An overview of *Klebsiella pneumoniae* septicaemia outbreaks in pigs in England since emergence in 2011

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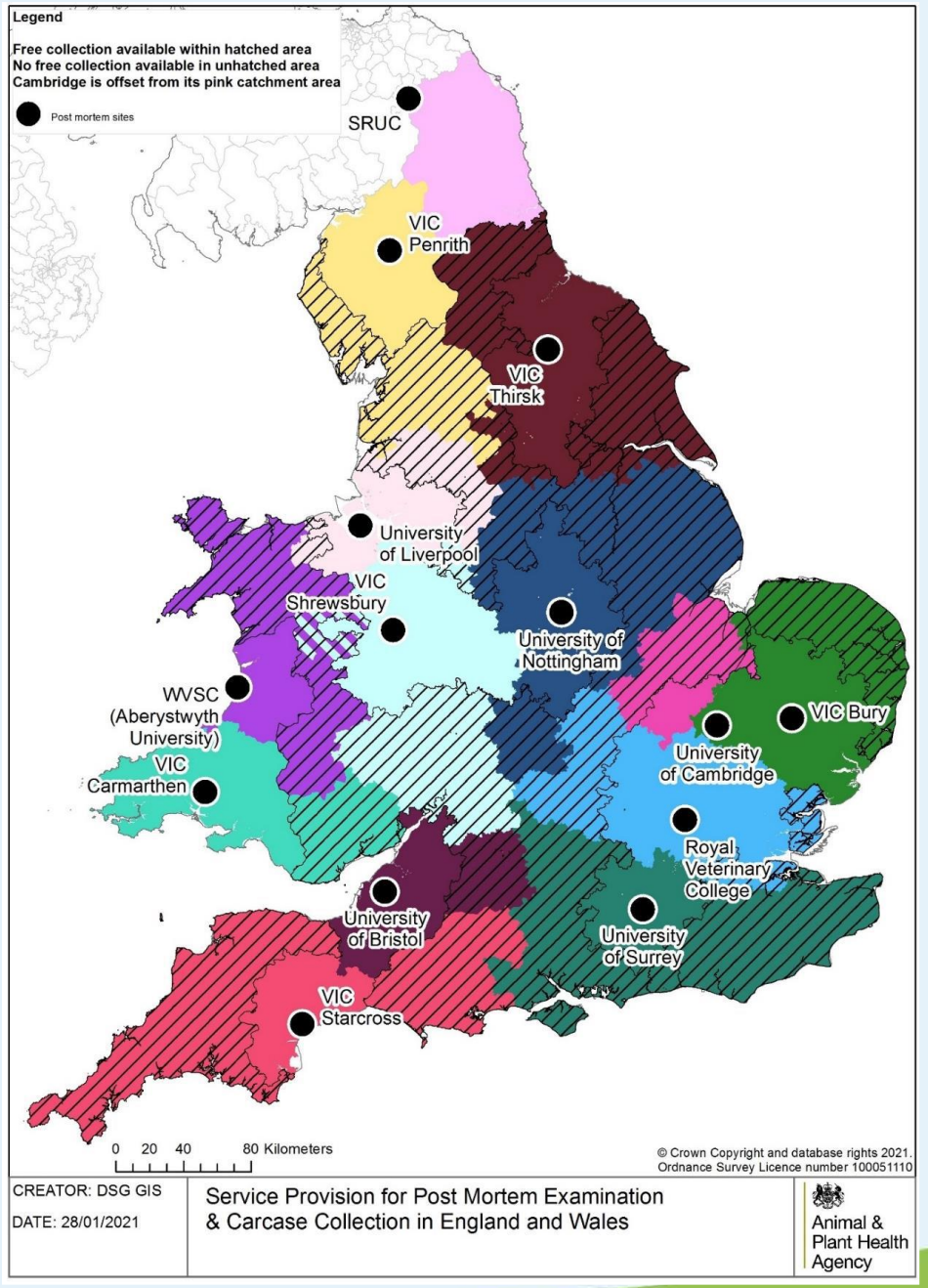
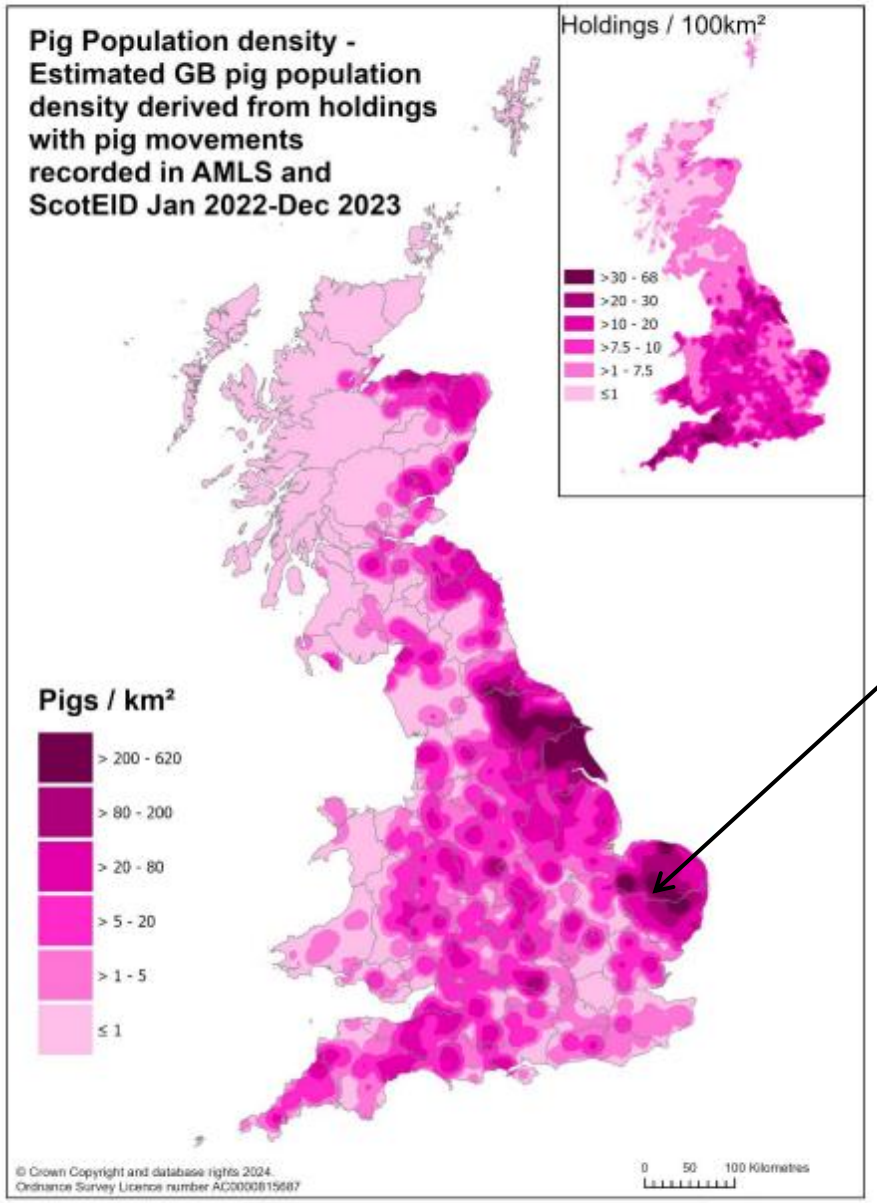
GB Scanning Surveillance Network

- 14 postmortem sites in England and Wales (APHA and surveillance pathology partners)
- SRUC Disease Surveillance Centres in Scotland
- Voluntary diagnostic submissions
- Government subsidises diagnostic submissions
- Free carcase collection (shaded areas)

Regular reports of findings: https://www.gov.uk/government/collections/animal-disease-surveillance-reports

A main aim of Government-funded scanning surveillance is detection of new and (re)emerging animal disease threats





APHA Veterinary Investigation Centre Bury St Edmunds

https://assets.publishing.service.gov.uk/media/674f2908d7e2693e0e47d02f/LDDG_Pig_Population_data_2022-23_published_2024-25_v3_Final.pdf

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July 2011…acute deaths of multiple piglets…. *Klebsiella pneumoniae* subsp *pneumoniae* (Kpp) isolated – an <u>unusual diagnosis</u>

- Kpp considered an opportunistic pathogen in animals and humans
- Gram-negative facultative anaerobic bacterium in the Enterobacteriaceae family
- Non-haemolytic, lactose fermenting mucoid colonies

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Six outbreaks in summer 2011:

- Summer outbreaks
- All well-grown preweaned piglets
- All with septicaemia
- All were in outdoor breeding herds in Eastern England (East Anglia)

case definition + diagnostic criteria established

"Pigs found dead with lesions consistent with septicaemia and pure/predominant growths of Klebsiella pneumoniae subsp. pneumoniae isolated from internal sites in multiple pigs"

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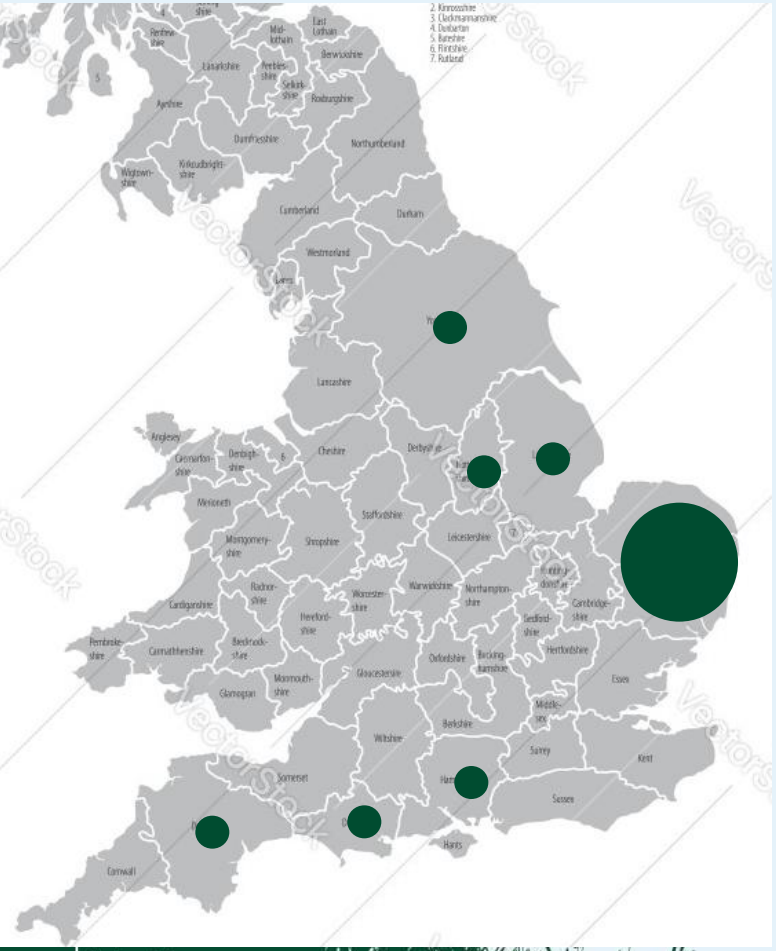
Summary of Kpp outbreaks 2011 to end December 2024



- **68 outbreaks on 54 English farms**
  - @80% farms in East Anglia, others in counties in England
  - 49 are outdoor breeding farms
  - **1 outbreak in Scotland (indoor unit) September 2024**

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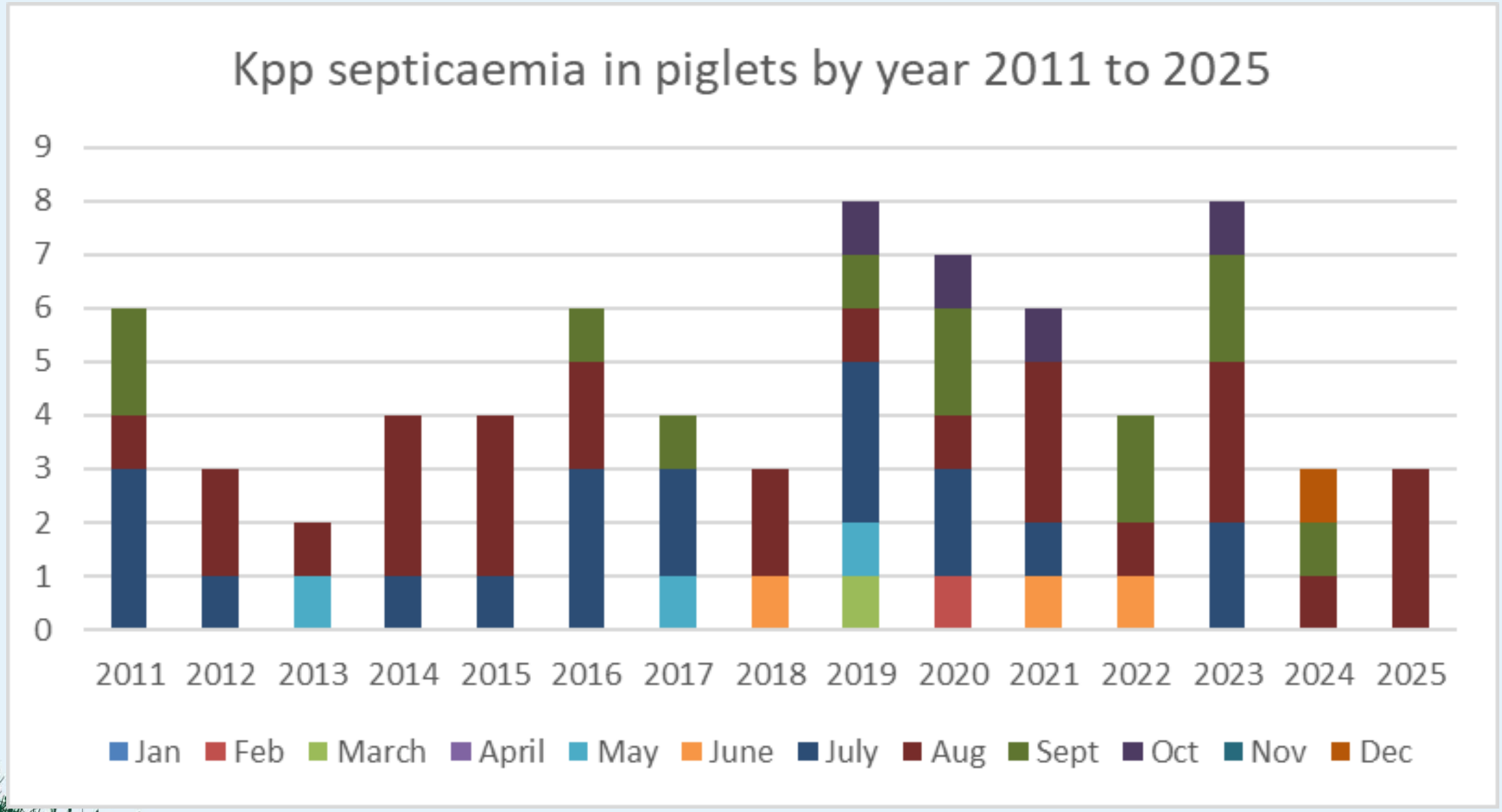

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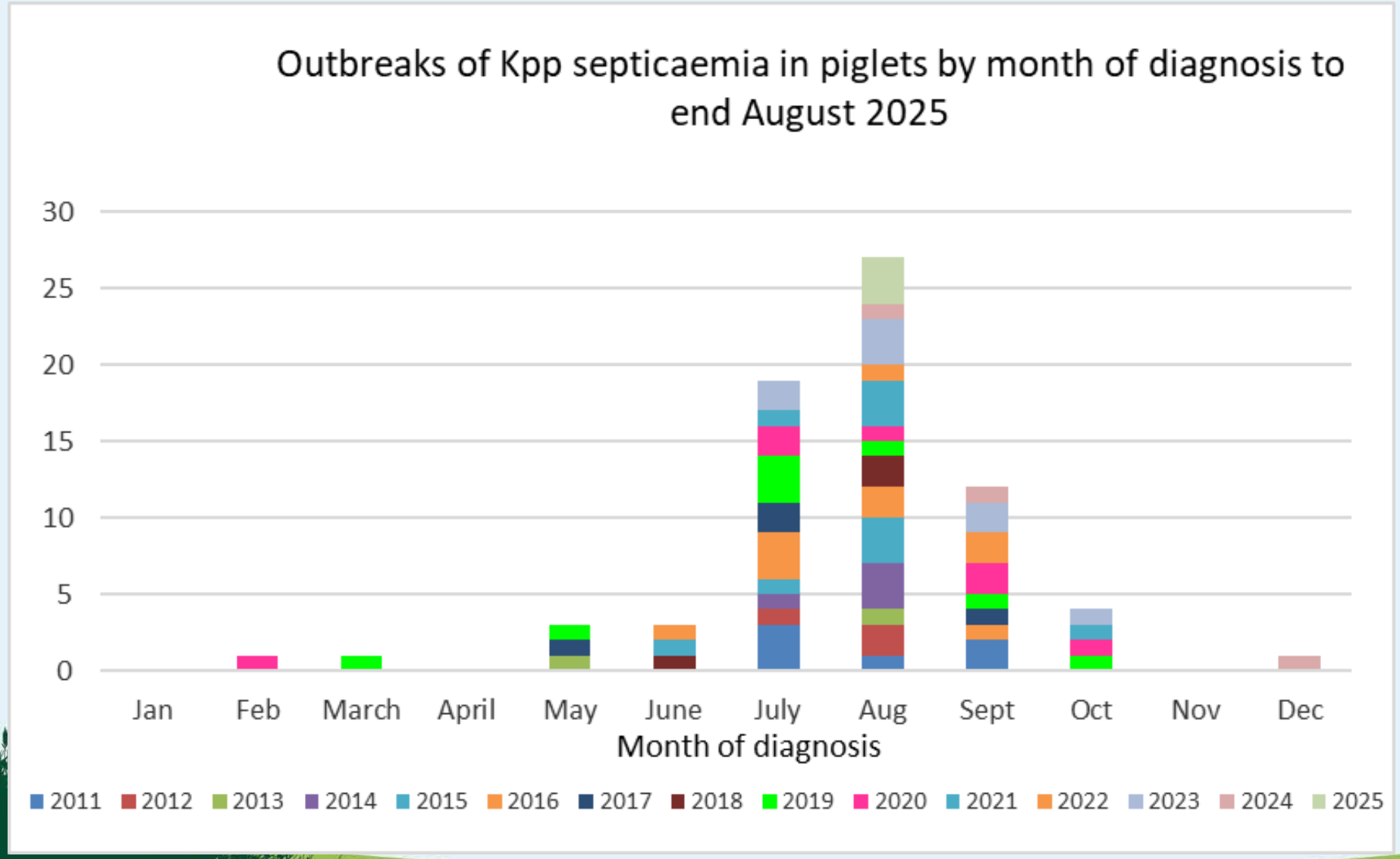
Outbreaks each year since 2011 with a marked seasonal pattern… now endemic in some herds



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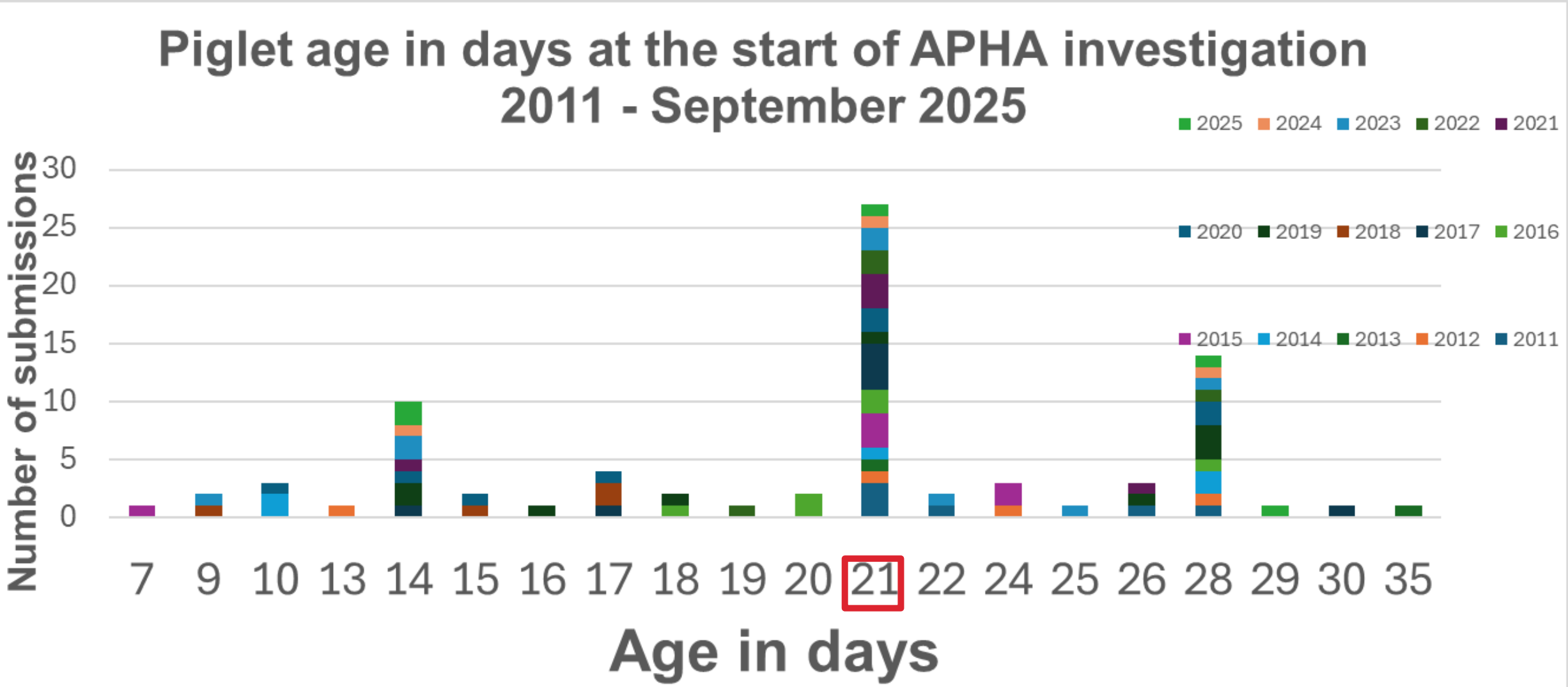

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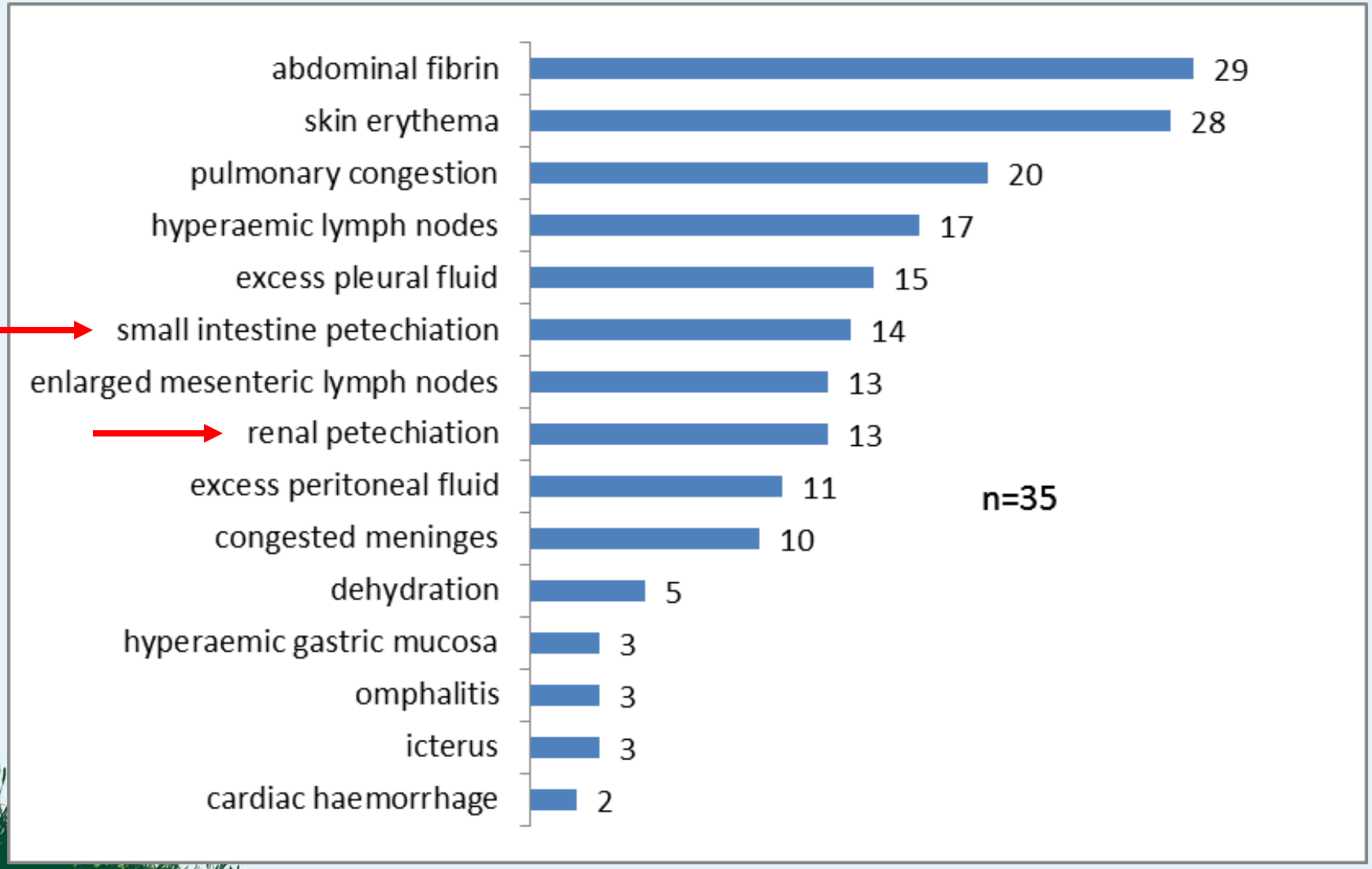
Clinical presentation of *Klebsiella pneumoniae* septicaemia outbreaks

- Predominantly preweaned pigs
- Less commonly first week after weaning
- Age range 7 – 35 days
- Up to 50% of litters with affected piglets (range 8% - 50%)
- Within litter mortality usually less than 50%
- Batch mortality usually less than 5% but up to 16%
- Outdoor breeder herds affected more than indoor
- Seasonal occurrence range February to December mainly May to September
- Duration of outbreaks one day to three months.
- Appears self-limiting, but at least 8 farms have had outbreaks in more than one year
- Pigs in good condition, found dead
- Severe lethargy, moribund rarely
- Lethargy and shaking (due to polyarthritis in one herd)
- Severe sow mastitis with deaths in one herd

Klebsiella pneumoniae septicaemia in pigs
Frequency of gross lesions (2011 – 2015)



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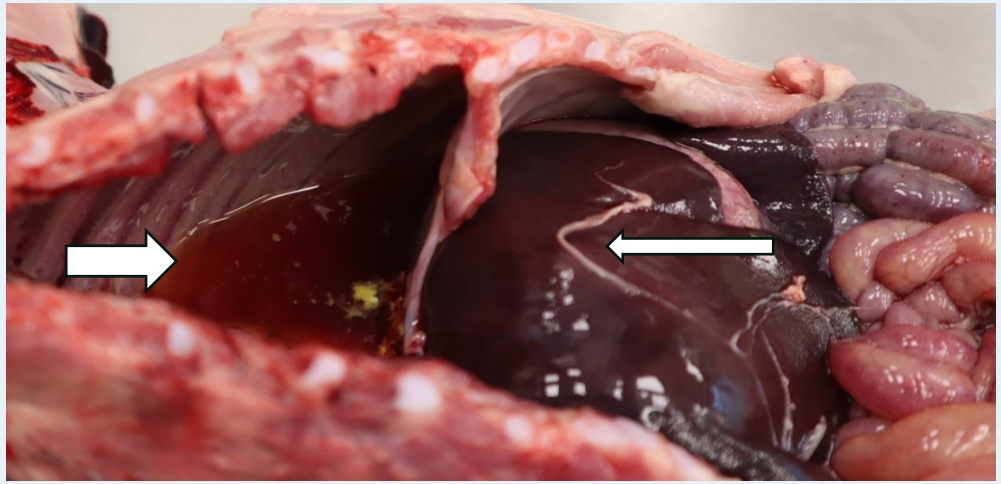
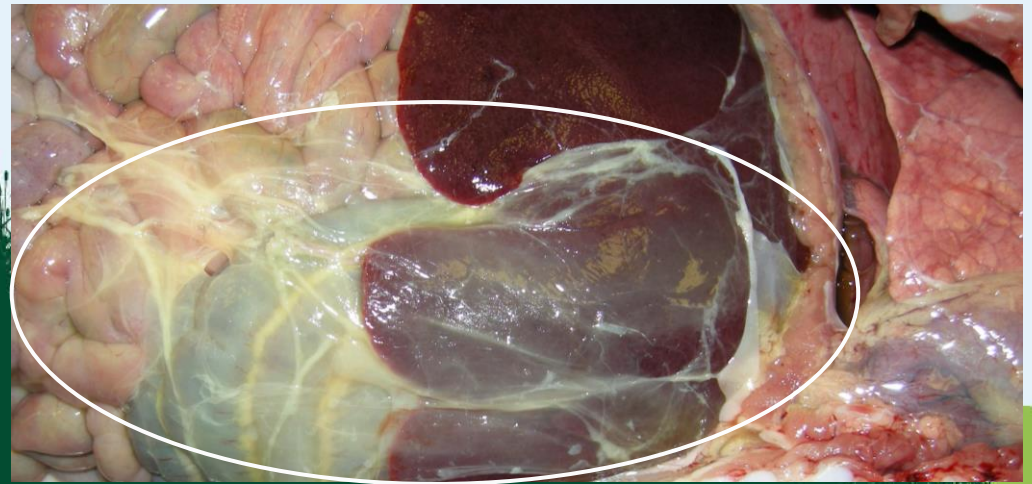
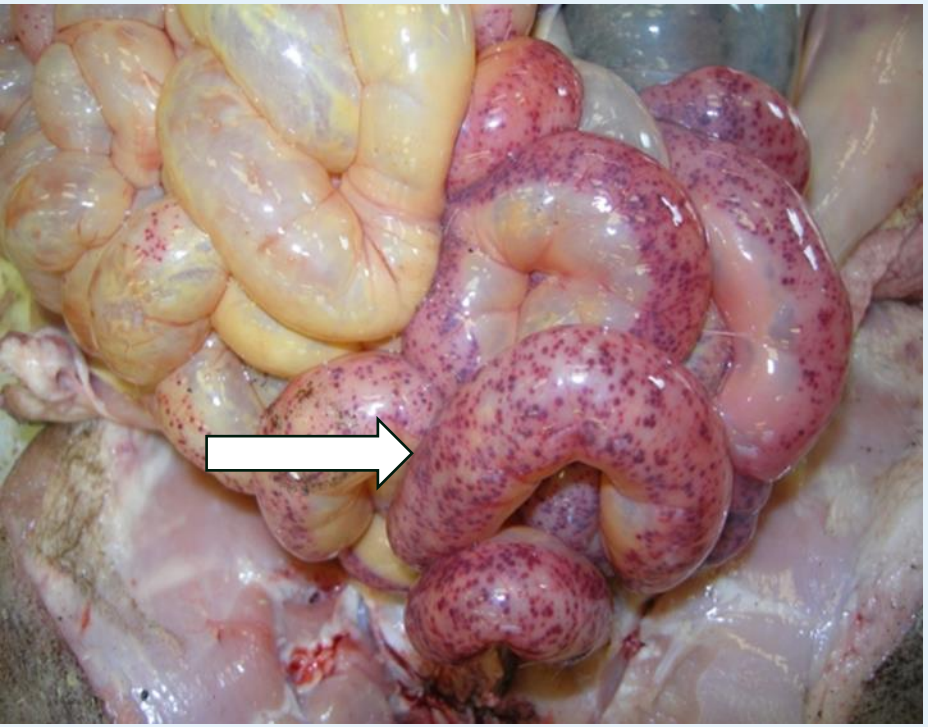
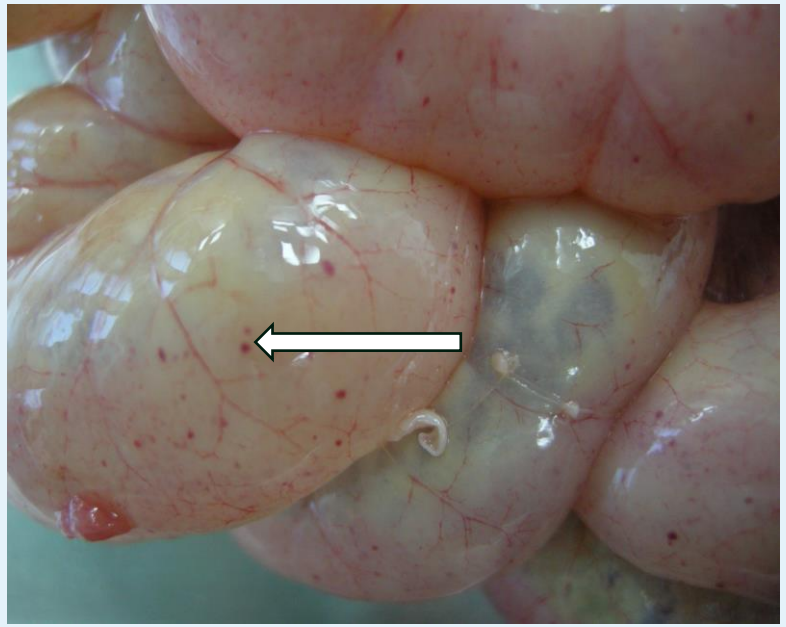
Kpp septicaemia gross lesions

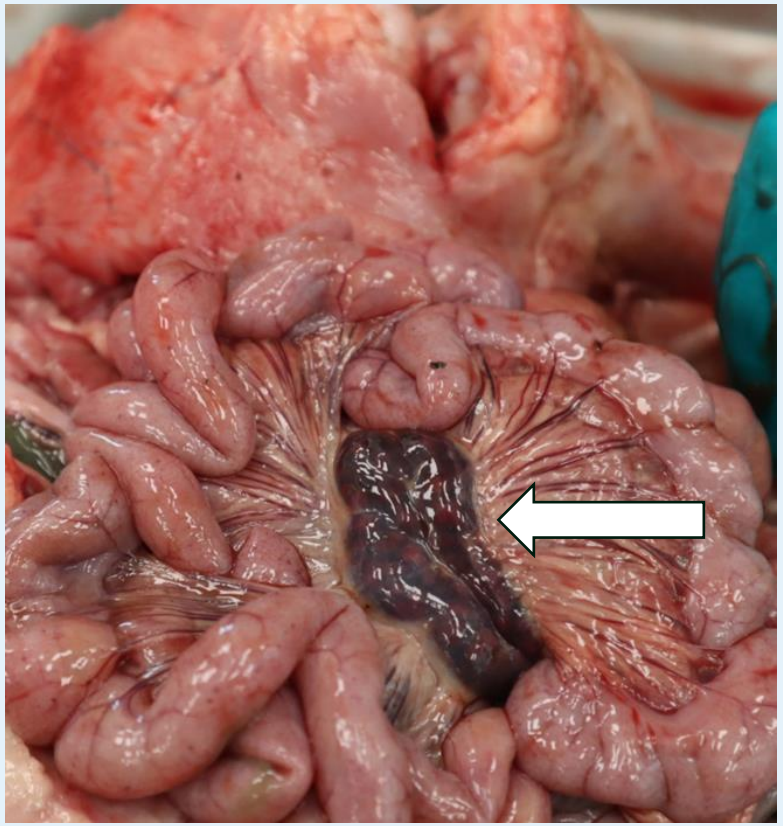
- Skin erythema
- Variable amounts of abdominal fibrin
- Excess serous pleural fluid
- Pulmonary congestion











Jejunum - variable serosal petechiation
Enlarged hyperaemic mesenteric lymph nodes

Klebsiella pneumoniae septicaemia
Good culture sites

- **Meninges**
- **Liver**
- **Lung**

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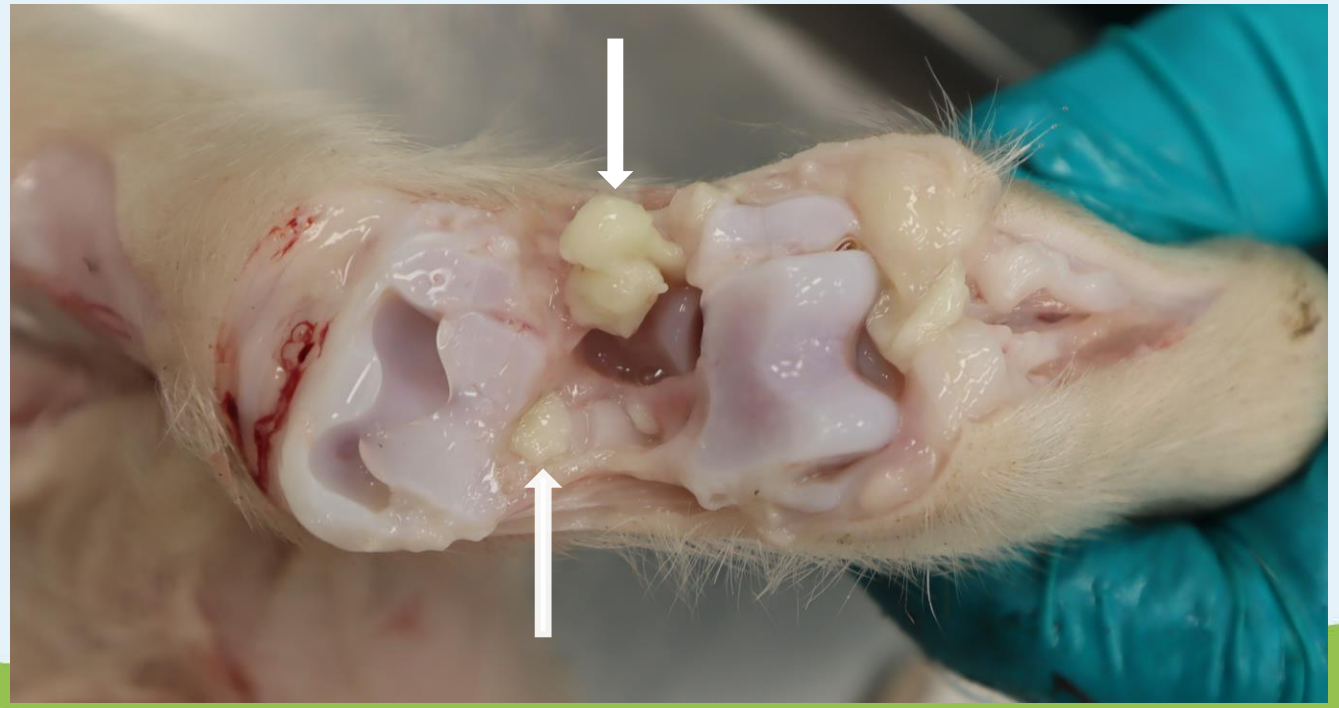
2025 Kpp septicaemia outbreak with unusual presentation

Pigs presented at 7 -14 days old with:

- Found dead
- Diarrhoea
- Few pigs shaking leading to euthanasia
- Mortality at 2 weeks was 12% (piglet batch size 1071)
- Typical Kpp septicaemia diagnosed but also -
- Polyarthritis due to Kpp in a shaking euthanased pig

Fibrinopurulent material in a hock joint due to Kpp (not sequenced yet)



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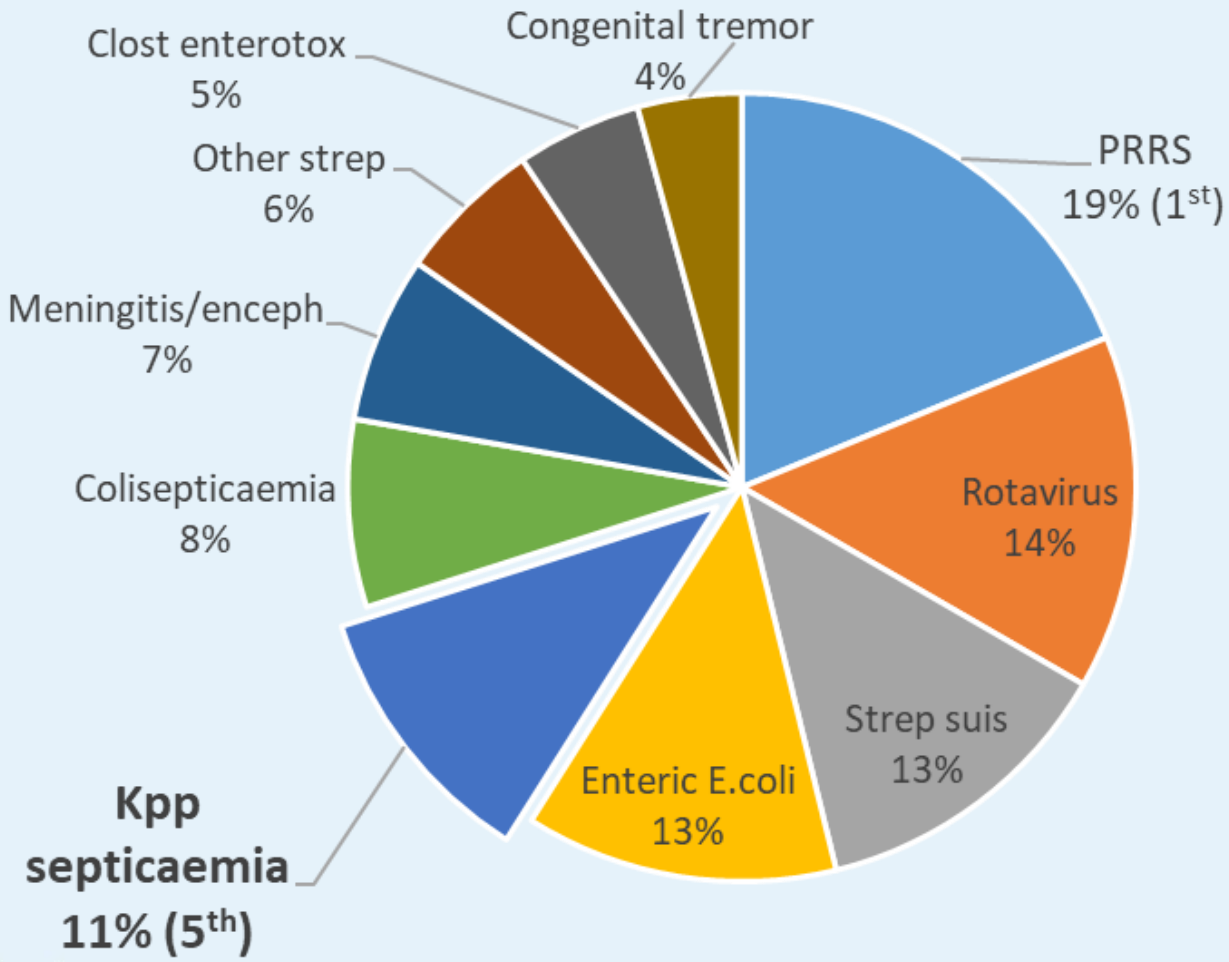
Sow mastitis due to Kpp ST25

Sows

- All farms except one reported that adult pigs were healthy at the time of the outbreak.
- On one farm in 2014 contemporaneous with piglet deaths due to Kpp septicaemia -
- Eight sows had severe acute lethargy, anorexia, purple skin around the perineum, vulva and multiple mammary glands.
- Five sows died from group of 150.
- The cause of mastitis was confirmed as Kpp ST25.
- Affected sows did not necessarily have litters affected with Kpp septicaemia.

Top ten diagnoses of infectious disease in preweaned pigs postmortemed within the GB surveillance network 2022-2023



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Laboratory investigation of Kpp from the 2011 outbreaks

- All outbreak isolates were **sequence type ST25**
- All outbreak isolates carried a small **4kb plasmid**

Kpp isolated from visceral sites are routinely stored (APHA archive)

Outbreak isolates were compared with archived isolates from pigs from 1990 onwards (28 isolates) and contemporary non-outbreak isolates

- No ST25 were identified in archive or contemporary non-outbreak isolates

Value of archives was demonstrated –

Disease due to a <u>new and emerging</u> pathogenic strain of *Klebsiella pneumoniae* in pigs was confirmed

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Emergence of a new and pathogenic strain of *Klebsiella pneumoniae*, ST25, in pigs – evidence and surveillance

- **Surveillance for Kpp ST25 – how frequent in non-outbreak situations at APHA?**

- 2012 – 2013 **frequency of nasal and tonsil carriage** study – diagnostic subs
- no Kpp ST25 identified outside outbreaks

	Nasal	Tonsil
Number tested	199	199
Number Kp positive	36 (18%)	22 (11%)
Kpp ST25	0	0

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Emergence of a new and pathogenic strain of *Klebsiella pneumoniae*, ST25, in pigs – evidence and surveillance

- 2015 **frequency of enteric carriage study using selective culture media**
  - 100% of Kpp outbreak pigs had enteric carriage of Kp ST25
  - 0.3% (1) of pigs without Kp septicaemia carried Kp ST25

	Non-outbreak	Outbreak	Total
Number faeces/intestine	327	9	336
Number Kp positive	49	9	58 (17%)
Kpp ST 25	1 (0.3%)	9 (100%)	10

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Emergence of a new and pathogenic strain of *Klebsiella pneumoniae,* ST25, in pigs – evidence and surveillance

Since 2011 there is ongoing surveillance of porcine Kp isolates.
To the end of 2024:
ST25 has been isolated in non-outbreak situations – mostly as a culture contaminant in cases with an alternative diagnosis (prewean to adults).
ST25 isolated 3 times as the cause of disease but not part of an outbreak
- either only 1 pig submitted or only one of multiple carcases submitted diagnosed with septicaemia (prewean pigs).

- Kp ST25 is present in pigs without septicaemia (probable enteric) but

→ **Not commonly detected in non-Kp outbreak pig submissions**

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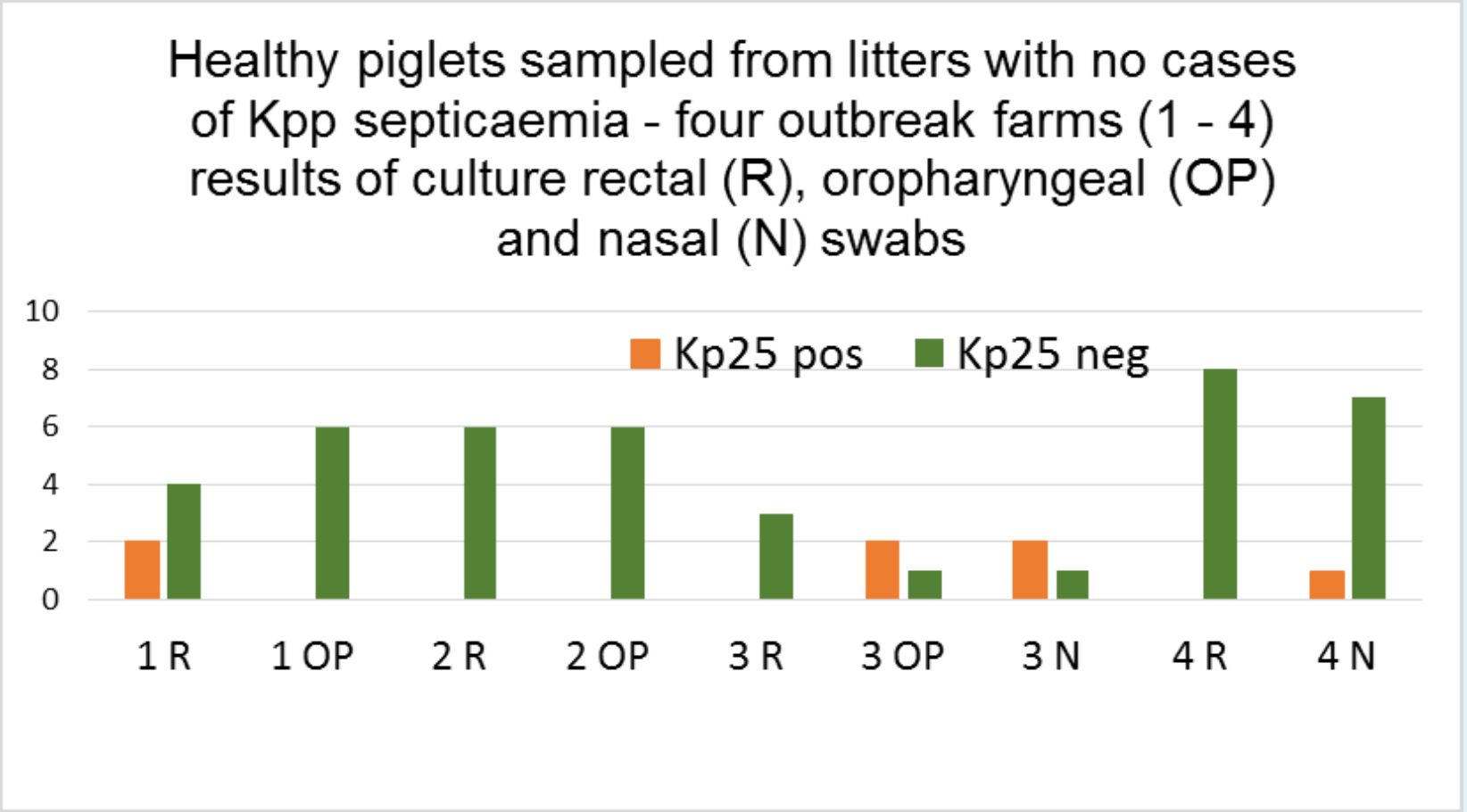
Sampling of cohort piglets contemporaneous with Kpp septicaemia outbreak



Results demonstrate that the presence of Kp ST25 is not sufficient to cause disease where all other management is similar to pigs with disease

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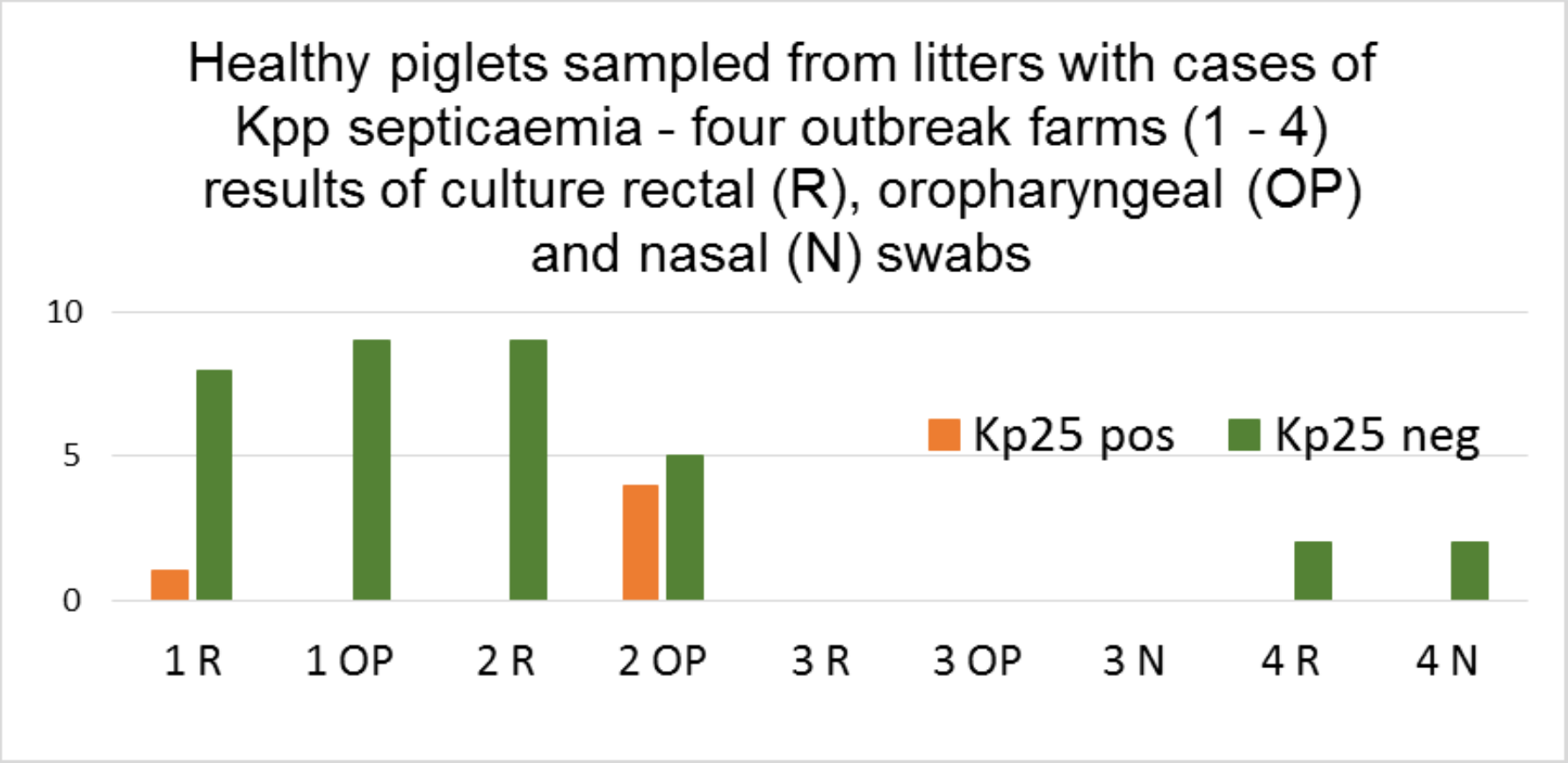
Sampling of cohort piglets contemporaneous with Kpp septicaemia outbreak



Results demonstrate that the presence of Kp ST25 is not sufficient to cause disease where all other management is similar to pigs with disease

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Klebsiella pneumoniae isolated from some samples from water troughs or wallows – 23 Kp isolates analysed, **none were ST25**. No Kpp isolated from bore-hole water sources

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Klebsiella pneumoniae isolated from wild bird faeces, **none were ST25**.

Free-living mammals have not been sampled.

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Concurrent disease

Iron-deficient piglets present in affected and unaffected litters with marginal/low packed cell volumes (piglets on 2 outdoor farms sampled)

No clinical signs of selenium or vitamin E deficiency evident but some pigs with low blood selenium (piglets on 2 outdoor farms sampled)

From all outbreaks - rarely PRRS, no influenza

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Summary of surveillance findings

- Enteric carriage of Kpp ST25 in pigs affected by diseases other than *Kpp* septicaemia is very low.
- There is evidence that Kpp ST25 can be present in pigs in which disease is not apparent.
- At the time of an outbreak **healthy** piglets in both litters with and without cases of septicaemia due to Kpp ST25 can carry the outbreak strain of Kpp in faeces, nares or oropharynx.
- **The presence of Kpp ST25 alone is not sufficient to cause disease.**
- Kpp ST25 was not detected in wild bird faeces or water on outbreak farms.
- Some outbreak farms tested had piglets with sub-clinical iron deficiency and/or low blood selenium.

• *Klebsiella pneumoniae* ST25 antimicrobial resistance

- Majority of outbreak isolates show no acquired resistance by disc diffusion.
- All Kpp (all ST) are innately resistant to ampicillin.

- A few isolates have resistance genes (tetracycline, TMPS, spectinomycin, streptomycin, lincomycin) *bla*$_{\text{LAP-2}}$ and *bla*$_{\text{TEM-1}}$.
- Genetic evidence of accumulating reduced susceptibility to fluoroquinolones.
- Use of FQs would provide strong selective pressure for further resistance to develop – submitting veterinary practitioners are informed.
- Kp production of ESBL and carbapenemases is an emerging problem in human disease-associated Kp isolates – **carbapenem and/or colistin resistance genes not found to date in our pig Kp ST25 isolates.**

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Analysis of *Kpp* outbreak isolates to 2024

Virulence gene analysis - ALL are **sequence type ST25 e**xcept one **ST558 isolated once in 2017**

- **ST25** are **K2** capsular type and harbour the virulence gene **rmpA** (not unique to ST25) conferring **hypermucoid phenotype**
- Contain genes for the siderophores yersiniabactin (ybt), aerobactin (iuc3 version AbST64) enterobactin and salmochelin (iro)

Plasmid analysis

- All outbreak ST25 carry a small novel 4kb plasmid pKPMC25
- **ST558 isolated in one outbreak** is a K3 capsular type (ST25 is K2)
- Does not contain the virulence gene *rmp*A
- It does harbour the pKPMC25 plasmid associated with ST25 Kpp isolates and previously unique to ST25, does have iuc3 version AbST25

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Kpp outbreaks – interventions reported for litter cohorts

Treatment to cohorts	Reported efficacy
Parenteral penicillin	
Parenteral amoxycillin	
Parenteral marbofloxacin	
Parenteral ceftiofur	
Start creep feed	

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Kpp outbreaks – interventions reported for **future** batches

Prophylaxis next batch	Reported efficacy
Parenteral penicillin	
Parenteral tulathromycin + Fe to neonates	
Creep feed with Tmp-S from 10 days	
Creep feed	
Kpp autogenous vaccine	

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Kpp outbreaks – interventions described by vets

Caveats: evidence to assess success/lack of success absent as no controls, disease is self-limiting on some farms without interventions and, sometimes, more than one intervention applied at one time.

- Provision of creep feed
- Antimicrobial use to litter mates, or to prevent disease in subsequent batches
  - Parenteral or in creep feed (TMPS, tulathromycin +/- iron)
  - Failure of penicillin treatment reflects innate resistance of Kpp to penicillins
  - Increase vitamin E in sow diets (180iu lactation, 150iu dry sow diets)
- **Kpp ST25 autogenous vaccine to sows**

Kpp ST25 autogenous vaccine to sows

- Kpp autogenous vaccine appears to control pre-weaning septicaemia effectively.
- Not aware of any outbreaks in herds currently using vaccine in sows. Use has been in outdoor breeder herds.
- Some units use Kpp vaccine as routine especially for new herds and repopulating herds.
- Example use: Gilts get 2 vaccinations 6 - and 2-weeks pre-farrowing regardless of the time of year.
- After parity 1 booster sows two weeks pre-farrowing during the risk period March to October.
- Side effects not seen, short shelf-life, plan ahead to order.

Kpp septicaemia – why only pre or just weaned pigs?

- All outbreaks have been in pigs 7–35-day old pigs
- Piglet innate immune systems are not mature until 36 days
- In-vitro studies demonstrated that the aerobactin gene iucA was critical for Kp proliferation in piglet blood (Krieger 2022)
- Septicaemia is a function of both the piglet's immature immune system and the presence of virulence genes in *K. pneumoniae*

Kpp septicaemia – why is it seasonal?

- 2011 to 2018 cases only May – September
- From 2019 extended to February and October and in 2024 one case in December
- Cases outside the peak of May – September occurred at a time of unseasonal warm weather
    - Australian cases occurred in their summer
        - Seasonality not explained

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Kpp ST25 septicaemia – reports from elsewhere

- APHA contacted by 5 countries experiencing similar disease, four in confidence.
- Johanna Fjelkner, DVM, presented at ECPHM 2023, Case in Sweden 2022
- Australia and the Netherlands have published their own findings which includes outbreaks due to ST25

- A dominant virulent genotype of *K. pneumoniae* associated with septicaemia in pre-weaned piglets has emerged in GB and other countries

Is Kpp in pigs a zoonosis?

Klebsiella pneumoniae is one of the most common MDR pathogens worldwide.
Human disease - pneumonia, bacteraemia, wound infections and meningitis
Acquired endogenously (from the patient's own gut flora) or exogenously from the healthcare environment.
Faecal contamination is how infection is usually acquired and spread.

- There is no evidence in GB of Kpp from pigs infecting humans.
- ST25 are uncommon in human infections and the ST25 detected in humans differ from our English pig Kp outbreak ST25.
- Naing (Netherlands) reported their porcine KpST25 with virulence scores 3 or 4 (scale 0-5) compared to human KpST25 with score 0-1.

‘’Take home’’ messages - *Kpp* septicaemia emergence

- Diagnosis requires postmortem examination and culture, retain isolates
- Sequencing is essential to determine emergence.
- AM sensitivity testing is important – most isolates are sensitive.
- Evidence that AMR genes can be acquired.
- AMR likely to develop in the face of AM use.
- Various interventions used in the face of disease, including autogenous vaccines, no efficacy trials.

Acknowledgements

- Farmers and their veterinary surgeons for submitting pigs and information
- APHA colleagues in Bury St Edmunds, Starcross, Thirsk and Weybridge
- Pig Expert Group members, Chris Teale, APHA Shrewsbury for AMR advice
- Defra and Welsh Governments for funding pig disease surveillance

...and my co-authors




There are gaps in our understanding of Kpp septicaemia in piglets and we are interested to hear about, and learn from, others' experiences with disease due to Kpp in pigs

Any enquiries regarding this publication should be sent to: cornelia.bidewell@apha.gov.uk

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References for Kpp septicaemia in piglets

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