“How do our daily decisions as veterinarians influence antibiotic resistance?”

E. Marco

Marco Vetgrup; S.L.

5th Animal Health and Veterinary Medicine Congress
(Valencia)
26-27 September 2016

Outline

- Antibiotics
  - History
  - Antibiotic resistance
- One health problem
- Daily decisions
  - Type of antibiotic
  - Administration route
  - Duration of treatment
  - Other variables
- Conclusions

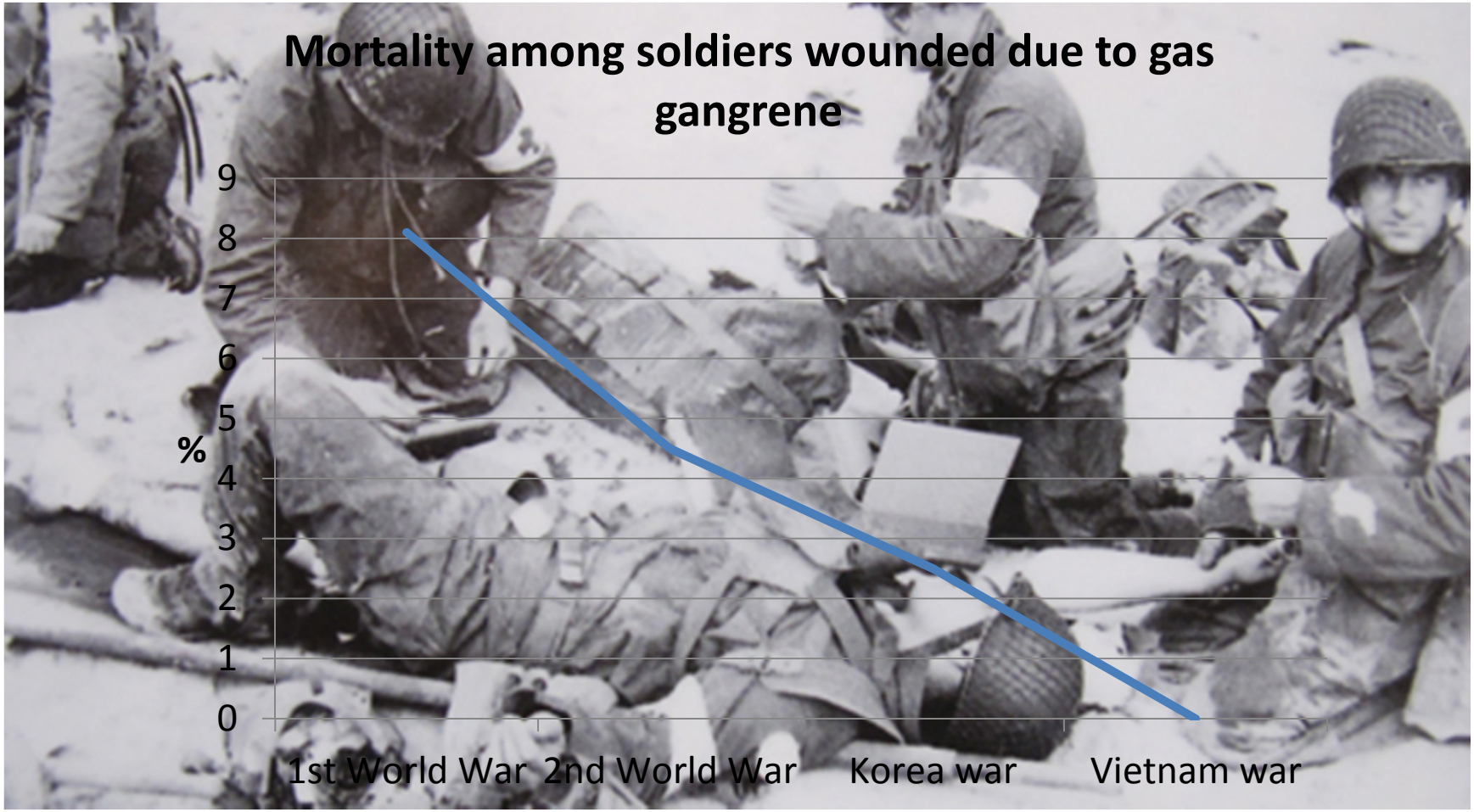
Alexander Fleming

- 1928 discover Penicillin.
- 1945 Alexander Fleming is awarded with Nobel Prize



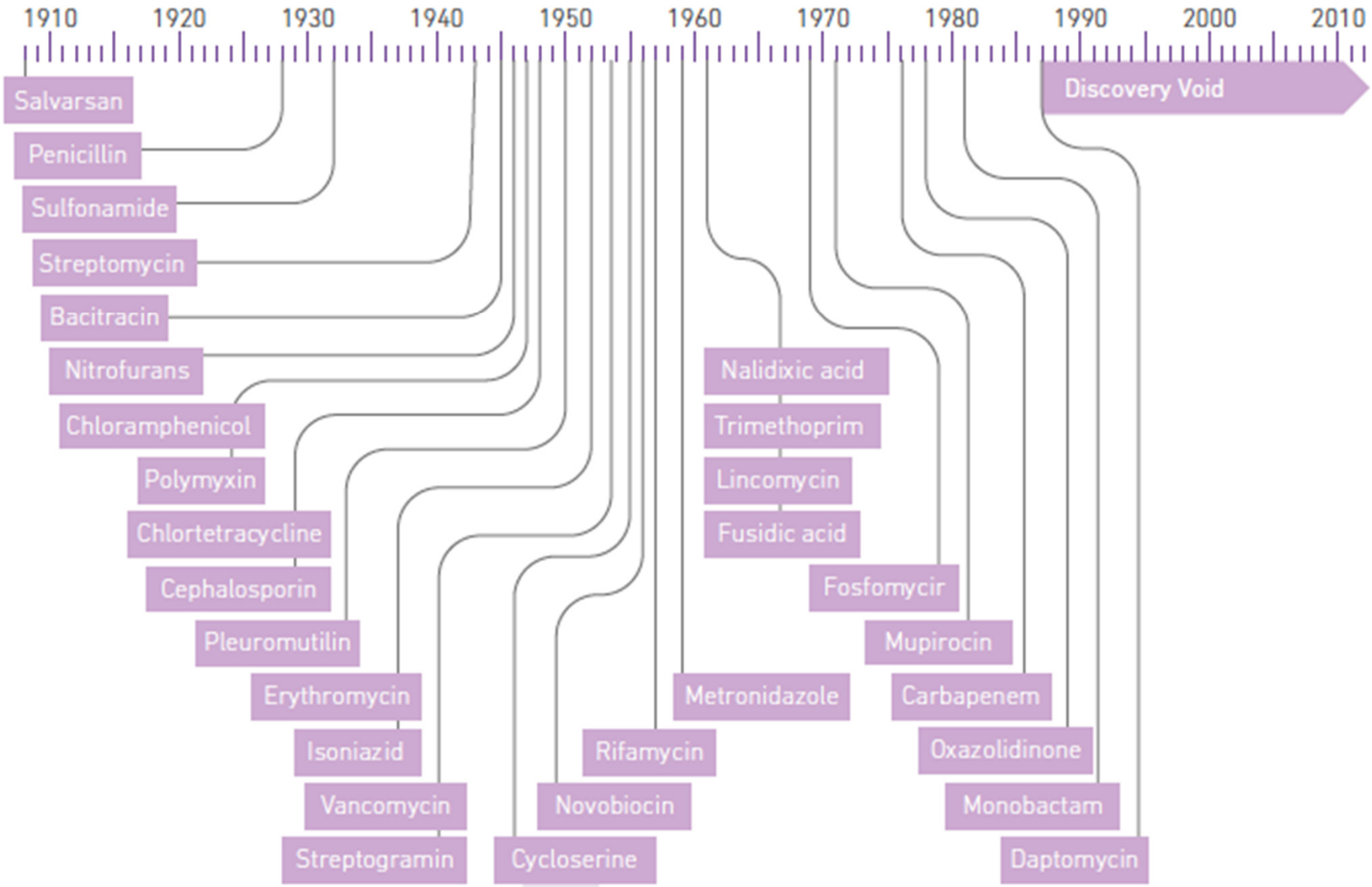
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Alexander Fleming



Calzadilla, V. Et al. Rev Cubana Med Milit 2005;34(3)

Dates of discovery of distinct classes of antibacterial drugs



Adapted from Silver 2011 (1) with permission of the American Society of Microbiology Journals Department.

Antimicrobial Resistance. Global Report on surveillance. 2014 WHO

Antibiotic resistance

- ABR exists even before antibiotics were discovered.
- Majority of drug resistance microorganisms have emerged as a result of genetic changes
  - Mutation
  - Tranfer of genetic material
  - Natural selection

Antibiotic resistance

- Use of Antibiotics can promote selection of spontaneous resistance mutants.
- But is estimated that major part of acquired resistance is plasmid mediated.
- Micro-organisms resistant to a certain anti-biotic may also be resistant to other antibiotics that share a mechanism of action or attachment.

Antibiotic resistance

- Micro-organisms may be resistant to several unrelated antibiotics.
- Use of one such antibiotic will therefore also select for resistance to the other antibiotics.

Human medicine concerns

- Community-acquired infections such as pneumonia may not respond to available or recommended drugs.
- Infections which normally respond to oral treatments in the past, may need to be treated by injected drugs, imposing additional costs, or become untreatable.
- Common infections in neonatal and intensive care are increasingly becoming extremely difficult, and sometimes impossible, to treat.
- Patients receiving cancer treatment, organ transplants and other advanced therapies are particularly vulnerable to infection. If treatment fails in such patients, the infection is likely to become life-threatening and may be fatal.
- Antibacterial drugs used to prevent postoperative surgical site infections have become less effective or ineffective.

Antimicrobial Resistance. Global Report on surveillance. 2014 WHO

Veterinary medicine concerns

- Some infection can become more difficult to treat.
- Forced to use newer molecules which can put on risk use in humans.
- Increase cost of disease.

Veterinary medicine concerns

"From the overview, it is clear that veterinary practice cannot afford to lose any of these important antimicrobials. The indications for using some of them may be very specific; nevertheless, losing any of them as an effective medicine or no longer having them available for veterinary purposes will have very direct consequences for animals, their owners and society at large."

Vaarten J. Clinical impact of antimicrobial resistance in animals. *Rev Sci Tech*, 2012, 31(1):221-229. (http://www.ncbi.nlm.nih.gov/pubmed/22849278, accessed 8 April 2014).


Jean Rozé
Label Rouge
2 COTES ECHINE
Par face
A point : 6 min
À GRILLER
A consommer jusqu'au : 20/08/16
PRIX A PAYER :
4.09€
Prix au Kilo 9.10€/kg
Poids net en kg 0.449kg
JEAN ROZÉ
Selection
NOUVEAU
Irrésistible Caractère de cochon
Porc élevé Sans Antibiotique*
* viande issue de porcs
Emballage à jeter avec les déchets.
2 PAVES
A consommer jusqu'au 16/08/16
Prix au kg 13.20€/kg
Poids Net 0.244kg
Prix à Payer 3.22€
À GRILLER
Conseils de cuisson
Par face
A point : 4 min
Numéro de tracabilité E62190551
Origine France
Ingrédient Carré sans os
FR 47-091-002 CE

Resistance transfer

- Possible sources of resistant micro-organism
  - *Animals and their faeces*
  - *Food of animal origin that may have been contaminated during processing*
  - *Fruits or vegetables that may come from a contaminated environment*
  - *Contaminated water*
  - *Humans*

Resistance transfer

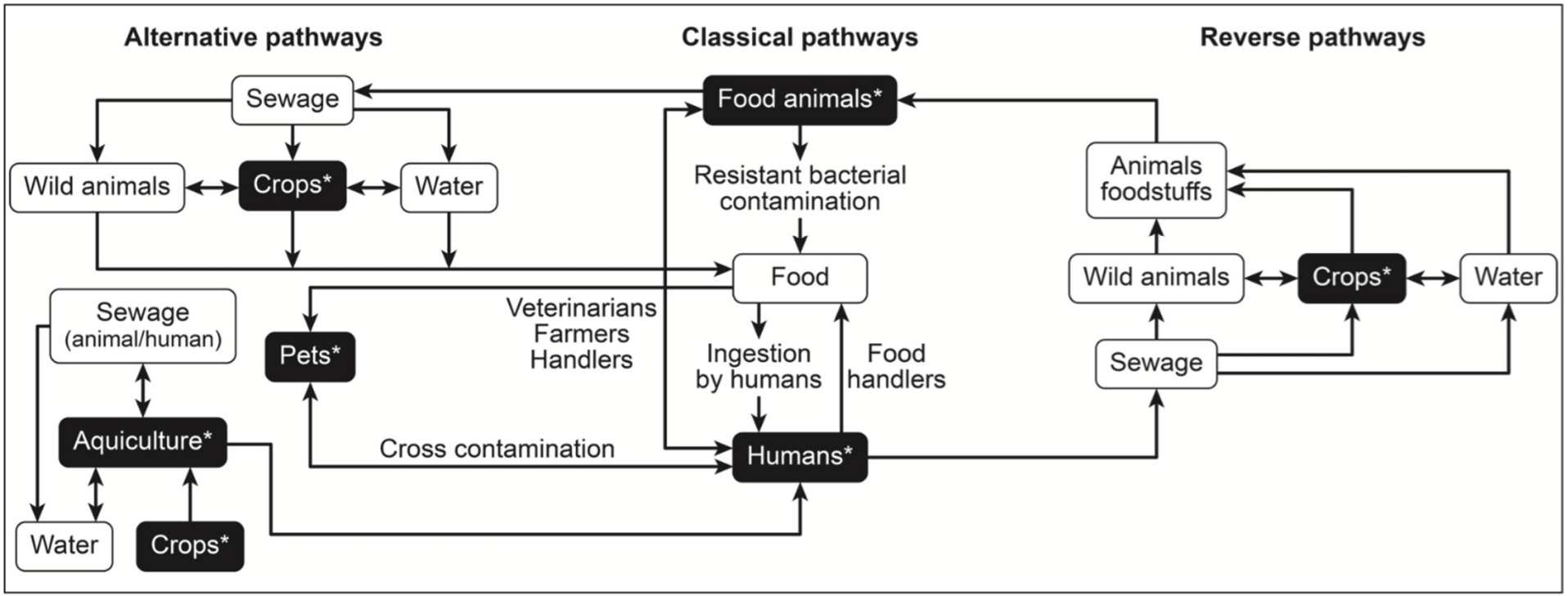
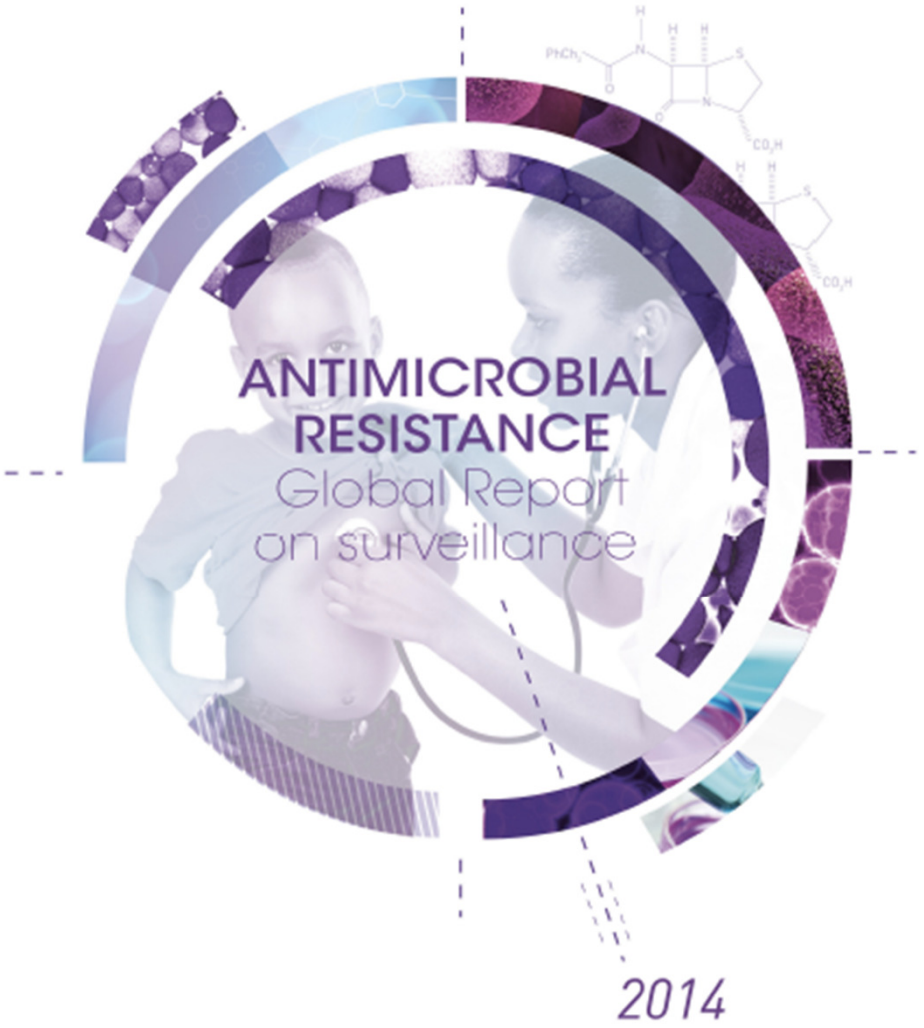


Figure 1 - Possible pathways and routes of transmission of gastrointestinal pathogens and bacteria from microbiota between animals (wild animals, pets and food animals) and humans
Fonte: Adapted from Phillips et al. (2004).

Silva K.C. *Et al.* Braz. J. Vet. Res. Anim. Sci., São Paulo, v. 50, n. 3, p. 171-183, 2013

One health


ANTIMICROBIAL
RESISTANCE
Global Report
on surveillance
2014

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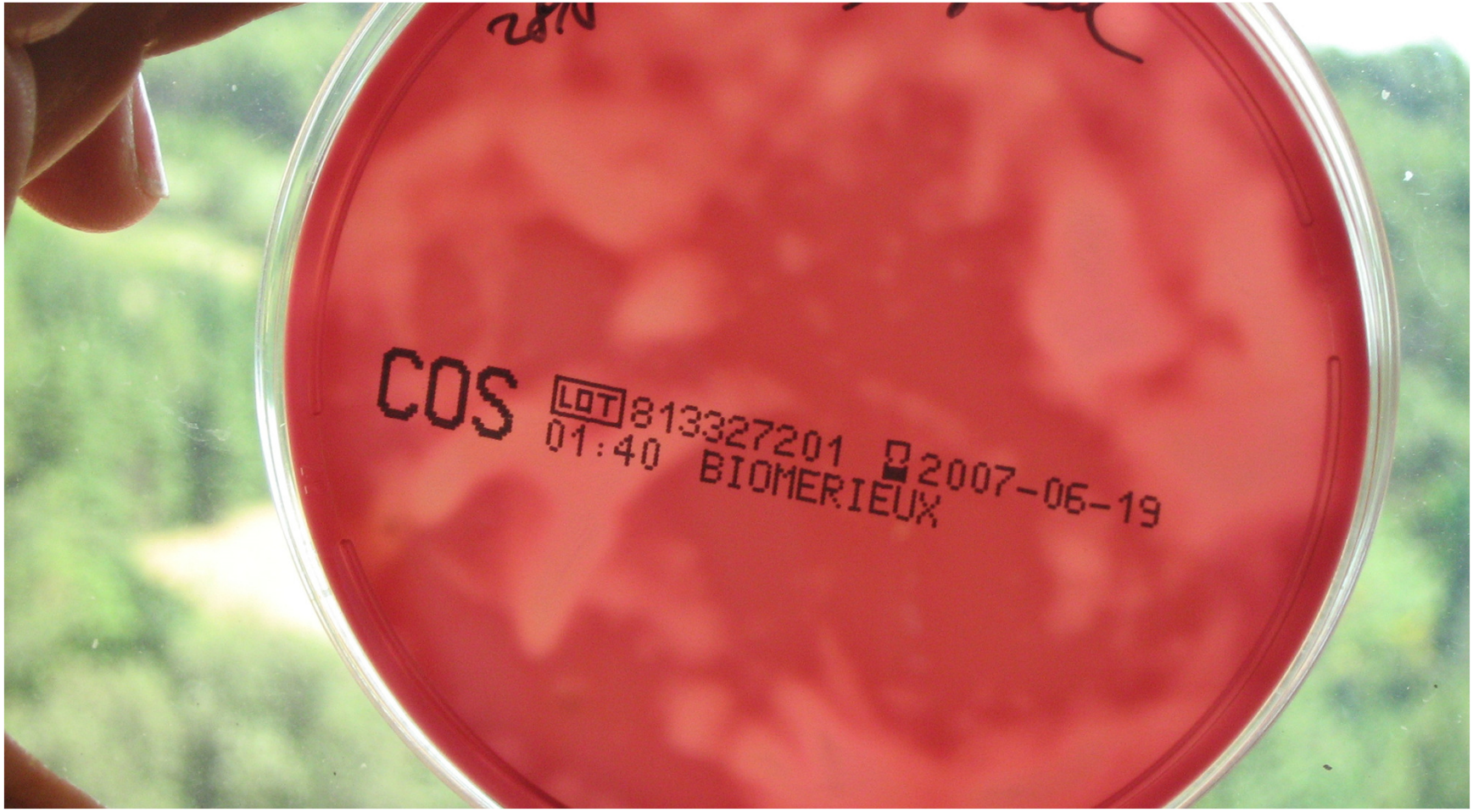
DAILY DECISIONS

Accurate Diagnosis



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Accurate Diagnosis



Sensitivity test

INFORME DE ENSAYO

ANTIBIOGRAMA*

ANTIBIOTICO			1-Escherichia Coli
PEN	Penicilina	10 IU	R
AMP	Ampicilina	10 ug	R
AML	Amoxicilina	30 ug	R
AMC	Amoxi+Clavulanico	30 ug	S
EFT	Ceftiofur	30 ug	S
CEQ	Cefquinoma	30 ug	S
TET	Tetraciclina	30 ug	R
DOX	Doxiciclina	30 ug	I
FFC	Florefenicol	30 ug	S
ERY	Eritromicina	15 ug	R
SPN	Espiramicina	100 ug	R
VAL	Valnemulina	30 ug	R
TIA	Tiamulina	30 ug	R
TY	Tilosina	30 ug	S
LS	Linco-Espetinomic	109 ug	R
LCN	Lincomycine	15 ug	R
GMN	Gentamicina	10 ug	R
SMN	Estreptomicina	10 ug	R
KMN	Kanamicina	30 ug	R
NEO	Neomicina	30 ug	R
APR	Apramicina	15 ug	R
CST	Colistina	10 ug	S
SXT	Sulfa-Trimetroprim	25 ug	R
UBN	Flumequina	30 ug	S
ENR	Enrofloxacina	5 ug	R
OA	Ac. Oxolinic	2 ug	S
MAR	Marbofloxacina	5 ug	S

INTERPRETACION DE RESULTADOS:

Sensible - Intermedio - Resistente S - I - R

Método Analítico PNT/P21-001

Daily decisions

- Sensitivity test are not perfect.
  - They should be considered as a guide.
  - Results obtained form them will work in practice as long the antibiotic is able to contact with pathogen.
    - Famacokitetics have to be know to choose the right product for a specific problem.

Avoid massive treatments



Daily decisions

- Better to use a narrow spectrum antibiotic than a broad one.
  - broad spectrum of activity lead to development of resistance in non-target micro- organisms more rapidly that those with narrow spectrum.
- Avoid mixing antibiotics for the same reason

Broad espectrum concequences

Just one shoot of Antibiotic can alter microbiota for a period of 5 weeks

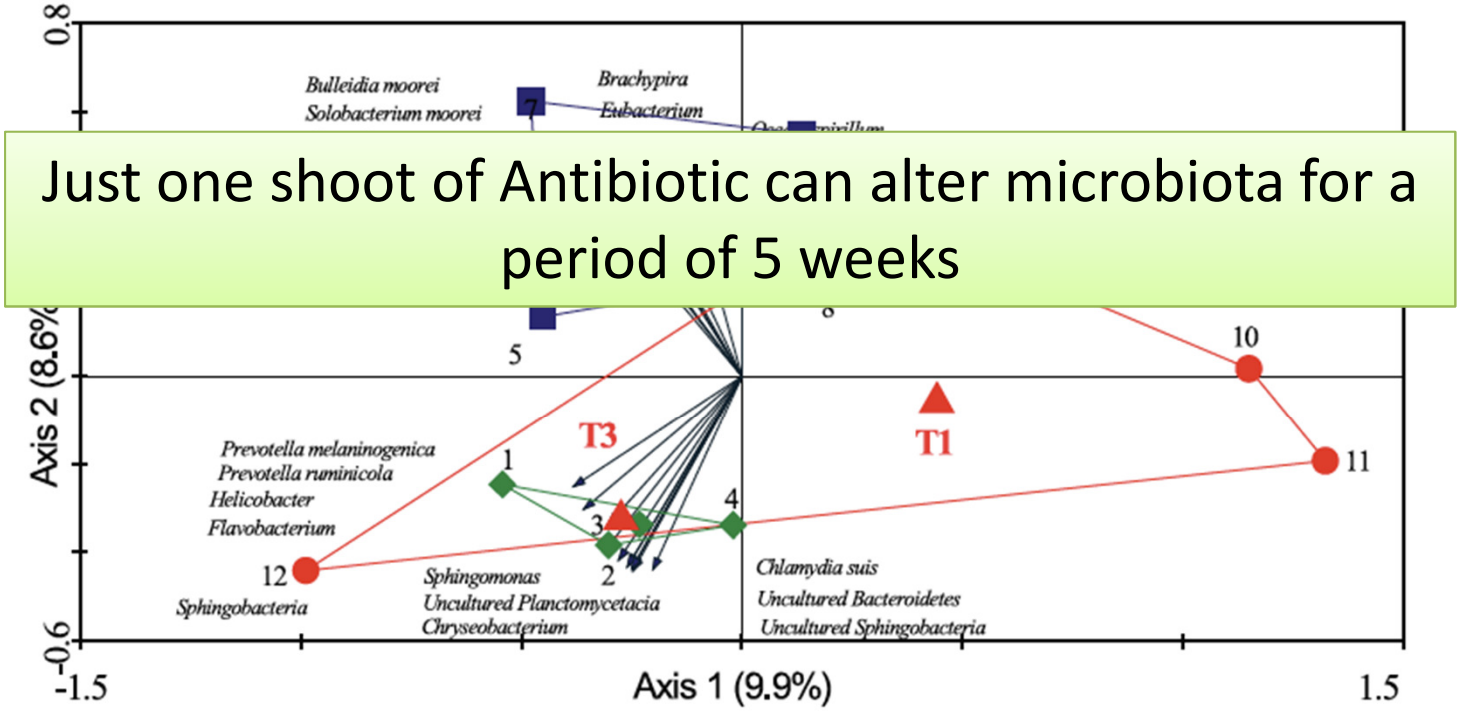


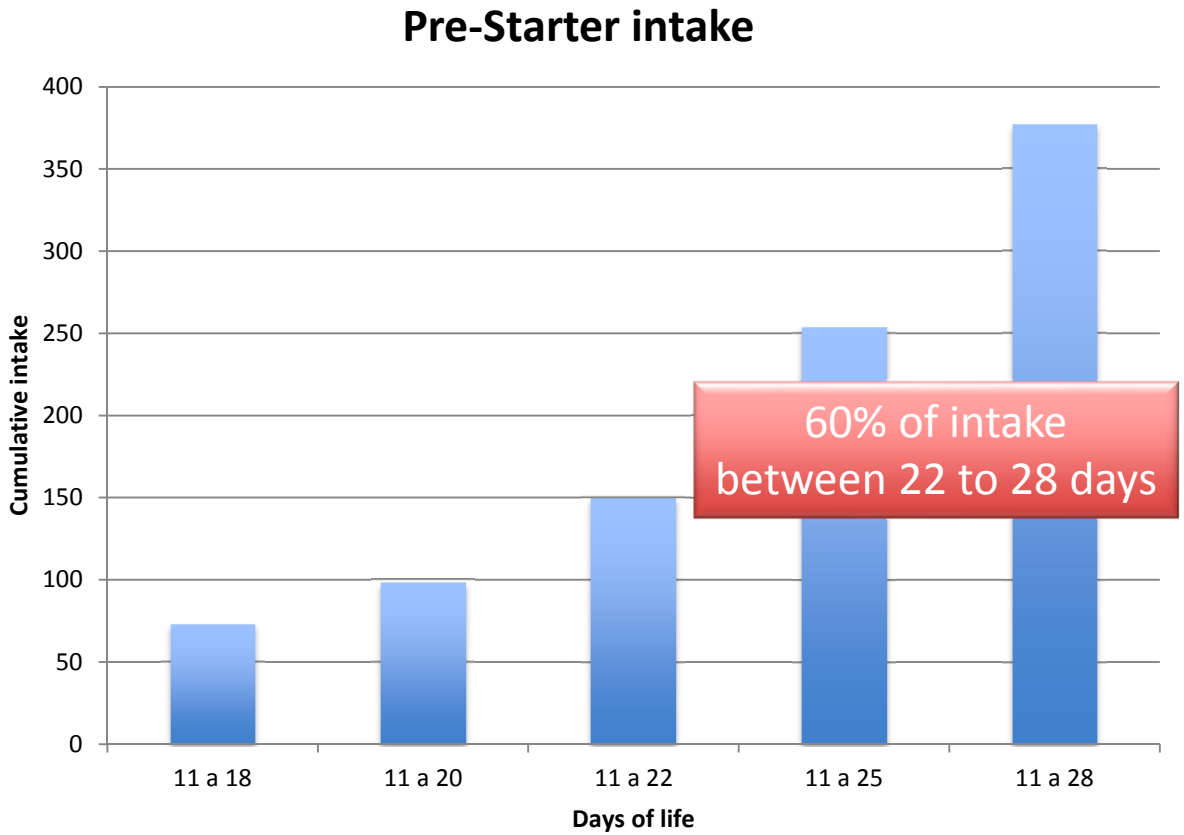
Figure 1. Triplot for RDA analysis of jejunal microbiota composition. Nominal environmental variables T1, T2 and T3 are represented by red triangles (▲). Samples are grouped by treatment: T1 (red; ○), T2 (blue; □) and T3 (green; ◇), each symbol represents a pool of four pigs, and numbers represent pool identity number. Microbial groups contributing at least 60% to the explanatory axes are represented as vectors. Both axes together explain 18.5% of the total variance in the dataset.
doi:10.1371/journal.pone.0100040.g001

Dirkjan Schokker *et al.* 2014. *Early-Life Environmental Variation Affects Intestinal Microbiota and Immune Development in New-Born Piglets.* PLoS ONE 9(6): e100040. doi:10.1371/journal.pone.0100040

Daily decisions

- Choose the right treatment
  - Has to be approved for swine and with indication to treat the disease.
- Correct dosage
  - Avoid under-dosage
  - Weight the animals in order to be precise

Does it make sense to medicate Pre-starter diets?



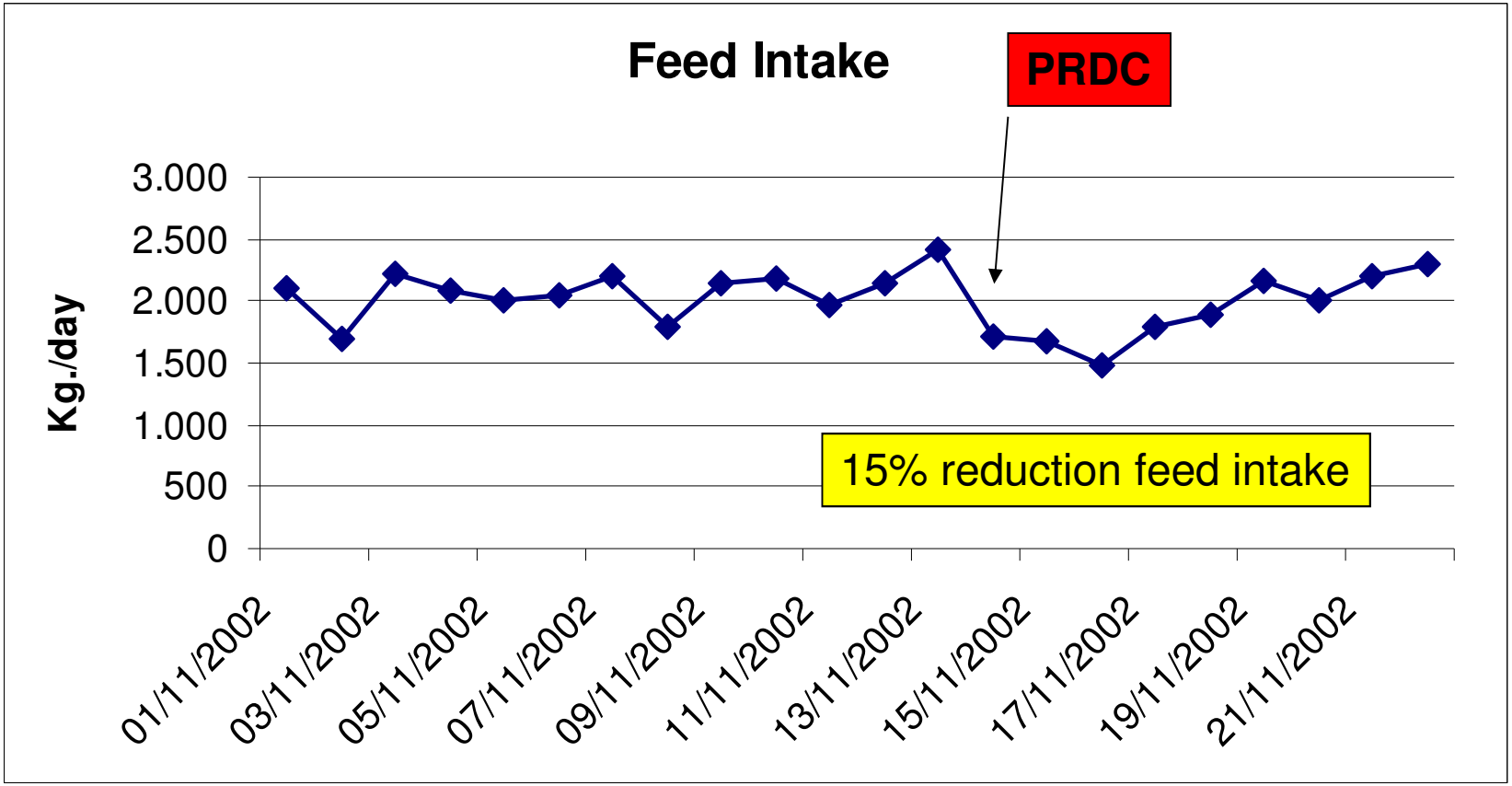
Brunix, et al. *Effect of creep-feed consumption on individual feed intake characteristics and performance of group housed weanling pigs*. J. Anim. Sci. 2002, 80: 1413-1418

Does it make sense to medicate Pre-starter diets?

- Weaning weight: 6 Kg
- Average feed intake 1st week: 100 g/pig/day
- Amoxicilline dose: 300 ppm
- **Amoxicilline dose pig/day: 5 mg/Kg. PV**

It does anything good?

Do we know how much they eat ?

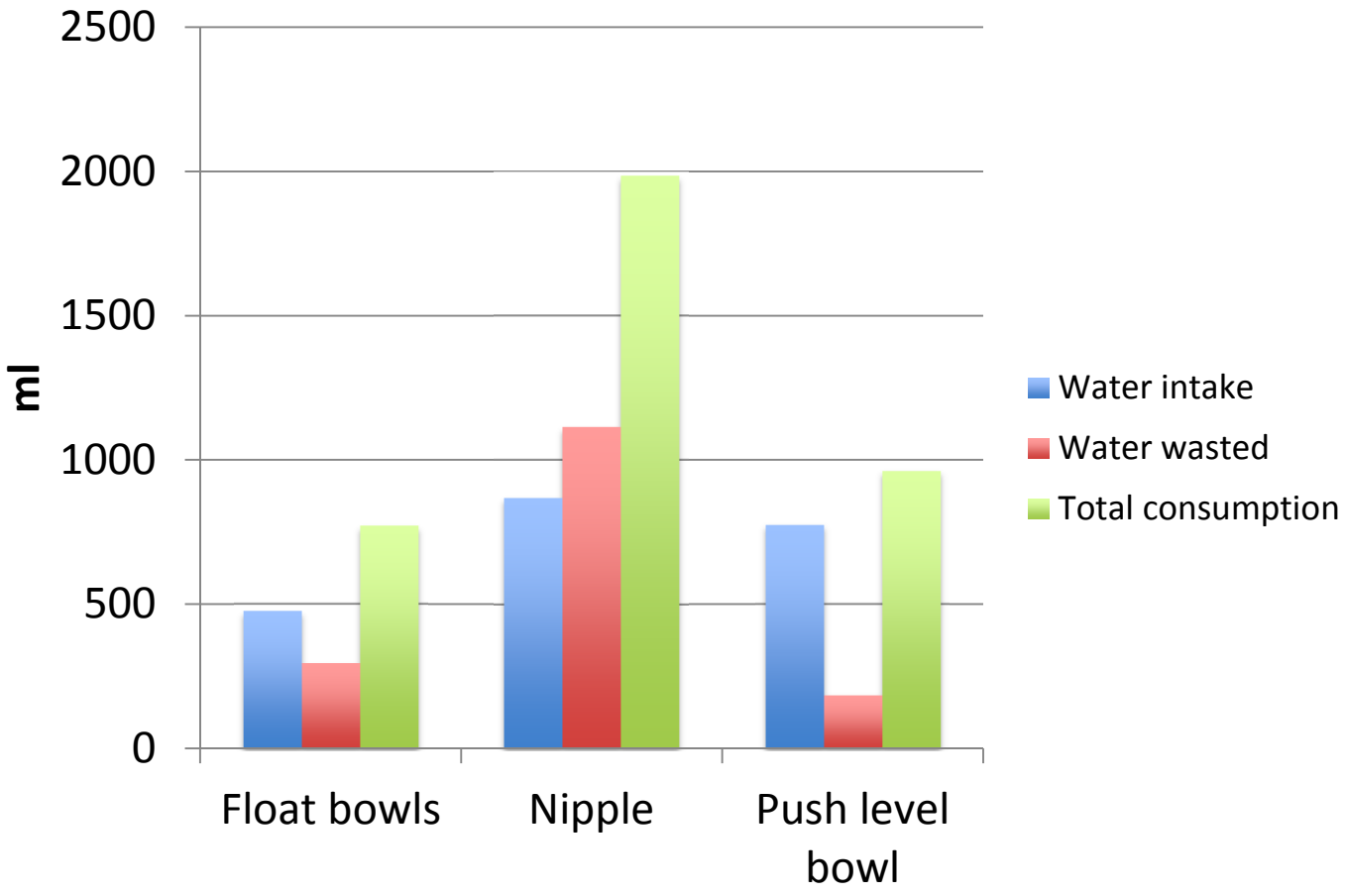


Alberto Morillo Alujas, 2002.Tests and Trials, S.L.

Do we know how much they drink?

Water consumption stimated for different pigs (l/day).							
Authors	Productive stage						
	Lactating pigs	Weaned pigs	Gorwing phase	Finishing phase	Gestating sows	Lactating sows	Boars
Pederson (1984)	1-2	1-5	5-10	5-10	12-20	25-35	8-10
Lumb (1998)	0,27	1,20	2,25	6,00	5-8	15-30	-
Cleary (1983)	-	-	3-7	7-12	12-15	18-23	12-15
Anderson (1984)	-	1,3-2,5	2,5-3,8	3,8-7,5	13-17	18-23	13-17
Almond (1995)	-	2,8	8-12	12-20	15-25	10-30	20
Patience (2005)	-	1-2,5	2,5-7	-	-	12-20	-
Carroll (2003)	1-2	1-5	8-12	12-20	12-25	10-35	8-20
Bpex (2008)	-	1-1,5	2-5	5-6	5-8	15-30	5-8
Shannon (2008)	1-2	1-5	5-10	10-20	12-20	20-60	10-20
Taylor (2006)	-	2-5	5-7	9-12	10-20	20-30	-
Muirhead (1997)	-	1-2,5	3,3	4,2	9-18	18-36	-
Forcada(1997)	1,2-1,5	2,25-2,5	3-5	6-8	5-8	10-30	5-8
Taylor DJ (1995)	0,3-0,5	1,5-2,0	-	6-12	10-20	25-40	-

Water consumption depends on type of drinker



Torrey et al. Journal Anim. Science, 2008. 86, 1439-1445

Daily decisions

- Long oral based treatment should be avoided.
  - Concerns associated with the selection and transfer of resistant bacteria that inhabit the gut.
- When immunosuppression is present
  - Bactericidal antibiotics are the choice

Daily decisions

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Daily decisions

- Correct duration of the treatment
  - Insufficient duration of administration can lead to:
    - recrudescence of the infection
    - increasing the likelihood of selecting organisms with reduced sensitivity.



Daily decisions

- How can we approach group medication?
  - Has to be evaluated in a particular situation
    - Ej. App infection

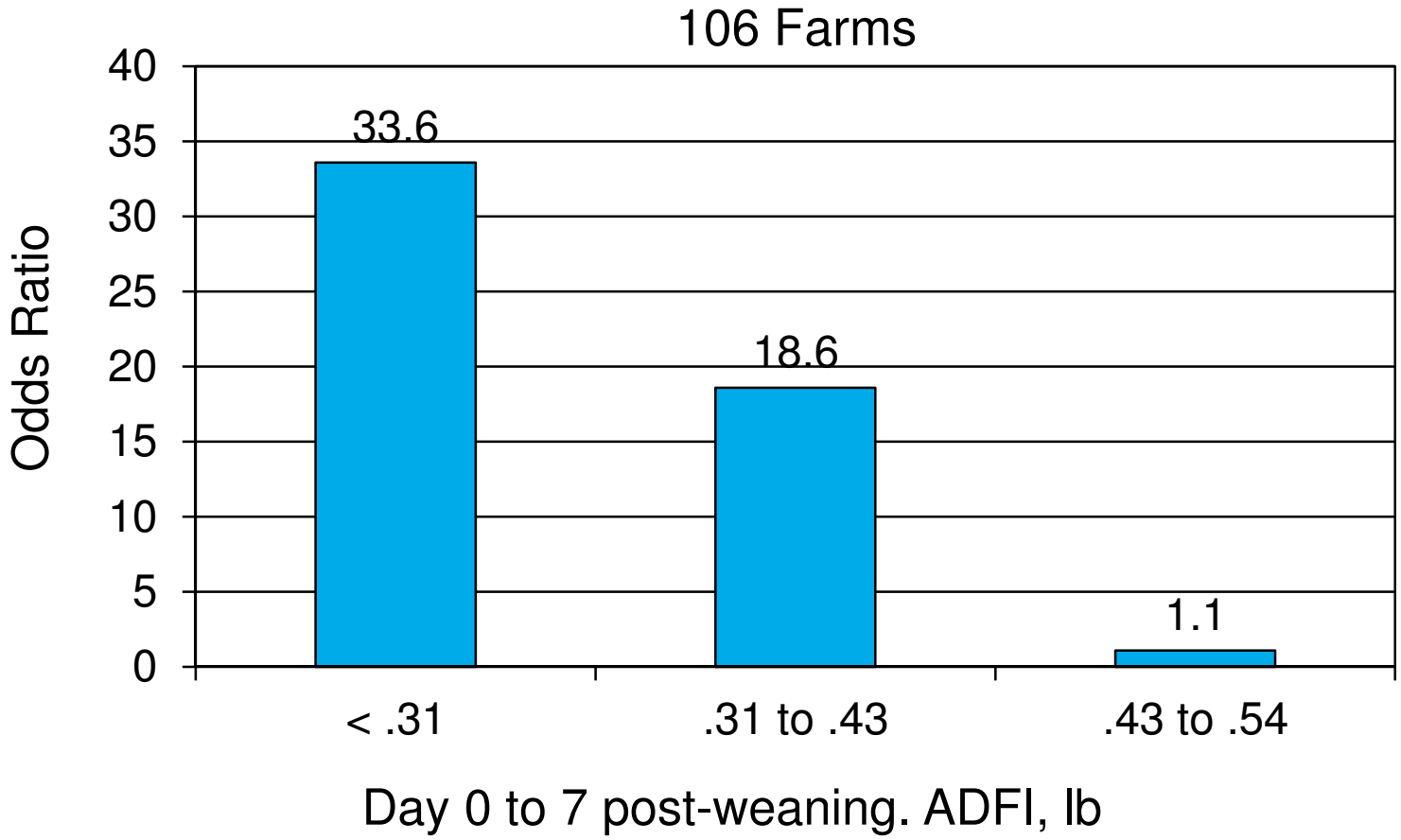




Other variables

DAILY DECISIONS

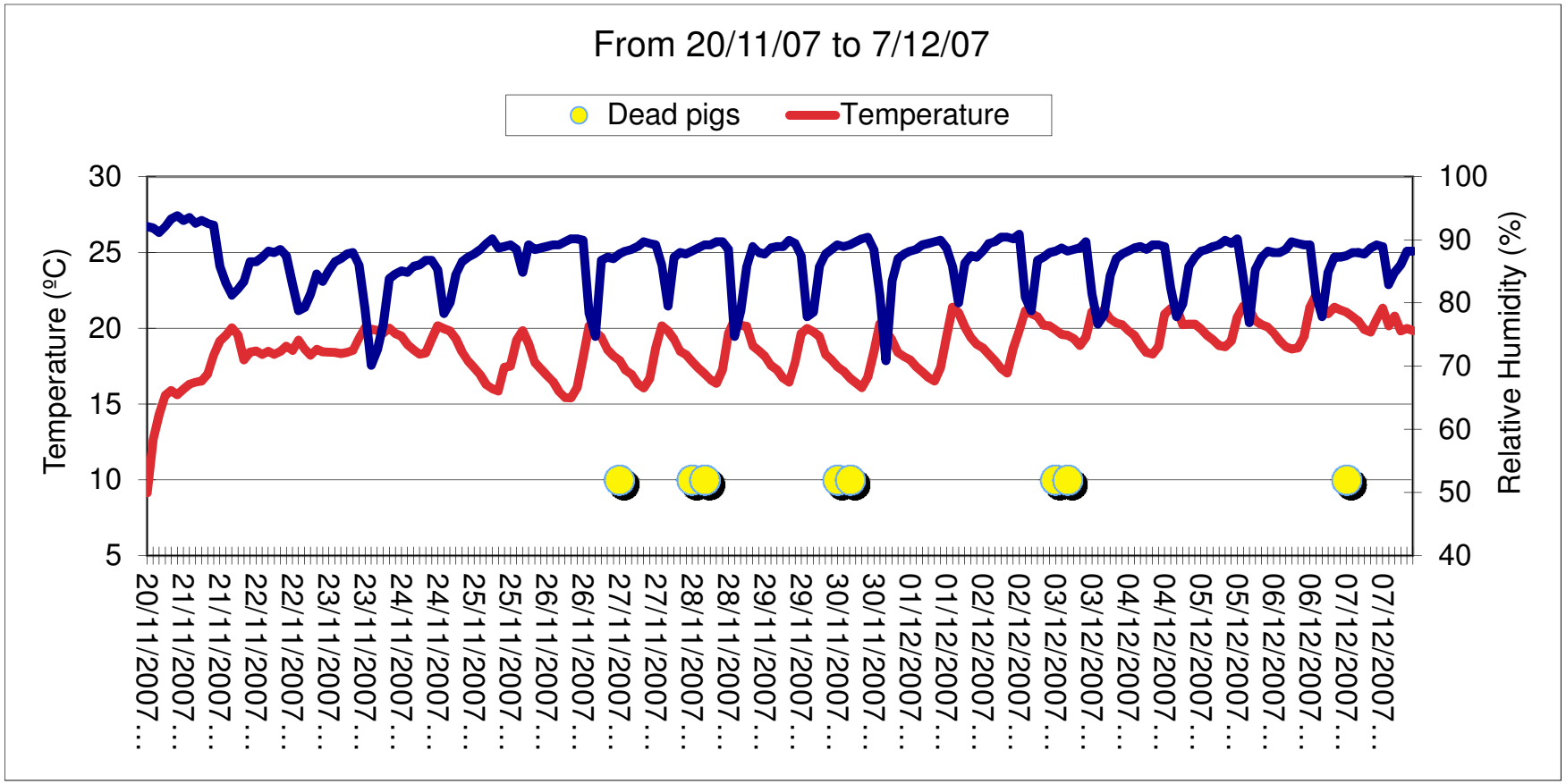
Relation between low feed intake first week after weaning and and diarrhoea



Madec et al., 1998



Temperature and problems



Good hygiene





Good hygiene

Pen Floors			Enterobacteriaceae[a]				Salmonella[b]			
			Before washing		After washing		Before washing		After Washing	
Category	Farm	Samples Tested (n)	Range	Median	Range	Median	Positive samples (n)	Range	Positive samples (n)	Range
3	A	64	1.7-6.6	4.5	0-5.8	0.8	–[c]	–	–[c]	–
High 2	B	64	3.5-6.1	4.6	0-1.6	0	–[c]	–	–[c]	–
High 2	C	72	0-5.1	1.2	0-1.6	0	1	1.1	–[c]	–
1	D	84	2.6-6.1	4.6	0-3.6	0.8	26	36->106	1	7.2
1	E	84	0-3.6	1.6	0-3.2	0	–[c]	–	–[c]	–
1	F	60	1.2-5.1	3.3	0.7-4.2	2.9	–[c]	–	–[c]	–
1	G	72	0-6.0	2.0	0-3.6	0	–[c]	–	1	0.36
1	H	48	0.8-4.2	3.7	0.7-4.1	2	–[c]	–	–[c]	–

Table 1. Effect of cleaning procedure on levels of *Salmonella* and *Enterobacteriaceae* on the pen floors. [a]Log10 cfu/cm^2. [b]MPN/cm^2; detection limit, 0.36 MPN/cm^2. [c]Negative for *Salmonella* (detection limit, <0.36 MPN/cm^2).

Mannion, C. *Et* al. 2005. *The efficacy of cleaning and disinfection on pig farms.* Safepork 2005

Good hygiene

Feeder/Drinker Units			Enterobacteriaceae[a]				Salmonella[b]			
			Before washing		After washing		Before washing		After Washing	
Category	Farm	Samples Tested (n)	Range	Median	Range	Median	Positive samples (n)	Range	Positive samples (n)	Range
3	A	16	3.0-5.6	4.4	2.4-6.8	5.2	–[c]	–	1	4600
High 2	B	16	3.7-5.7	5	0.7-6.8	5.6	–[c]	–	3	11-240
High 2	C	24	0-6	2	2.0-6.0	5	–[c]	–	–[c]	–
1	D	27	3.7-6.1	5.5	0-6.1	4.9	6	0.92-105	2	0.6-7.2
1	E	36	1.5-4.9	3.4	0-5.5	3	–[c]	–	–[c]	–
1	F	24	0.5-4.9	3.5	3.2-5	4.4	–[c]	–	–[c]	–
1	G	24	0-5..5	2.8	0-4.1	2.8	–[c]	–	–[c]	–
1	H	20	3.4-4.9	3.9	3.3-6	4	–[c]	–	–[c]	–

Table 2. Effect of cleaning procedure on levels of *Salmonella* and *Enterobacteriaceae* in feeder/drinker units
[a]Log10 cfu/cm^2. [b]MPN/cm^2; detection limit, 0.36 MPN/cm^2. [c]Negative for *Salmonella* (detection limit, <0.36 MPN/cm^2).

Mannion, C. *Et* al. 2005. *The efficacy of cleaning and disinfection on pig farms.* Safepork 2005



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Neddle transmision

- PRRS infected pigs and non infected vaccinated against *M. hyo* with the syringe.
- 2 out of 4 trials PRRS was transmitted in 100% of negative pigs.



S. Otake et al. Vet Rec. 2002, 150(4):114-115.

Facilities



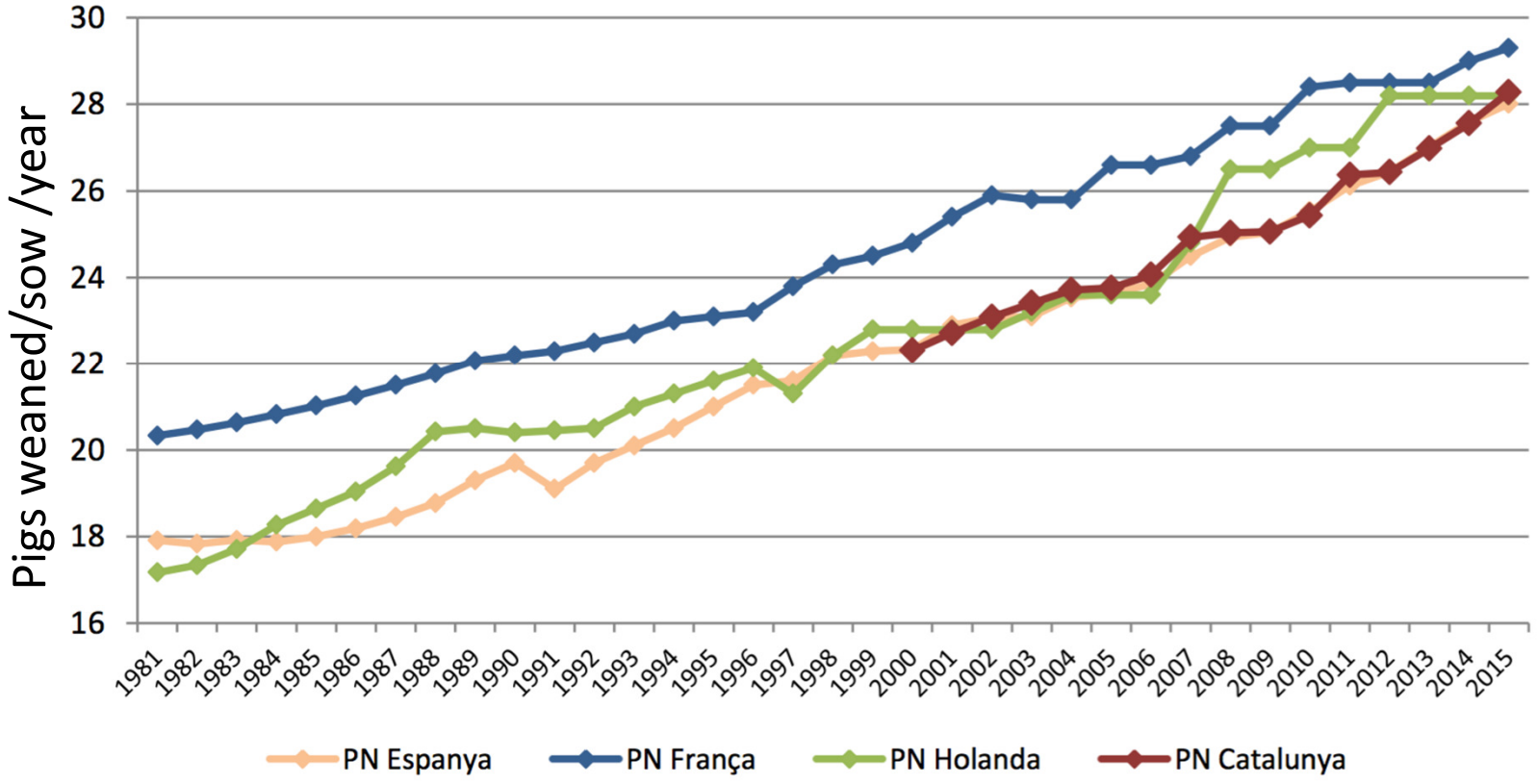
All in - all out

Differences between AI-AO and continuous flow

Parameter	AI- AO.	CONTINUOUS
Mortality (%)	1,8	3,4
ADWG (g/day)	548	512
FE	3,84	4,1

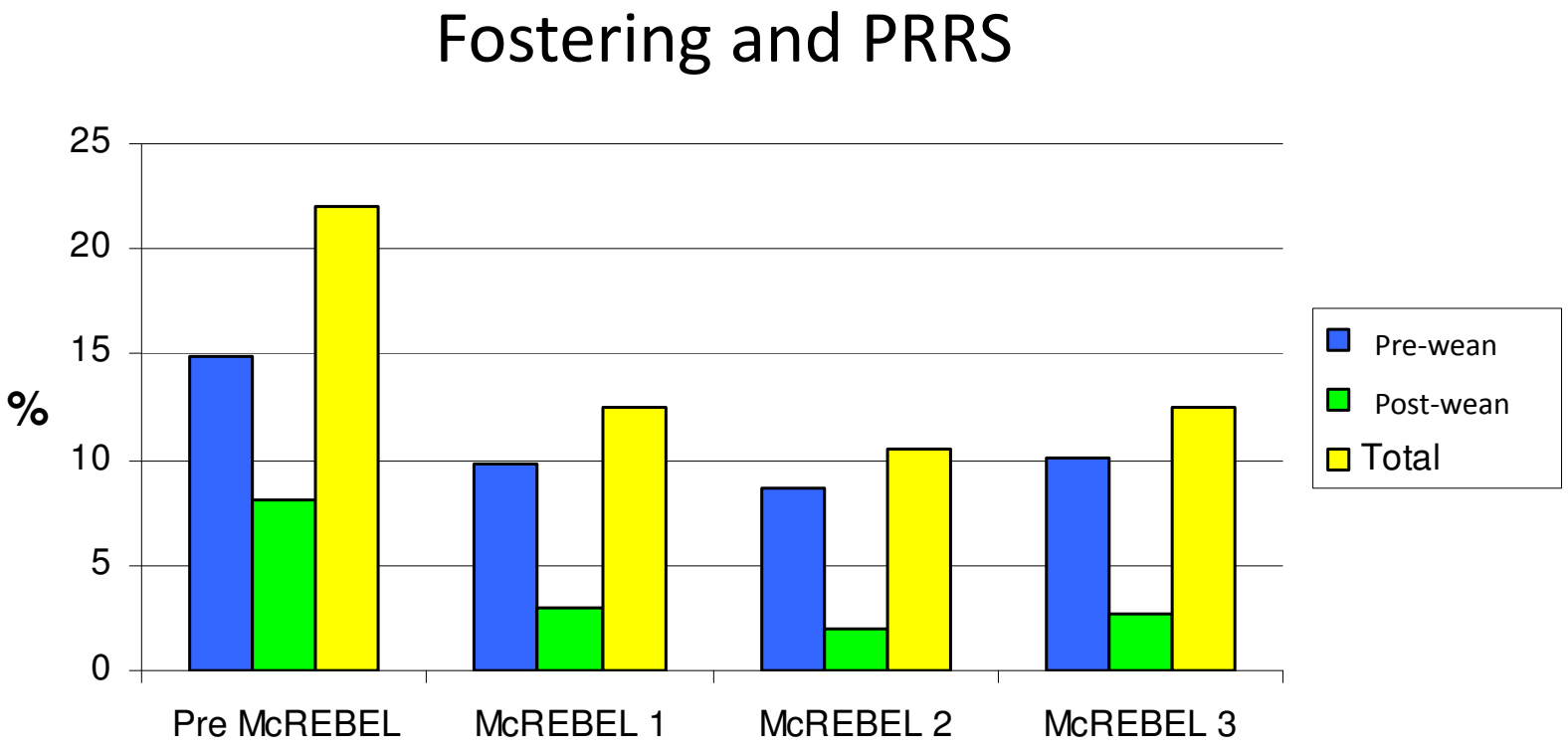
Jourdaum, 1972

Production (weaned/sow/year)



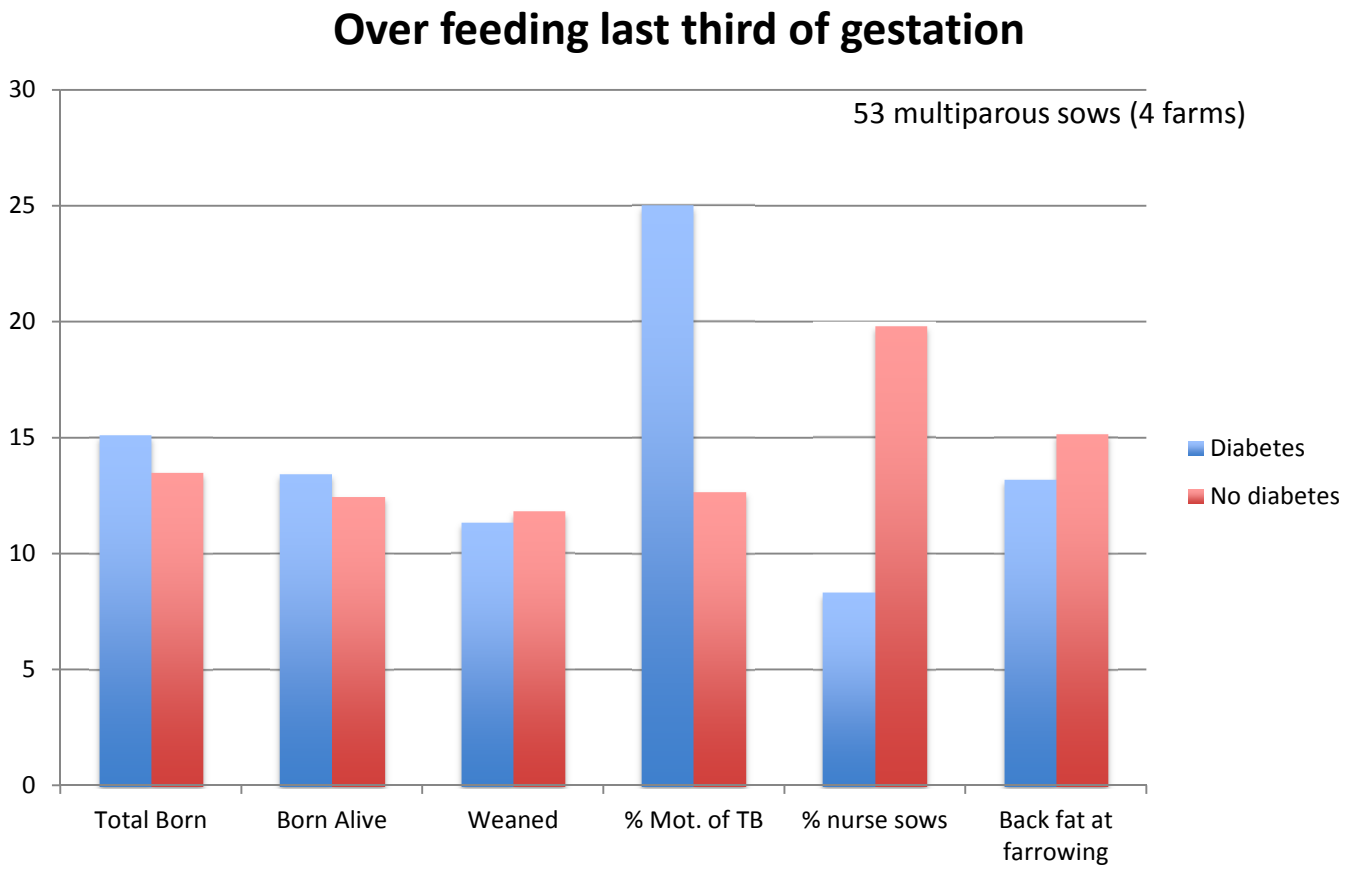
Grup de Gestió Porcina UdL. Informe Anual 2015

Management



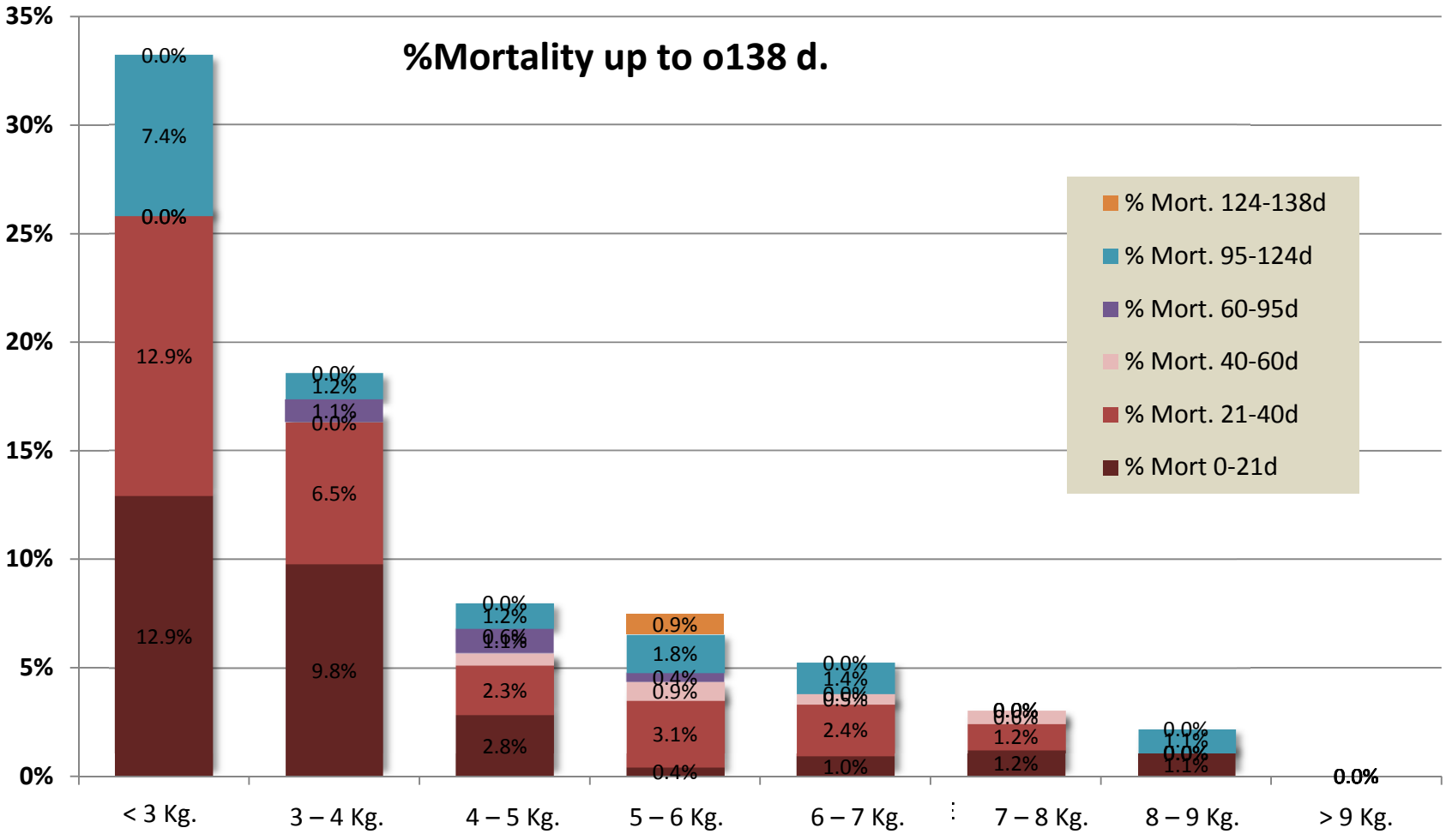
Monte B.McCaw, 1999

Feeding last weeks of gestation



L. Flores and J. Mayol, 2014

Influence of weaning weight



Vall Companys private trial, 2014 (1009 animals).



Conclusions

- Daily decisions have to be taken in any aspect of swine health and production.
- Good advise in management, feeding, facilities, environment and hygiene would be crucial.

THANK YOU