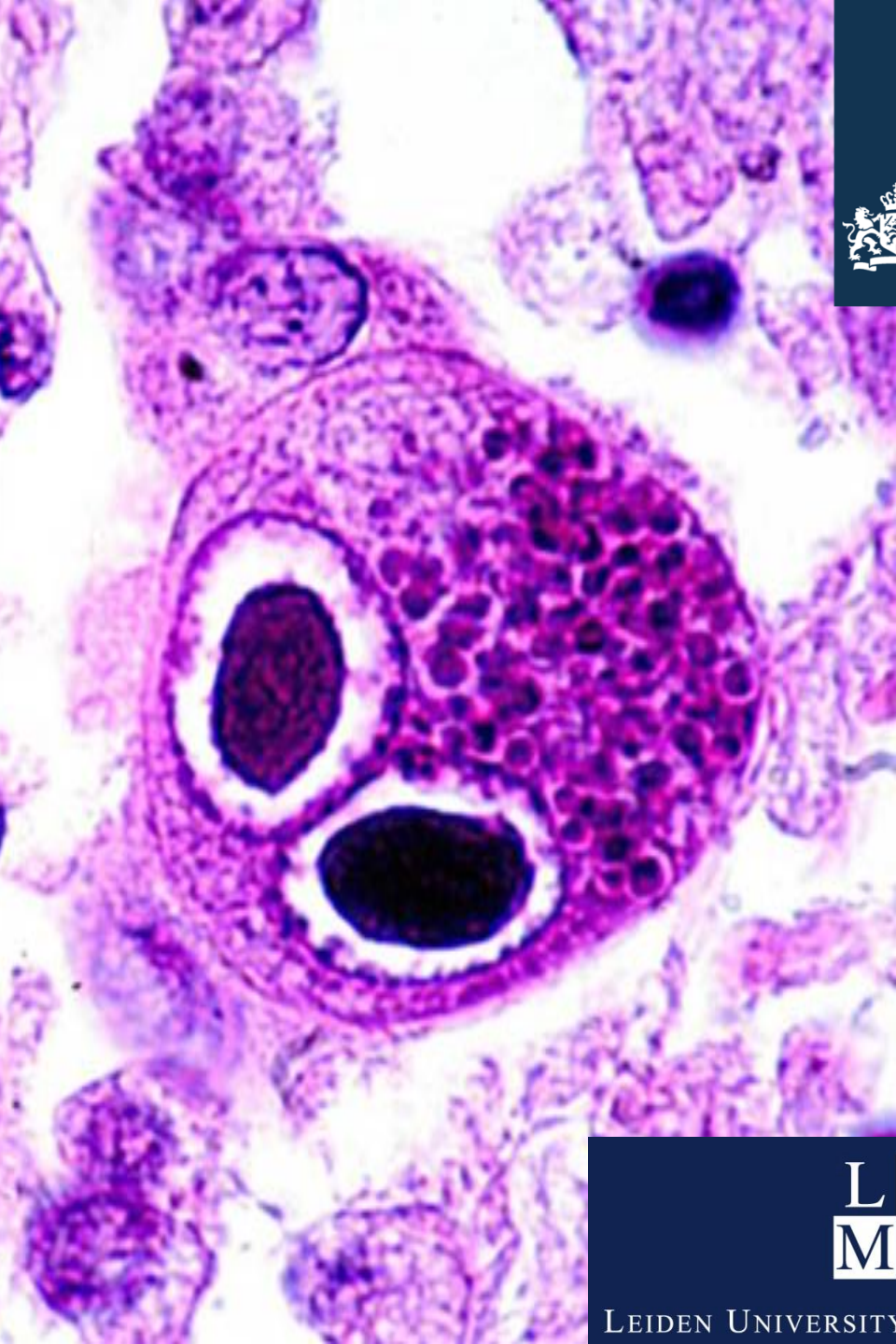




National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

CMV-infections in the Netherlands - Seroprevalence, risk factors and implications

Marjolein Korndewal

September 26th 2014

CMV Public Health &
Policy Conference



LEIDEN UNIVERSITY MEDICAL CENTER

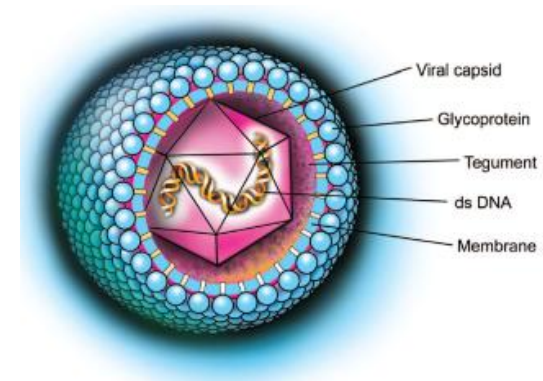


Introduction

Cytomegalovirus (CMV)

- Beta-Herpes Virus
 - Primary infection → Latency
 - Recurrent infection
- Clinical symptoms
 - Healthy individuals
 - Immunocompromised
- Transmission

Saliva, urine, sexual contact, placenta, blood, organ transplant





PIENTER 2-study



- Population-based, serum bank (2006-2007)
 - › National sample and Oversampling of migrant
 - › Individuals: 0-79 year
 - › Invited: N = 19.781 (response rate: 32%)
- Serum test: CMV-specific IgG antibodies using ELISA
(ETI-CYTOK-G PLUS DiaSorin, Saluggia, Italy)
- Questionnaire: general, vaccination, health and disease,
occupation and activities, sexual contact



Risk factors

- Age
- Gender
- Educational level
- Origin
 - › Western: Europe, North America, Oceania, Japan
 - › Non-Western: Africa, South America, Asia, Turkey
- Migrants
 - › First generation: born abroad
 - › Second generation: parent born abroad
- Number in household
- Child in household (< 4 years)
- Number of contacts – outside household
- Contact with child (< 4 years) – outside household



Analysis

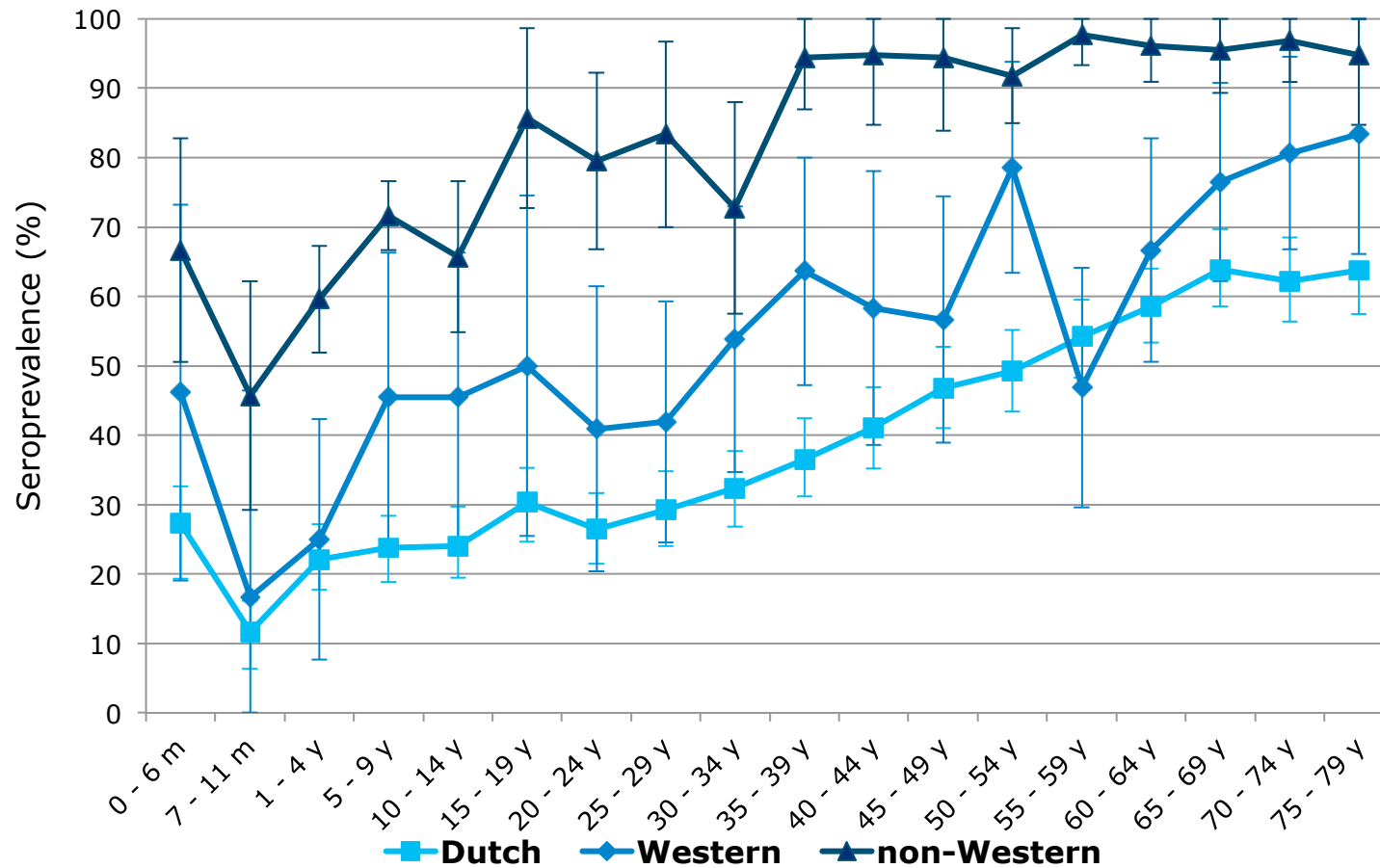
- Children < 6 months: excluded
- Stratified analysis: Dutch/Western and non-Western
- Seroprevalence
 - Risk factors for seropositivity
- Geometric Mean Concentration – **seropositive only**
 - Risk factors for high antibody concentration
- Subgroup analysis
 - Women of reproductive age (20-45 years)



Seroprevalence and Risk factors

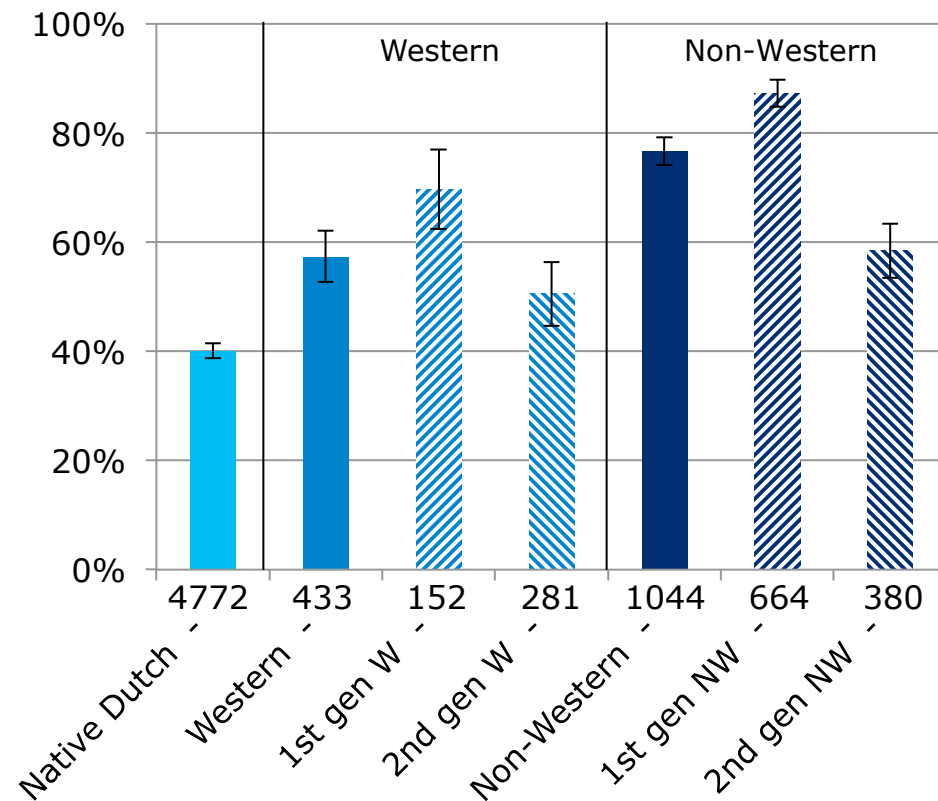


Seroprevalence





Seroprevalence – Geographic origin





Risk factors for seropositivity – Dutch / Western

Characteristics	Number	Seroprev. %	Multivariable OR 95% CI
Age			
6 m-9 y	830	21.8	1 (ref)
10-19 y	629	28.0	1.28 0.96 - 1.69
20-29 y	643	28.9	1.52* 1.16 - 1.99
30-39 y	646	36.8	2.09* 1.64 - 2.66
40-49 y	603	45.3	3.04* 2.33 - 3.95
50-59 y	609	52.7	4.04* 3.06 - 5.32
60-69 y	703	62.2	5.88* 4.40 - 7.85
70-79 y	542	64.6	6.59* 4.83 - 8.97
Gender			
male	2348	38.7	1 (ref)
female	2857	43.9	1.26* 1.12 - 1.42
Education	<i>57 missing</i>		
high	2113	36.2	1 (ref)
middle	2646	42.9	1.17* 1.04 - 1.33
low	389	59.9	1.85* 1.44 - 2.38



Risk factors for seropositivity – **non-Western**

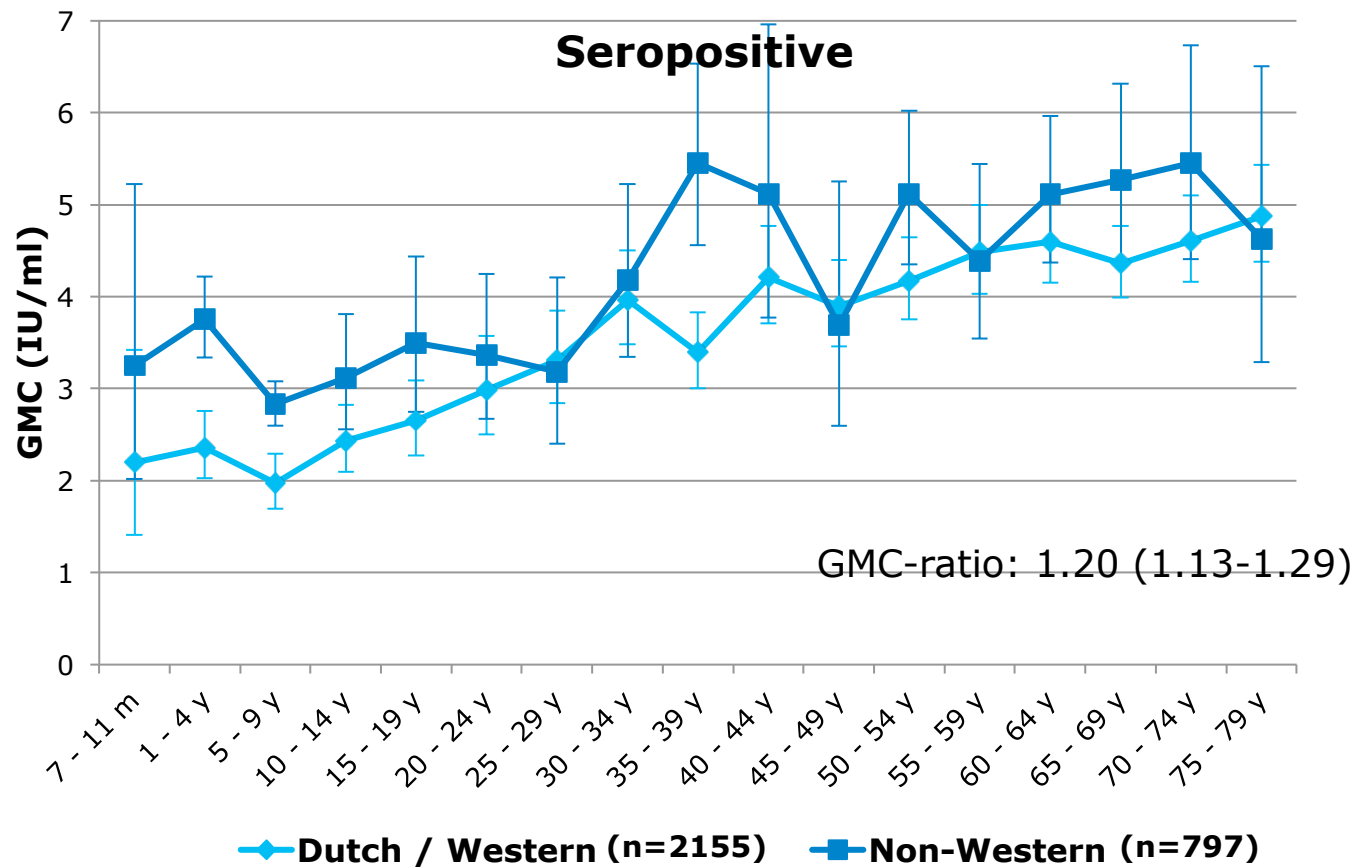
Characteristics	Number	Seroprev. %	Multivariable OR 95% CI
Age			
6 m-9 y	516	65.9	1 (ref)
10-19 y	101	71.3	1.62 0.95 - 2.76
20-29 y	69	81.2	3.66* 1.79 - 7.48
30-39 y	69	84.1	2.85* 1.36 - 5.99
40-49 y	37	94.6	8.18* 1.86 - 36.0
50-59 y	105	94.3	6.19* 2.49 - 15.4
60-69 y	96	95.8	8.62* 2.78 - 26.8
70-79 y	51	96.1	11.4* 2.39 - 54.4
Gender			
male	489	77.5	1 (ref)
female	555	76.0	0.83 0.60 - 1.15
Education	<i>58 missing</i>		
high	229	62.9	1 (ref)
middle	425	76.0	2.59* 1.73 - 3.87
low	332	85.8	3.92* 2.45 - 6.27



Geometric Mean Concentration and Risk factors

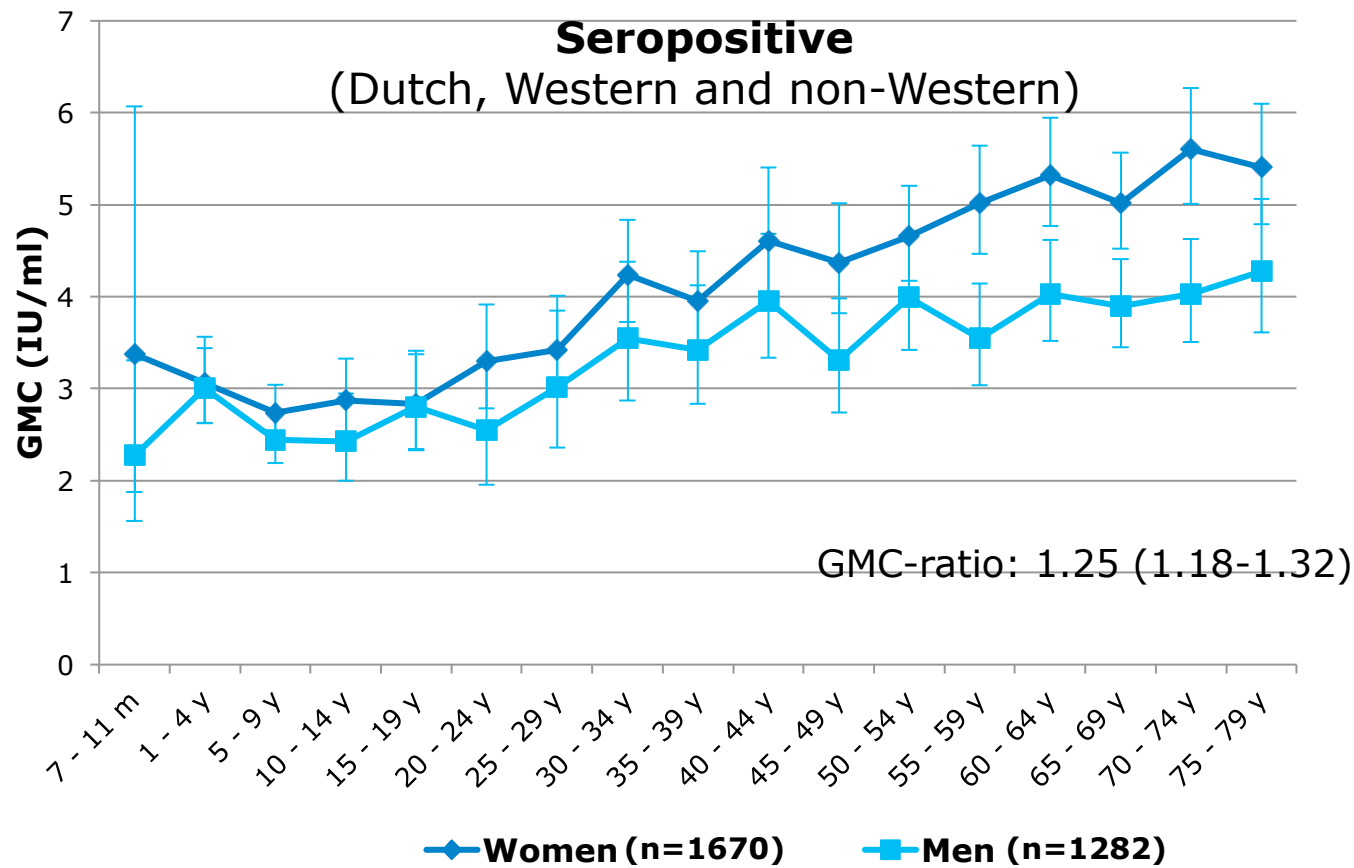


Geometric Mean Concentration - Origin





Geometric Mean Concentration - Gender





Risk factors for high GMC – Dutch / Western

Characteristics	Number	GMC (IU/ml)	Multivariable GMC-ratio	95% CI
Age				
6 m-9 y	174	2,17	1 (ref)	
10-19 y	176	2,54	1,34*	1,12 - 1,62
20-29 y	186	3,15	1,63*	1,36 - 1,94
30-39 y	238	3,63	1,79*	1,53 - 2,09
40-49 y	273	4,03	2,16*	1,83 - 2,55
50-59 y	321	4,33	2,28*	1,93 - 2,71
60-69 y	437	4,48	2,53*	2,13 - 3,01
70-79 y	350	4,72	2,76*	2,30 - 3,31
Gender				
male	906	3,29	1 (ref)	
female	1249	4,19	1,28*	1,20 - 1,37
Education				
high	761	3,49	1 (ref)	
middle	1132	3,92	1,06	0,98 - 1,14
low	233	4,23	1,04	0,92 - 1,18



Risk factors for high GMC – non-Western

Characteristics	Number	GMC IU/ml	Multivariable GMC-ratio 95% CI	
Age				
6 m-9 y	336	3,08	1 (ref)	
10-19 y	72	3,24	1,12	0,92 - 1,35
20-29 y	56	3,28	1,11	0,90 - 1,37
30-39 y	58	4,89	1,60*	1,31 - 1,96
40-49 y	35	4,37	1,70*	1,32 - 2,19
50-59 y	99	4,79	1,73*	1,45 - 2,06
60-69 y	92	5,18	1,82*	1,50 - 2,22
70-79 y	49	5,13	1,79*	1,39 - 2,30
Gender				
male	376	3,51	1 (ref)	
female	421	4,03	1,14*	1,03 - 1,26
Education				
high	142	3,59	1,00	
middle	323	3,63	1,03	0,89 - 1,18
low	284	4,11	1,15*	1,00 - 1,34



Conclusion



Conclusion

- Risk factors for seropositivity
 - Origin (generation)
 - Age
 - Gender (Dutch/W)
 - Educational level
 - Contact with child (Dutch/W)
- Risk factor for high GMC
 - Origin
 - Age
 - Gender
 - Educational level (NW)
 - Child in household (Dutch/W)

NW > Dutch/W (1st > 2nd)

elderly > young

women > men

low > high

yes > no

NW > Dutch/W

elderly > young

women > men

low > high

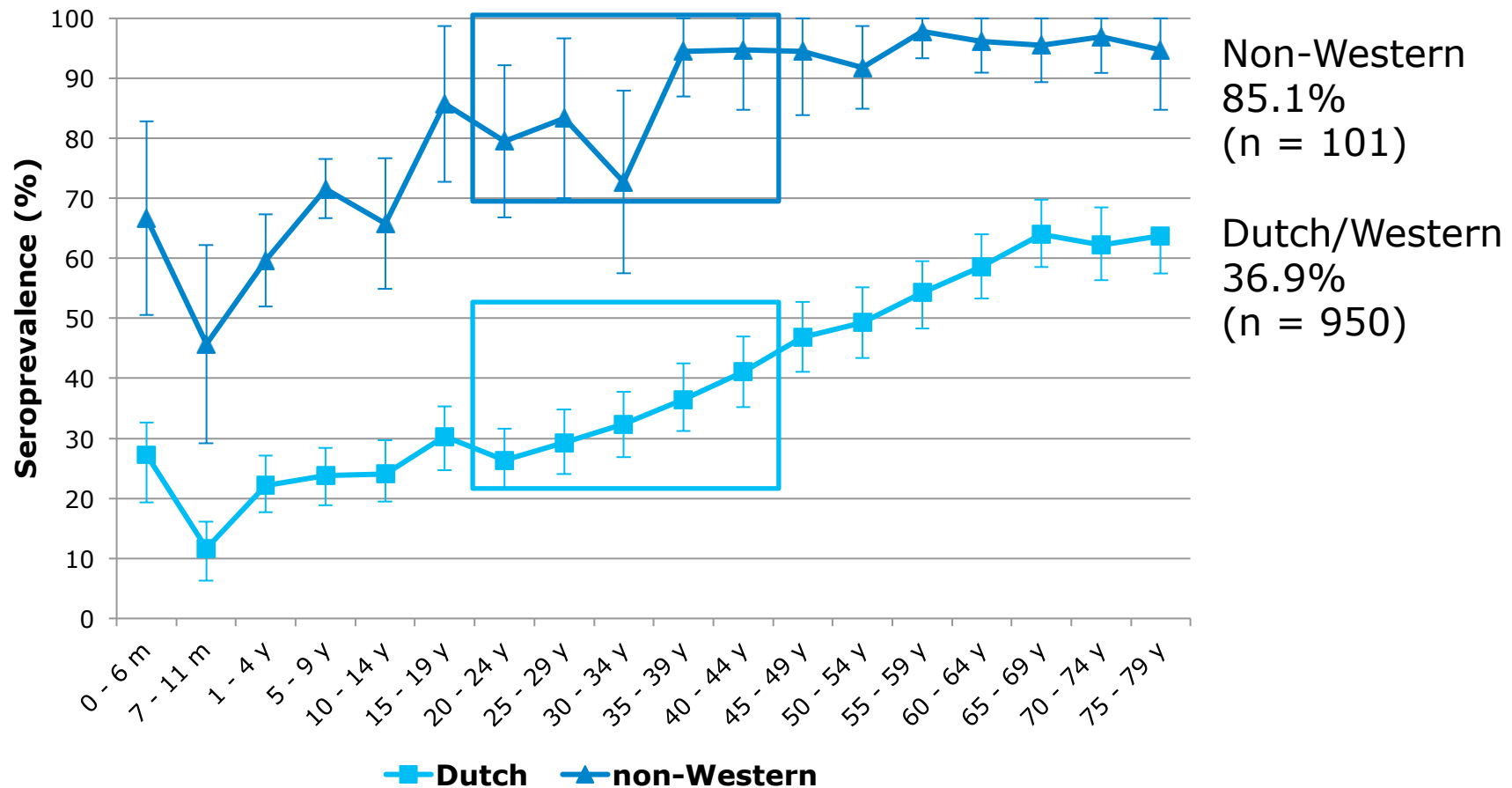
yes > no



Women of reproductive age



Women of reproductive age





Implications

- Women of reproductive age
 - Dutch / Western: 36.9% seropositive
 - Non-Western: 85.1% seropositive
- Risk of congenital CMV infection
 - Primary maternal infection
 - Recurrent maternal infection
- Prevention
 - Vaccination: not yet
 - Hygienic measures!





Acknowledgement



Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*



LEIDS UNIVERSITAIR MEDISCH CENTRUM

- Epidemiology & Surveillance
 - › Hester de Melker
 - › Liesbeth Mollema
 - › Marianne van der Sande
- Centre for Infectious diseases, Diagnostics and Screening
 - › Fiona van der Klis
 - › Irina Tcherniaeva
- Medical microbiology
 - › Ann Vossen
 - › Louis Kroes
- Willem-Alexander Children's Hospital
 - › Anne Marie Oudesluys



Questions







Risk factors for seropositivity – Women (20-45 yr)

Characteristics	Number	Seroprev. %	Multivariable OR	95%CI
Age				
20 - 24 y	202	32,7	1 (ref)	
25 - 29 y	200	32,0	1,04	0,65 - 1,66
30 - 34 y	187	36,4	1,12	0,69 - 1,81
35 - 39 y	194	42,8	1,41	0,92 - 2,17
40 - 44 y	167	41,9	1,43	0,93 - 2,21
Education				
High	491	34,4	1 (ref)	
Middle	448	39,1	1,23	0,93 - 1,63
Low	7	57,1	1,54	0,29 - 8,19
Number in household				
1 or 2 persons	353	30,9	1 (ref)	
3 or 4 persons	457	41,1	1,40	0,98 - 2,01
>4 persons	134	38,8	1,29	0,80 - 2,07



Seroprevalence of CMV-infection

- Overall:
 - Women of reproductive age: 45-100%
- Geographic:
 - South America, Africa and Asia: highest CMV seroprevalence
 - Western Europe and USA: lowest CMV seroprevalence
- Ethnicity:
 - Non-white > white: 20–30% (PR: 1.59 [1.57–1.61])
- Gender:
 - Females > males (PR: 1.13 [1.11–1.14])
- Socio economic status:
 - Low SES > high SES (PR: 1.33 [1.32–1.35])

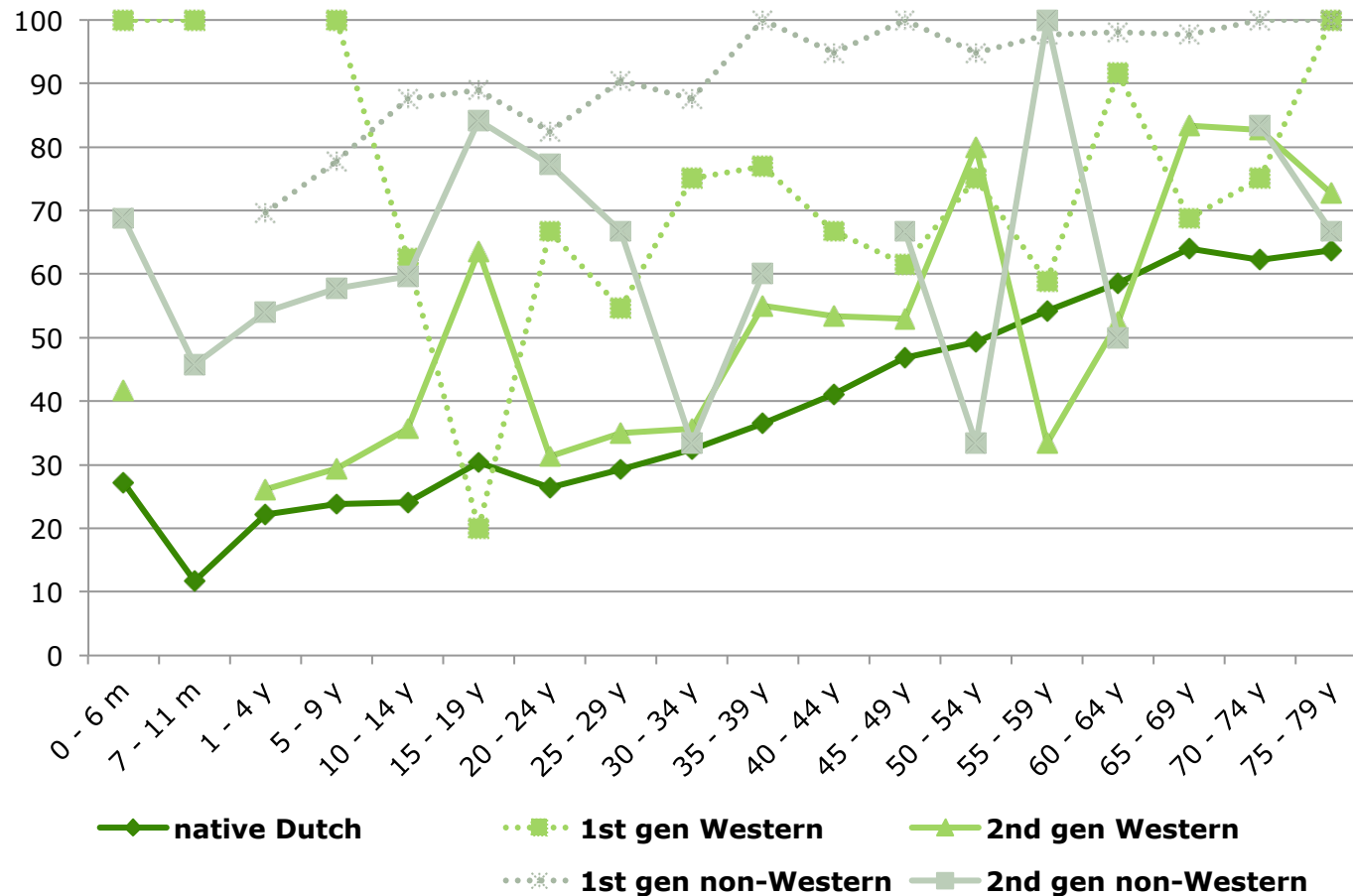


Seroprevalence CMV-infection

- Medline database: English articles (1966-2008)
- Inclusion: 'CMV' or 'cytomegalovirus' AND 'seroprevalence', 'prevalence', 'IgG' or 'antibody'
- Exclusion: < 40 participants, non-human, HIV-, transplantation- or hemodialysis patients
- 112 studies included
 - Categories: age, ethnicity, gender, SES or other
 - Variability of definitions (e.g. SES) → study definitions
 - Persons from very variable risk groups: Child day care / health care personnel or STD-clinics
 - Compare different geographical areas: Women of reproductive age (without other risk factors)

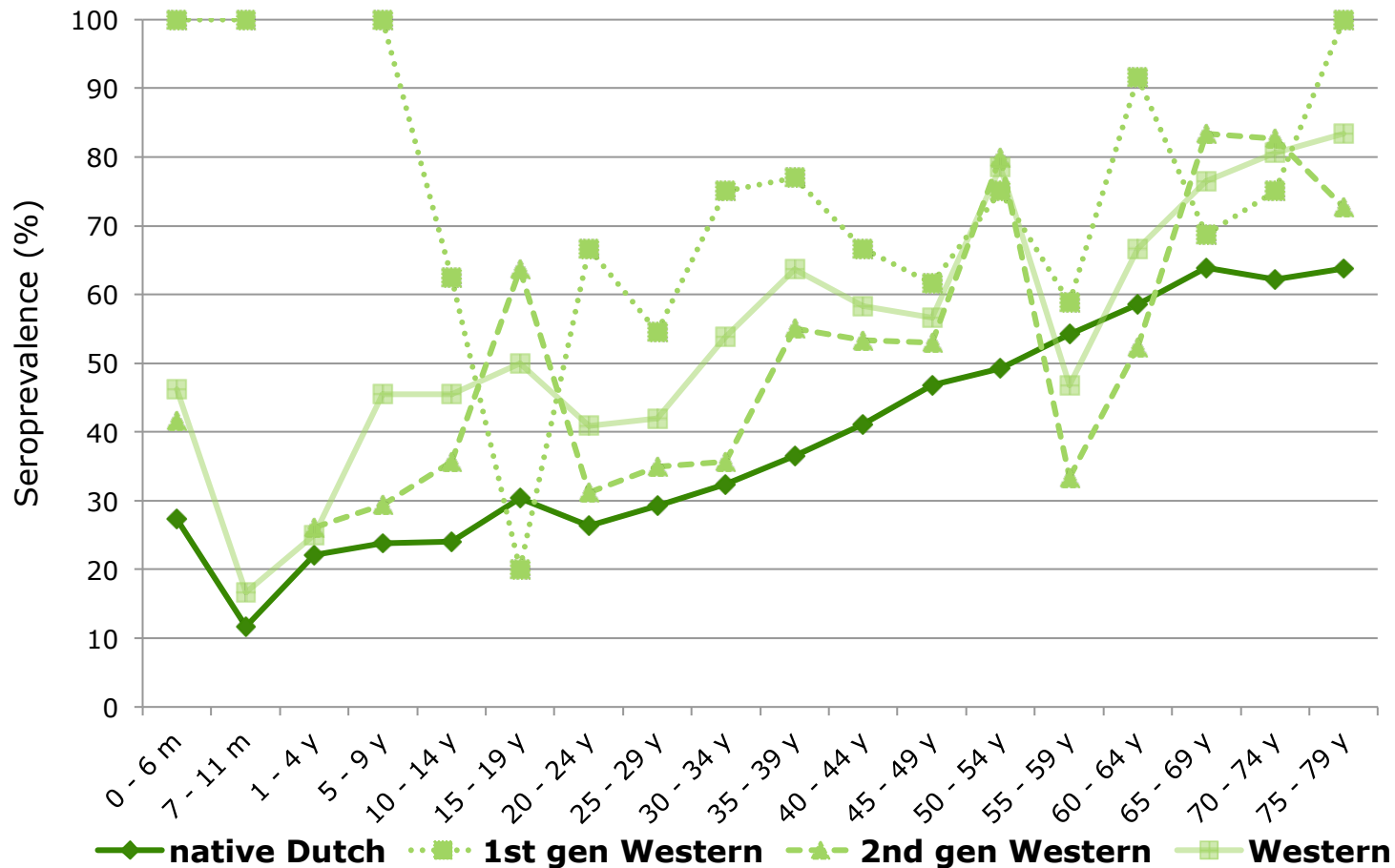


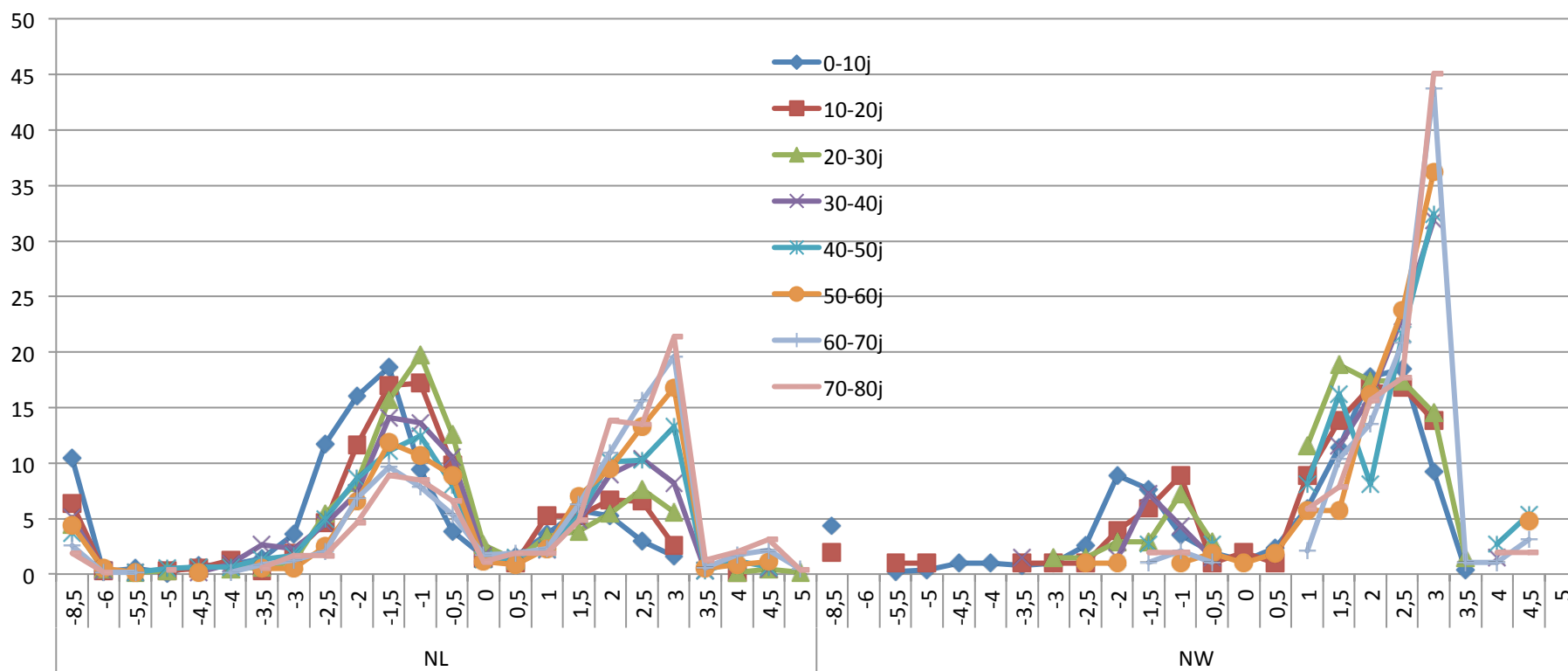
Seroprevalence





Seroprevalence





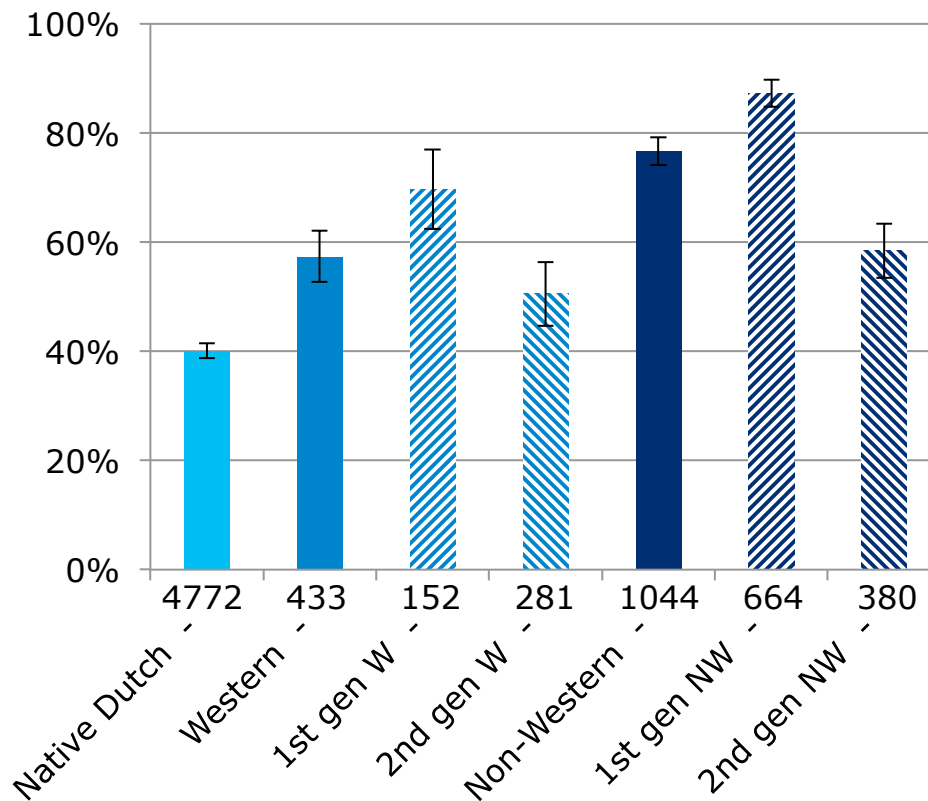


Seroprevalence – Geographic origin

Geographic origin	Number	Seroprevalence	
		%	95% CI
Overall	6249	45.6	41.9 - 49.3
Native Dutch	4772	40.1	38.7 - 41.5
Western	433	57.3	52.6 - 61.9
1 st generation	152	69.7	62.4 - 77.0
2 nd generation	281	50.5	44.7 - 56.4
Non-Western	1044	76.7	74.2 - 79.3
1 st generation	664	87.2	84.7 - 89.7
2 nd generation	380	58.4	53.5 - 63.4
Non-Western			
Morocco / Turkey	338	84.0	80.1 - 87.9
Surinam / Aruba	351	69.5	64.7 - 74.3
Other countries	355	76.9	72.5 - 81.3



Seroprevalence – Geographic origin

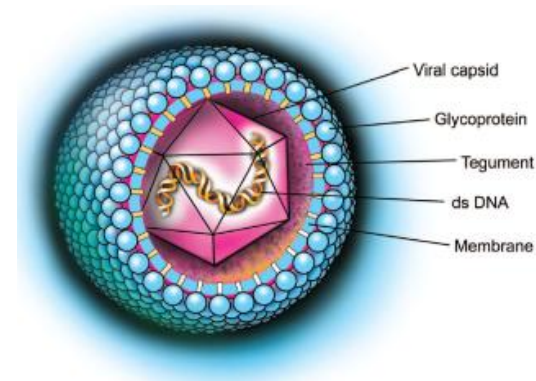


Geographic origin	Seroprevalence	
	%	(95% CI)
Overall	45.6	(41.9 - 49.3)
Native Dutch	40.1	(38.7 - 41.5)
Western	57.3	(52.6 - 61.9)
1 st generation	69.7	(62.4 - 77.0)
2 nd generation	50.5	(44.7 - 56.4)
Non-Western	76.7	(74.2 - 79.3)
1 st generation	87.2	(84.7 - 89.7)
2 nd generation	58.4	(53.5 - 63.4)

Cytomegalovirus (CMV)

- Human Cytomegalovirus
 - Beta-Herpes Virus (HHV 5)
- Infection
 - Primary infection → Latency
 - Recurrent infection:
Reactivation or Reinfection
- Transmission

Saliva, urine, sexual contact,
placenta, blood, organ transplant





Cytomegalovirus

- Clinical symptoms
 - Healthy individuals
 - › Asymptomatic, Pfeiffer-like symptoms
 - Immunocompromised
 - › Pneumonia, hepatitis, colitis, retinitis, encephalitis
 - Congenital CMV infection
 - › At birth: jaundice, hepatosplenomegaly, seizures, microcephaly, “blue berry muffin”
 - › Long term: development delay, hearing loss

