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Lever VC Insights

Bovine Disease Detection and Diagnostics

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Current Landscape

I. Introduction

Beef Cattle Mortality

Over the past several decades, the beef cattle industry has witnessed a discernible upward trend in feedlot death loss rates. According to data from the United States Department of Agriculture's National Animal Health Monitoring System (USDA-NAHMS), since 1999, average death rates in both small (1,000–7,999 head capacity) and large feedlots (>8,000 head capacity) have increased by 36% and 23%, respectively. Moreover, from January 1992 to July 2017, steer death loss percentages more than doubled, indicating a significant shift in the industry's mortality landscape. In 2015 the leading cause of death in cattle and calves was respiratory problems at 23.9% and 26.9%, respectively. These findings indicate a persistent upward trajectory in feedlot death loss rates, raising concerns about economic implications, animal welfare, and potential industry-wide repercussions. Researchers point to various factors, including structural changes, controllable elements like technology adoption and feed rations, and uncontrollable aspects such as disease outbreaks and weather conditions, contributing to this concerning trend. Addressing the complex interplay of these factors is imperative for mitigating the impact on the beef industry's sustainability and profitability. The figure below **(Figure 1)** also illustrates how the mortality rates change across the lifetime of beef cattle. These numbers indicate that the cow/calf and backgrounder operations can significantly benefit from new diagnostics.

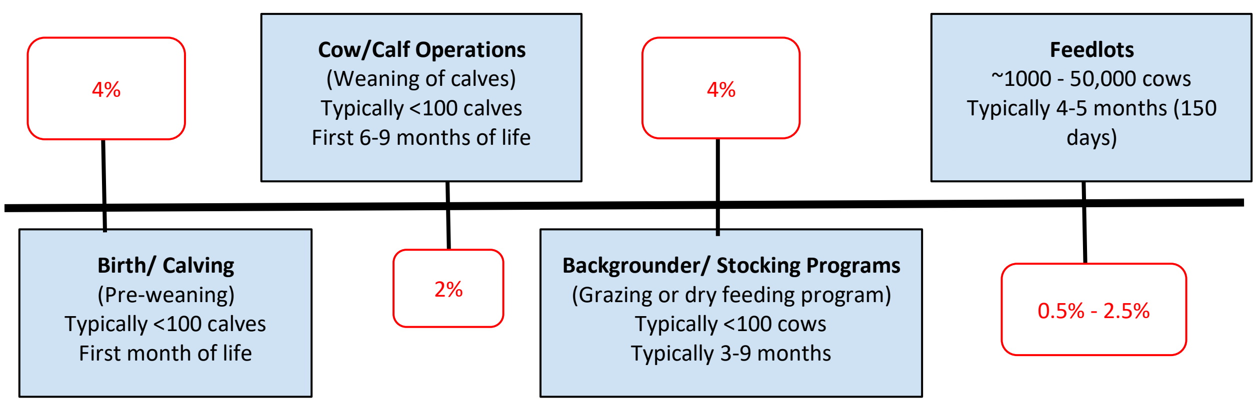
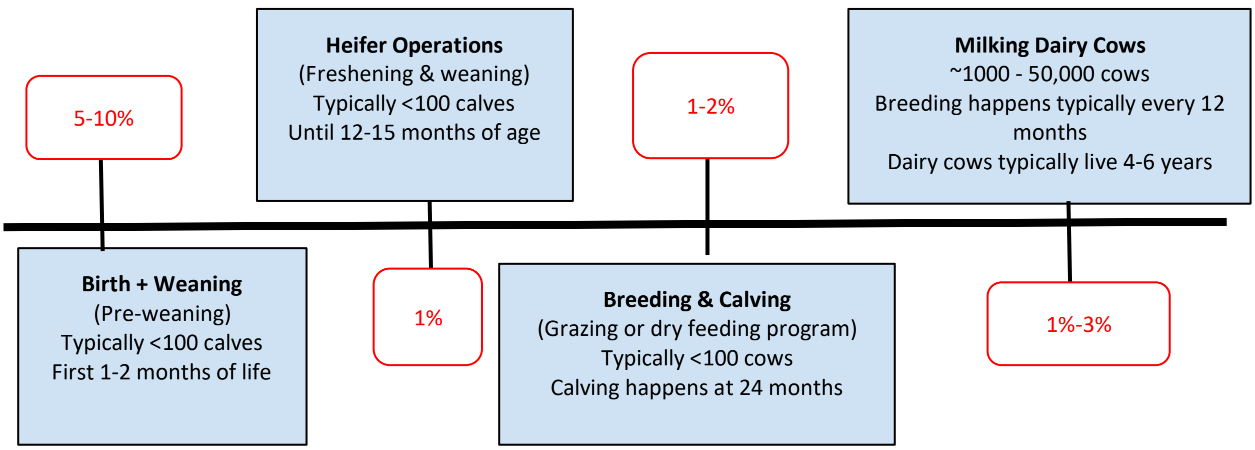


Figure 1. *Representation of mortality across the beef industry*

Dairy Farm Mortality

The increase in death rates on dairy farms, as highlighted by the Dairy 2007 USDA survey, has become a growing concern within the industry. One survey reported a notable rise from 4.8% in 2002 to 5.7% in 2006, indicating a substantial increase in DHIA Provo-recorded dairy cattle death rates in 8 Western states from 3%

in 1992 to 10% in 2002.[1] This trend is alarming, particularly when compared to annual death rates of 1 to 1.5% in beef cows and feedlot cattle. In 2008, lameness or injury emerged as the leading cause of cow death, accounting for 20%, followed by mastitis (16.5%), calving problems (15.2%), and unknown reasons (15%).[2] However, in 2015 the leading non-predator cause of death was respiratory problems (16%), and lameness only caused 12% of deaths. Factors such as herd size, milk production level, fresh cow management, reproductive problems, and health issues like respiratory problems, lameness, diarrhea, and clinical mastitis were identified as contributors to higher mortality rates. The intricate interplay of intensive management practices, environmental changes, and insufficient training and experience in identifying early signs of disease contributes to the heightened loss of animals on dairy farms, underscoring the need for comprehensive strategies to address these multifaceted challenges. The figure below **(Figure 2)** outlines the mortality rates across the dairy cow lifecycle. Similar to the feedlot life cycle graph, the early cow/ calf operations are ripe for new methods of early disease detection and calving predictions.



Zhang, Hailiang, Yachun Wang, Yao Chang, Hanpeng Luo, Luiz F. Brito, Yixin Dong, Rui Shi, Yajing Wang, Ganghui Dong, and Lin Liu. "Mortality-Culling Rates of Dairy Calves and Replacement Heifers and Its Risk Factors in Holstein Cattle." *Animals : An Open Access Journal from MDPI 9*, no. 10 (2019). Accessed January 23, 2024. https://doi.org/10.3390/ani9100730.

Ahmedin, Umer M., and Alula A. Assen. "Calf Morbidity, Mortality, and Management Practices in Dairy Farms in Jimma City, Southwestern Ethiopia." *BMC Veterinary Research 19*, (2023). Accessed January 23, 2024. https://doi.org/10.1186/s12917-023-03815-w.

Figure 2. *Representation of mortality across the dairy industry*

As the cattle and dairy industry grapples with rising mortality rates and the consequential economic and animal welfare implications, there is a growing imperative to explore innovative technologies for disease detection and diagnostics. The surge in demand for cattle has led to the expansion of farm operations, making efficient and reliable disease monitoring crucial for maintaining herd health and productivity. Traditional methods of

[1] McConnel et al., "Evaluation of Factors Associated with Increased Dairy Cow Mortality on United States Dairy Operations."
[2] {Updating}

disease detection may prove insufficient in larger farm settings, necessitating the integration of cutting-edge technologies. Embracing advancements in diagnostics not only enhances the early identification of health issues but also facilitates timely intervention, mitigating the impact of diseases on both individual animals and the overall herd. Additionally, the adoption of advanced disease detection technologies holds the potential to reduce the widespread reliance on antibiotics and the need for broad-spectrum treatments, which are shown to lead to antibiotic resistance. This white paper will explore new and innovative technologies that can improve disease detection on cattle and dairy farms.

II. Primary Beef Cattle and Dairy Cow Diseases

- Mastitis
  - Mastitis is an inflammatory condition of the udder in dairy cattle, characterized by the infection of mammary glands by pathogens including Staphylococcus aureus, Streptococcus agalactiae, Escherichia coli, and Mycoplasma species.[3]
  - Environmental factors, such as poor udder health management practices, unhygienic milking conditions, contaminated bedding, and wet environments, contribute to the risk of mastitis. The disease results in changes in milk composition, reduced milk quality and quantity, and veterinary costs.
  - The estimated worldwide economic losses caused by mastitis are more than US$40 billion annually.[4]

- Bovine Respiratory Disease (BRD)
  - BRD is a multifactorial condition caused by complex interactions between various viral and bacterial pathogens, host immune status, and environmental stressors.
  - Behavioral changes and clinical signs in BRD-sick cattle include ocular and nasal discharge, cough, extended head, dry snout, floppy ears, poor coat, dull eyes, lethargy, social isolation, hypo-/anorexia, pyrexia, dehydration, tachypnea, and dyspnea.[5]
  - BRD is responsible for half of all disease-based cattle deaths in North America and costs the US beef industry $900 million annually.[6]

- Bovine Viral Diarrhea (BVD)
  - BVD is a disease caused by a pestivirus that can manifest as generalized immunosuppression, with evidence of synergistic effects with other pathogens, fertility problems in male and female cattle, and other often more variable signs such as decreased milk production and weight gain, fever, diarrhea, and respiratory dysfunction.[7]
  - The average economic impact of dairy and beef cattle herds across the world ranges from £46.50 - £82.80 per cow per year in affected herds.[8]

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[3] Cheng and Han, “Bovine Mastitis.”
[4] Neculai-Valeanu and Ariton, “Udder Health Monitoring for Prevention of Bovine Mastitis and Improvement of Milk Quality.”
[5] Puig et al., “Technological Tools for the Early Detection of Bovine Respiratory Disease in Farms.”
[6] Service, “Pen-Side Test for Bovine Respiratory Disease May Save Cattle Industry Millions, Reduce Antibiotic Use.”
[7] Fulton, “Host Response to Bovine Viral Diarrhea Virus and Interactions with Infectious Agents in the Feedlot and Breeding Herd.”
[8] Yarnall and Thrusfield, “Engaging Veterinarians and Farmers in Eradicating Bovine Viral Diarrhoea.”

- Foot-and-mouth Disease (FMD)
  - Foot-and-mouth disease is one of the world's most economically important viral diseases of livestock. The virus infects cattle, pigs, and sheep, and many cloven-hoofed wildlife species. The infection results in vesicular lesions in and around the mouth and on the feet, resulting in the reluctance of an animal to eat or move. [9]
  - The United States prioritizes preparedness for FMD outbreaks due to the disease's contagious nature and potential trade and transportation disruption.
  - The 2001 foot and mouth disease (FMD) outbreak in the UK cost an estimated US$10 billion to the agriculture and food sectors[10]

- Bovine Tuberculosis (BTB)
  - Bovine tuberculosis is a serious infectious disease affecting a wide range of domesticated and wild animals, representing a worldwide economic and public health burden. The disease is caused by Mycobacterium bovis and infrequently by other pathogenic mycobacteria. The problem of bovine tuberculosis is complicated when the infection is associated with multidrug and extensively drug-resistant M. bovis.[11]
  - Within the last 10 years, the USDA-Animal and Plant Health Inspection Service (APHIS) program has directed $342 million of its budget to US BTB surveillance and control[12]
  - In 2013, the UK government spent £99 million on BTB with 35.6% of the cost going toward cattle compensation costs[13]

- Johne's Disease
  - Johne's disease (JD) is a major gastrointestinal disease of cattle caused by Mycobacterium Avium subspecies Paratuberculosis (MAP). This cattle disease causes premature culling and reduced milk production.[14]
  - In the U.S. dairy industry, economic losses from reduced productivity associated with JD are estimated to cost between $200 and $250 million annually.[15]

III. Existing Diagnostics

As outlined in the section above, there are significant economic gains if farms can promptly identify and diagnose diseases, maintain herd health, and ensure sustainable practices. This section explores the current state of disease detection diagnostics, focusing on key indicators and technologies that are used on farms. Identifying the current state of diagnostics will help predict areas of significant economic value for modern diagnostic technologies.

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[9] Office, "Foot and Mouth Disease."
[10] "Foot-and-Mouth Disease in Animals - Generalized Conditions."
[11] Borham et al., "Review on Bovine Tuberculosis."
[12] Kelley et al., "Accuracy of Two Point-of-Care Tests for Rapid Diagnosis of Bovine Tuberculosis at Animal Level Using Non-Invasive Specimens."
[13] Kelley et al.
[14] "Sensors | Free Full-Text | Comparison between a Conductometric Biosensor and ELISA in the Evaluation of Johne's Disease."
[15] "Sensors | Free Full-Text | Comparison between a Conductometric Biosensor and ELISA in the Evaluation of Johne's Disease."

Body Temperature as an Indicator

When properly used, body temperature serves as a crucial indicator of illness in cattle. A rectal temperature of 104°F or higher is commonly designated as a sign of sickness in beef cattle.[16] However, normal temperature fluctuations during the day must be considered when using this method. Temperature is typically measured using a rectal probe and more recently with advanced RFID ear tags.[17]

Appetite Suppression as a Signal

Visual appraisal of appetite suppression is another significant signal of illness in cattle. Feed consumption decreases about 48 hours before an increase in body temperature is observed.[18] However, it can be difficult to monitor each animal's feeding patterns on self-feeders. Instead, farm operators need to be able to visually identify animals that look gaunt, have abdomens that bounce when they walk, or experience rapid weight loss.[19]

Behavioral Changes as an Indicator

Behavioral changes such as lethargy, depression, and reduced water intake are recognized indicators of febrile infectious diseases.[20] However, similar patterns can be caused by other diseases or environmental conditions. Moreover, it requires a knowledgeable and trained operator to detect such changes in behavior.

Mastitis Detection via Somatic Cell Count (SCC)

In the realm of udder health monitoring within dairy herds, the Somatic Cell Count (SCC) of composite cow milk stands as a standard indicator in current practices.[21] Monitoring the SCC is integral for early mastitis detection. Elevated SCC signals the presence of pathogens, and additional tests like milk culture and PCR help identify the specific pathogen. SCC is routinely measured using flow cytometry-based laboratory techniques (L-SCC).[22] However, the traditional laboratory-based approach involves costly and time-consuming sample collection and shipping. Testing with the Dairy Herd Improvement program is typically conducted every 3–6 weeks, indicating a need for more frequent monitoring methods.

Recognizing the need for more frequent and cost-effective on-farm testing, the online California Mastitis Test (O-CMT) emerges as a promising solution.[23] This automated sensor facilitates mastitis monitoring on dairy farms equipped with automatic milking systems, enabling more timely and efficient detection of udder health issues.

Typical Bovine Respiratory Disease (BRD) Diagnostics

BRD is commonly identified through observation of cattle behavior. This is often paired with diagnostic methods including in-vivo and post-mortem sampling of blood, nasopharyngeal swabs, and bronchial lavage utilizing techniques like histopathology, PCR, ELISA, and microbiological culture.[24] BRD is difficult to detect because it is a multifactorial condition caused by a variety of viruses and bacteria that result in the infection of the respiratory tract.

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[16] "Identifying Sick or Injured Cattle."
[17] Murugeswari et al., "Monitoring Body Temperature of Cattle Using an Innovative Infrared Photodiode Thermometer."
[18] McManus et al., "Thermography for Disease Detection in Livestock."
[19] "Identifying Sick or Injured Cattle."
[20] Puig et al., "Technological Tools for the Early Detection of Bovine Respiratory Disease in Farms."
[21] Deng et al., "Performance of Online Somatic Cell Count Estimation in Automatic Milking Systems."
[22] Deng et al.
[23] Deng et al.
[24] Puig et al., "Technological Tools for the Early Detection of Bovine Respiratory Disease in Farms."

Merck BRD Diagnostics: Whisper on Arrival Diagnostic

Merck has developed a technology, Whisper on Arrival, that uses a handheld wand to analyze lung and heart sounds. In combination with rectal temperature and weight, the algorithm can predict an individual animal's risk of developing BRD.[25] This allows for more objective decision-making and reduced need for antibiotics. Merck also recently released SenseHub™, a system that provides a 24/7 connection to every animal, measuring temperature and movement to predict diseases.[26] Priced at 50-70 $/ear tag, it is one of the few automated monitoring ear-tag products on the market, reducing BRD mortality by ~40% compared to traditional observation methods on feedlots.[27]

In the world of cattle diagnostics, the tools currently employed by ranchers globally are, in many ways, rudimentary when compared to the precision and specificity prevalent in modern human health diagnostics. Traditional methods often necessitate seasoned expertise and involve invasive procedures such as blood sampling or rectal probes, presenting challenges in terms of both accuracy and animal welfare.

Modern diagnostics, such as SenseHub and Whisper on Arrival, promise a paradigm shift by offering less invasive, yet more effective and precise methods. The potential to monitor cattle health in real-time, predict diseases, and make informed decisions without subjecting animals to unnecessary stress opens new horizons for sustainable and humane cattle farming practices. Additionally, the potential economic benefits are manifold. Reduced mortality rates mean healthier herds and less financial loss for ranchers. By minimizing the need for intense medical intervention, these diagnostics contribute to cost savings and more sustainable practices. Real-time monitoring and disease prediction allow for better supply predictions, enabling ranchers to optimize resource allocation and production efficiency. Moreover, the decreased reliance on labor-intensive diagnostic methods translates to operational efficiency.

IV. Start-Ups

Company	**Location**	**Diagnostic Device**	**Disease Focus**
Isomark	USA	Breathalyzer	Bacterial and viral infection
AgScent	Australia	Breathalyzer (Hand-held)	BRD
Krishi	USA	Nasal Swab and LAMP testing	BRD and other diseases
SmaXtec	Austria	Reticulum bolus sensor	General health, mastitis, pneumonia (via temperature)
HerdStrong	USA	Reticulum bolus sensor	General Health
Moonsyst	Ireland	Reticulum bolus sensor	General health, mastitis,

[25] Nickell et al., "Comparison of a Traditional Bovine Respiratory Disease Control Regimen with a Targeted Program Based upon Individualized Risk Predictions Generated by the Whisper On Arrival Technology."
[26] "SenseHub_Homepage."
[27] "SenseHub_Homepage."

			pneumonia (via temperature)
Dropnostix	Germany	Reticulum bolus sensor	General health and disease detection
UlikeKorea Co. Inc.	Korea	Reticulum bolus sensor	General health, mastitis, pneumonia (via temperature)
Cattle Scan	Canada	Reticulum bolus sensor	SARA and general health
HerdDogg	USA	Ear Tag temp. Sensor and accelerometer	General health (via movement, feeding patterns, temp.)
Q Scout Lab	USA	Milk leukocyte differential test and blood leukocyte differential test	Mastitis and BRD
Mastatest	New Zealand	Milk sample for bacteria detection (24 hrs for results)	Mastitis
Soma Detect	USA	In-line continuous somatic cell counter for milk	Mastitis
MyAniml	USA	Facial recognition and computer vision	Disease (eg. pink eye, respiratory disease, etc.)
EIO Diagnostics	USA	Computer imaging and sensors of udders	Mastitis
Cattle Care	USA	Computer imaging and video analytics	Mastitis & General Health

New Diagnostic Technologies

V. At Farm Sensing Technologies and Precision Agriculture

The integration of big data and machine learning in IoT solutions, combined with metabolomics as disease markers, offers promising avenues for further advancements. Monitoring physical and spatial behaviors through accelerometers, GPS, and RFID systems provides a comprehensive approach to disease detection. However, challenges, including cost and data management, necessitate further investigation into the cost-benefit of implementing behavioral analysis methods.

Movement and Feeding Analysis

In one study, published in IEEE Access, a machine learning-based IoT technology was showcased which included wearable sensors and automatic feeders, for closely monitoring dairy calves. By employing leg bands and automatic feeders, the system achieved an impressive 88% accuracy in labeling sick and healthy calves.[28] Seventy percent of sick calves were predicted four days before diagnosis, demonstrating the potential for early intervention and improved farm efficiency.

Computer Vision and Analysis

Another study used deep learning and computer vision to monitor the respiratory behavior in dairy cows within modern farming practices. This study leveraged the YOLACT (You Only Look At CoefficienTs) model for the recognition and segmentation of multiple cows based on 4000 manually labeled images.[29] Specific resting states (lying resting, standing resting) are identified using a combination of convolutional neural networks and bidirectional long and short-term memory algorithms. Test results on 60 videos show an average accuracy of 93.56%, proving effectiveness despite interference factors such as movement, occlusion disturbance, and behavioral changes.[30] This study illustrates potential applications for the automatic diagnosis of respiratory-related diseases in dairy cows through health-sensing robots and noncontact monitoring using computer vision. Despite advancements, challenges persist in monitoring respiratory behavior in dairy cows due to poor obedience and interference from uncontrollable factors.

Automated Infrared Thermography (IRT)

IRT works by utilizing infrared sensors to detect radiation in the long-infrared range of the electromagnetic spectrum emitted by an object's surface. These sensors capture temperature-related data, producing thermograms that visually represent variations in temperature, with elevated core body temperature and regional temperature increases serving as key indicators for infectious diseases and inflammatory processes in livestock.

IRT is a non-invasive method that can detect BRD through the measurement of nostril and nasal plane temperatures and orbital temperature. Studies show early diagnosis up to a week before clinical signs.[31]

[28] "A Machine Learning and Optimization Framework for the Early Diagnosis of Bovine Respiratory Disease | IEEE Journals & Magazine | IEEE Xplore."
[29] Wu et al., "Monitoring the Respiratory Behavior of Multiple Cows Based on Computer Vision and Deep Learning."
[30] Wu et al.
[31] Puig et al., "Technological Tools for the Early Detection of Bovine Respiratory Disease in Farms."

One study on IRT testing for Foot and Mouth Disease demonstrates IRT's potential. IRT cameras can identify at-risk cattle 48 hours before clinical symptoms appear, aiding in rapid containment during outbreaks.[32] The combination of IRT with rapid diagnostic tests enhances outbreak response capabilities.

Moreover, research on IRT's relationship with residual feed intake (RFI) in cows and feedlot cattle suggests its potential as a low-cost, non-invasive method for approximating feed efficiency.[33] IRT readings, affected by stress and environmental factors, could be valuable in managing cattle entering the feedlot and mature cows based on available resources.

Challenges in IRT research include inconsistencies in practice, lack of measured emissivity values, and the need for standardized protocols.[34] Recommendations for optimizing IRT accuracy involve considering factors like ambient temperature, humidity, and camera specifications. Continuous research is essential to build confidence in results and explore the potential of IRT in early disease detection, potentially revolutionizing disease surveillance systems in livestock.

Sound Analysis

Sound analyzers are another option for diagnosing various issues in cattle and cows, offering insights into their physical well-being. For instance, rumination microphones can observe cud chewing in cows, providing valuable behavioral indicators of digestion. Wasting diseases in livestock, requiring 24-hour monitoring, can be successfully detected through audio and video data, particularly by analyzing cough sounds through audio analysis and motion detection.[35] In pigs, sound analysis aids in assessing stress levels, with recent advancements in automatic scream-detection methods offering significant breakthroughs in health management.[36] Similarly, sound data from Korean native cows has contributed to detecting abnormalities in the oestrus cycle.[37] However, challenges include interference from environmental noise and the need for sophisticated algorithms to differentiate relevant sounds.

VI. On Cow Sensing Technologies

The integration of sensors and wearable technologies in animal farming has ushered in transformative capabilities, enhancing the monitoring and management of livestock on a granular level. These sensors are strategically placed on and inside the cow, covering areas such as the neck, legs, body, vagina, tail, rumen, rectum, and subcutaneous tissue.[38] Implantable sensors offer a myriad of functions, from detecting sweat constituents to preventing diseases.[39] Biosensors seamlessly integrated with cellphones and handheld devices streamline farm monitoring processes, replacing traditional manual recording methods. RFID tags, recording farming tasks and aiding health control factors, are already employed in millions of animals to track the locations of animals and record farming tasks that contribute to control factors like fattening and milking management.[40]

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32 McManus et al., "Thermography for Disease Detection in Livestock."
33 "Identifying Efficient Cattle Using Infrared Technology."
34 McManus et al., "Thermography for Disease Detection in Livestock."
35 Neethirajan, "Recent Advances in Wearable Sensors for Animal Health Management."
36 Vandermeulen et al., "Discerning Pig Screams in Production Environments."
37 "Automatic Detection of Cow's Oestrus in Audio Surveillance System."
38 Hajnal, Kovács, and Vakulya, "Dairy Cattle Rumen Bolus Developments with Special Regard to the Applicable Artificial Intelligence (AI) Methods."
39 Neethirajan, "Recent Advances in Wearable Sensors for Animal Health Management."
40 Neethirajan.

Biosensing Devices and Commercial Collars

Notable advancements include biosensing devices attached to animals' ears, measuring body temperature, and commercial biosensor collars for detecting estrus periods in cows.[41] The biosensing ear devices cost roughly $100,000 for 10,000 cattle.[42]

Motion, Movement, and Behavior Sensors

Reduced activity in cattle due to lameness or diseases necessitate advanced technologies like accelerometers, pedometers, and GPS.[43] Commercially available accelerometer devices, such as IceTag and IceQube, prove effective in disease detection, estrus detection, and continuous study of mobility and behavior.[44] GPS collars combined with activity sensors provide real-time tracking of cattle behavior and location, enhancing overall monitoring efficiency. Moreover, through strategically located sensors or RFID tagging platforms, the feeding and drinking behavior can be monitored on feedlots. These technologies can provide valuable insights to farmers on the behavior of their cattle and through ML algorithms can be used to identify sick or injured cattle early.

Solar-powered GPS collar-based virtual fence systems, like NoFence, offer promising solutions for tracking and confining animals.[45] Robotic grazing systems utilize electronic leg bands interacting with sensors to record feeding and milking behavior.[46]

Studies reveal the efficacy of biosensors, including electromyography, mechanical/pressure, and acoustic sensors, in recognizing jaw movements indicative of grazing behavior. The RumiWatch noseband sensor stands out as an example, effectively monitoring feeding and rumination activity in dairy cows.[47] Real-time physiological parameter measurement through these sensors offers advantages over traditional herd-based observation systems.

The main challenge with motion and movement sensors is getting the hardware to withstand the conditions of the farm or feedlot, provide an easy application or attachment, have low power requirements, and low cost per animal.

Rumen Bolus Sensors

Rumen bolus sensors, introduced after the 2000s, focus on reticulo-ruminal pH and temperature.[48] Initially used in research with fistulated cattle, these sensors have evolved to provide integral data about various aspects of the animal condition, welfare, estrus, feeding, disease symptoms, lameness, and calving prediction. While rumen boluses offer valuable diagnostic insights, their use in cattle farming is limited due to high costs compared to external sensors in smart herd diagnostic systems.

[41] Džermeikaitė, Bačėninaitė, and Antanaitis, "Innovations in Cattle Farming."
[42] Neethirajan, "Recent Advances in Wearable Sensors for Animal Health Management."
[43] Džermeikaitė, Bačėninaitė, and Antanaitis, "Innovations in Cattle Farming."
[44] Džermeikaitė, Bačėninaitė, and Antanaitis.
[45] Džermeikaitė, Bačėninaitė, and Antanaitis.
[46] Neethirajan, "Recent Advances in Wearable Sensors for Animal Health Management."
[47] Džermeikaitė, Bačėninaitė, and Antanaitis, "Innovations in Cattle Farming."
[48] Hajnal, Kovács, and Vakulya, "Dairy Cattle Rumen Bolus Developments with Special Regard to the Applicable Artificial Intelligence (AI) Methods."

Rumen boluses play a role in detecting sub-acute rumen acidosis (SARA) through continuous pH measurements in the ventral rumen.[49] Challenges include the short lifespan of pH boluses and associated costs. Alternative noninvasive methods involve challenges in pH probe calibration, signal recording, conversion to radiofrequency, and reception. In addition to pH measurement, bolus sensors can assess changes in ruminal temperature. Monitoring temperature changes aids in the early detection of estrus, inflammatory conditions, and overall physiological states.[50]

Temperature Determination

Various methods are employed to measure animal temperatures, ranging from invasive techniques like intra-vaginal radio transmitters and rectal probes to non-invasive solutions like infrared thermometers.[51] Invasive methods, while informative, pose challenges such as the rapid drop in rumen temperature during water intake and the potential for vaginal sensors to fall out and cause stress. Miniaturized ambulatory receivers/loggers have been used for core body temperature calculations in various animals, and recent advancements explore automatic monitoring systems for subcutis, vagina, skin surface, and rumen. Challenges persist in standardizing these methods. Endoceliac sites and the tail base have been proposed as viable options, but implantable sensors come with risks of infection. Ear tag or collar sensors are fairly sensitive and can provide accurate temperature guidance when compared to the entire herd's average temperature and ambient temperature. Temperature monitoring can indicate certain physiological changes in cows, however they are often not the most effective in detecting disease early, since by the time the temperature of the animal increases, they are usually already quite sick.

Sweat and Saliva Detection

The development of diagnostic devices for animals testing sweat and saliva represents a significant stride in non-invasive health monitoring. Saliva emerges as a promising non-invasive alternative to blood sampling for disease diagnosis in animals. The comprehensive composition of saliva, containing local and systemic components, offers valuable insights into the physiological or pathological status of the organism.[52] Salivary biomarkers have diverse applications, including early disease detection, decision support for animal management, and monitoring disease progression. Studies have explored saliva for detecting oral cancer biomarkers and determining estrous time in buffalo for precise insemination planning.[53] Additionally, saliva has been investigated for indications of physiological conditions such as pregnancy status in cattle. Despite its potential, challenges exist in understanding the protein composition of saliva under various conditions, ensuring accurate diagnostic results.

In the realm of saliva analysis, mouth guard biosensors equipped with the uricase enzyme provide real-time, wearable monitoring for uric acid detection.[54] This technology offers non-invasive and continuous monitoring, making it highly valuable for detecting mouth conditions and diseases like Gastrophageal Reflux Diseases (GERD).[55] The non-invasive nature of saliva analysis is particularly advantageous in mitigating the stress associated with drawing blood from animals.

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[49] Hajnal, Kovács, and Vakulya.
[50] Hajnal, Kovács, and Vakulya.
[51] Murugeswari et al., "Monitoring Body Temperature of Cattle Using an Innovative Infrared Photodiode Thermometer."
[52] Džermeikaitė, Bačėninaitė, and Antanaitis, "Innovations in Cattle Farming."
[53] Džermeikaitė, Bačėninaitė, and Antanaitis.
[54] Neethirajan, "Recent Advances in Wearable Sensors for Animal Health Management."
[55] Neethirajan.

Wearable sweat analyzers present another avenue for animal health monitoring, relaying valuable information about the health of animals.[56] Despite not being commercialized yet due to size constraints, low-cost robust designs have been developed in laboratories. Real-time sweat monitoring systems have been designed to detect sodium levels, multiple electrolytes, and metals, showcasing potential for comprehensive and non-invasive health monitoring in animals. [57]

VII. Point-of-Care Testing

The increasing demand for efficient and rapid diagnostic solutions has led to the widespread adoption of Point-of-Care Tests (POCTs) in various fields, including veterinary medicine. POCTs, defined as devices delivering same-day diagnostic results outside traditional laboratory settings, come in diverse formats such as paper-based lateral flow assays, portable nucleic acid detection systems, wearable electronic sensors, and more.[58] The World Health Organization (WHO) has set criteria for ideal POC applications under the acronym ASSURED, emphasizing affordability, sensitivity, specificity, user-friendliness, rapidness, robustness, and deliverability.[59] With the ability to detect single or multiple analytes or disease agents, POCTs play a crucial role in screening, diagnosis, monitoring, prognosis, surveillance, and staging. The development of POCTs has seen significant growth, with clinical chemistry POCTs dominating the market, while infectious disease POCTs are predicted to experience rapid expansion. The COVID-19 pandemic has popularized POC testing globally, but a similar trend is yet to be observed in POC diagnostics for farm animal diseases.

Types of Samples	Types of POCT Systems
• Milk • Blood • Nasal mucus • Breath • Urine • Imaging	• Paper-based fluidic devices • Miniaturized isothermal amplification tests • Lateral Flow Assays • Chemiluminescence • Nano-particle based assays • Microfluidic devices • Multiplex Diagnostics • Electronic Nose or GC-MS • Conductometric Biosensors • Ultrasound

Disease Specific Detection

Bovine Tuberculosis Detection

[56] Neethirajan.
[57] Neethirajan.
[58] Hobbs et al., "The Potential of Diagnostic Point-of-Care Tests (POCTs) for Infectious and Zoonotic Animal Diseases in Developing Countries."
[59] Manessis, Gelasakis, and Bossis, "Point-of-Care Diagnostics for Farm Animal Diseases."

The study assessed the suitability of two rapid diagnostic tests, the Alere Determine TB Lipoarabinomannan Antigen (LAM-test) and the Lionex Animal TB Rapid Test (Lionex-test), for bovine tuberculosis (BTB) detection in cattle.[60] The LAM-test, endorsed by WHO for human TB, demonstrated poor agreement with routine USDA BTB tests when applied to urine and milk samples. Despite inconsistencies, the Lionex-test, designed for BTB, showed positive trends in milk samples, suggesting potential viability for non-invasive and rapid BTB diagnosis in cattle.[61] The study highlights the challenges of BTB diagnosis, the economic burden of surveillance efforts, and the need for further validation of novel tests to enhance field-based BTB detection.[62]

Bovine Leukemia Diagnosis

Yamazaki et al. employed a combination of EZ fast DNA extraction and LAMP to amplify bovine leukemia virus DNA from blood for diagnostic purposes.[63] This approach demonstrated comparable sensitivity and specificity to rRT-PCR and offered rapid results, with the extraction step completed in less than 10 minutes.

Mastitis Diagnosis

Loop-mediated isothermal amplification (LAMP) has become a prevalent platform for mastitis diagnosis in cattle. LAMP assays, used in-line, in-parlor, and in the laboratory, offer advantages over PCR or rRT-PCR, such as reduced sensitivity to inhibitory substances in milk.[64] However, challenges include the heterogeneity of mastitis pathogens and resistance determinants, along with limited multiplexing capacity.

Bacterial Detection

Researchers developed a wax-printed paper-based ELISA using a microfluidic device for Escherichia coli O157:H7 detection in artificial beef samples.[65] The assay exhibited high specificity, sensitivity, and repeatability, completing within 3 hours and requiring only 5 μl of sample. Another study by Liebes et al. introduced a chemiluminescence immunosensor for Brucella antibodies in milk, outperforming conventional ELISA with a superior limit of detection at 0.207 μg/ml.[66]

Bovine Respiratory Disease

Researchers at Purdue University have developed technology that can identify three significant strains of bacteria causing BRD: Pasteurella multocida, Mannheimia haemolytica, and Histophilus somni.[67] Using a nasal swab and a vial with specific primers and reagents, the technology, based on loop-mediated isothermal amplification (LAMP), provides results within an hour by detecting bacterial DNA and triggering a color change in the assay.[68] The results of this innovative on-site test closely match those of the standard polymerase chain reaction (PCR) test, with a matching rate ranging from 60% to 100%.

Catalase Detection in Milk for Mastitis Disease

An aptamer-based Surface Plasmon Resonance (SPR) biosensor has been developed for the detection of catalase in milk samples, serving as a key indicator of mastitis disease.[69] The aptamer, immobilized onto a gold

[60] Kelley et al., "Accuracy of Two Point-of-Care Tests for Rapid Diagnosis of Bovine Tuberculosis at Animal Level Using Non-Invasive Specimens."
[61] Kelley et al.
[62] Kelley et al.
[63] Velayudhan and Naikare, "Point-of-Care Testing in Companion and Food Animal Disease Diagnostics."
[64] Velayudhan and Naikare.
[65] Velayudhan and Naikare.
[66] Velayudhan and Naikare.
[67] Service, "Pen-Side Test for Bovine Respiratory Disease May Save Cattle Industry Millions, Reduce Antibiotic Use."
[68] Service.
[69] Ashley and Li, "An Aptamer Based Surface Plasmon Resonance Biosensor for the Detection of Bovine Catalase in Milk."

surface, exhibits good specificity toward catalase. The biosensor demonstrates a limit of detection in the nanomolar range and a dynamic range suitable for catalase detection in milk.[70] Aptamers, as ligands in SPR biosensors (aptasensors), offer stability, small size, cost-effectiveness, and versatility for easy immobilization onto the SPR surface.

Johne's Disease Detection

Conductometric biosensors have been employed for the detection of Johne's disease (JD), caused by Mycobacterium avium subspecies paratuberculosis (MAP).[71] JD is a major gastrointestinal disease in cattle, leading to economic losses. Conductometric biosensors combine immunomigration technology with electronic signal detection, offering a non-laboratory-based assay using samples of serum from cattle. The biosensors, focusing on the detection of IgG antibodies against MAP, provide a potential tool for more frequent testing and improved control of JD.[72]

Bovine Herpes Virus-1 (BHV-1) Antibodies Detection

A biosensor assay, specifically Vantix™, has been developed for the quantitative analysis of bovine herpes virus-1 antibodies in milk samples.[73] This biosensor platform, designed for rapid routine immunological testing, provides an efficient method for detecting BHV-1 antibodies in a milk matrix.

Bovine Tuberculosis Diagnosis

One method of diagnosing bovine tuberculosis involves analyzing volatile organic compounds (VOCs) in breath for specific biomarkers.[74] Breath biomarkers like ammonia, methane, carbon dioxide, acetone, and nitric oxide are examined using laser spectroscopic techniques. GC-MS further reveals VOCs associated with M. bovis infection. Nanotechnology-based array sensors offer real-time monitoring of M. bovis-infected cattle through breath samples, providing a promising approach for early diagnosis.[75]

Foot-and-Mouth Disease Detection

Noninvasive screening for foot-and-mouth disease utilizes hand-held air samplers with electrostatic particle capture to identify sources of the disease.[76] Real-time PCR is applied to captured airborne infectious agents for monitoring the foot-and-mouth disease virus. Monolayer-capped gold nanoparticle (GNP) sensors, along with pattern recognition methods, offer fast and cost-effective diagnostic results from breath samples.[77] Recent patent developments even detect carbon dioxide from fluids to determine respiratory health in animals, showcasing diverse approaches in noninvasive disease detection.[78]

Bovine Respiratory Disease

One study explored the utility of thoracic ultrasonography (TUS) in diagnosing BRD in experimental settings.[79] Calves were infected with bovine respiratory syncytial virus or Mannheimia haemolytica to simulate viral and bacterial infections, respectively. TUS, conducted alongside clinical scoring, revealed weak overall correlations

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[70] Ashley and Li.
[71] "Sensors | Free Full-Text | Comparison between a Conductometric Biosensor and ELISA in the Evaluation of Johne's Disease."
[72] "Sensors | Free Full-Text | Comparison between a Conductometric Biosensor and ELISA in the Evaluation of Johne's Disease."
[73] Neethirajan, "Recent Advances in Wearable Sensors for Animal Health Management."
[74] Neethirajan.
[75] Neethirajan.
[76] Neethirajan.
[77] Neethirajan.
[78] Neethirajan.
[79] Porter et al., "Use of Thoracic Ultrasonography to Improve Disease Detection in Experimental BRD Infection."

but effectively identified abnormal lung pathology, providing valuable insights beyond clinical assessment.[80] The study suggests TUS as a promising tool for enhancing BRD diagnosis and potentially offering an alternative to terminal studies.[81]

Analysis of POCTs

Challenges in POCTs	**Opportunities in POCTs**
Validation and Complexity ● Focus on comprehensive validation using diverse clinical samples and large animal populations. ● Ensure validation data, performance metrics, and confidence intervals (CIs) represent the variability in animal populations.	*Telemedicine and Precision Farming* ● Integrate animal tracking and telemedicine to enable real-time epidemiological surveillance. ● Facilitate evidence-based disease-control strategies through data-driven insights.
Cost-Effectiveness and Simplicity ● Emphasize low-cost and simple designs for consumer acceptance and successful marketing. ● Automation of complex handling processes (e.g., pipetting, sample pre-treatment) is crucial for efficiency.	*Multiplexing for Improved Disease Detection* ● Develop multiplexed POC devices to enhance the accuracy of disease detection. ● Offer benefits such as reduced sample volumes, faster analysis times, and increased testing throughput.
Portability and Multiplexing ● Develop portable and multiplexed POC devices to address the lack of permanent infrastructure on farms. ● Multiplexing is essential for efficient testing, considering the diverse range of diseases and limited expertise among farmers	*Public-Private Collaboration for Development and Commercialization* ● Foster collaboration between the public and private sectors for successful research, development, and commercialization of novel POC diagnostics. ● Combine resources and expertise to expedite the implementation of innovative solutions.

[80] Porter et al.
[81] Porter et al.

Interdisciplinary Collaboration and Funding ● Form interdisciplinary research teams, involving animal experts, to fully leverage technological advancements. ● Collaborate with both public and private sectors, relying on public funding for the research and development of innovative POC diagnostics.	*Flexible Legal Framework* ● Advocate for a unilateral and flexible legal framework that supports the commercialization of POC devices. ● Ensure consumer protection while facilitating the dissemination of cutting-edge technologies.
Legal Framework and Commercialization ● Establish a flexible legal framework to streamline the commercialization and dissemination of novel POC devices. ● Provide financial incentives for private companies to undertake commercialization efforts.	

VIII. Conclusion

The white paper reveals a concerning upward trend in feedlot and dairy farm death loss rates within the cattle industry. The escalating mortality rates, attributed to factors such as structural changes, technology adoption, and uncontrollable elements like disease outbreaks and environmental conditions, pose significant economic risks and animal welfare concerns. Improved and early detection of Bovine Respiratory Disease and Mastitis offer a substantial economic opportunity, given the prevalence of the disease which increases with larger farmers and higher stocking densities.

Addressing this complex challenge necessitates a shift towards innovative technologies for disease detection and diagnostics. Traditional methods, outlined in the paper, often prove insufficient due to their invasiveness, lack of precision, and required veterinarian expertise. This prompted a crucial exploration of modern diagnostics such as SenseHub and Whisper on Arrival. These technologies offer real-time monitoring and predictive analytics, presenting potential solutions for reducing mortality rates and enhancing operational efficiency.

The paper also delves into new diagnostic technologies, emphasizing the promise of farm sensing technologies, precision agriculture, and the integration of big data and machine learning. Wearable sensors, biosensing devices, and point-of-care testing emerge as avenues for non-invasive and early disease detection. However, challenges, including cost considerations and the need for standardization, highlight the importance of continuous research to optimize accuracy, build confidence in results, and explore the full potential of these technologies.

Furthermore, a significant challenge that demands attention is the intricate process of integrating these advanced technologies onto farms. Cattle and dairy operators often approach promising new diagnostics with skepticism, fueled by past experiences of misleading solutions and unmet promises. A key consideration is simplifying the integration of technologies into existing farm infrastructure, ensuring success by avoiding disruption to established practices.

The potential of computer vision, particularly if it becomes more cost-effective and enhances predictive capabilities, holds promise for delivering substantial value to farmers. Technologies that can autonomously collect samples without operator intervention are likely to gain traction, provided they are economically viable. Given the narrow profit margins in the beef and dairy sectors, operators will only invest in new technologies if a clear Return on Investment (ROI) is evident, contributing to increased annual revenue.

Recommendations include early partnerships with farms to test diagnostic functionalities in day-to-day operations. Launching new diagnostic technologies at the stage of the cattle or dairy life cycle with the highest returns for operators is crucial. For instance, focusing on disease detection during backgrounder or cow/calf operations may yield more significant benefits due to higher mortality rates in these stages. Successful integration hinges on understanding and respecting the economic constraints and operational dynamics of beef and dairy operators.

In conclusion, the white paper highlights the critical role of advanced technologies in mitigating the impact of rising mortality rates in the cattle industry. Future investments should prioritize the development and implementation of cutting-edge diagnostics to address economic, welfare, and sustainability concerns faced by the beef and dairy sectors. The potential benefits of reducing mortality rates, minimizing antibiotic use, and optimizing resource allocation underscore the transformative impact that technological advancements can have on the overall health and profitability of the cattle industry if built with the end-user in mind.

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