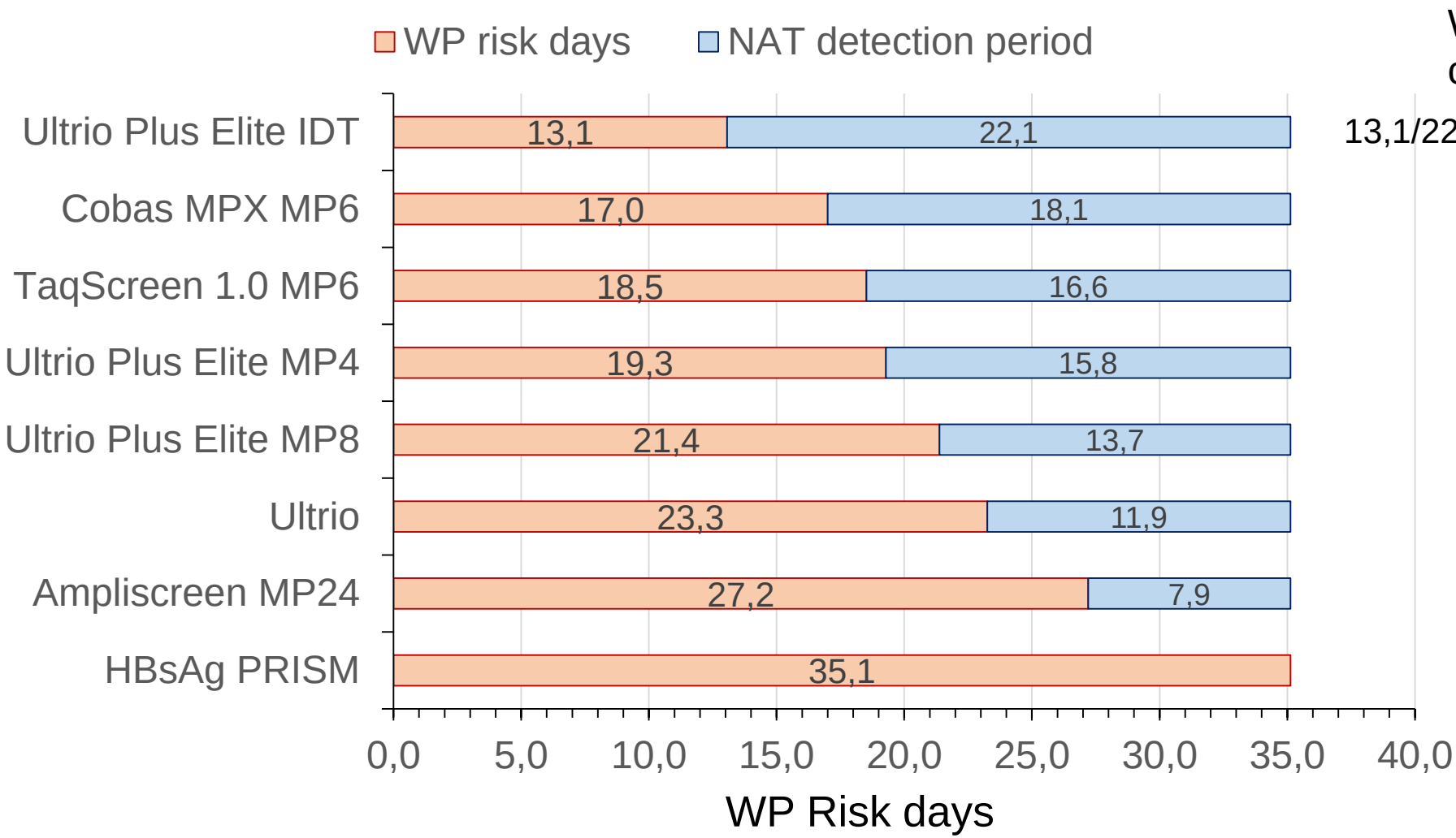
HBV-DNA genotype A standard	panel	NAT method	n	50% LOD (CI) cp/mL	95% LOD (CI) cp/mL
S0011 VQC-Sanquin	PeliCheck	Multiprep Ampliscreen	24	5,9 (3,9-9,3)	72,4 (37,3-211,4)
S0011 VQC-Sanquin	PeliCheck	Ampliprep Ampliscreen	24	8,6 (5,9-12,9)	88,2 (48,7-215,7)
S0011 VQC-Sanquin	PeliCheck	TaqScreen 1.0 cobas s201	12	2,9 (1,6-4,9)	26,9 (13,9-71,0)
S0010 Eurohep	P0001	TaqScreen 1.0 cobas s201	12	2,3 (1,3-3,8)	14,1 (7.2-56.6)
S0011 VQC-Sanquin	P0007	cobas MPX	24	1,9 (1,3-2,7)	13,0 (7,7-29,6)
S0010 Eurohep	P0272	cobas MPX	48	1,7 (1.0-2.4)	10,3 (6,2-28,8)
S0011 VQC-Sanquin	P0007	Ultrio Plus	48	4,8 (3,7-6,2)	38,8 (25,6-68,5)
S0010 Eurohep	P0001	Ultrio Plus	96	3,6 (2,9-4,4)	40,4 (29,2-60,2)
S0011 VQC-Sanquin	P0007	Ultrio Elite	74	3,4 (2,3-4,8)	43,2 (24,8-98,0)
S0010 Eurohep	P0001	Ultrio Elite	24	7,9 (5,5-11,2)	49,1 (29,4-116)



NAT method	n	Geomean 50% LOD	Geomean 95% LOD
Ampliscreen	48	7,1	79,9
TaqScreen MPX1.0	24	2,6	19,5
Cobas MPX	72	1,8	11,1
Ultrio Plus and Elite	216	4,1	41,7

NAT method	50% LOD cp/mL	95% LOD cp/mL	Literature reference
Ultrio	63,0	391,6	Vermeulen et al. Transfusion 2009:59:2922-2930
HBsAg PRISM	1493		Van Drimmelen and Lelie. Viruses 2022, 14,1942

WP NAT yield rate ratio modeling for RBCs# using risk days in Weusten model



WP NAT yield rate conversion factor

13,1/22,1 =	0,592
	0,938
	1,116
	1,217
	1,555
	1,959
	3,432

ID50 3,16 virions or HBV-DNA copies 20 mL plasma/RBC

Weusten et al, Transfusion 2011;51:203-15

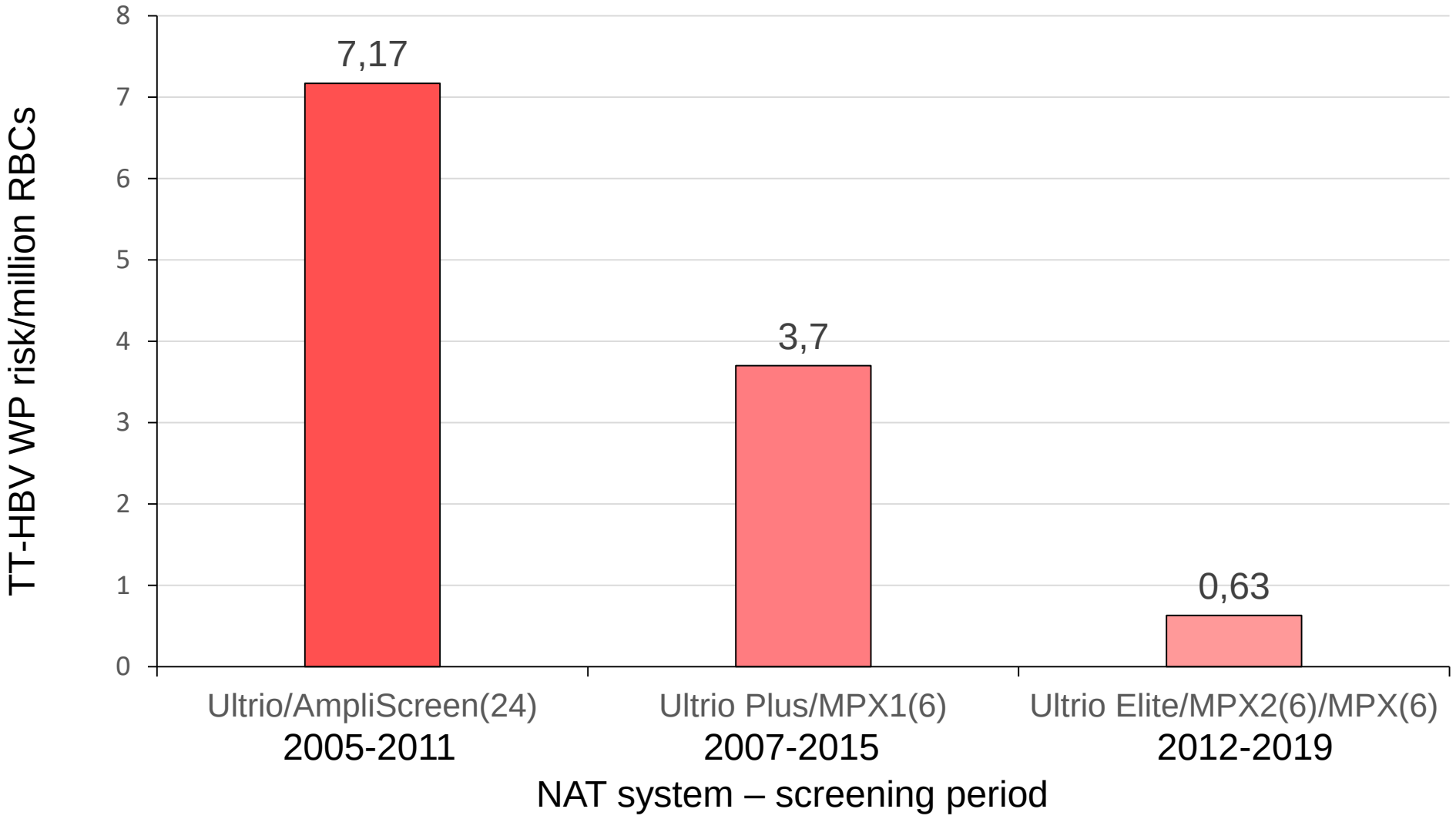
TT-HBV risk per million RBCs calculated with Weusten WP model

All donations - Residual TT-HBV risk per million									
Assay **NAT-Format** **Period**	**Ultrio** **ID** 2005-2011	**Ampliscreen** **MP24** 2005-2007	**cobas** **MPX1** **MP6** 2007-2013	**Ultrio Plus** **ID** 2010-2015	**Ultrio Plus** **MP8** 2013	**cobas** **MPX2/MPX** **MP6** 2012-2019	**Ultrio Elite** **ID** 2013-2019	**Ultrio Elite** **MP4** 2017-2019	**All NAT** **Assays** 2005-2019
All donations	**2.262.854**	**1.426.157**	**3.639.201**	**1.480.734**	**227.429**	**6.012.089**	**2.027.013**	**133.614**	**17.209.091**
WP yield rate	4,42	1,40	3,57	5,40	0,00	0,33	2,47	0,00	2,32
WP RR conversion factor	1,959	3,432	1,116	0,592	0,969^	0,938	0,592	0,874^	
TT-HBV WP risk/milion RBCs	**8,66**	**4,81**	**3,99**	**3,20**	**5,24^**	**0,31**	**1,46**	**2,16^**	**3,02#**

^in the absence of WP-NAT yields in the Ultrio Plus MP8 and Ultrio Elite MP4 screening periods the TT-HBV risk was derived from the Ultrio Plus ID-NAT and Ultrio Elite ID-NAT screening periods respectively

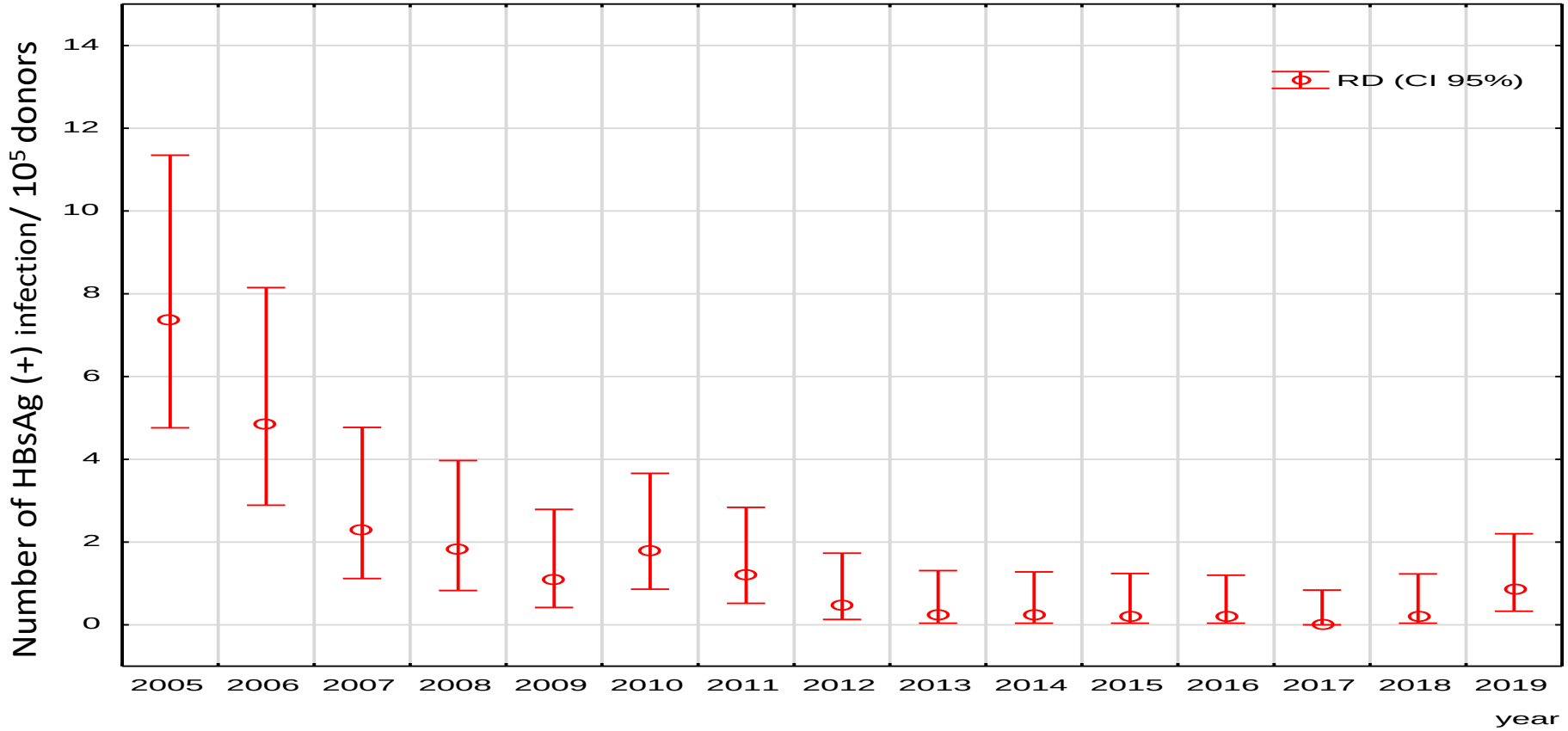
#calculated after correction for numbers of donations in screening periods

TT-HBV risk per million RBCs in 3 screening periods calculated with Weusten WP model



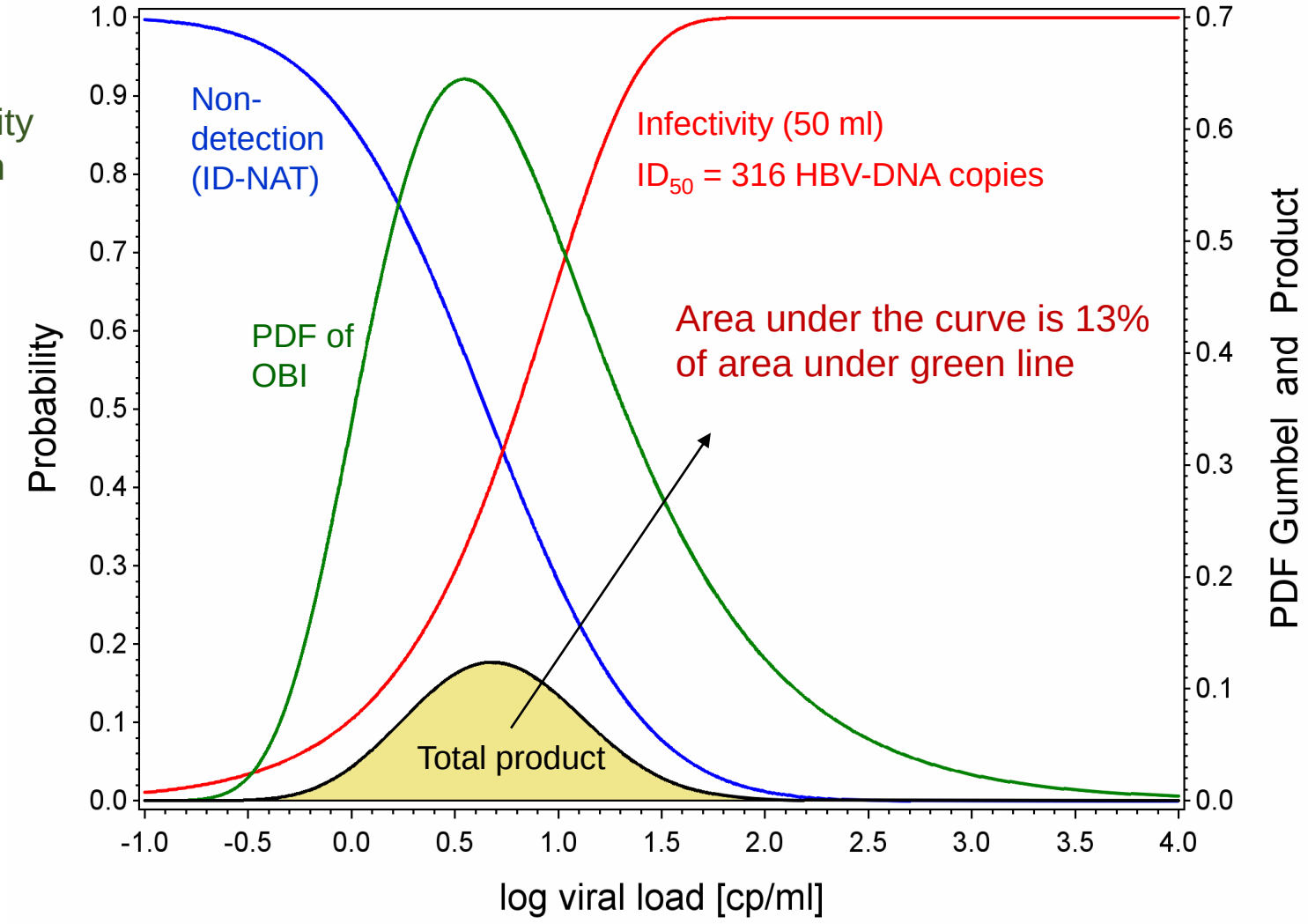
TT-HBV risk per million RBCs from Weusten WP model in 3 screening periods vs frequency of HBsAg(+) in RDs

TT-HBV risk/mln RBCs NAT methods 95% LOD period	**7,17** Ultrio/Ampliscreen (MP24) **10,5 -106 IU/ml** 2005-2011	**3,7** Ultrio Plus/MPX1 (MP6) **4,6 -22,8 IU/ml** 2007-2015	**0,63** Ultrio Elite/MPX2(MP6)/MPX(MP6) **4,3-8,4 IU/ml** 2012-2019



TT-HBV risk calculation for OBI donations

PDF = probability density function



PDF Gumbel is based on VL distribution in large amount of OBI donations in South Africa and includes donations with VL below the NAT detection limit

Weusten et al, Transfusion 2017;57;841–849

TT-HBV risk per million RBCs calculated with Weusten OBI model

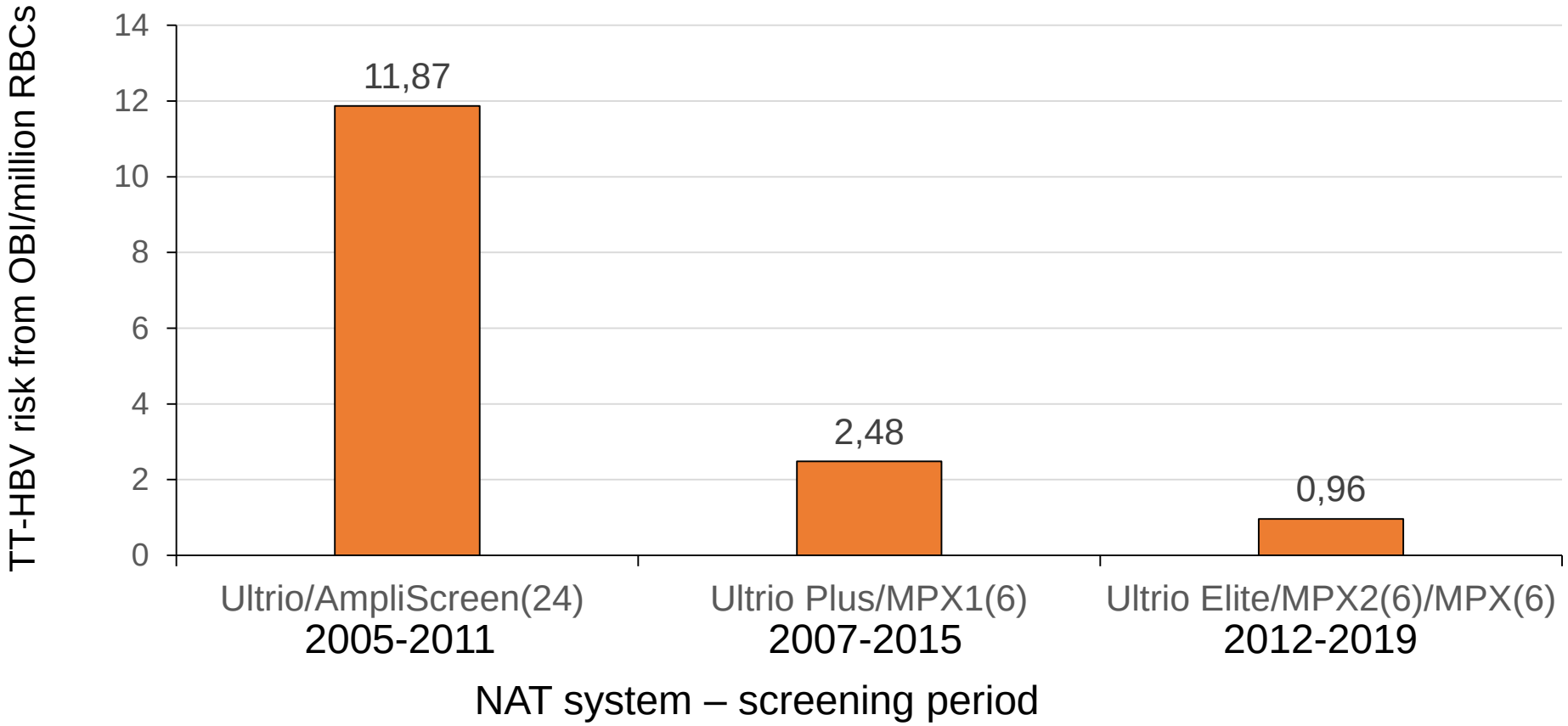
All donations - Residual TT-HBV risk per million									
Assay **NAT-Format** **Period**	**Ultrio** **ID** 2005-2011	**Ampliscreen** **MP24** 2005-2007	**cobas** **MPX1** **MP6** 2007-2013	**Ultrio Plus** **ID** 2010-2015	**Ultrio Plus** **MP8** 2013	**cobas** **MPX2/MPX** **MP6** 2012-2019	**Ultrio Elite** **ID** 2013-2019	**Ultrio Elite** **MP4** 2017-2019	**All NAT** **Assays** 2005-2019
All donations	**2.262.854**	**1.426.157**	**3.639.201**	**1.480.734**	**227.429**	**6.012.089**	**2.027.013**	**133.614**	**17.209.091**
OBI + 2nd WP yield rate	18,12	3,51	14,84	6,75	8,79	6,99	12,33	7,48	10,46
OBI TT-HBV risk percentage^	**84%**	**170%**	**22%**	**5,3%**	**43%**	**15%**	**5,3%**	**24%**	
TT-HBV OBI risk/milion RBCs	**15,22**	**5,96**	**3,26**	**0,36**	**3,78**	**1,05**	**0,65**	**1,80**	**3,72#**

^TT-HBV risk conversion percentages in this table were adjusted from [PDF Gumbel = 100%] to [OBI NAT yield rate = 100%]

ID_{50}= 316 virions
RBC 20 mL plasma
Infecivity of 50% of OBI donations assumed to be completely neutralized by anti-HBs

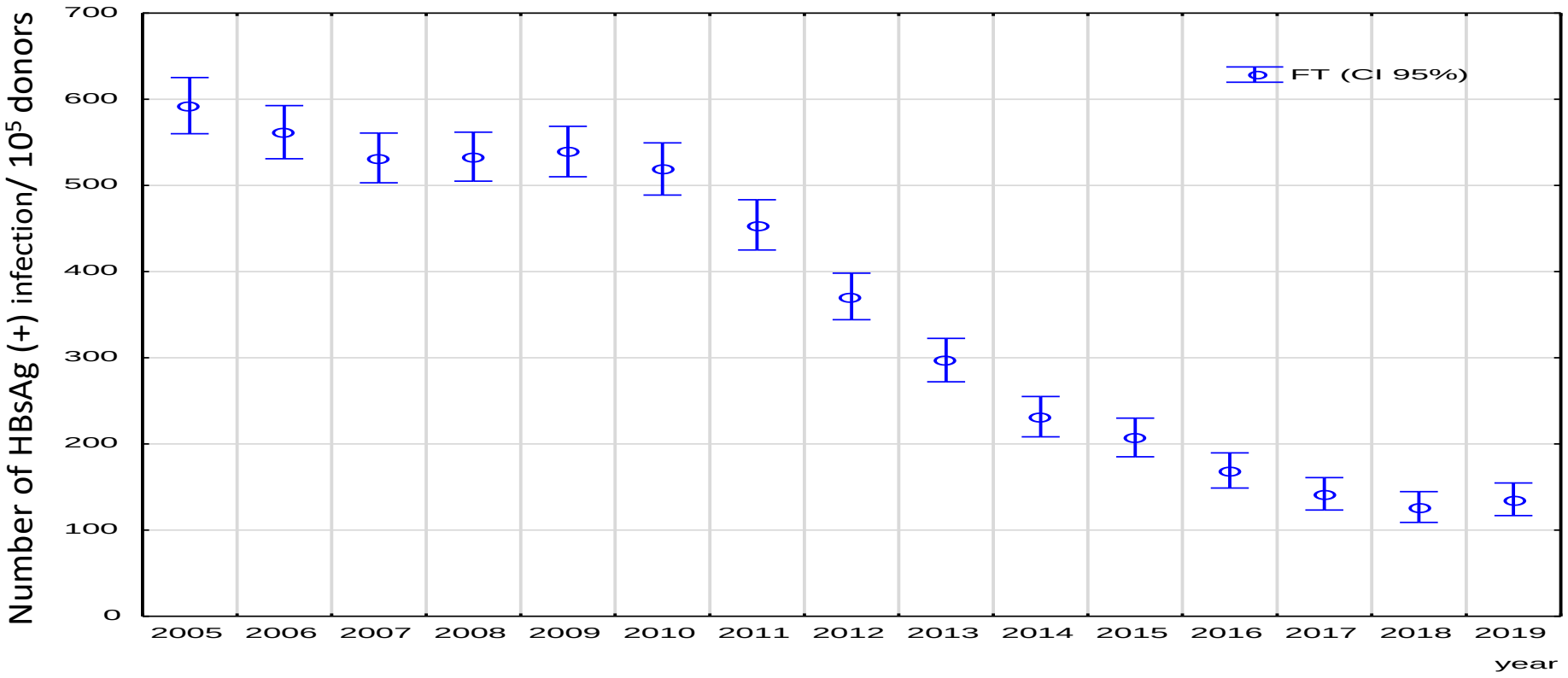
Weusten et al, Transfusion 2017;57;841–849

TT-HBV risk per million RBCs in 3 screening periods calculated with Weusten OBI model

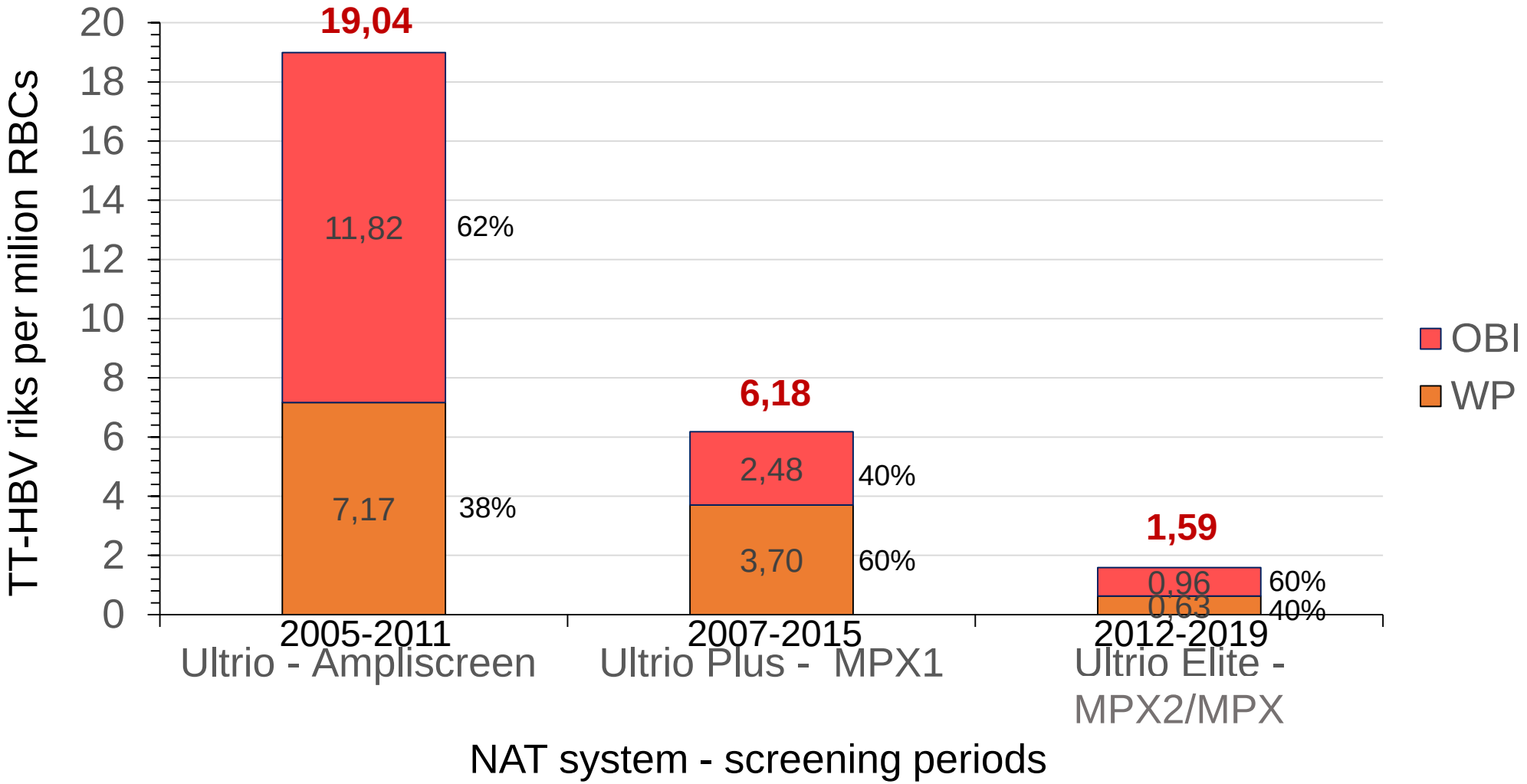


TT-HBV risk per million RBCs from Weusten OBI model in 3 screening periods vs HBsAg(+) in FTD

TT-HBV risk/mln RBCs NAT methods 95% LOD period	**7,17** Ultrio/Ampliscreen (MP24) **7,5 -106 IU/ml** 2005-2011	**3,7** Ultrio Plus/MPX1 (MP6) **4,6 -22,8 IU/ml** 2007-2015	**0,63** Ultrio Elite/MPX2(MP6)/MPX(MP6) **4,3-8,4 IU/ml** 2012-2019



TT-HBV risk per million RBCs in different screening periods calculated with Weusten WP and OBI models



Limitations TT-HBV risk modelling

- Differences in HBsAg seroconversion points for different assays ignored.
- Acute occult HBV WP infections ignored (estimated <5-10%).
- Not all WP NAT yields confirmed by HBV marker conversion in follow up.
- Of donors with OBI and in 2nd WP 59% had anti-HBs <10 mIU/mL, and 50% neutralization of infectivity was assumed.
- Number of donations and NAT yields was too low in MP4 and MP8 Ultrio Plus/Elite screening periods and therefore risk was converted from ID-NAT screening data.
- Number of WP NAT yields in Ampliscreen MP24 and cobas MPX screening periods were in fact too low (n=2) for ratio modelling.
- Weusten WP risk modeling using HBsAg and HBV-DNA seroconversion rate in repeat donors (and incidence rate adjustment factors for transient viremia) has so far not been performed.
- Recipient immunity or anti-HBs neutralization in cotransfusions ignored.

Conclusions

- TT-HBV risk in the screening period of the currently used NAT systems (2012-2019) has reduced >10-fold as compared to the time when the first less sensitive NAT systems were used (2005-2011)
- Risk reduction is caused by enhanced sensitivity of newer NAT assay versions and improving epidemiology of HBV in Poland
- Current residual TT-HBV risk is estimated at 1,6 per million
- Introduction of anti-HBc testing would reduce theoretical risk by 1 per million
- No TT-HBV transmission cases reported