



UNIVERSITAT DE
BARCELONA



Generalitat de Catalunya
Agència de Salut Pública de Catalunya



Agència
de Gestió d'Ajuts
Universitaris
i de Recerca

“Outbreaks of norovirus gastroenteritis: An emergent health issue”

SCIENTIFIC SESSION

Monday, 23 November 2015

Norovirus outbreaks: A growing public health problem

NV as an increasing cause of AGE in Catalonia

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Acute Gastroenteritis (AGE):

The most common clinical presentation of food and waterborne infections

A major health problem worldwide *

In developing countries

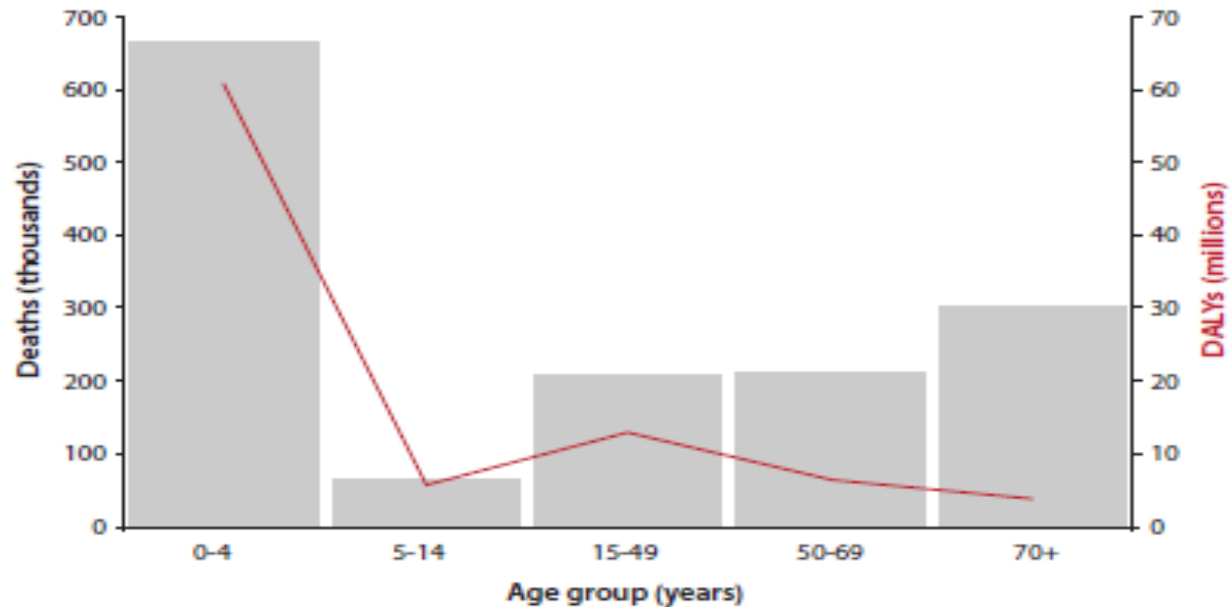
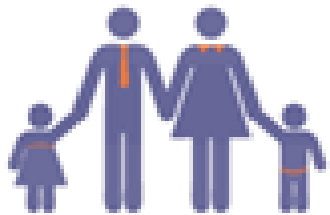
Leading cause of morbidity & mortality in children < 5 yrs

In developed countries

10% of hospitalizations in children aged < 5 yrs

Severe disease (hospitalization/death) in > 60yrs *

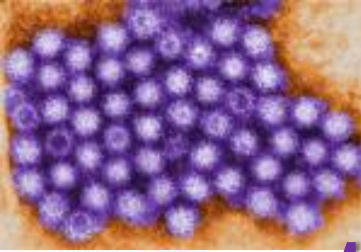
Figure 1.
Global Deaths and
DALYs from diarrheal
disease, 2010



- ☐ Considerable use health services and significant economic costs
- ☐ Viral AGE outbreaks show significant increase in last decade
- ☐ Viral etiology in 80% of AGE but important under detection

Overview on NV

- ☐ What is Norovirus? **(Stomach flu; winter vomiting; Norwalk virus)**
- ☐ Transmission
- ☐ Symptoms
- ☐ Treatment
- ☐ Prevention



Norovirus

the *perfect human pathogen*

- Able to survive freezing and high temperatures
- Able to survive in environmental surfaces up to 7 days or more



Rönnqvist, M., et al., Swabs as a tool for monitoring the presence of norovirus on environmental surfaces in the food industry, Journal of Food Protection, 2013, 76:8, 1421–8

Rönnqvist, M. et al. Norovirus transmission between hands, gloves, utensils, and fresh produce during simulated food handling. Applied and Environmental Microbiology, 2014, 80:17, 5403-5410

How contagious is norovirus?



Just a **very small amount** - as few as 18 viral particles - of norovirus on your food or your hands can make you sick.

In fact, the amount of virus particles that fit on the head of a pin would be enough to infect **more than 1,000 people!**

Highly contagious



1gr feces / 5 billion virus

Rapid evolution



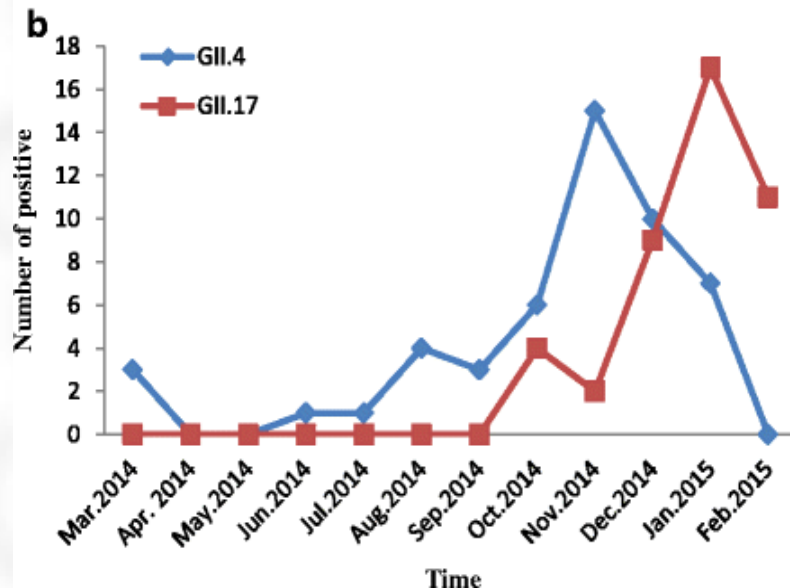
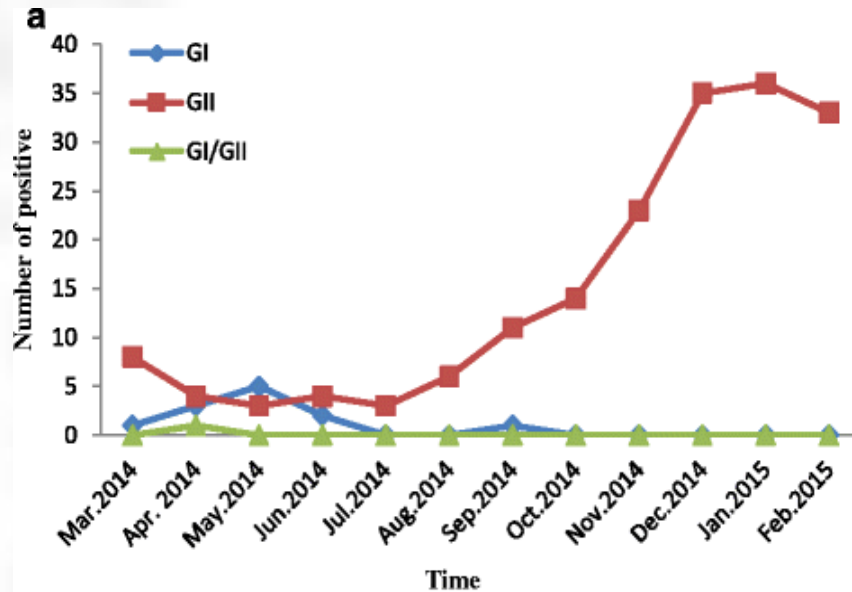
Adaptative changes



Limited host Immunity



Reinfection



Emergence and predominance of norovirus GII.17 in Huzhou, China, 2014–2015

Jiakang Han, Lei Ji, Yuehua Shen, Xiaofang Wu, Deshun Xu and Liping Chen*

Transmission



(DoD photo by Tech. Sgt. Jeremy Lock, U.S. Air Force/Released)

□ Fecal-oral route ; airborne

- Shedding of virus in stool up to 3 weeks after onset of illness
- Secondary cases (person-person transmission) high attack rate in nursing homes *

□ Indirect contact with the virus on

- Feces
 - Vomits
- } contaminated surfaces

Transmission

□ Via contaminated food and water

- Shellfish
 - Produce
 - Berries
- } sewage contaminated water

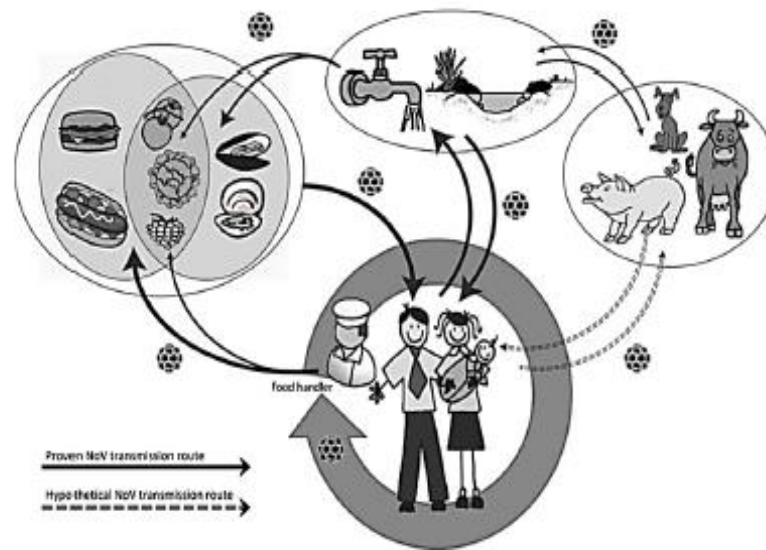


Fig 4. Overview of the proven and hypothetical transmission routes of HuNoVs, as presented by Mathijis and colleagues (16). The thickest arrows present the most common transmission routes for HuNoV, while the thin arrows indicate less frequent transmission routes. Dashed lines represent hypothetical transmission routes for HuNoV. NoV=HuNoV



Symptoms

Symptoms usually **start** within 12 to 48h

- ☐ Vomiting
- ☐ Watery diarrhea
- ☐ Stomach cramping.
- ☐ Low grade fever ($\pm$ 50%)



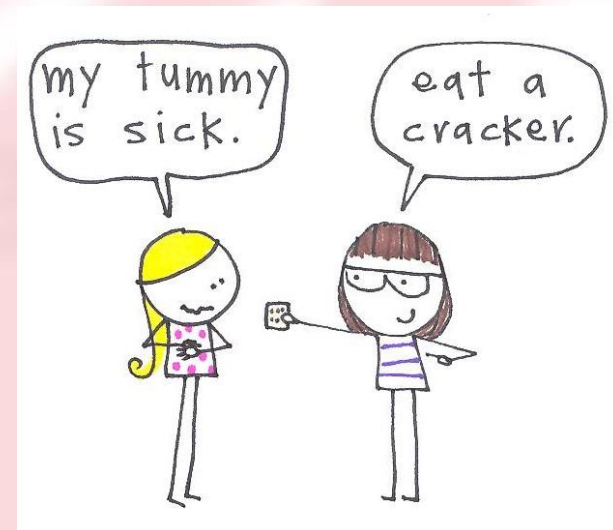
Symptoms usually **last** 24- 48 hours after onset
(range 1-11 days)*

Shedding of virus in stool continues long after the resolution of
symptoms**.

*Sala MR et al. CMI, 20, 793–798 ; ** Rockx, B., et al., Clin. Infect. Dis., 2002. 35(3): p. 246-253.

Treatment

- ❑ There is no specific treatment
- ❑ Liquid replacement to prevent dehydration
- ❑ Avoid medication
 - Antibiotics should be avoided unless specifically recommended by a physician.
 - No Antivirals



Prevention

- Frequent thorough hand washing



http://seguretatdelspacients.gencat.cat/ca/detalls/article/higiene_de_mans

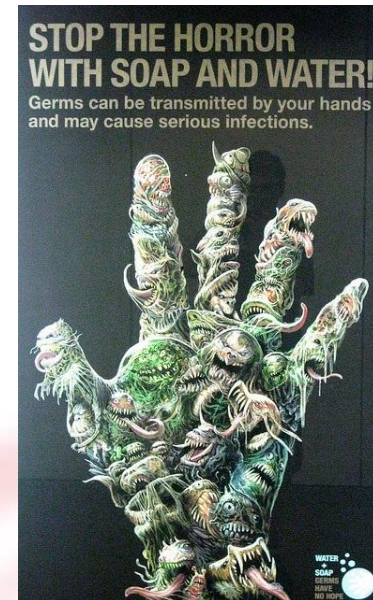


Foto from Flickr by tbSMITH: <https://www.flickr.com/photos/10819063@N06/3654276952>

No Vaccine

...yet

Transgenic plant-based norovirus vaccine

Norovirus P particle and combination vaccines

Trivalent norovirus /rotavirus combination vaccine

Bivalent, intramuscular VLP vaccine.

Prevention

- Prompt disinfection of contaminated surfaces



- Wash soiled clothing and fomites



NV causes ≈50% FB outbreaks of AGE



- Avoid food or water from contaminated or unsafe sources
- Avoid uncooked shellfish
- Stay home when sick

Point source outbreaks can be the beginning of a neverending story



Epidemiology of Norovirus Acute Gastroenteritis in Catalonia



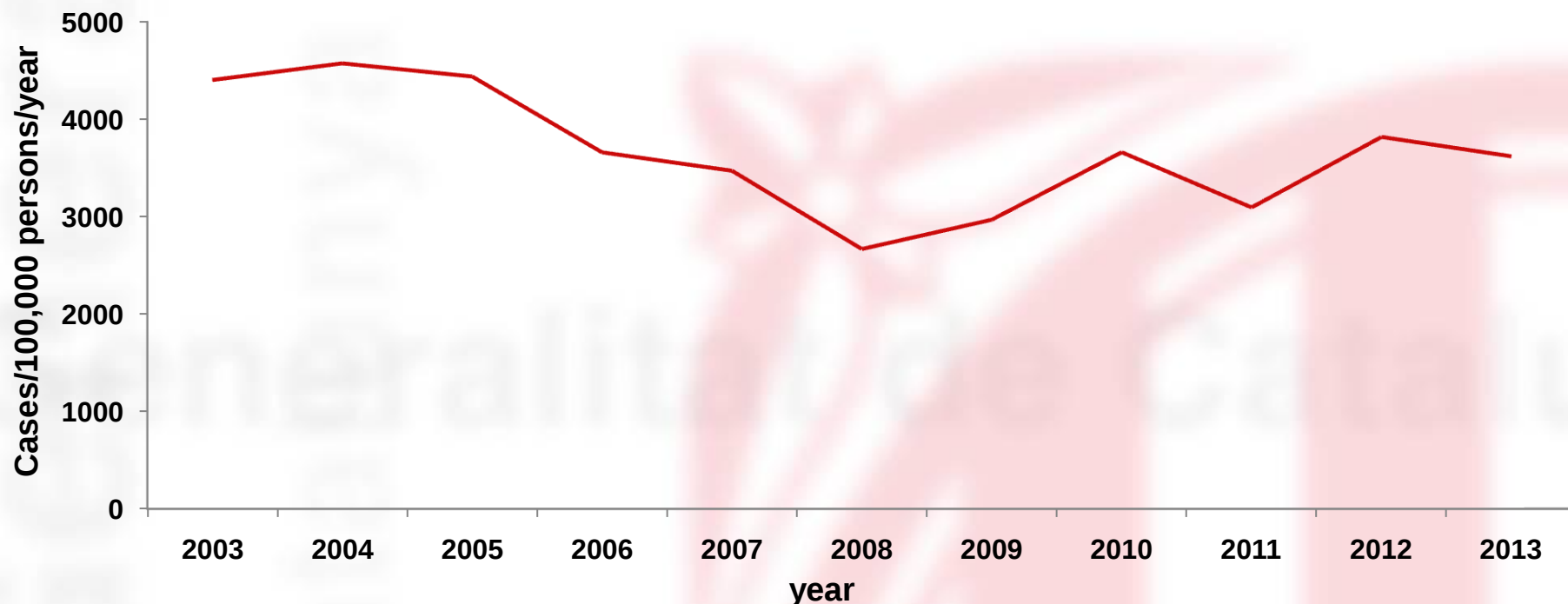
Acute Gastroenteritis :

Incidence rate in Catalonia, 2013

3619/100.000 persons/year (273.409 cases reported in 2013)*

Resum de les malalties de declaració obligatòria. 2013. Butlletí Epidemiològic de Catalunya Maig 2015

AGE incidence rates of cases reported . Statutory reporting system, Catalonia 2003-2013

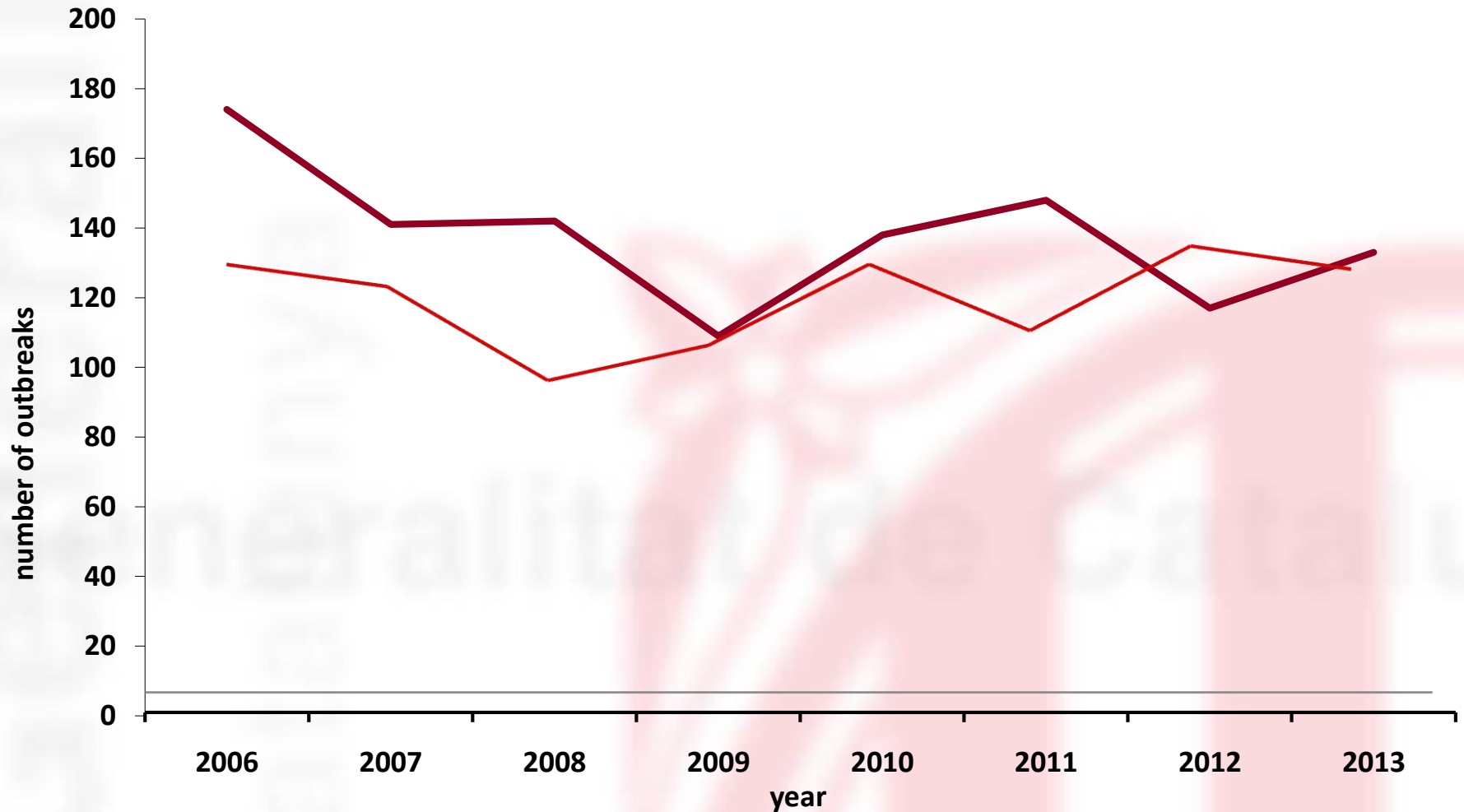


Source: Butlletins Epidemiològics de Catalunya BEC . Resums MDO 2003-2013

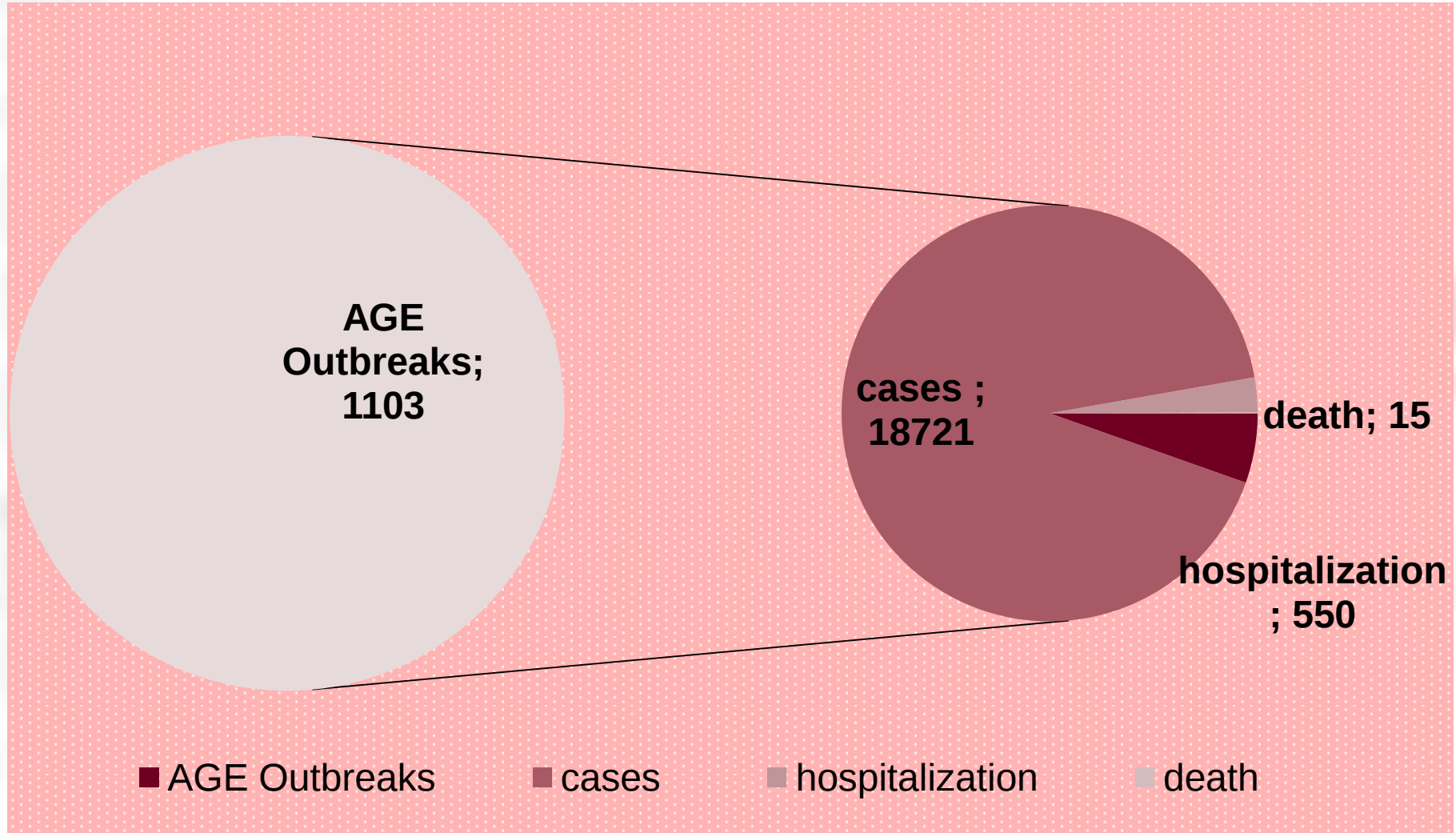
Servei de Control Epidemiològic i Resposta a Alertes i Emergències SG de Vigilància i Resposta a Emergències de Salut Pública

ACUTE GASTROENTERITIS OUTBREAKS

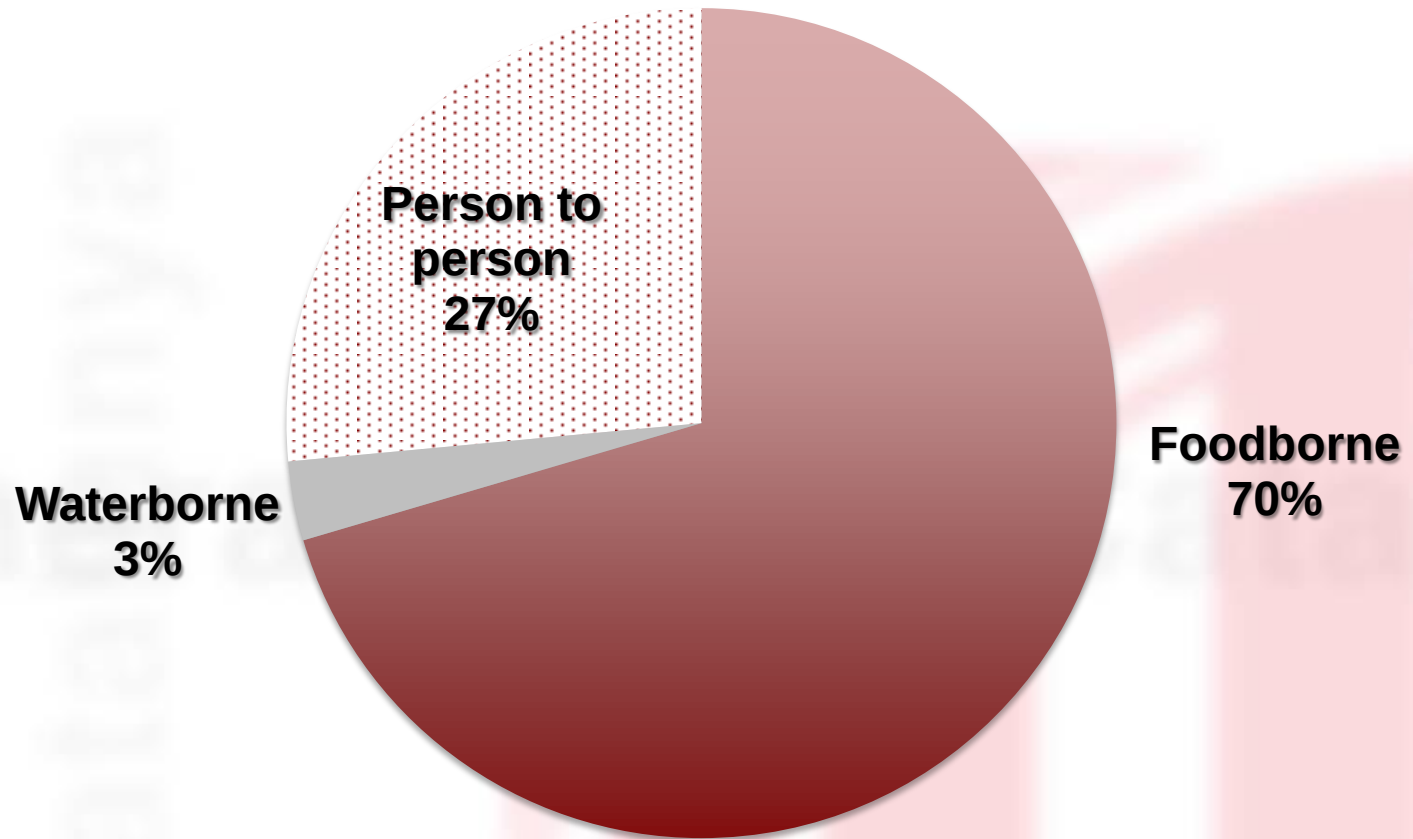
CATALONIA 2006-2013



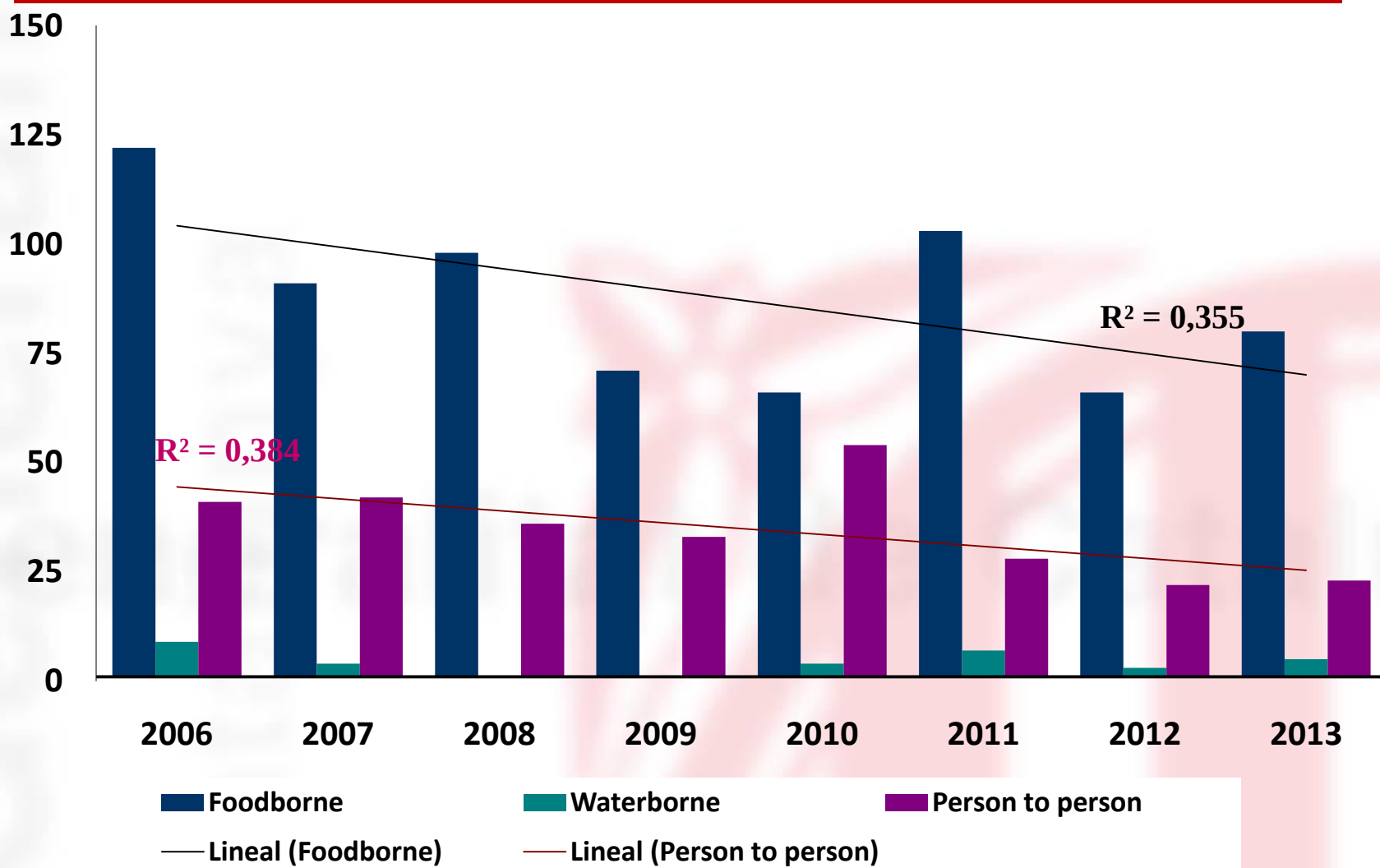
Burden of disease: AGE Outbreak cases, hospitalizations and death 2006-2013



TRANSMISSION MODE OF ACUTE GASTROENTERITIS OUTBREAKS. CATALONIA 2006-2013



TRANSMISSION MODE OF ACUTE GASTROENTERITIS OUTBREAKS. CATALONIA 2006-2013



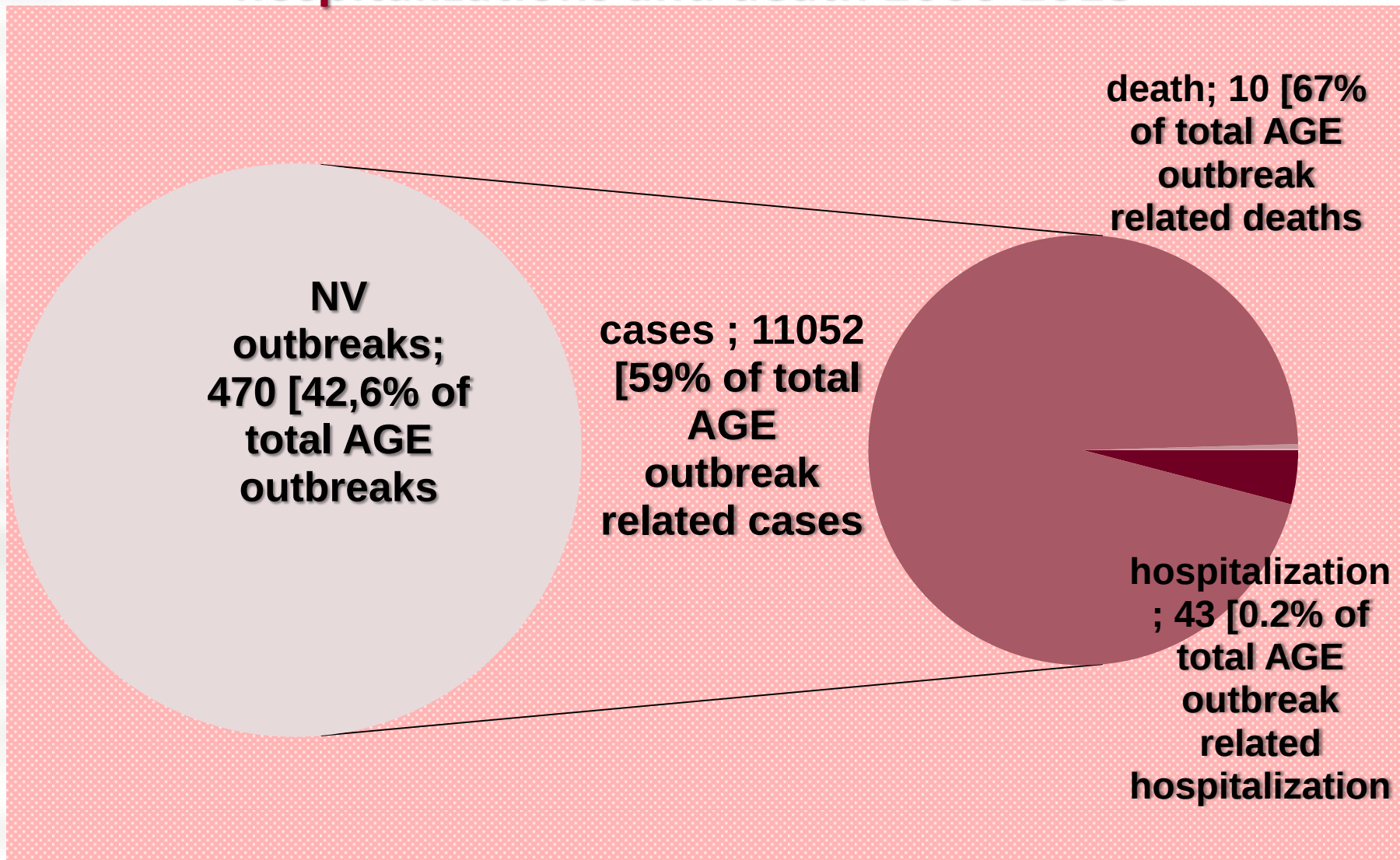
So how much is Norovirus?

Challenges for quantifying NV disease burden:

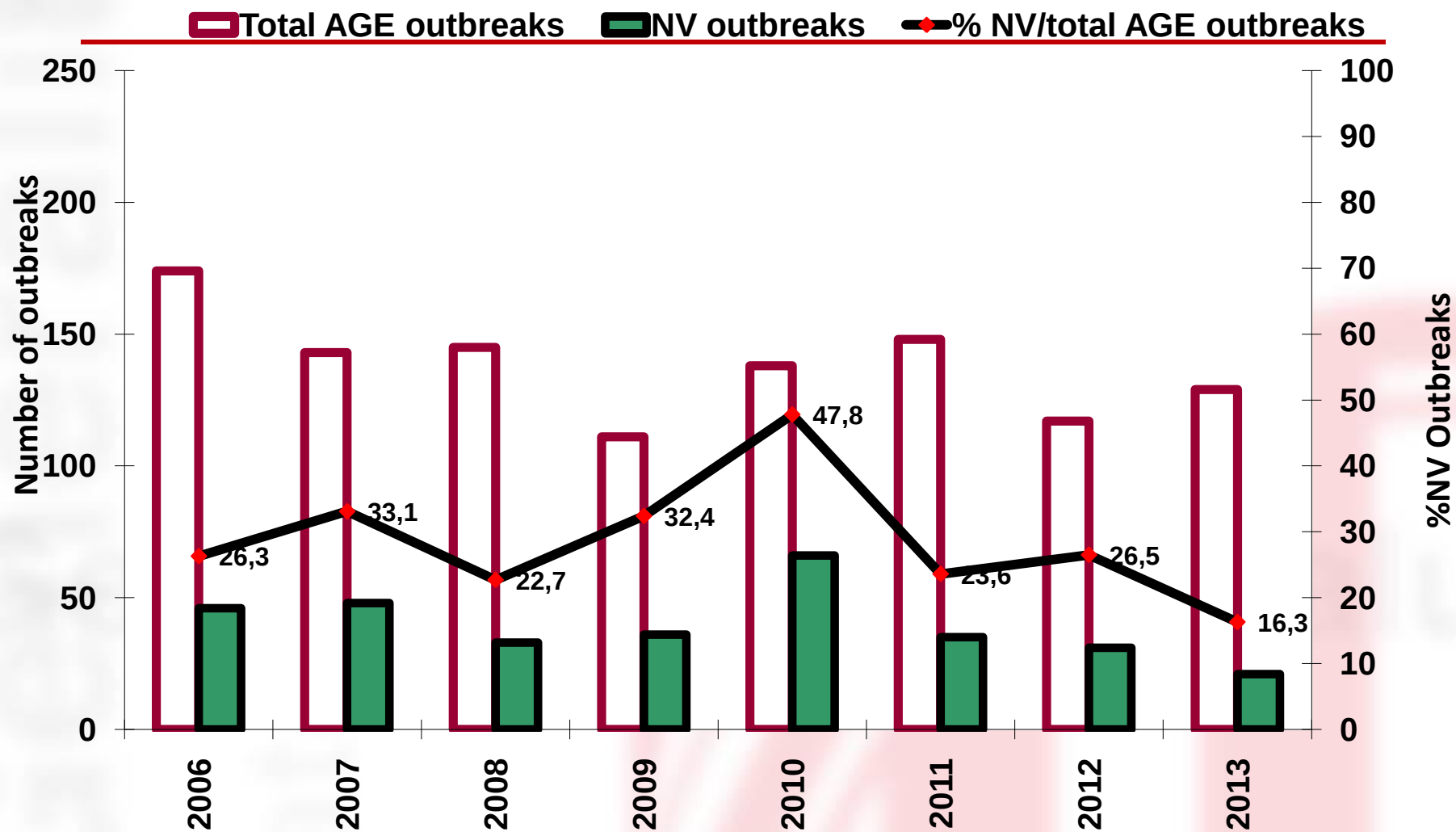
- ❑ Lack of accurate data
(especially developing countries)
- ❑ Robust laboratory diagnostics not widely available
(only in public health and research laboratories in middle and high income settings)
- ❑ Detection in asymptomatic
(high sensitivity real-time quantitative RT-PCR)
- ❑ Hyper-endemicity

So how much is Norovirus?

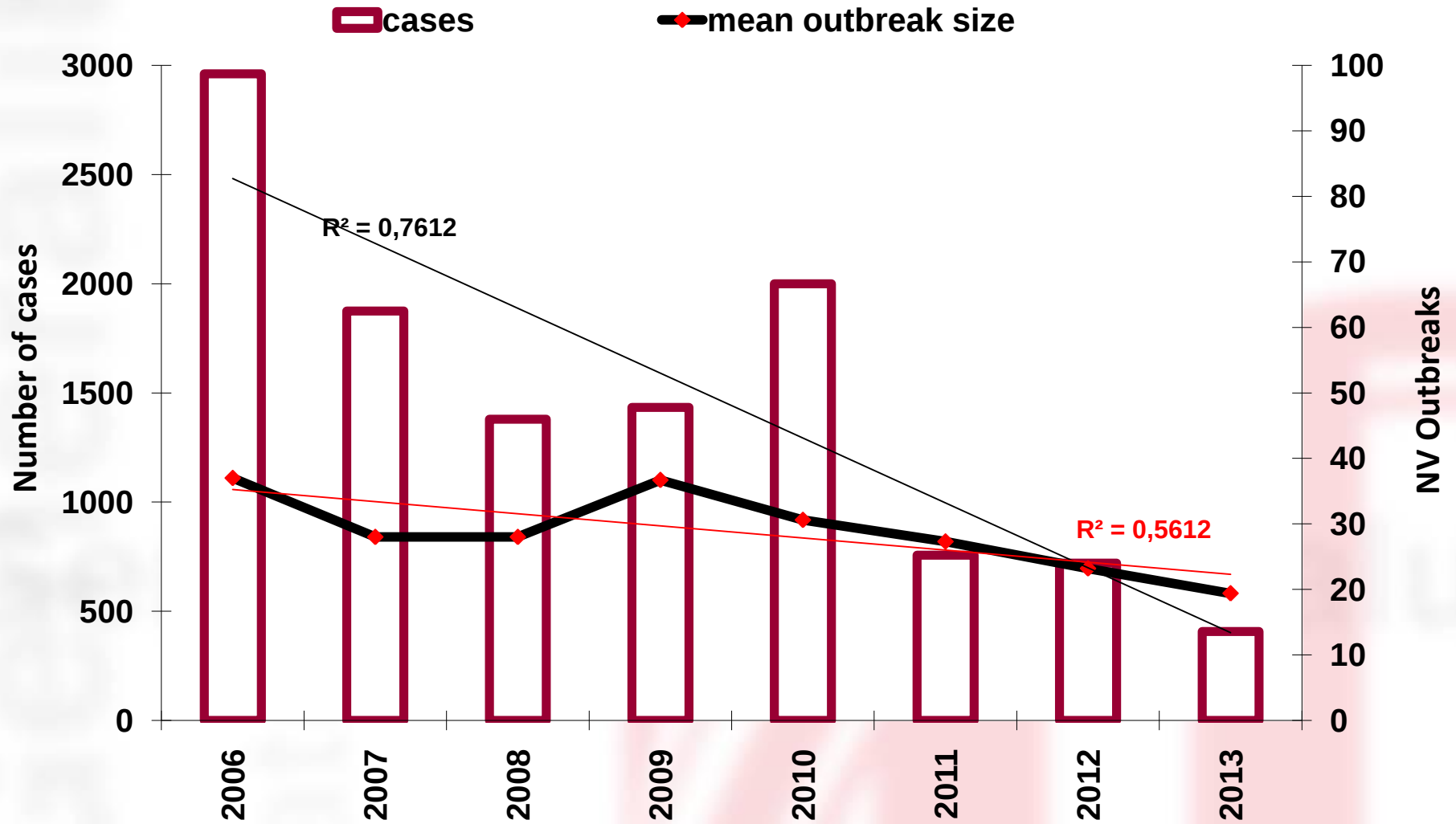
**Burden of disease: NV Outbreak cases,
hospitalizations and death 2006-2013**



% NV -AGE Outbreaks in Catalonia. 2006-2013



NV Outbreaks in Catalonia. 2006-2013



Norovirus: Epidemiology in Catalonia

Due to limitations in the detection of sporadic cases ➡ Study of Outbreaks

Epidemiological study of outbreaks of acute gastroenteritis due to norovirus and sapovirus in Catalonia

PS0902516 (2010-2011)

Objective:

- To describe basic features of NV& SV outbreaks
- To study the frequency of secondary cases in outbreaks of gastroenteritis (GE) due to norovirus and sapovirus occurring only in closed or semi-closed institutions
- Involvement of food handlers in outbreaks of foodborne disease (FBD) and of carers in GE outbreaks with person-person transmission
- To determine the viral load and excretion of persons with symptomatic and with asymptomatic infections due to these viruses.



Kaplan criteria allows to identify NV AGE outbreaks

- ☐ $\geq 50\%$ cases presenting vomitus
- ☐ Incubation period :mean 24-48 h
- ☐ Duration of symptoms: mean 12-60 h
- ☐ Abscene of bacterial pathogen in feces culture*

* Kaplan et al. *Am. J. Public Health*,1982; 72 :1329–1332 ;Turcios et al. *Clin Infect Dis* 2006; 42::964–9

Distribution of NV outbreaks according to setting and mode of transmission.

Catalonia 2010-2011

Setting	No. of outbreaks(%)	Persons affected (%)	Foodborne		Waterborne		Person to person		Persons affected Median(range)	Persons exposed Median(range)	Median age (range)
			No. of outbreaks	Persons affected	No. of outbreaks	Persons affected	No. of outbreaks	Persons affected			
Household	11(10.9)	84(3)	6 ^a	45	1	15	4	24	6 (2-15)	11 (2-30)	29 (0-82)
Foodservice	40(39.6)	1257(45.6)	35 ^{b(2+)}	869	-	-	5	388	17 (3-191)	46 (4-3474)	56 (0-93)
School	12(11.9)	436(15.8)	3 ^c	75	1	103	8	258	19 (6-103)	71 (25-488)	10 (0-74)
Holiday camp/ cottage	4(3.9)	53(1.9)	1 ^d	7	1 ⁺	17	2	29	13 (7-20)	60 (13-77)	10 (8-55)
Nursing home	14(13.9)	445(16.2)	4 ^e	122	-	-	10	323	28 (12-65)	85 (43-213)	81 (21-102)
Longterm care/ Hospital	13(12.9)	371(13.5)	1 ^f	48	-	-	12	323	23 (6-76)	57 (20-203)	76 (19-100)
Other*	7(6.9)	110(4.0)	-	-	2	33	5	77	12 (6-28)	43 (26-83)	37 (0-91)
Total	101 (100%)	2756 (100%)	50 (49.5%)	1166 (42.3%)	5 (5%)	168 (6.1%)	46 (45.6%)	1422 (51.6%)	17 (2-191)	50 (2-3474)	51 (0-102)

* Closed institutions (prison, youth fostering center , mentally disabled facility) ,free camp site, popular race.

+ Positive sample to NoV

a 1 oysters, 1 cake, 4 unknown

b 3 clams, 1 durum, 1 pork roast, 2(1+) mussels, 5(1+) oysters, 22 unknown

c 1 sandwich, 2 unknown

d 1 unknown

e 4 unknown

f 1 unknown

NV Incidence rates and risk of infection according to gender and age group. Catalonia 2010-2011



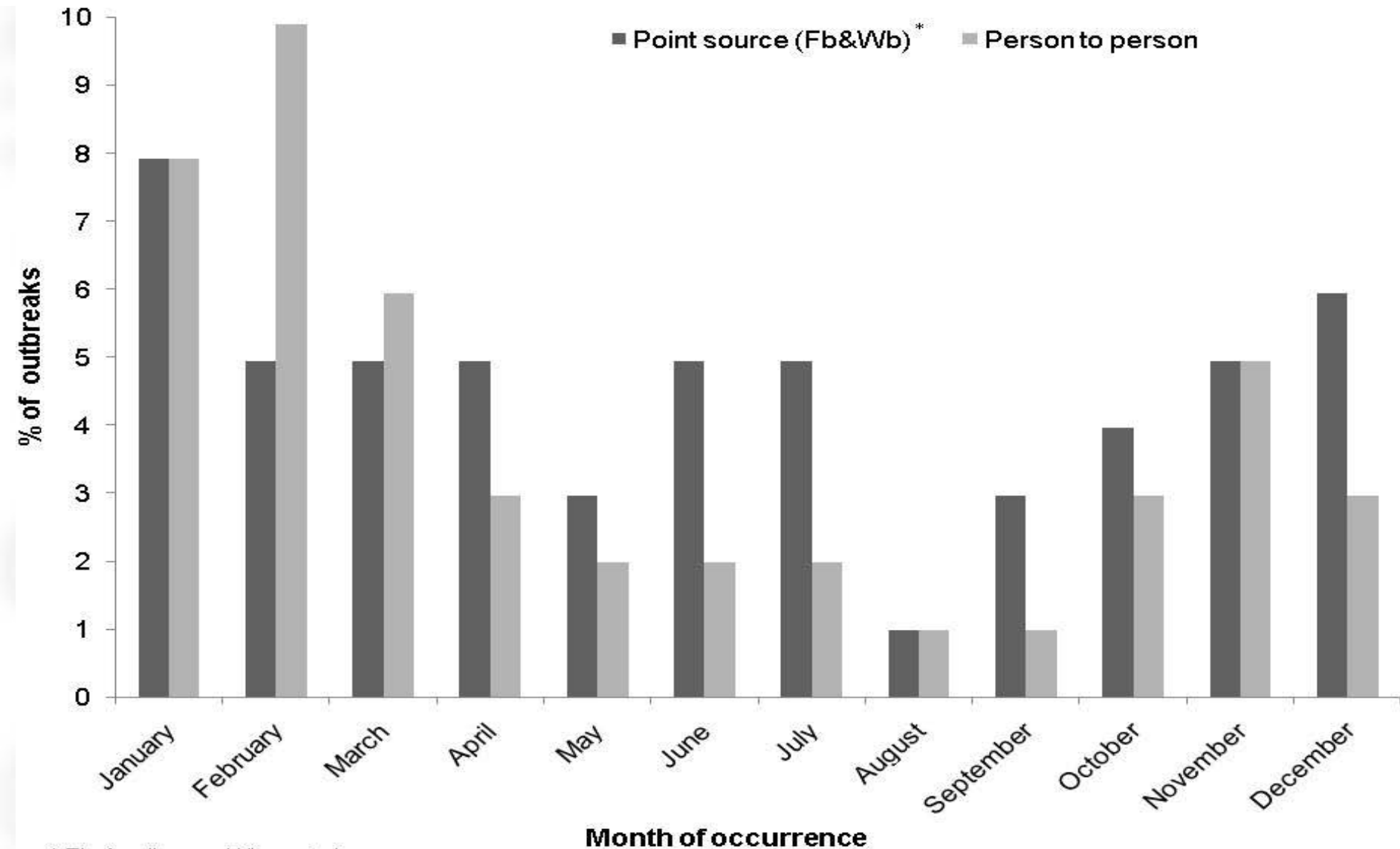
Age group*	IR (95% CI)	RR (95%CI)	p
0 a 14 years	17.19 (15.55-18.97)	1.87 (1.66-2.11)	< 0.001
15 a 64 years	9.18 (8.60-9.78)	1	
≥ 65 years	43.56 (41.01-46.22)	4.75 (4.35-5.19)	< 0.001
Gender**			
Men	13.69 (12.87-14.56)	1	
Women	19.91 (18.92-20.94)	1.45 (1.34-1.58)	< 0.001

*219 of the 2758 affected persons were not surveyed

*109 out of 2537 surveyed lacked information on age and 4 on gender

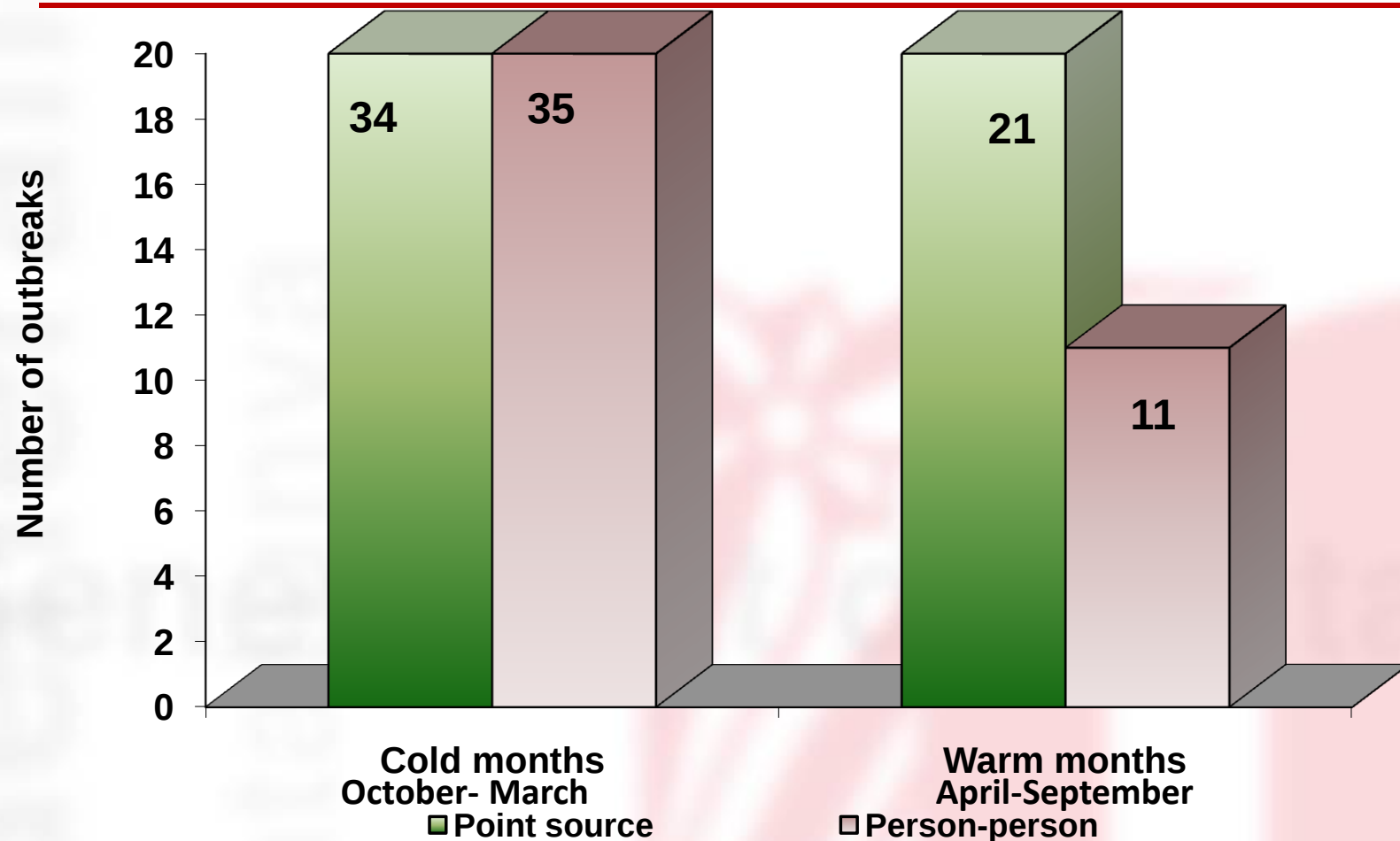
NV Seasonality according to transmission.

Catalonia 2010-2011



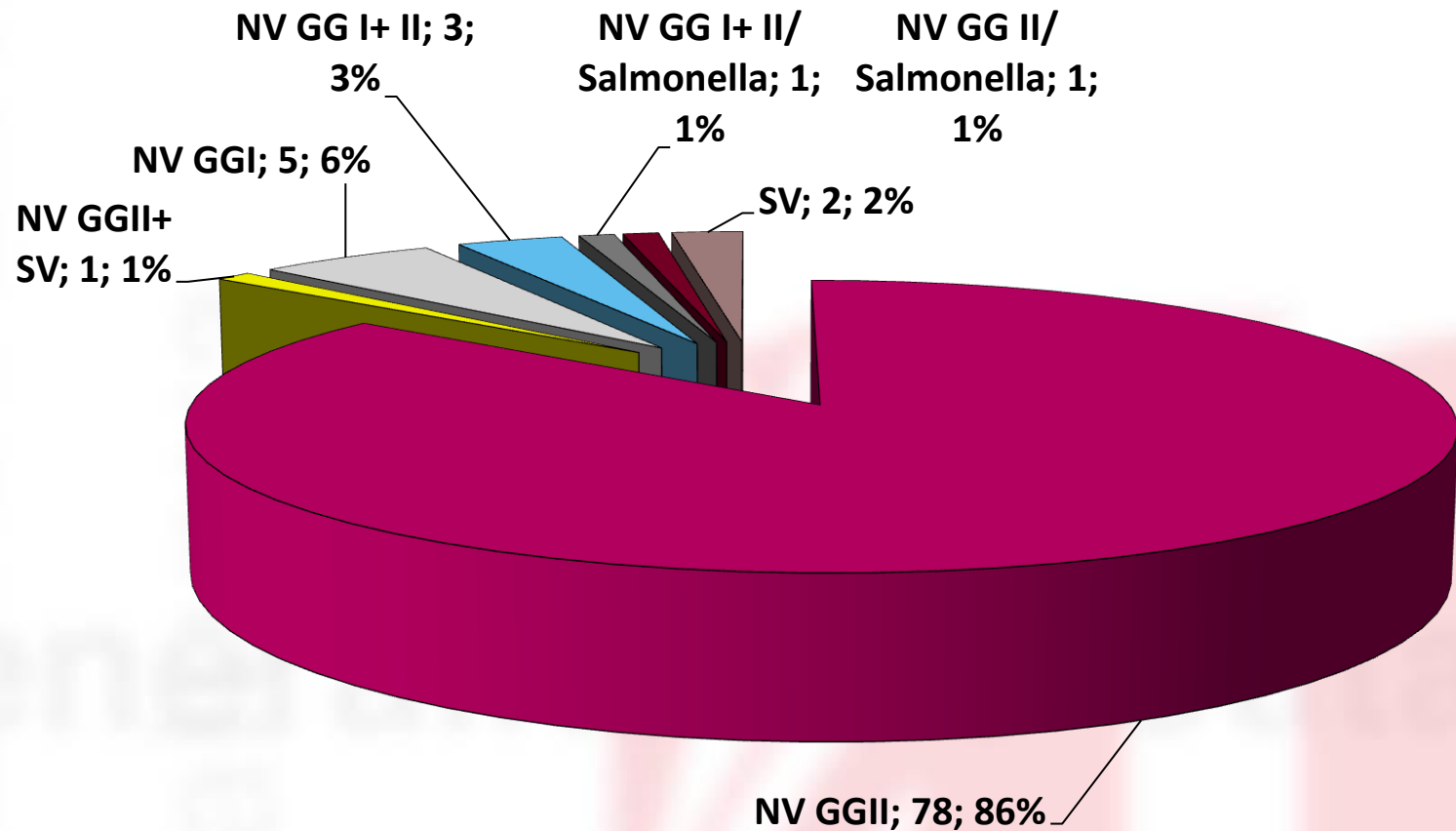
* Fb: foodborne; Wb: waterborne

NV Seasonality according to transmission. Catalonia 2010-2011



OR=1.97 (95%CI :0.82-4.69 ; p=0.12)

NV Genogrup distribution Catalonia,2010-2011



Conclusions

- ❑ Epidemiological studies of outbreaks allow for upgraded knowledge and awareness on NV disease trends.
- ❑ The easiness with which noroviruses are transmitted and the low infecting dose required to set an infection results in extensive outbreaks.
- ❑ The accurate diagnosis of virus gastroenteritis is essential to reduce the impact of the disease on the growing aging population

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