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## Exploring the link between poor welfare, production diseases, antimicrobial usage and resistance on Irish pig farms (WELPIG)



### Key external stakeholders:

Policy makers (DAFM, DOH), veterinary/public health officials/inspectors, pig farmers/IFA, private pig veterinarians, Bord Bia, pig meat processors, pig advisors, veterinary practitioners and animal scientists.

### Practical implications for stakeholders:

There is no foundation to the belief of pig producers that antibiotic (AB) use is essential to protect pig welfare. Environmental/management factors such as repeated re-mixing and a failure to adhere to biosecurity practices had a stronger influence on pig welfare than AB use. Such management deficiencies had negative implications for pig welfare, health and performance and were associated with AB use. Comprehensive investigation of AB resistance at a molecular level on one farm with high levels of AB use revealed potential risks to public health. Many resistance and virulence genes that may be transmissible to human and animal pathogens were detected, some of which were identified for the first time in pigs. Further work is necessary to quantify the extent of these risks. Importantly, improving management strategies offers huge potential to reduce AB use. Indeed high feed prices combined with poor pig prices means that good herd management and high welfare standards have never been more important to maximise efficiency and profitability of pig units. However, as this project identified strongly held misconceptions about pig welfare among some members of the pig industry, it is essential that all stakeholders work together to bring about positive changes for pig welfare while addressing animal and public health concerns.

### Main results:

Pig farmers' background, education level and type of communication/network influenced their use of AB. They considered that there is a lack of proper communication among stakeholders (e.g. farmers, vets and advisors) and that there was a need for reliable people from whom they could get advice on AB use. Pig farmers' attitudes to animal welfare and related practices (e.g. euthanasia, use of hospital accommodation etc.) were identified as potential barriers to the adoption of practices consistent with prudent AB usage. Ultimately, many pig farmers strongly believed that AB use was essential to protect pig health and welfare. However, an on-farm study revealed minimal effects of removing prophylactic AB from weaner diets on the overall performance, health and welfare of pigs from weaning to slaughter with the exception that a greater likelihood of ear lesions was found in pigs without AB in their diet, suggesting that AB have a protective effect on this welfare lesion. Most of the welfare conditions investigated were more strongly influenced by environmental and management factors than whether or not AB were used. In a second on-farm study, pigs not managed according to 'all-in/all-out' (AIAO) were 3 times more likely to be lame prior to slaughter, to have pleurisy, pericarditis and heart condemnations at slaughter and to have lower carcass weights (c. 10 kg less) as well as welfare problems. However, healthy, thriving/fast growing pigs managed according to correct AIAO practices were those at highest risk of having lesions indicative of poor welfare (i.e. tail, ear and body lesions), possibly due to increased competition between animals in this group.

Human infections with *E. coli* and other enteric bacteria resistant to ABs in the carbapenem group (CPEs) were declared a public health emergency in Ireland in 2017. CPEs were not detected in any pig samples during this study although carbapenemase genes were detected in bacteria other than *E. coli*. ESBL-producing *E. coli* are another type of resistant organism that produces infections in both animals and humans that are difficult to treat. ESBL-producing *E. coli* were detected in one pig farm but the levels of these organisms in faeces decreased as pigs grew and moved through the production cycle. Overall, findings on the intensively studied farm showed that there was a decrease in resistance genes and the genetic elements associated with the spread of resistance two weeks before slaughter, which is an important positive finding

for public health. One *E. coli* isolate (serotype O155:H21) sampled from a farrowing pen carried the genes *stx2a* and *stx2b*, both associated with food-borne diarrhoea but never previously described in pigs.

#### Opportunity / Benefit:

- Few negative effects of removing in-feed AB were found on the overall performance, health and welfare of pigs from weaning to slaughter. This finding can be used to encourage pig producers to reduce and ultimately withdraw AB from pig diets
- From a practical perspective, managing a population of pigs coming from the same batch is not easy to do on most Irish farms. However, different management approaches can be developed for pigs with different requirements (i.e. in different 'flows') to improve pig health and welfare and thereby reduce the need for AB
- The social science work suggests that there are opportunities to implement initiatives among stakeholders in the Irish pig sector (e.g. workshops etc.) to increase knowledge and 'buy-in' on pig welfare issues and on appropriate management practices to maximise pig health and welfare and for more prudent AB use
- The findings raise concerns for the health and welfare of the national pig herd as there was evidence of mismanagement of pigs and of imprudent AB usage as well as high incidences of welfare lesions and pathologies at slaughter. This is of societal relevance and also raises concern at a wider level because of the threat of antimicrobial resistance (AMR)
- The pilot studies on mechanisms of resistance associated with critically important antimicrobials provide a basis for future much needed work in this area

#### Collaborating Institutions:

##### Teagasc project team:

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Ms. Alessia Diana (PhD Walsh Fellow)

##### External collaborators

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#### Project background:

Intensification in the Irish pig industry has been accompanied by larger herd sizes, low labour and barren, densely populated environments that facilitate the spread of disease. In addition, genetic selection has seen higher metabolic rates and new physiological settings (e.g. higher growth/lean deposition rate, increases in litter size etc.). Such changes place huge stresses on the pigs' ability to cope reflected in growing health and welfare problems. Indeed, damaging behaviours (i.e. tail and ear biting) and the associated lesions are considered major welfare issues in intensive pig production systems as are production diseases such as lameness, enteric and respiratory disease. Unsurprisingly, there has been a concurrent increase in the use of antibiotics (AB) which were viewed as the most effective way of controlling these health and welfare challenges. This reliance on AB is thought to mask housing and husbandry deficiencies and to be associated with the risk of AMR which poses a global threat to human and animal health. There are also important social and cultural factors driving AB use by pig producers. Addressing this challenge is hampered by the dilemma for pig production which is driven by narrow profit margins and the demand for cheap food on one side and regulatory requirements for food safety, animal welfare and environmental protection on the other. The recent EU proposal to ban the prophylactic use of AB (Anon., 2016) further complicates this dilemma and means that there is an urgent need to explore the implications of such a ban for the pig industry.

AMR poses a complex threat to the human-animal-environment interface. Global use of AM in human medicine, veterinary medicine and plant agriculture compromises AM efficacy worldwide. Over the past decades, following the introduction of AM, the number of resistant bacteria causing infection in human and animal settings has increased significantly, challenging physicians and veterinarians. The complexity involved in the emergence and dissemination of AMR due to the interaction between humans, animals and the environment needs to be addressed by researchers, medical professionals, policy makers and society. AMR is the quintessential One Health problem that needs to be addressed with a holistic approach. There is a lack of knowledge on AMR in Irish pig populations and particularly on mechanisms of resistance associated with critically important antimicrobials (CIA).

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#### Questions addressed by the project:

- What effects does the withdrawal of prophylactic, in-feed antibiotics have on pig health, welfare and performance from weaning to slaughter?
- Is there an association between on-farm management practices and pig health and welfare on

commercial farms?

- What are the underlying social, cultural and attitudinal factors driving Irish pig farmers use of AB?
- What is the impact of using CIA in piglets (according to veterinary practices in Ireland) on pig farms with no history of previous use?
- What are the mechanisms of resistance associated with critically important antimicrobials (CIA) on Irish pig farms?

#### The experimental studies:

WELPIG employed a combination of qualitative (social science) and quantitative (epidemiological and controlled) animal/veterinary science based studies all of which were conducted on commercial pig farms in Ireland. We conducted semi-structured interviews with 30 pig farmers, four farm staff focus groups and five pig veterinarians after which a qualitative analysis of the transcribed data led to the identification of 7 convergent themes driving AM use namely: concept of pig welfare, concept of best practice, perceptions about legislation, perceptions about AM use on farm, communication/network, economics and culture. Studies were carried out on two commercial farms with intensive AB use: 1) in-feed AB were either maintained in the diet of pigs post-weaning or removed; 2) a batch of c. 1000 pigs was retrospectively classified into 3 production flows according to the time they took to reach slaughter. Effects on health and welfare indicators and performance were measured in pigs both during the production cycle and at slaughter in both studies. A cross-sectional study was conducted investigating the molecular features of *E. coli* and *Acinetobacter* species sampled in a pig farm positive for ESBLs (extended spectrum beta-lactamases), using whole genome sequencing technology. A longitudinal study (from farrowing (D0) to 2 weeks before slaughter (D133)) was performed in a commercial pig farm with ESBL-producing *E. coli*. The effect of medicating piglets with a 3rd generation cephalosporin injection was also investigated on a farm with no previous use of 3rd generation cephalosporins using conventional and molecular methods.

#### Main results:

- There was an initial difference in growth between pigs with and without AB in their diet with 'AB pigs' being heavier than those without ('NO pigs') during the first weaner stage;
- Variation in performance traits was not significantly different at the end of the 2<sup>nd</sup> weaner and finisher stages and there was no effect on health indicators collected on-farm and at slaughter;
- NO pigs received almost double the amount of injections than AB pigs during the weaner stage; this difference disappeared at finisher stage; removal of in-feed AB represented a 97% reduction in AB use;
- AB pigs performed more fighting behaviour and were more likely to have tail lesions compared to NO pigs potentially attributable to increased competition for access to feed, higher growth rates and associated lower space allowance;
- AB pigs had a lower likelihood of having ear lesions as a result of biting compared to NO pigs, perhaps due to a curative effect provided by the in-feed AB;
- Pigs repeatedly delayed from the normal production flow on-farm (i.e. Flow 3 pigs) were <10 kg lighter prior to slaughter, had more health (higher likelihood of lameness, pericarditis, pleurisy and heart condemnation) and welfare problems than flow 2 pigs (pigs delayed only one week);
- Flow 1, pigs which adhered to an AIAO system of management, had higher performance and fewer health problems but were at greater risk of having welfare issues (i.e. ear, tail and body lesions) compared to flow 2 and 3 pigs;
- 7 major themes were identified driving AM use by pig producers namely: concept of pig welfare, concept of best practice, perceptions about legislation, perceptions about AM use on farm, communication/network, economics and culture;
- The concept of animal welfare and perceptions about best practice were identified as new factors influencing farmers' motivation to use AB. Farmers generally believe that use of in-feed AB represents best practice in preserving pig welfare;
- Irish pig vets considered pig advisors as competitors between themselves and the farmers in terms of providing advice and this conflict could prohibit a team approach to solving problems on farm;
- Pig farmers considered that there was a lack of proper communication among stakeholders (e.g. farmers, vets and advisors) and that there was a need for people whom they, the farmers, considered reliable when seeking advice;
- Quantitative analysis conducted on data obtained through a questionnaire provided to pig farmers revealed that factors such as background (P=0.02), education level (P=0.09) and type of communication/network (P=0.05) were associated with the use of AB;
- Pig farmers' attitudes to animal welfare and related practices (e.g. euthanasia, use of hospital accommodation, etc.) were identified as potential barriers to the adoption of practices consistent with

prudent AM usage;

- Carbapenemase encoding genes were not detected in *E. coli* although some isolates appeared resistant to carbapenams when cultured; The ESBL gene *bla*<sub>CTX-M-107</sub> was detected in *Acinetobacter* while the genes *bla*<sub>CTX-M-33</sub>, *bla*<sub>CTX-M-55</sub> and *bla*<sub>TEM-4</sub> were detected in *E. coli*;
- A single *E. coli* isolate (serotype O155:H21) sampled from a farrowing pen carried *stx2a* and *stx2b*, virulence genes associated with food-borne diarrhoea but never previously described in pigs;
- No carbapenem-resistant *E. coli* were identified in a commercial pig farm with ESBL-producing *E. coli* however the genes encoding the carbapenemases *bla*<sub>NDM</sub> and *bla*<sub>GES</sub> were detected in pig faecal DNA; the public health significance of this finding is currently unclear.
- Levels of Cefotaxime-resistant *E. coli* (CefRE) reduced throughout the production cycle with few animals shedding CefRE by 2 weeks before slaughter;
- Cefotaxime-resistant *E. coli* were not detected on a pig farm which medicated piglets with a 3<sup>rd</sup> generation cephalosporin injection however, molecular techniques (qPCR array) detected  $\beta$ -lactamases CTX-M, CMY-2, AmpC and NDM in pig faecal DNA;
- Additionally, there was no increase in the levels of the resistance genes AmpC and CMY-2 in faecal DNA obtained from animals injected with ceftiofur (a critically important antimicrobial, CIA) when compared to control group piglets.

#### Opportunity/Benefit:

- WELPIG is a good example of the efficacy of multidisciplinary approaches to research questions;
- An ESBL-positive farm allowed us to investigate in detail the presence of  $\beta$ -lactamases and mobile genetic elements throughout the production cycle; there was a reduction in cefotaxime-resistant *E. coli* shed by pigs at the end of production cycle which is relevant for public health;
- Findings suggest that it is possible to use ceftiofur on a naïve farm without selecting for AMR traits associated with the use of ceftiofur, although further studies are essential to investigate if other management practices, during the production cycle, affect the shedding of cefotaxime-resistant *E. coli*;
- Some of the findings of the AMR work suggest that factors other than AM use may provide selective pressure and promote the emergence and spread of AMR. Thus, there is scope to expand research on AMR to different disciplines including areas such as microbial endocrinology;
- Faecal community DNA was investigated to gather information on the role of non-culturable bacteria in the spread and emergence of AMR however, further studies targeting the community DNA are needed to allow comparison with our findings;
- Greater understanding of the miscommunication between stakeholders could help to develop efficient intervention strategies for the promotion of responsible AB use;
- These findings can also be used to inform the development of Irish policies regarding AB use and to design appropriate education strategies for people working in the pig industry;
- Good health and performance are not necessarily synonymous with good welfare for pigs; this is a novel finding which highlights the complexity and multifactorial nature of animal welfare problems;
- There is huge potential for more targeted prophylaxis and possibly reduced AB use through training, education and improved management practices on farms leading to improved health and welfare of the national pig herd which will also enhance the country's marketing image;
- The decrease in AMR genes and MGEs associated with AMR on a commercial pig farm two weeks before slaughter is an important positive finding for public health.

#### Dissemination:

##### Main scientific publications:

A. Diana, E.G. Manzanilla, J.A. Calderón Díaz, N. Leonard, L. Boyle. 2017. Do weaner pigs need in-feed antibiotics to ensure good health and welfare? *PLoS ONE* 12(10): e0185622.

J.A. Calderón Díaz, A. Diana, L.A. Boyle, F.C. Leonard, M. McElroy, S. McGettrick, J. Moriarty, E.G. Manzanilla. 2017. Delaying pigs from the normal production flow is associated with health problems and poorer performance. *Porcine Health Management*. 3:13.

J.A. Calderón Díaz, L.A. Boyle, A. Diana, F.C. Leonard, J. Moriarty, M. McElroy, S. McGettrick, D.J. Kelliher, E.G. Manzanilla. 2017. Early life indicators predict mortality, illness, reduced welfare and carcass characteristics in finisher pigs. *Preventive Veterinary Medicine*. 146: 94-102.

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