Pushing the Boundaries of Environmental Health Monitoring: What's Next?

Kerith Luchins| The 3Rs Collaborative
Rodent Health Monitoring Initiative

AALAS 11-04-2024
12:30-2pm

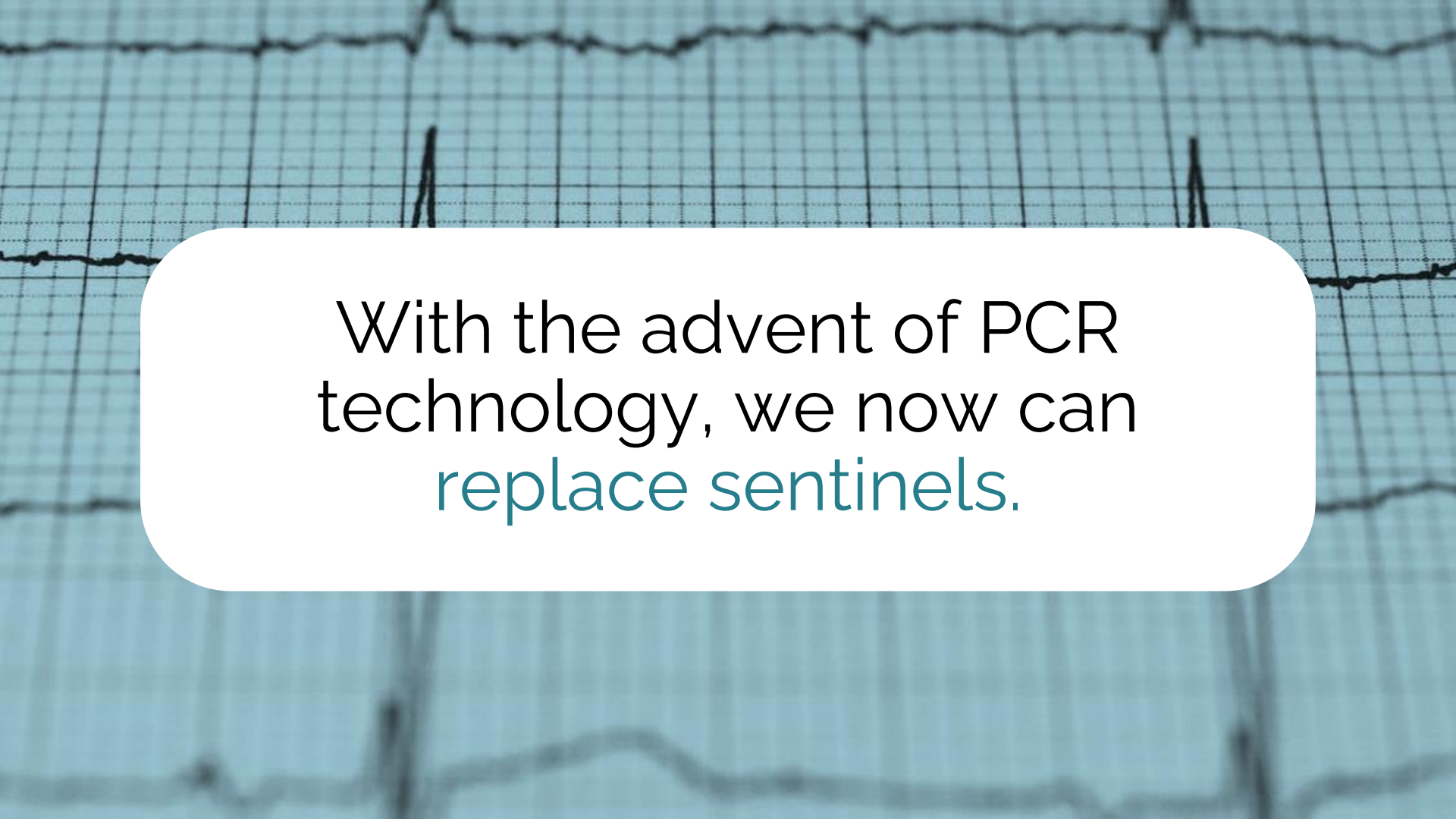
Today's Schedule

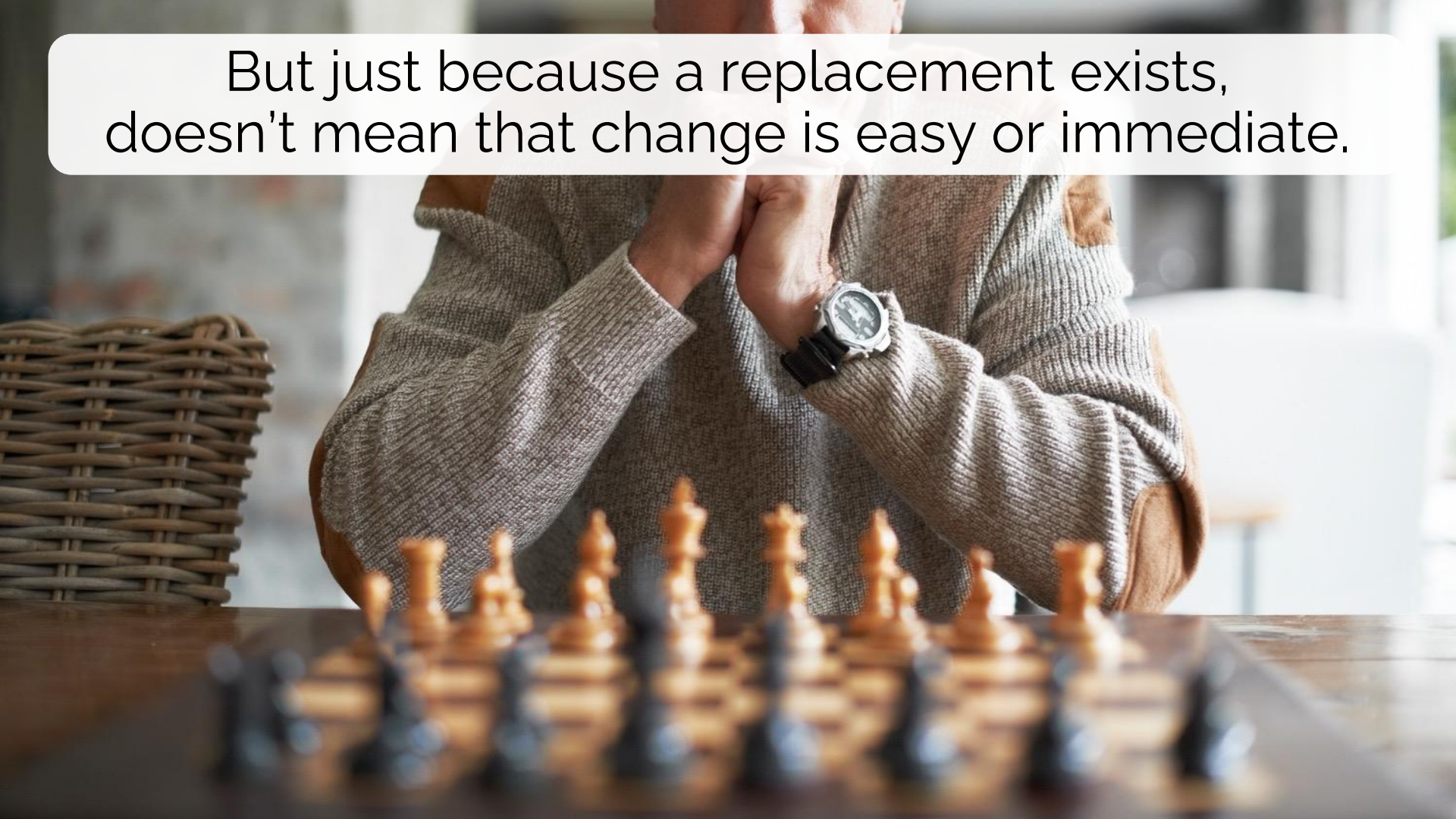
- Introduction– Kerith Luchins
- EHM Systematic Literature Review– Joe Garner
- Detection and Origin of LDV by EHM– Kerith Luchins
- Detection and Elimination of *P. murina* by EHM– Chris Manuel
- EHM for Other Rodents & Unexpected False Positives– Wai Hanson
- EHM and role of the IACUC– Trish Foley

Time for 1-2 questions after each presentation

Additional time for questions at the end

Traditionally, soiled bedding sentinel rodents were used to ensure colony health status.


With the advent of PCR technology, we now can replace sentinels.


But just because a replacement exists,
doesn't mean that change is easy or immediate.

The 3Rs Collaborative was created by professionals who understand challenge of 3Rs change firsthand.

The 3RsC's mission is to advance better science – for both people & animals

There are two core types of rodent health monitoring programs.

- Soiled Bedding Sentinels (SBS) = traditional rodent health monitoring that involves transferring soiled bedding to cage with live rodents which are periodically sampled/euthanized to determine colony health status. (Sometimes referred to as “sentinels")

- Environmental Health Monitoring (EHM) = any type of health monitoring that does not require use of live animal sentinels

Major difference = use of live animals

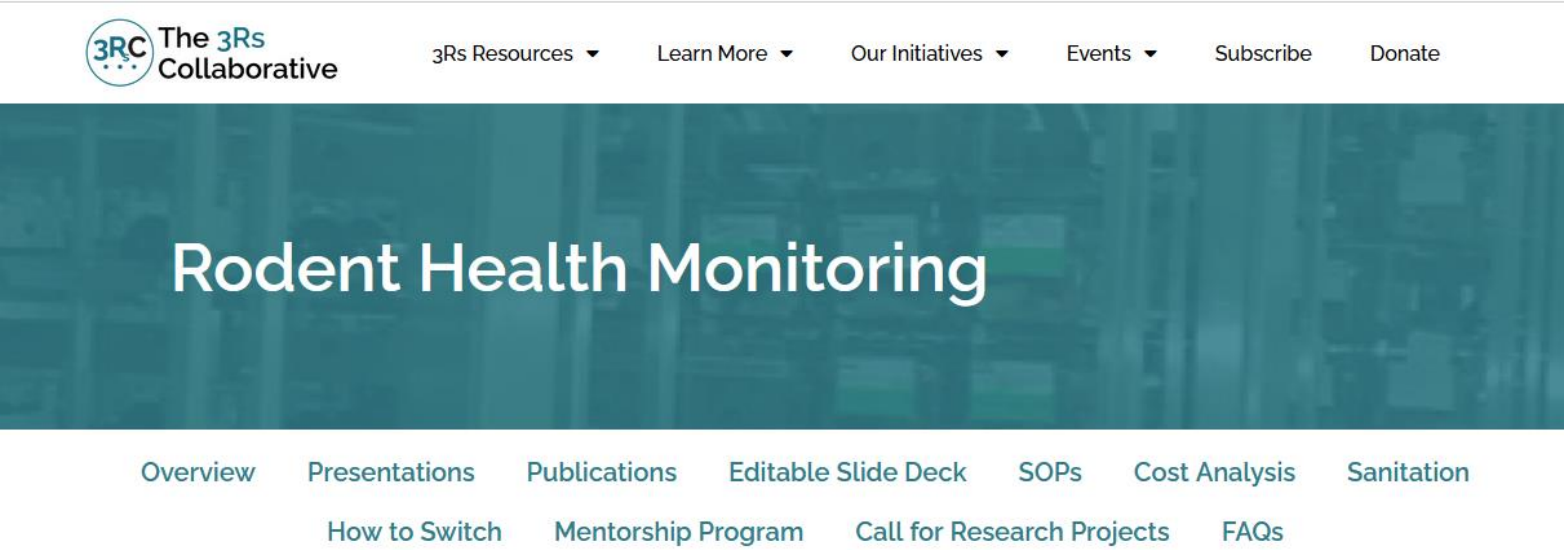
There are two major types of EHM:

- Exhaust Dust Testing (EDT) = use of swabs or a media to collect dust and nucleic acid that accumulates in **primary housing equipment** such as an individually ventilated cage (IVC) exhaust system
  - This is vendor-independent terminology, but you may have heard this called, Exhaust Air Dust (EAD®), Environmental Diagnostics (Edx), EnviroRax, Sentinel™ or Sentinel2™, or Intercepter EAD®
  - Use with certain types of IVC units
- Sentinel-Free Soiled Bedding (SFSB) = serial pooling of soiled bedding from rodent colony cages which is then sampled by either swabs and/or media for particulates and nucleic acid
  - This is vendor-independent terminology, but you may have heard this called, Shake & Bake, PathogenBinder™, REPLACE, or Sentinel Swab
  - Procedurally resembles soiled bedding sentinel program
  - Can be used on all caging and rack types

Supplemental EHM can include:

- Direct Colony Sampling (DCS) = collection of feces, fur swabs, oral swabs, or blood to non-invasively (or minimally invasive) sample specific animals or their cage microenvironment
  - Typically used for quarantine testing or confirmatory testing after positive result by different EHM method
- Room & Equipment Monitoring (REM) = use of swabs or media to sample husbandry or facility support equipment where dust and nucleic acid accumulate
  - Uncommon as main strategy

3RsC has created a resource hub to help institutions make the switch to EHM.



Many institutions have replaced their sentinels.

- University of Washington
- Pfizer Comparative Medicine sites
- University of Florida
- University of Colorado Anschutz Medical Campus
- Emory University
- University of Chicago
- University of Texas at Austin
- University of Southern California
- Emory National Primate Research Center
- Medical College of Wisconsin
- Northwestern University
- Benaroya Research Institute
- UT Southwestern Medical Center
- University of Alabama at Birmingham
- University of Arizona
- Seagen
- GSK
- Chapman University
- The Research Institute of the McGill University Health Centre
- Comparative Medicine Animal Resources Centre at McGill
- Montreal Clinical Research Institute
- University of Saskatchewan

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- John Hansenau, Tecniplast Consultant
- Jon Moll, VRL
- Julita Ramirez, Astrazeneca
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- Ken Henderson, Charles River Laboratories
- Kerith Luchins, U. of Chicago
- Lauren Young, 3RsC
- Lise Phaneuf, Centre for Phenogenomics
- Marnie Metzler, NC State
- Massimo Foa, IDEXX
- Megan LaFollette, 3RsC
- Norman Peterson, Seagen
- Ovidiu Jumanca, ICRM
- Patricia Foley, Georgetown U.
- Theresa Faughnan, Long Island U.
- Wai Hanson, Emory U.

Subscribe to The 3Rs Collaborative's newsletter for copy of these slides & practical 3Rs Resources

https://bit.ly/3RC_Newsletter

Environmental Health Monitoring: A Systematic Review

Dr. Joseph Garner
Comparative Medicine
Psychiatry & Behavioral Sciences
Stanford School of Medicine

STANFORD UNIVERSITY

AALAS, November 2024
Nashville, KY

Acknowledgments

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- 3RsC Board and EHM subcommittee
- Megan LaFollette
- Caroline Clement
- Katherine Gates
- David Chu

JPG: Disclosures / Conflicts of Interest

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- Consulting:
  - Roche; Genentech; Eli-Lilly; American Humane
- Donors:
  - Charles River Labs; Fibrecore; SSP; Private Philanthropy
- No Conflicts

2023 Benchmarking Survey

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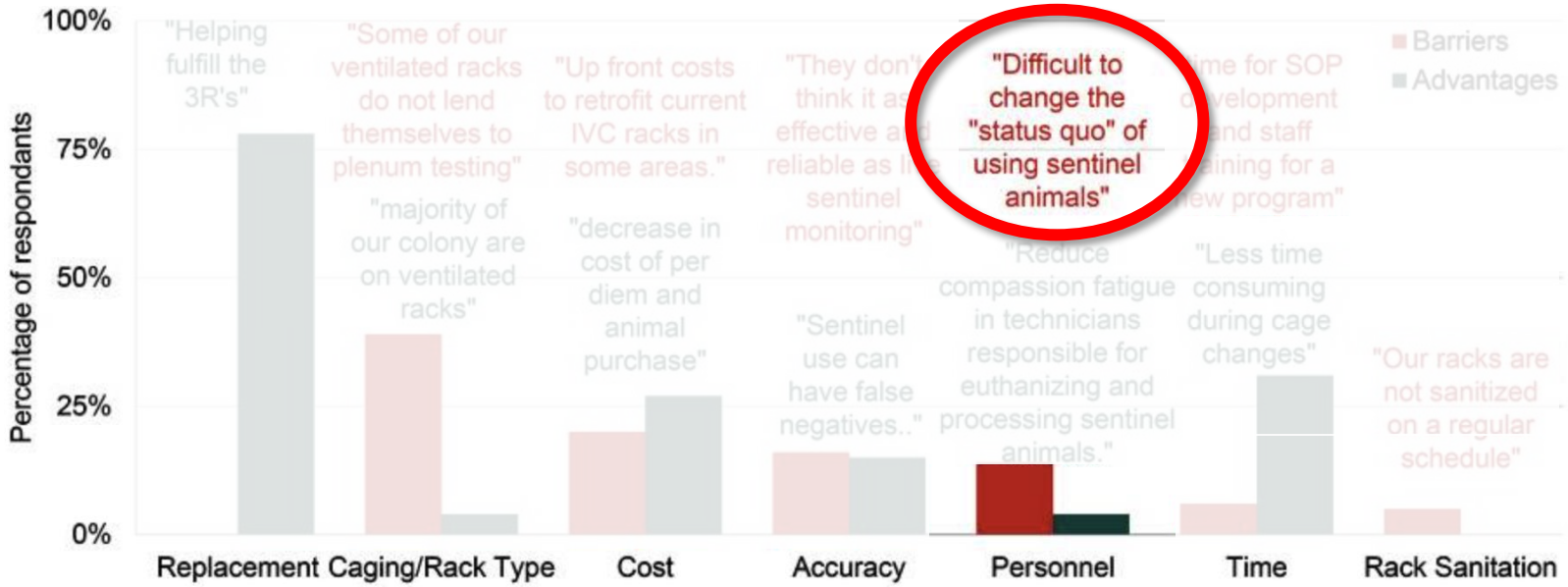
Pages 1–10

A Cross-sectional Survey on Rodent Environmental Health Monitoring Practices: Benchmarking, Associations, and Barriers

Kerith R Luchins,[1,‡,*] Kate V Gates,[2,‡] Caroline B Winn,[3] Christopher A Manuel,[4] Christina Pettan-Brewer,[5] Patricia L Foley,[6] Norman C Peterson,[7] Joseph P Garner,[8] Wai Hanson,[9] and Megan R LaFollette[10]

2023 Benchmarking Survey



A Cross-sectional Survey on Rodent Environmental Health Monitoring Practices: Benchmarking, Associations, and Barriers

2021 Benchmarking Survey

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This begs the question – How strong is the evidence base for Soiled Bedding Sentinels prior to EHM?

RESEARCH ARTICLE

Efficacy of Soiled Bedding Transfer for Transmission of Mouse and Rat Infections to Sentinels: A Systematic Review

W. C. C. de Bruin[1]*, E. M. E. van de Ven[1], C. R. Hooijmans[2]

1 QM Diagnostics BV, Nijmegen, The Netherlands, 2 Radboud University Medical Centre, SYRCLE at Central Animal Laboratory, Nijmegen, The Netherlands

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- 15 studies, including Grey literature
- SBS are EFFECTIVE for
  - MHV
  - MPV
  - TMEV
  - Helicobacter spp.
  - Fur Mites
- SBS are INEFFECTIVE for
  - Sendai Virus
- Insufficient evidence for 11 further pathogens

The right time for a Systematic Review of EHM *versus* SBS

- SBS has been shown to be ineffective for many pathogens…
- … However the literature does not make adopting EHM easy
  - Relevant studies are hard to find
  - Almost every relevant study is methodologically different
    - Terminology; Exact EHM methodology; Pathogens
- To be fair, this problem isn't uncommon in young literatures…

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- To be fair, this problem isn't uncommon in young literatures…
- … and Systematic Reviews are the established answer
  - **They bring together ALL relevant literature**
  - **They are the antidote to confirmation bias and cherry-picking**
  - They expose methodological issues, and establish best practice
- But this clearly needs both veterinary and biostats expertise

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We wanted to answer the following:

- Is there evidence to show that EHM works?
  - For what pathogens?
  - For what types of EHM?
- How does EHM perform *versus* SBS?

Best practice for rigor & objectivity.

PRISMA Guidelines

Preferred **R**eporting **I**tems for **S**ystematic Reviews and **M**eta-**A**nalyses

SYRCLE Guidelines

Systematic **R**eview **C**enter for **L**aboratory Animal **E**xperimentation

Liberati 2009; Moher 2009; Hooijmans 2014

We searched 3 databases with broad terms, and then filtered down to the relevant articles

- Biological monitoring [MESH] OR
- "health monitoring" OR "hygienic monitoring" OR "health surveillance" OR "microbiological monitoring" OR "diagnostic surveillance" OR "routine surveillance" OR "sampling of bedding debris" OR "Hygienic surveillance" OR "environmental sampling"
- "exhaust air" OR "exhaust debris" OR "exhaust dust"

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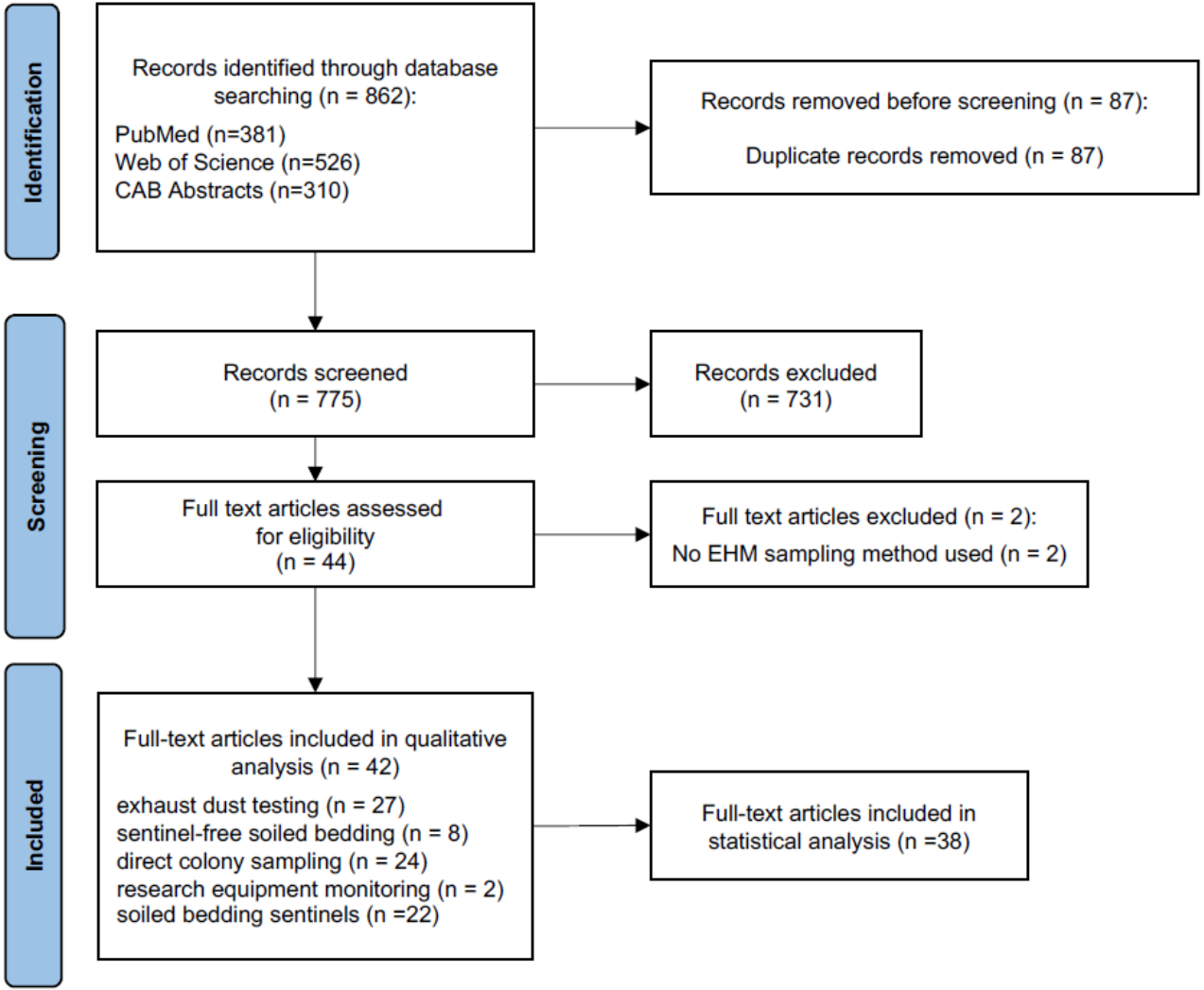
- No “Grey Literature”
  - Peer-reviewed
  - E.g. Conference Abstracts
- In English
- Rats or Mice

- Search performed on 10/15/2023
- 20% of data assessed in duplicate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Records identified through database searching (n = 862):
PubMed (n=381)
Web of Science (n=526)
CAB Abstracts (n=310)
Records removed before screening (n = 87):
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Screening
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Records excluded (n = 731)
Full text articles assessed for eligibility (n = 44)
Full text articles excluded (n = 2):
No EHM sampling method used (n = 2)
Included
Full-text articles included in qualitative analysis (n = 42)
exhaust dust testing (n = 27)
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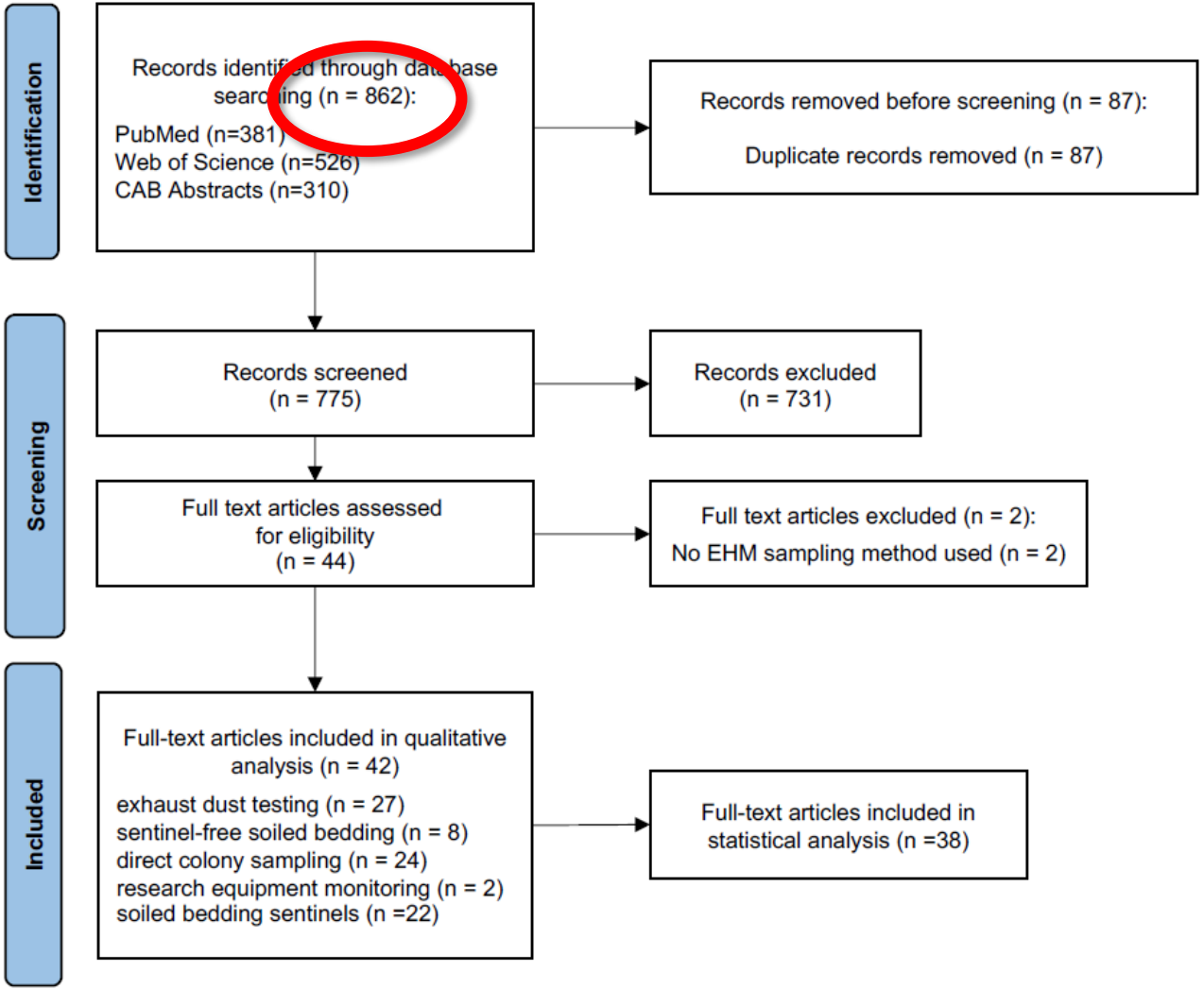
Full-text articles included in statistical analysis (n =38)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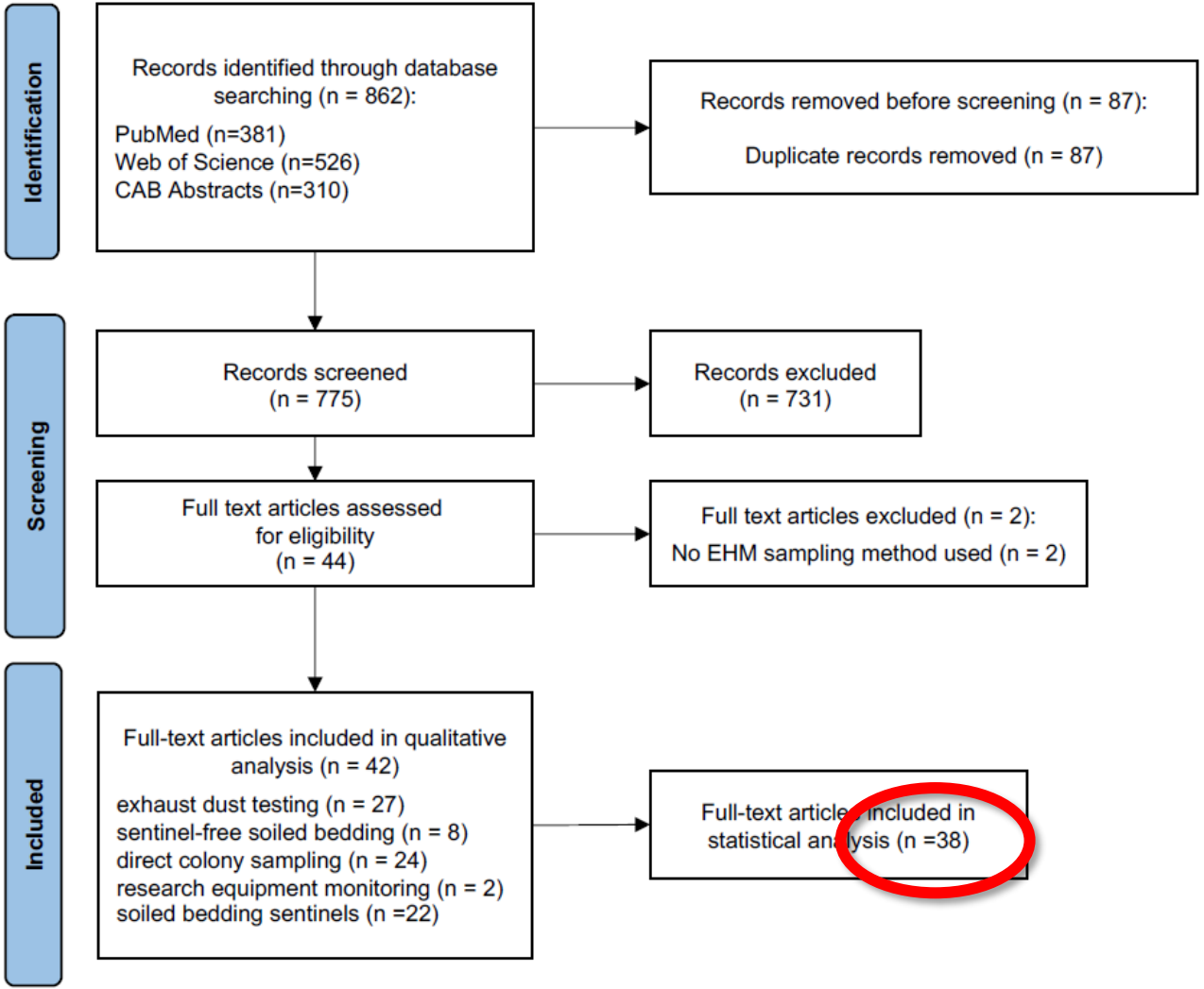
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Each article was coded in a universal format for later analysis, **per veterinary expertise**

- Sampling type: SBS vs EHM
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  - Type (Virus, Bacterial or Fungal, Endoparasites, Ectoparasites)
  - Importance (3Month or Annual Panel / Supplemental Panels)

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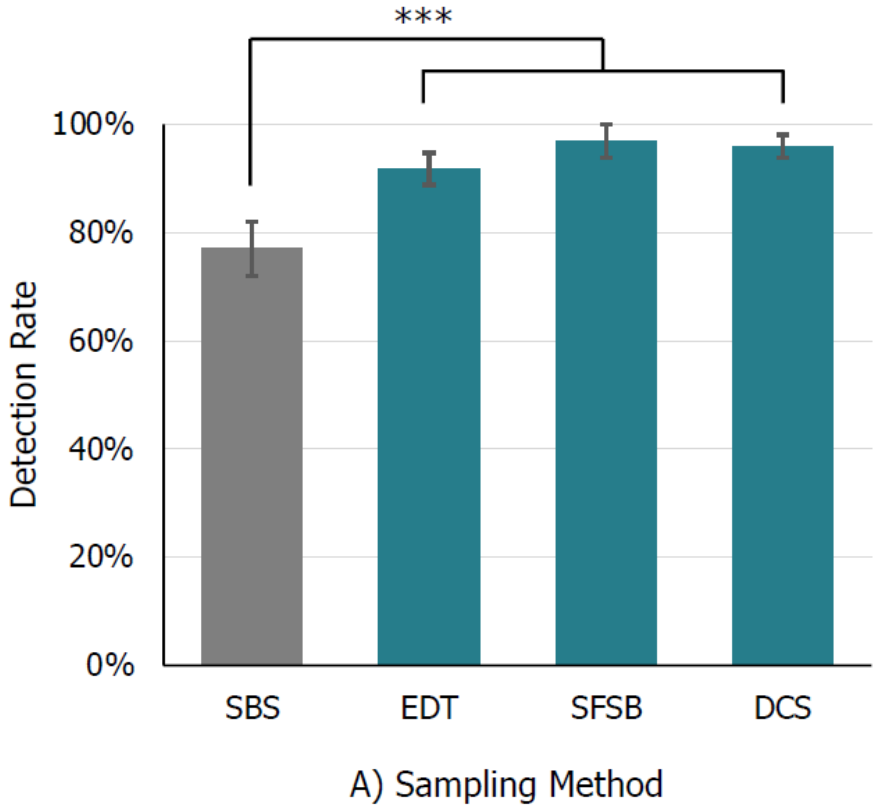
  - Importance (3Month or Annual Panel / Supplemental Panels)
- Did the sampling type detect the pathogen? (Yes/No)

Environmental health monitoring detects pathogens more often than soiled bedding sentinels (P<0.0001), regardless of EHM sampling method or pathogen type.



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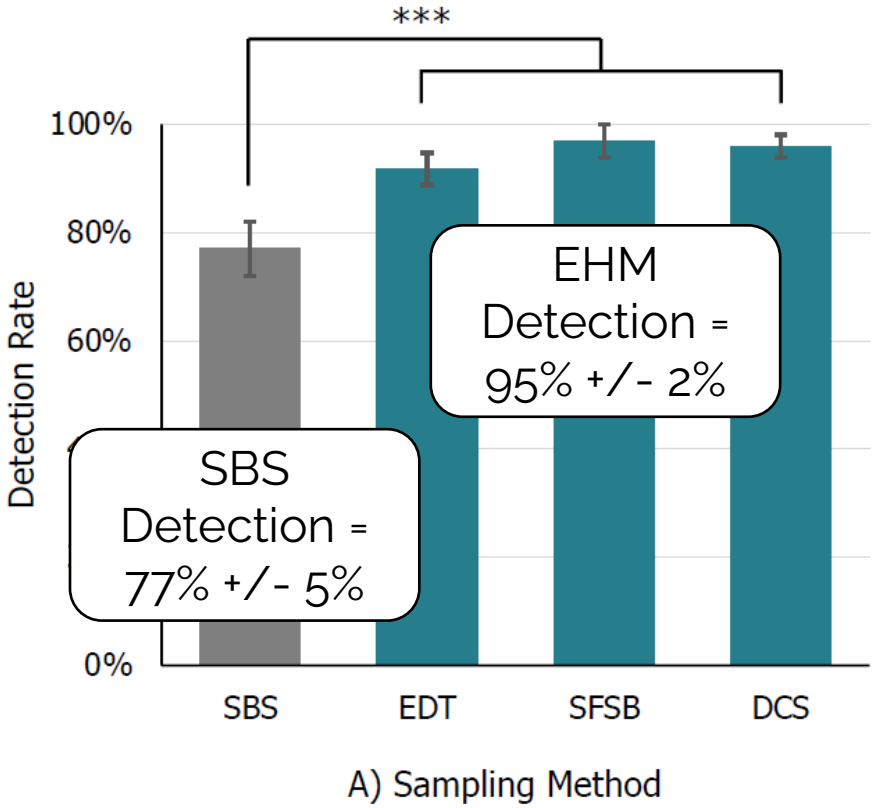

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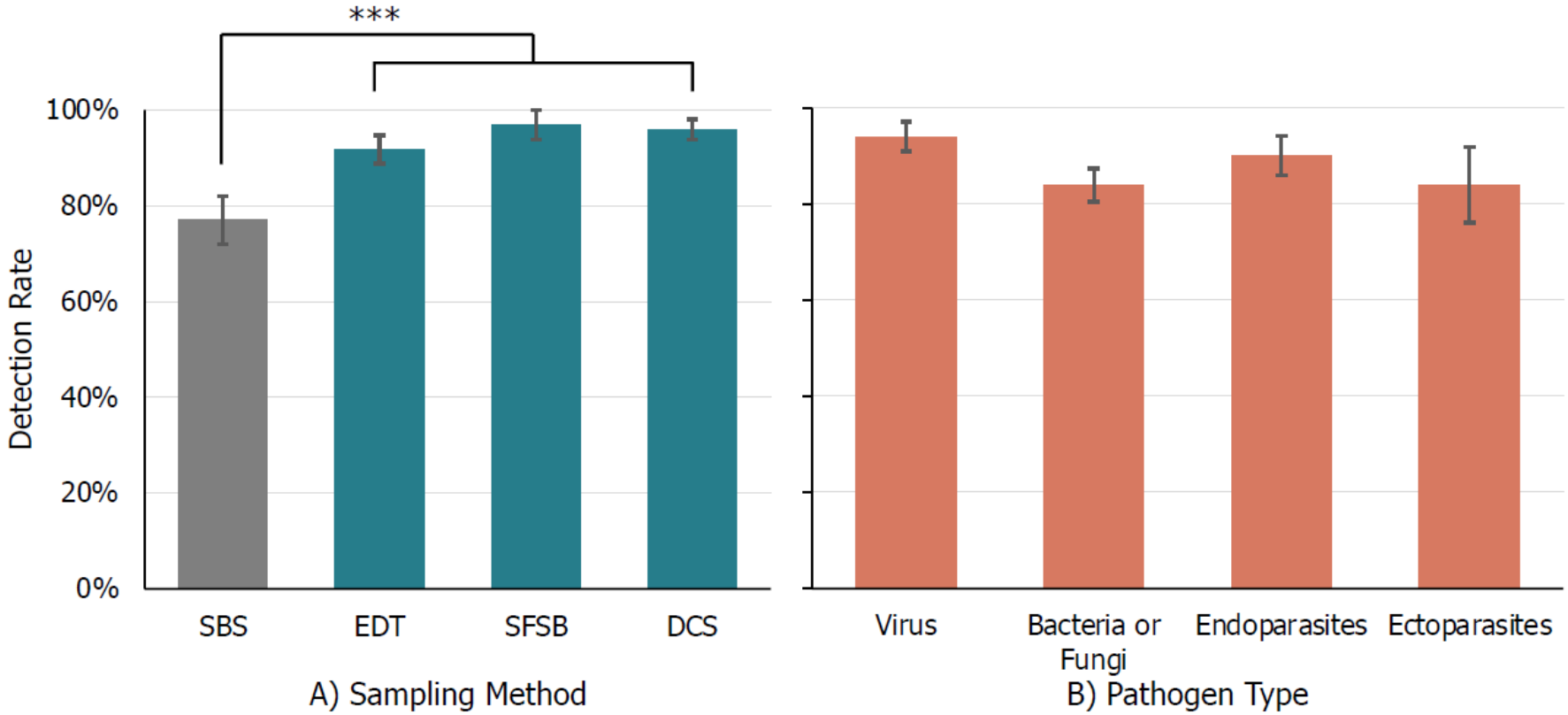

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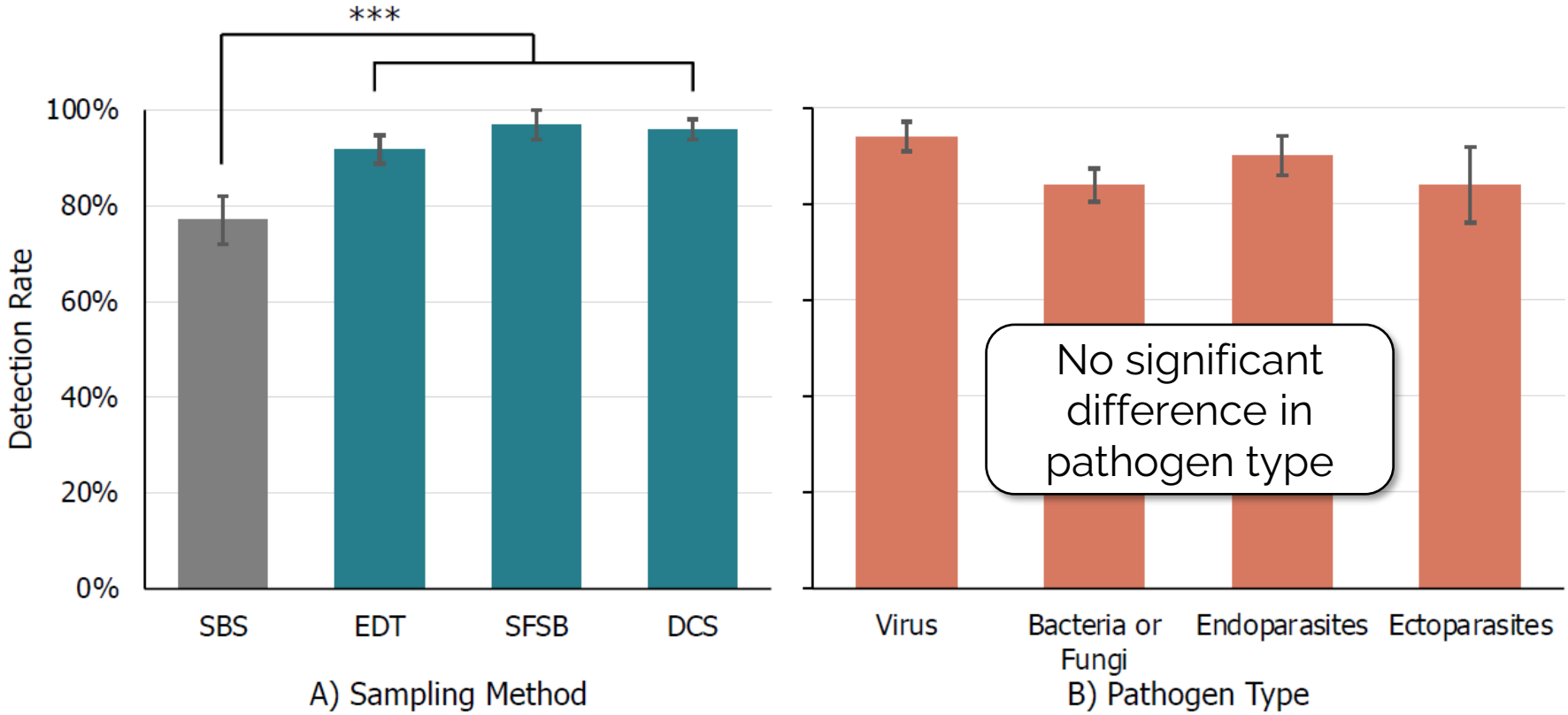
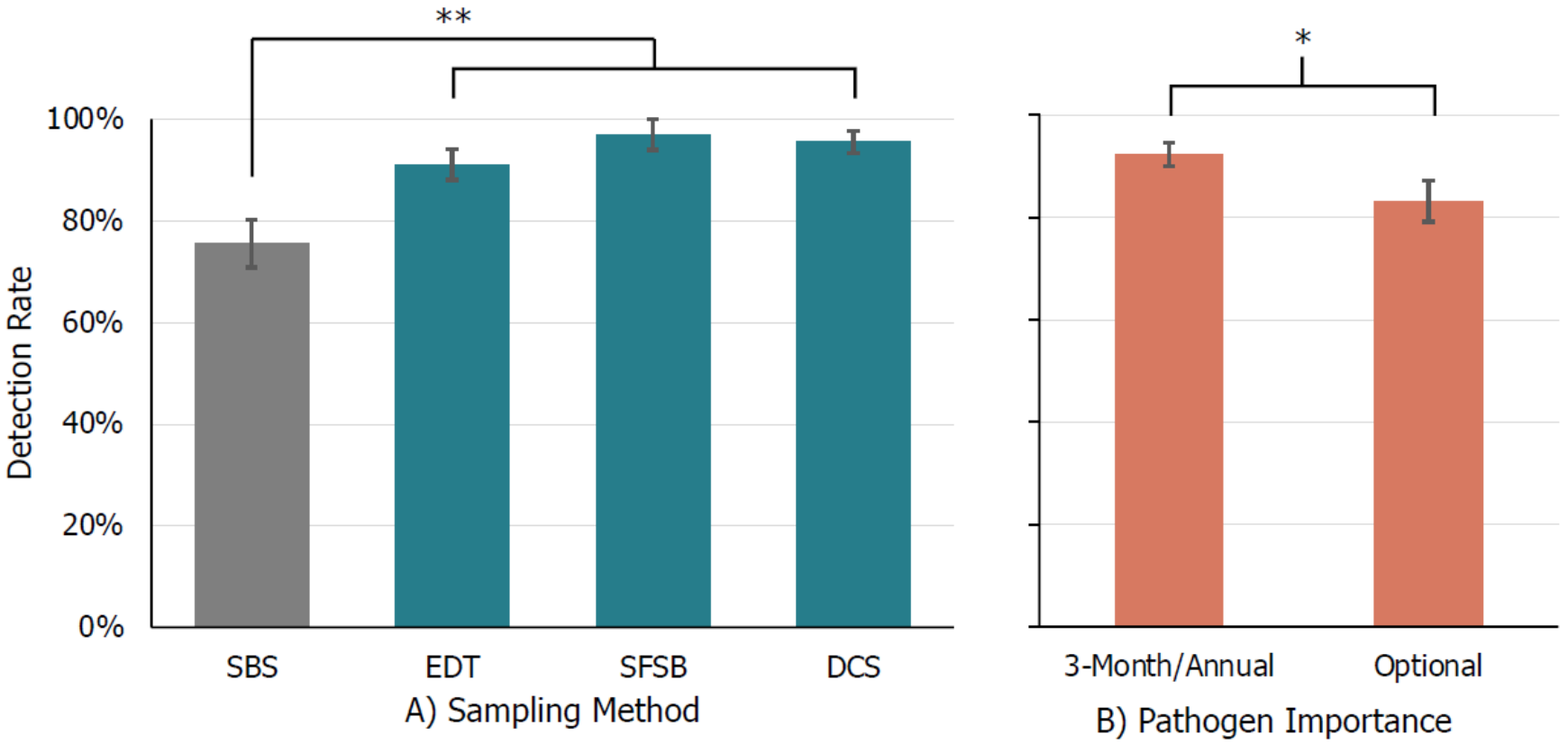


Environmental health monitoring detects pathogens more often than soiled bedding sentinels (P<0.0001), regardless of EHM sampling. Overall sensitivity is better for more important pathogens.



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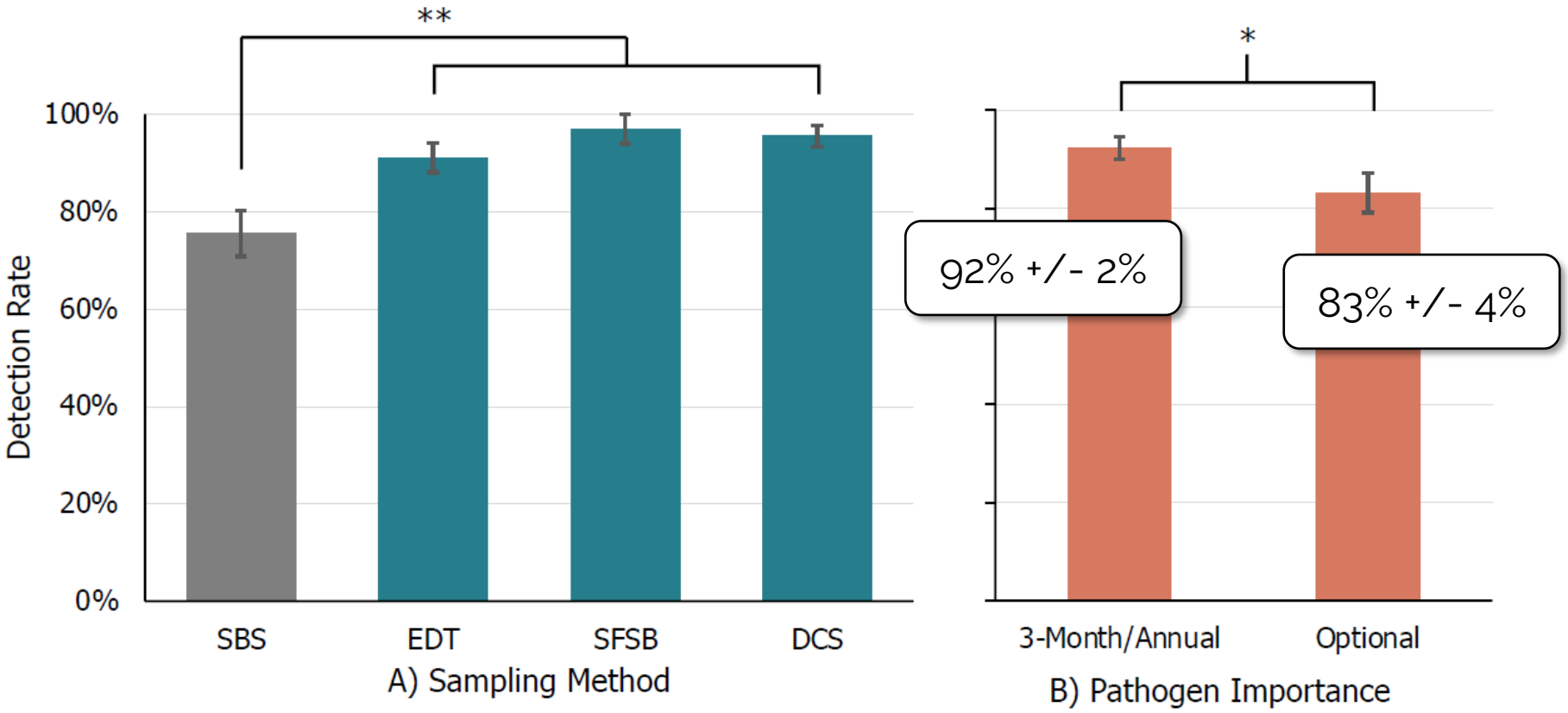

In Head-to-Head comparisons, where SBS detects a pathogen, EHM fails to detect the in 1/66 (1.5%) of cases

		SBS	
		No	Yes
EHM	No	1	1
	Yes	20	65

- *Streptococcus* spp.
- But EHM detects *Streptococcus* spp. in 2 other studies.

In Head-to-Head comparisons, where EHM detects a pathogen, SBS fails to detect the pathogen in 20/85 (23.5%) of cases

		SBS	
		No	Yes
EHM	No	1	1
	Yes	20	65

- *Pneumocystis* spp. SBS +ve (0/2), 0%
- Sendai Virus SBS +ve (0/1), 0%
- *Proteus mirabilis* SBS +ve (2/5), 40%
- Ectoparasites SBS +ve (3/7), 43%
- *Rodentibacter* spp. SBS +ve (5/8), 63%
- *Spironucleus* spp. SBS +ve (2/3), 67%
- *Tritichomonas* spp. SBS +ve (3/4), 75%
- *Entamoeba* spp. SBS +ve (4/5), 80%
- Pinworms SBS +ve (4/5), 80%
- *Helicobacter* spp. SBS +ve (12/14), 86%
- *Staphylococcus* spp. SBS +ve (6/7), 86%

EHM is a win for everyone: “good welfare = good business = good animal health = happier human staff”

3Rs
Replaces Sentinel Rodents

Operations
Reduces labor & cost

Veterinary
Increases health monitoring sensitivity & accuracy

Staff
Reduces emotional / compassion fatigue

Detection and Origin of Lactate Dehydrogenase-Elevating Virus by EHM

Kerith Luchins, DVM, DACLAM
Director, Rodent Clinical Services

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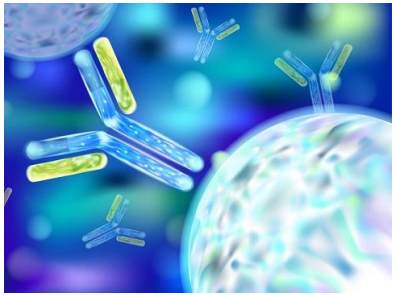
BIOLOGICAL SCIENCES

Immediately after Exhaust Dust Testing (EDT) implementation, we detected presumably long-standing Lactate Dehydrogenase-Elevating Virus (LDV) outbreak.

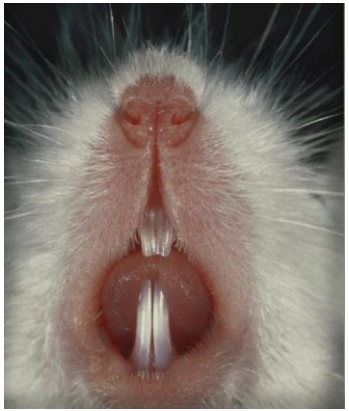
- LDV is mouse-specific arterivirus
  - Small and enveloped → unstable in environment
- Clinical signs do not usually manifest
  - Immunologic research effects
- Common contaminant of biologic products
  - Products derived from or passaged in rodents
  - Cell lines, blood products, feces



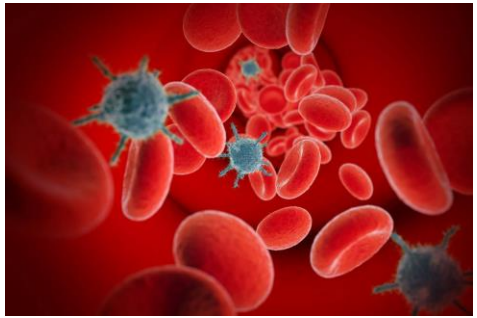
https://www.qps.com/category/bioanalytical-services/

LDV is not reliably detected by soiled bedding sentinels.

- Blood-borne virus
  - Natural transmission is rare
  - Most commonly due to bite wounds
- Causes a lifelong viremia



https://fineartamerica.com/featured/pet-mouse-teeth-jerome-wexler.html?product=poster



https://magbiosense.com/technology/

Directly after switching to EDT, one IVC rack was detected to be positive for LDV.

July 2018
EDT + (12 copy #)
Confirmatory testing –
Presumed false +
Testing frequency ↑

October 2018
EDT + (1 copy #)
Presumed true +
Patient Derived Xenograft (PDX) tumors
+
Mice w/PDX euthanized
Breeder dams (oral swab) –
No rack sanitation

January 2019
EDT + (unknown copy #)
Non-PDX tumors –
Rack sanitation performed

Outbreak investigation identified two sources of LDV, PDX tumors and breeding colony animals.

July 2019
EDT –

April 2019
EDT + (12 copy #)
Breeders (blood) +
Breeders euthanized
Experimental (blood) –
Rack sanitation performed

Outbreak highlights importance of understanding characteristics of pathogen.

- Plenum swab not preferred method for confirmatory testing for LDV
  - Nucleic acid copy number is higher on collection media than horizontal plenum swab
  - Media specifically designed to capture dust
- Testing by oral swabs is poor method for diagnostic detection of LDV
  - Oral swabs missed detection initially in breeding colony animals
  - Minimal viral excretion of LDV in saliva

PDX tumors are not of rodent origin, but may require rodent pathogen testing.

- Patient Derived Xenografts (PDX) are tumor tissues from human patients
  - Superiority in recapitulating cancer characteristics
- Even though they are human derived, PDX tumors are commonly contaminated with LDV
  - Historically, basement membrane complex, Matrigel, has been identified as cause of LDV contamination
  - LDV persists in transplantable tumors

We now know rodent pathogen testing of all biological materials is important for biosecurity.

- Now require rodent pathogen testing of PDX tumors
  - Previously passaged in rodents
  - Mixed with Matrigel
  - Unknown history of use
- Testing must occur before use of PDX in barrier facility

EHM was able to detect a pathogen when soiled bedding sentinels did not.

- LDV will not transmit to sentinel mice
  - Not fecal-oral transmitted agent
- Due to its transmission properties, LDV will be shed minimally in environment
  - Minimal transmission of urine, saliva, feces, milk in first week of infection
- EHM was able to detect LDV due to sensitivity of PCR

Outbreak Summary

- Necessary to understand pathophysiology of agent
- Did not figure out cause of LDV in breeding colony animals
  - Most importantly, resolved outbreak
- Superiority of EHM for LDV over soiled bedding sentinels

THE UNIVERSITY OF CHICAGO BIOLOGICAL SCIENCES

Questions?

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Detection of Lactate Dehydrogenase Elevating Virus in a Mouse Vivarium Using an Exhaust Air Dust Health Monitoring Program

Kerith R Luchins,[1,2,*] Darya Mailhiot,[1] Betty R Theriault,[1,2] and George P Langan[1,2]

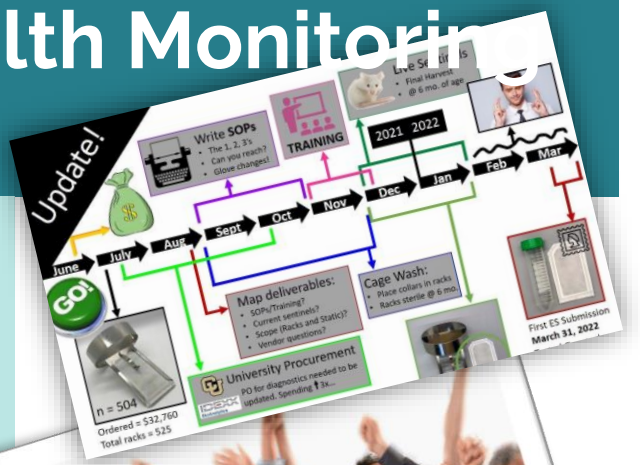
Pneumocystis murina
Finding and Eliminating with EHM Methods

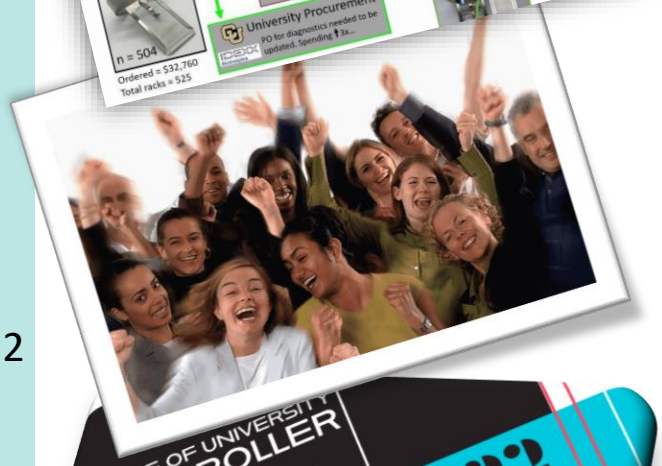
Chris Manuel, DVM, PhD, DACLAM
Senior Associate Director, Office of Laboratory Animal Resources
Associate Professor, Department of Pathology

Environmental Health Monitoring (EHM)

CU Anschutz Stats

- ✓ Sentinel animal-free March 2022
- ✓ 11 months to implement
- ✓ 2,200 rodents saved/yr.
- ✓ Widely Accepted
- ✓ Won the University of Colorado
  - ✓ Innovation & Efficiency Award - 2022
  - ✓ Controller's Choice Award - 2022





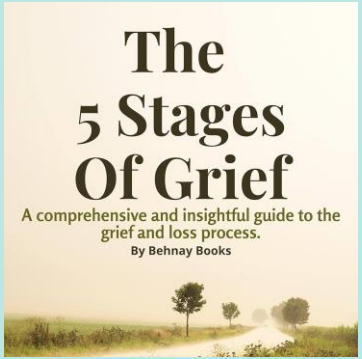
Lauren Habenicht, DVM, MS, DACLAM (left)
EHM Program Veterinarian

Christina Avena-Roman, CVT, ALAT (right)
EHM Program Coordinator

…then we found *Pneumocystis murina*

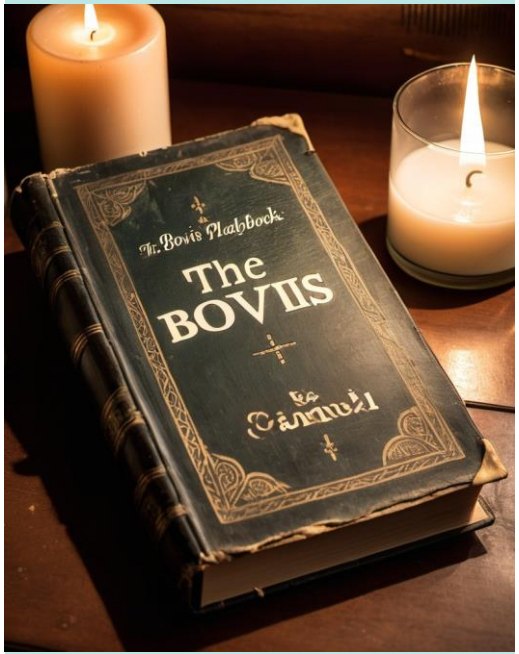
3 + Rooms
Multiple + racks

Pneumocystis murina
GMS "Silver" stain of lung tissue
Image Acknowledgement: Lost to Time



…Acceptance

The ***C. bovis*** Playbook



~~C. bovis~~ *P. murina* next steps …

1. Rule-in and rule-out PI's
   - Localize the infection to the cage level
2. Determine the strains infected
   - Typically, immunodeficient mice right?
3. Work with PI's to replace or rederive

What is the best sample?

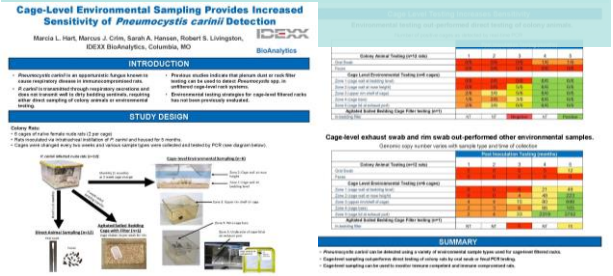
Contact your diagnostic lab to help!

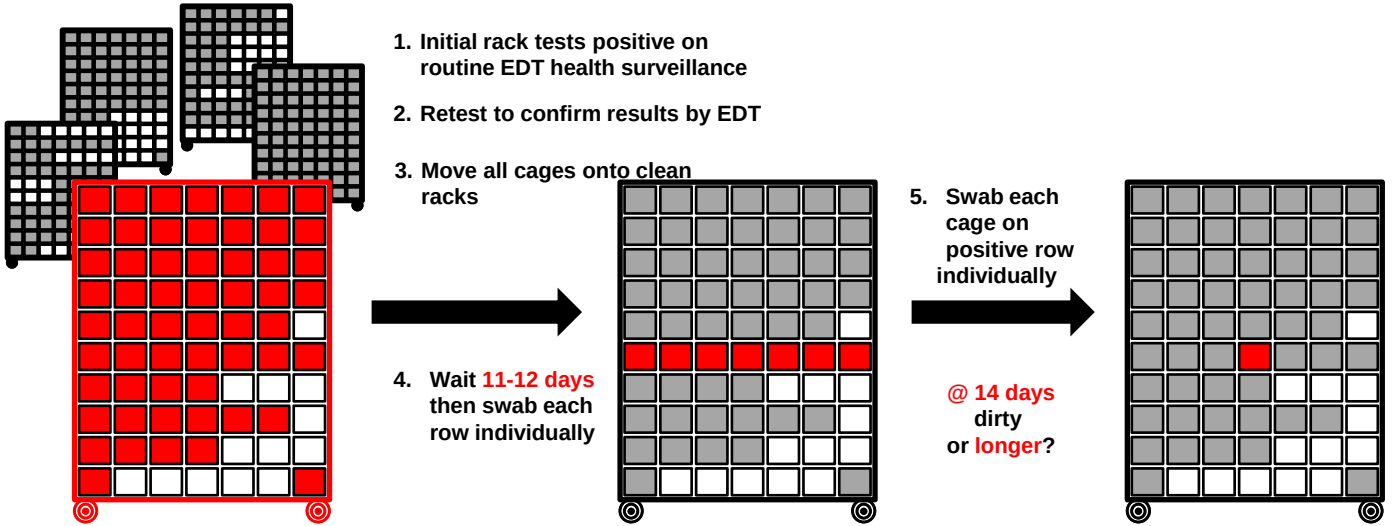
Marcia Hart, DVM, PhD, DACLAM
IDEXX BioAnalytics

FELASA 2022 Abstract

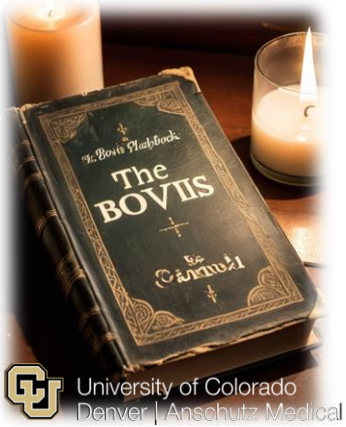
Cage-Level Environmental Sampling Provides Increase Sensitivity of *P. carinii*

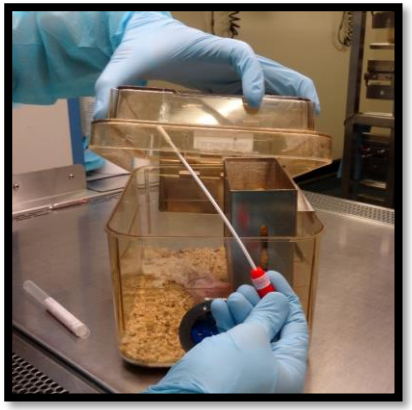
- Summary of "ideal" sample collection
  - Oral swabs & feces = ***bad***
  - Intracage dust accumulation =





Differential Swabbing





Cage Swabs:
Dust accumulation points

University of Colorado Denver | Anschutz Medical Campus

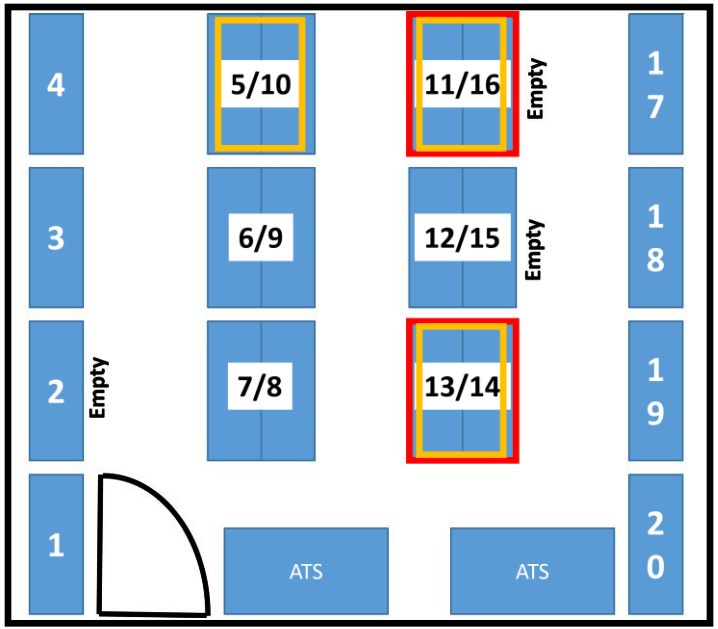
Manuel *et al.* 2017 Detection and Elimination of Corynebacterium bovis from Barrier Rooms with an Environmental Sampling Surveillance Program. *J Am Assoc Lab Anim Sci.* 56(2):202-

Rm 465

We have....

Allentown
Improving Life – it's in our DNA.®

DOUBLE SIDED RACKS!!!



Initial results (1/12/2023); media 3 mo.

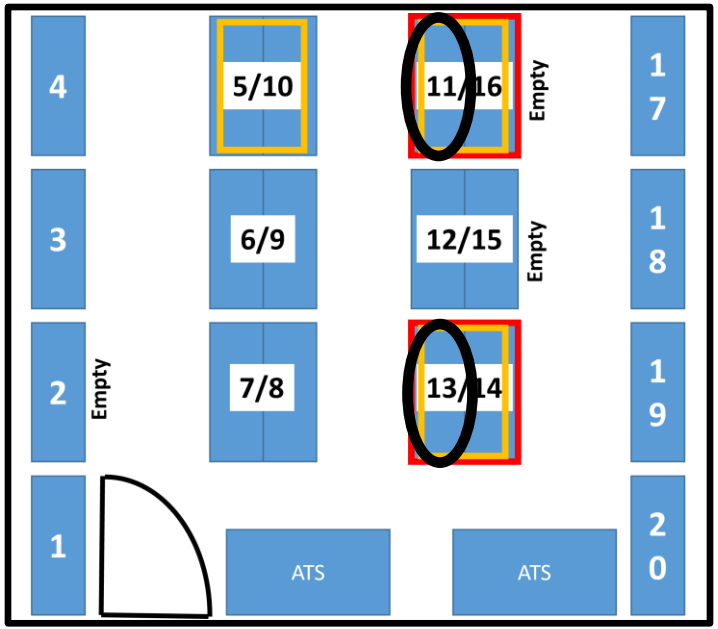
rack 5/10; copy 2
rack 11/16; copy 432
rack 13/14; copy 103

Confirmation (1/23/2023); media ~1 mo.

rack 11/16; copy 124
rack 13/14; copy 32

Rm 465

Pneumocystis murina



Row Level (2/1/2023); swab @ 11-12 days

Rack side 11 = **1 + row**

Rack side 13 = **3 + rows**

Rack 11

Rack 13

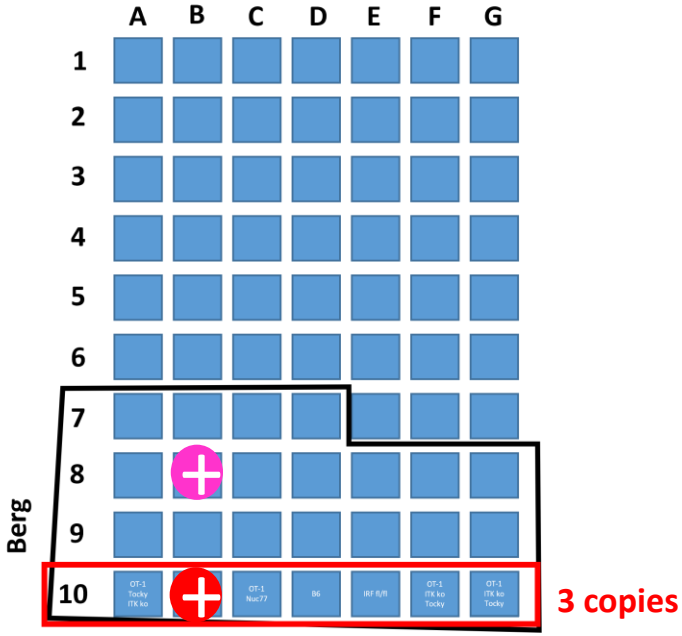
Row Testing Result 2/1/2023

Cage Testing 2/21/2024

Check other OT-1 PD1 KO cages

PI: Berg

Strain: OT-1 PD-1



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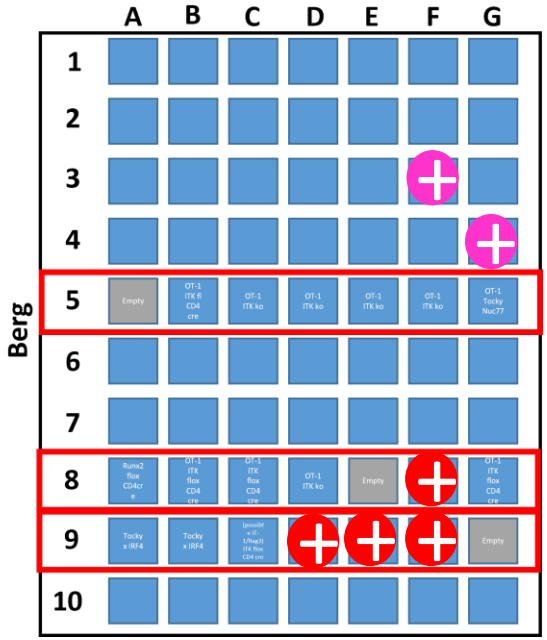


5 copies

12 copies

19 copies

University of Colorado
Denver | Anschutz Medical Campus

EHM Case Summary

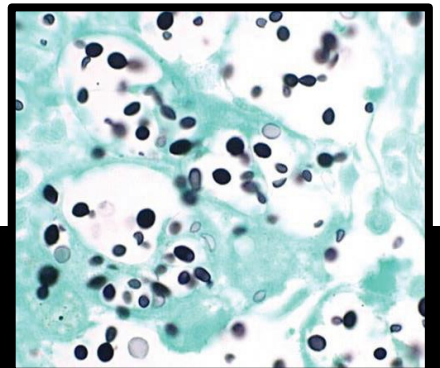
1. *P. murina* infection & shedding confirmed by:
   - PCR (n = 67)
   - Serology (n = 33)
   - Histopathology (n = 4)

   $5,050.50
   Not including time

2. Combination of **EDT** and **DCS** localized *P. murina* at the:
   - **Room**
   - **Rack**
   - **Row & Cage Level**

3. Differential Swabbing – ***makes life easier!***
   - 1 of 3 labs with mice on these racks
   - 1 of 12 strains used by the Berg lab

4. Resolved *P. murina* infection in **45 days**
   - Initial Detection → Confirmation
   - Localization → Elimination



Thank you

Chris.Manuel@cuanschutz.edu

Lauren Habenicht, DVM, MS, DACLAM
Senior Clinical Veterinarian
Associate Professor, Department of Pathology
Rodent Health Monitoring Supervisor

Extending EHM to Other Rodents & Encountering Unexpected Positives

Wai Hanson, DVM, PhD, DACLAM
Emory University

The 3Rs Collaborative

Extending EHM to Rats

Agent	EDT	SFSB
Rat Polyomavirus-2	X	X
β-Haemolytic Streptococcus Group B	X	X
Campylobacter spp.	X	X
Helicobacter spp.	X	X
Klebsiella spp.	X	X
Proteus mirabilis	X	X
Rodentibacter spp.	X	X
Staphylococcus spp.	X	X
Chilomastix, Hexamastix	X	X
Entamoeba spp.	X	X
Pinworms	Not yet reported	X
Pneumocystis carinii	X	Not yet reported
Spironucleus muris	X	X
Tritrichomonas muris	X	X

Extending EHM to Other Rodents

Gerbils

Agent	SFSB
Entamoeba spp.	X
Staphylococcus aureus	X

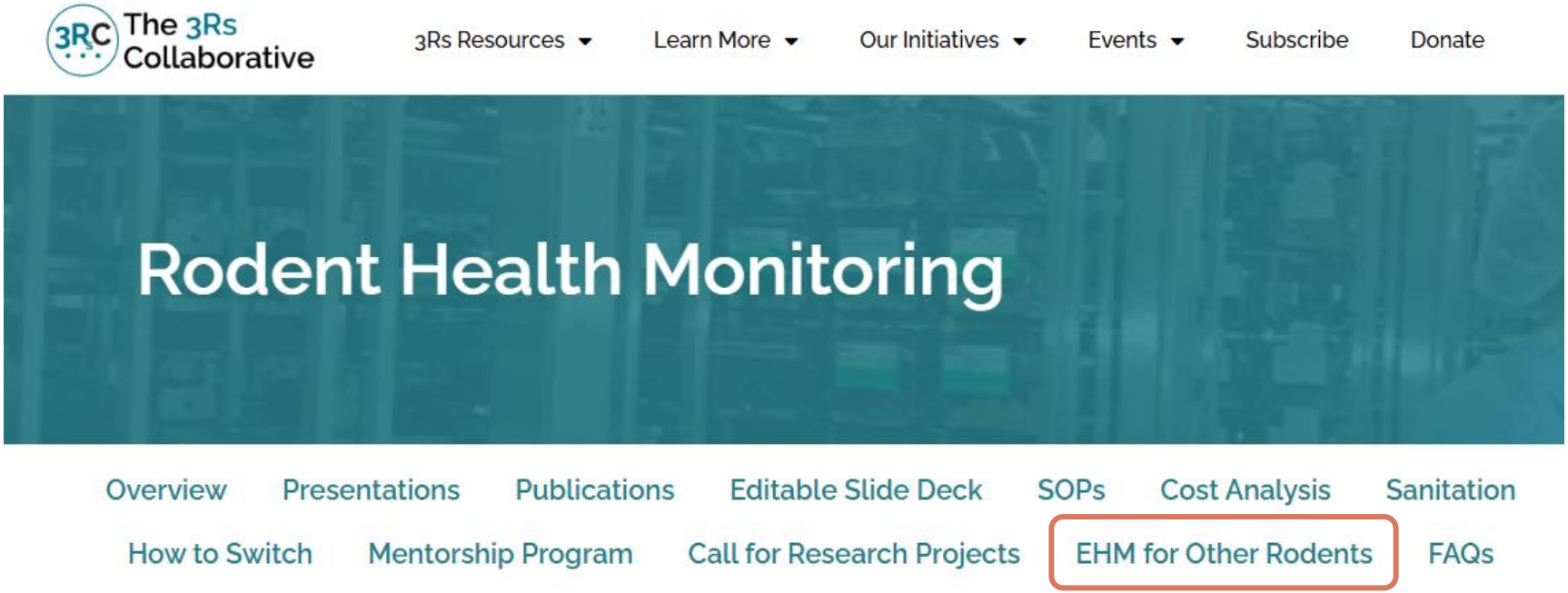
Hamsters

Agent	SFSB
Cryptosporidium spp.	X
Entamoeba spp.	X
Giardia spp.	X
Helicobacter spp.	X
Staphylococcus xylosis	X
Tritrichomonas muris	X

Spiny Mice

Agent	SFSB
Entamoeba spp.	X
Klebsiella spp.	X
Pseudomonas aeruginosa	X
Rodentibacter spp.	X
Tritrichomonas muris	X

EDT: Not yet reported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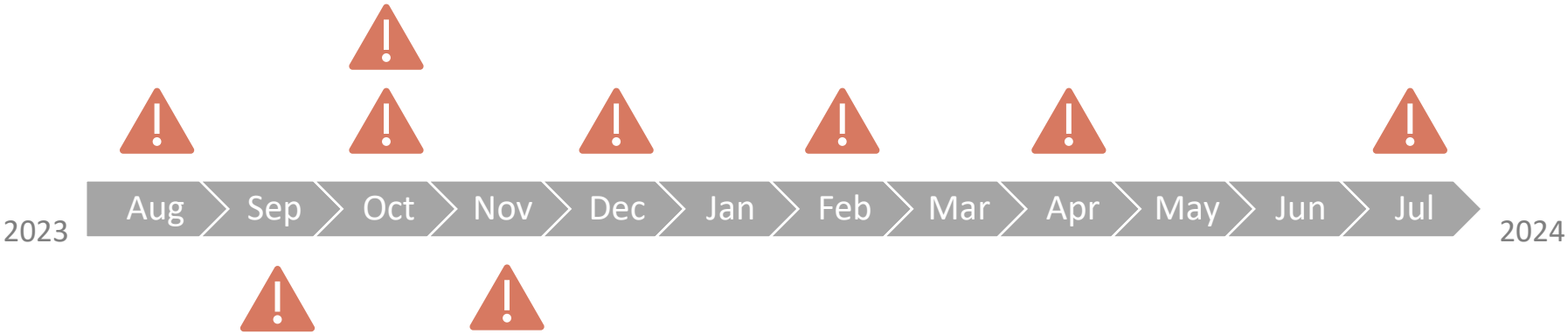
Life with EHM:
Hurdles with Unexpected Positives



1

2

3

4 Investigate the Potential Source

Have any staff or lab members acquired a new **pet rodent or snake**?

Is there any PI-managed **special diet** being used in the room?

Were any of these animals recently released from your **Quarantine** program?

Double check **vendor** health reports

Has the facility experienced a **wild rodent** incursion?

Are there any **biological products** being used that did not get pathogen testing?

MPV-2 in Mice

Initial Positive on Quarterly HM

- Dx Lab: Confirmed positive
  - #s: 25 MPV/MVM, 6 MPV-2
    - Start containment measures
      - Quarantine the room
      - Confirm negative room pressure
        - Collect and submit new samples (SFSB HM cages + DCS) - negative
          - Increased and enhanced surveillance for entire quarter (DCS)
            - All subsequent testing negative

Likely a real positive but either burned out or levels too low to detect

MAV in Mice

Initial Positive on Quarterly HM

- Dx Lab: Confirmed positive
  - #: 65
  - Detection of MAV by EHM >>> SBS
    - Collect and submit new samples - negative
      - All subsequent testing negative

Likely a real positive but animals have either been euthanized and removed or seroconverted and no longer shedding

Mycoplasma pulmonis in Mice

Initial Positive on Quarterly HM

- Dx Lab: Confirmed positive
  - #: 6
  - Never seen this agent positive in HM before! 
    (Mycoplasma genus is commonly found in biologicals, but not *M. pulmonis* specifically.)
    - This rack is all xenograft cancer models...
      - Collect and submit new samples - negative
        - All subsequent testing negative

Likely a real positive but majority of colony was euthanized due to experimental endpoint

Radfordia affinis in Mice

Initial Positive on Quarterly HM

Dx Lab: Confirmed positive

Collect and submit new samples

Positive

Treatment

Negative

Positive

No treatment

Negative

Real outbreak of live fur mites

Residual (dead) nucleic acids

Radfordia ensifera in Mice
Myocoptes musculinus in Rats

Initial Positive on Quarterly HM

Contact Dx Lab

R. ensifera

Confirmed positive.
Never seen this agent positive in mice before!

Cross reactivity with *R. affinis*

M. musculinus

Confirmed positive.
Never seen this agent positive in rats before!

Cross-contamination

(All subsequent testing negative)

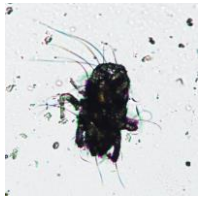
Unknown Ectoparasites in Rats

Initial Report by Lab Member

- Videos sent were blurry and “bugs” were unclear
  - Start investigation
    - Animals arrived from an approved vendor one week ago
    - Vet Staff examined multiple animals and pelage tapes microscopically - negative
      - Lab member sends new videos. Describes “some of the mites burst with blood when found and crushed”

Unknown Ectoparasites in Rats

Start diagnostics



- Successful pelage tapes
- Consultations:
  - Parasitologists from the Dx Lab
  - Parasitologists from the University of Georgia
  - Entomologist from Orkin

} Storage Mites (grain, flour, house)

- Dx Lab PCR: Fur mites, Demodex, Ornithonyssus - negative
- Dx Lab Sanger Sequencing: *Tyrophagus brevicrinatus* and *Tyrophagus putrescentiae*

A real infestation that could not be identified with current PCR primers

Grain Mite
(From CRL archives)

Take Home Messages

- DON'T PANIC
- Do the investigation.
  - Sometimes you won't get an answer.
  - Sometimes it may not become a full outbreak situation.
- Limitations of PCR
  - Cross reactivity / Cross-contamination
  - Alive vs. Dead / Past vs. Present
  - Are PCR primers available?
- Talk to your diagnostic lab colleagues

DAR Quality Assurance and Diagnostic Lab
Kat Judd, BA, RALAT

DAR Veterinary Residents
Julia Lazo, DVM, MPH

Charles River Laboratories
Research Animal Diagnostic Services
Ken Henderson, PhD, MSc
Cheryl Wood, BS

EMORY UNIVERSITY

Division of Animal Resources
Emory Integrated Core Facilities

3RsC

EHM and IACUC Considerations

Patricia Foley, DVM, DACLAM
Director, Animal Models Shared Resources, Georgetown University

Why should the IACUC care?

- Responsibility to ensure that the **3Rs are being considered**.
- IACUC has a responsibility to **enhance progressive animal research**
  - EHM has been shown to be superior to traditional soiled bedding sentinels more often than not.
  - Science evolves and protocols should as well.
  - What was okay for an IACUC to approve in prior years may be different from what is needed or expected now.
- IACUC has a role to **promote best science**, not just meet regulatory requirements.

Isn’t animal health monitoring the purview of the Attending Veterinarian and his/her veterinary team?

- **Yes… but….**
- The AV may be worried about going it alone and not having the support of the institution.
- Vet team may feel that internal trials are necessary to test out EHM and compare against SBS results for 1 or more cycles.
    - Now have 38 peer-reviewed papers (included in the recent systematic review paper demonstrating efficacy of EHM).
- **Look for the COLLABORATIVE OPPORTUNITIES between IACUC/Operations/Veterinary/Scientists**

The IACUC's role in Program Oversight

- Reviewing facility SOPs
- Is program staying current with best practices?
- Reviewing the protocol that approves use of
- sentinel animals – must be reconsidered in light of availability of non-animal alternatives that are equally if not more efficacious.
- Incentivize novel methods – make resources available to try EHM.

Financial considerations and securing institutional support

- Switching to EHM might incur additional costs to institutions at least initially depending on what current methods are in place for health monitoring.
- PCR vs. serology and in-house parasitology.
- Cost should not be primary consideration.
- Savings in labor, animal purchase, and housing costs.
- Several papers published showing that EHM can be cost effective.

Resistance from Investigators?

- No one likes change
- PIs might be concerned that EHM is less effective and that a pathogen might impact their own mouse/rat colonies and be less likely to be detected.
- IACUC can help with communication and provide institutional backing to support the decision to transition to EHM.

Advancing the 3Rs and Culture of Care

- Continuous improvement mindset.
- Promotion of alternatives and refinements
  (note 2 new proposed AAALAC Position Statements on the 3Rs and Culture of Care)
- Consideration for staff responsible for euthanizing large numbers of sentinel animals.

Questions?
Comments?

pf418@georgetown.edu

GEORGETOWN UNIVERSITY