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Advances in Anaesthesia and Analgesia for Laboratory Animals- Current Practices and Future Directions: A Review

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ABSTRACT

Laboratory animal anaesthesia and analgesia are essential for ethical research, balancing welfare with scientific rigor. This review synthesizes historical practices and contemporary innovations to refine perioperative care. We evaluate the shift to inhalant/hybrid protocols for precision and compliance with the 3Rs (Replacement, Reduction, Refinement). Advancements include multimodal pain assessment (*e.g.*, rat grimace scale) and technology-driven monitoring, enhancing detection of pain masked by anaesthesia. Innovations address physiological challenges like hypothermia and species-specific responses. Interdisciplinary One Health collaborations foster sustainable practices and translational biomarker discovery. However, barriers persist, including resource disparities, understudied chronic pain models and slow technology adoption, highlighting the need for global standardization. Case studies illustrate successes with pre-emptive analgesia and failures from outdated protocols. Practical recommendations include perioperative checklists and institutional training to harmonize welfare and research goals. Prioritizing animal welfare is fundamental to scientific excellence, urging innovation, equity and transparency.

Key words: Laboratory animal research, Pain, Rats, Refinement.

Anaesthesia and analgesia are integral to laboratory animal science, ensuring humane treatment and minimizing pain while maintaining the integrity of scientific research.

The use of Anaesthesia in laboratory animals has evolved significantly over the past century. Early anaesthetic techniques often relayed upon ether and chloroform, which had inconsistent effects and high mortality rates. With advancements modern anaesthetics such as isoflurane and sevoflurane have emerged, offering improved safety and precision in dosage (Miller *et al.,* 2016). Moreover, the refinement of analgesic protocols, including the use of multimodal analgesia combining opioids and local anaesthetics, has enhanced post-procedural recovery (Mumtaz *et al.,* 2024). The integration of standardized pain assessment methods, such as the rat grimace scale (RGS) and mouse grimace scale (MGS), has also contributed to refining anaesthetic and analgesic protocols (Miller *et al.,* 2015, 2016). These behavioural assessments help to manage pain effectively, reducing the impact of procedural stress on experimental outcomes as effective integration of Anaesthesia and analgesia in laboratory animal research is crucial to balancing animal welfare with scientific rigor. Ethical frameworks, such as the 3Rs (Replacement, Reduction and Refinement), emphasize the importance of minimizing pain and distress while maintaining experimental validity. Studies have shown that hypothermia during general Anaesthesia can interfere with pain assessment in rats, highlighting the necessity of comprehensive perioperative monitoring (Klune *et al.,* 2020). Furthermore, certain anaesthetic agents, (sodium pentobarbital; IP), may induce pain responses in laboratory rats, necessitating alternative approaches or adjunct analgesics (Reimer *et al.,* 2020). The adoption of preemptive and multimodal analgesia, combining local and systemic analgesics, has been shown to improve outcomes in surgical models, particularly in procedures inducing significant post-operative pain, such as uterine surgery in rats (Mumtaz *et al.,* 2024).

Traditional vs. advanced anesthesia practices

The evolution of anesthetic techniques in laboratory animal science has seen a transition from traditional, primarily injectable methods to advanced techniques that

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incorporate precise inhalant delivery and hybrid approaches.

Injectable anesthetics: Efficacy, limitations and species-specific risks

Injectable anesthetics have long been a mainstay in laboratory animal procedures because of their ease of administration and minimal equipment requirements. Agents such as sodium pentobarbital and ketamine-based combinations provide rapid induction and are widely used across various species. However, limitations exist regarding their efficacy and safety. For example, (Reimer *et al.,* 2020) reported that intraperitoneal injections of sodium pentobarbital may elicit pain responses in adult rats, raising concerns about animal welfare. Injectable agents also carry risks of tissue irritation and adverse cardiorespiratory events, particularly when dosing is not carefully adjusted for species-specific metabolic rates and sensitivities (Groeben *et al.,* 2003).

Inhalant anesthetics: Precision, safety and technological advances

In contrast to injectables, inhalant anesthetics such as isoflurane have become increasingly popular because of their rapid induction, ease of titration and predictable recovery profiles. Precision vaporizers allow for the exact delivery of anesthetic concentrations, reducing the risk of overdose and enabling fine control over anesthetic depth (Miller *et al.* 2016). Advances in scavenging systems further increase safety by minimizing occupational exposure to waste anesthetic gases. These technological improvements also help mitigate common side effects, such as hypothermia and cardiorespiratory depression, making inhalant anesthesia particularly well suited for prolonged or delicate procedures.

Hybrid approaches: Combining local and general anesthesia

Hybrid anesthetic strategies seek to capitalize on the strengths of both injectable and inhalant techniques while minimizing their respective drawbacks. By combining general anesthesia with local anesthetic techniques, researchers can achieve effective surgical conditions with lower doses of systemic anesthetics. This multimodal approach not only enhances pain control but also reduces the potential for adverse systemic effects. For example, (Mumtaz *et al.,* 2024) demonstrated that the concomitant use of preemptive analgesia (local anesthetics) with general anesthesia improved pain management in a rat uterine pain surgical model. Additionally, such hybrid protocols, which are often augmented with adjuncts such as buprenorphine, allow for reduced doses of general anesthetics, thereby minimizing risks such as respiratory depression and delayed recovery.

Pain assessment in anesthetized animals

Accurate pain assessment in anesthetized laboratory animals is critical for ensuring welfare and scientific validity. However, anesthesia complicates pain evaluation by masking behavioral cues and altering physiological responses.

Behavioral and physiological biomarkers (*e.g.*, grimace scales, activity monitoring)

Behavioral and physiological biomarkers remain foundational tools for pain assessment in anesthetized animals. The Rat Grimace Scale (RGS) and Mouse Grimace Scale (MGS) are validated tools for quantifying facial expressions associated with pain, even under anesthesia (Miller *et al.,* 2015, 2016). For example, (Miller *et al.,* 2016) demonstrated that isoflurane-anesthetized rats exhibit reduced orbital tightening and ear positioning, key RGS indicators, suggesting that pain may persist undetected if assessments rely solely on facial expressions. Similarly, (Miller *et al.,* 2015) reported strain-specific differences in MGS responses in mice, emphasizing the need for species- and strain-adjusted protocols.

Activity monitoring systems, such as telemetry and video tracking, complement grimace scales by capturing subtle postural changes (*e.g.*, hunched back) or reduced mobility postsurgery (Flecknell, 2016). However, these tools require baseline data for individual animals to account for intersubject variability. Physiological biomarkers, including heart rate variability and respiratory patterns, also provide indirect pain indicators. For example, (Groeben *et al.,* 2003) identified heritable differences in respiratory drive in anesthetized mice, which could confound pain-related interpretations without careful baseline comparisons.

Challenges of anesthesia-induced masking: Case studies in rodents

Anesthetic agents often suppress pain-related behaviors, leading to the underestimation of discomfort. In rodents, isoflurane, a widely used inhalant anesthetic, reduces the sensitivity of grimace scales by altering facial muscle tone (Miller *et al.,* 2016; Mumtaz *et al.,* 2024), highlighting this issue in a rat uterine pain model, where traditional opioid-only regimens failed to mitigate postoperative pain behaviors, whereas combining preemptive local anesthesia (bupivacaine) with isoflurane improved outcomes. This underscores the importance of multimodal analgesia to counteract anesthesia-induced masking.

Additionally, intraperitoneal sodium pentobarbital, a common injectable anesthetic, can itself elicit acute pain responses in rats, further complicating pain assessment (Reimer *et al.,* 2020). These findings advocate the use of alternatives such as inhalants with rapid titratability or adjunct analgesics to minimize masking effects.

Hypothermia and stress: Confounding factors in pain evaluation

Hypothermia during general anesthesia is a pervasive issue in rodents, altering pain perception and assessment accuracy. Klune *et al.* (2020) demonstrated that hypothermic rats (core temperature <36°C) presented diminished RGS responses despite confirmed surgical pain, likely due to reduced metabolic activity and stress hormone secretion. This necessitates rigorous temperature control, such as heated surgical surfaces or circulating water blankets, to maintain normothermia.

Stress from anesthesia and handling also confounds pain evaluation. (Groeben *et al.,* 2003) noted strain-specific respiratory stress responses in anesthetized mice, suggesting that genetic background influences physiological pain.

Physiological and metabolic impacts of anesthesia

Anesthesia induces profound physiological and metabolic changes in laboratory animals, influencing the cardio-vascular, respiratory and immune systems. Understanding these impacts is critical for optimizing animal welfare and experimental outcomes.

Cardiovascular and respiratory effects: Risks and mitigation strategies

Anesthetic agents significantly alter cardiovascular and respiratory functions. Injectable agents such as sodium pentobarbital depress myocardial contractility and reduce cardiac output, posing risks during prolonged procedures (Reimer *et al.,* 2020). In contrast, inhalants such as isoflurane cause dose-dependent vasodilation and respiratory depression, necessitating careful titration to avoid hypoxia (Flecknell, 2016). For example, (Groeben *et al.,* 2003) demonstrated strain-specific respiratory vulnerabilities in mice under anesthesia, with heritable differences in breathing patterns affecting gas exchange efficiency.

The mitigation strategies include the following:

· Heart rate, blood pressure and oxygen saturation are continuously monitored (Flecknell, 2016).

· Ventilatory support for prolonged procedures to counteract respiratory depression (Fish, 2008).

· Dosing was tailored on the basis of species, strain and individual health status to minimize cardiovascular strain (Groeben *et al.,* 2003).

Thermoregulation: Hypothermia management during prolonged procedures

Hypothermia is a common complication of anesthesia due to impaired thermoregulation and vasodilation. In rodents, core temperatures can decrease rapidly, with hypothermia (<36°C) altering drug metabolism and exacerbating pain assessment challenges (Klune *et al.,* 2020). For example, Klune *et al.* (2020) reported that hypothermic rats exhibited delayed recovery and reduced sensitivity to pain biomarkers, complicating postoperative evaluations.

Effective interventions include the following:

· External warming devices (*e.g.*, heated surgical pads and circulating water blankets) are used to maintain normothermia (Flecknell, 2016).

· Prewarming animals before induction to buffer heat loss (Klune *et al.,* 2020).

· Intraoperative fluid warming to stabilize the core temperature over a long period of time requires surgery (Janus and Golde, 2014).

Innovations in multimodal monitoring

The integration of advanced technologies into laboratory animal care has revolutionized perioperative monitoring, enhancing precision, welfare and data reliability.

Advanced technologies: ECG, pulse oximetry and capnography

Modern monitoring tools such as electrocardiography (ECG), pulse oximetry and capnography provide real-time insights into cardiovascular and respiratory stability during anesthesia. ECG systems detect arrhythmias induced by anesthetic agents such as ketamine or isoflurane, enabling rapid intervention (Flecknell, 2016). Pulse oximetry, while challenging in small rodents due to peripheral vasoconstriction, offers noninvasive measurement of oxygen saturation (SpO_2), which is particularly useful in prolonged procedures (Janus and Golde, 2014). Capnography, which measures end-tidal CO_2 ($EtCO_2$), is critical for assessing ventilatory efficiency. For example, (Groeben *et al.,* 2003) utilized respiratory pattern analysis in mice to identify strain-specific vulnerabilities to hypoxia under anesthesia, underscoring the need for tailored monitoring.

Telemetry and real-time data: Enhancing perioperative care

Implantable telemetry systems enable continuous monitoring of physiological parameters (*e.g.*, heart rate, blood pressure and temperature) in conscious and anesthetized animals, minimizing stress from external devices. Real-time data transmission to centralized platforms allows researchers to adjust anesthetic depth or analgesia instantaneously, aligning with the 3Rs' refinement principle (Flecknell, 2016).

Automated systems for anesthesia delivery and pain detection

Automation is transforming anesthesia administration and pain assessment. Closed-loop anesthesia delivery systems (CLADSs) use algorithms to titrate inhalant concentrations on the basis of real-time electro encephalo gram (EEG) or vital sign feedback, reducing overdose risk (Ching *et al.,* 2013). Machine learning (ML)-driven pain detection tools, such as AI-powered grimace scale analyzers, enhance objectivity in pain assessment. (Miller *et al.,* 2016) validated an automated RGS scoring system in rats, which detected subtle pain indicators masked by manual observation. Similarly, activity-monitoring algorithms can flag pain-related behavioral changes, such as reduced exploratory behavior, in real time (Miller *et al.,* 2015).

Species-specific considerations

To optimize welfare and scientific outcomes, laboratory animal anesthesia and analgesia protocols must account for species-specific anatomical, physiological and behavioral differences.

Rodents: Unique challenges in small-body models

Rodents, the most common laboratory animals, present distinct challenges due to their small size and high metabolic rates. Injectable anesthetics such as sodium pentobarbital, while convenient, can cause pain upon intraperitoneal administration (Reimer *et al.,* 2020) and require precise dosing to avoid overdose. Inhalants such as isoflurane are preferred for titratability but suppress pain-related facial expressions, complicating postoperative assessments (Miller *et al.,* 2016). Hypothermia during anesthesia is particularly problematic in rodents; (Klune *et al.,* 2020) demonstrated that core temperatures below 36°C reduce the sensitivity of the rat grimace scale (RGS), necessitating active warming strategies such as heated pads or circulating water blankets.

Preemptive analgesia, such as combining local anesthetics (bupivacaine) with general anesthesia, has proven effective in rodent models. For example, (Mumtaz *et al.,* 2024) reported reduced postoperative inflammation and pain behaviors in rats undergoing uterine surgery when preemptive analgesia was integrated. Strain-specific differences further complicate protocols, as observed in mice, where compared with CBA strains, DBA/2 strains exhibit heightened stress responses under isoflurane (Miller *et al.,* 2015). However, in one of those studies, the administration of bupivacaine resulted in a significant increase in muscle twitch parameters (Pelit *et al.,* 2018).

Nonhuman primates: Addressing complex pain behaviors

Owing to their cognitive complexity, social needs and ability to mask pain, nonhuman primates (NHPs) require specialized protocols. As Janus and Golde (2014) emphasized, NHPs often exhibit subtle pain indicators, such as reduced social interaction or altered feeding patterns, rather than overt grimacing. Inhalant anesthetics (*e.g.*, isoflurane) are standard but require meticulous monitoring to avoid respiratory depression. Postoperative analgesia must address both physical and psychological distress, often through multimodal approaches combining opioids (*e.g.*, buprenorphine) and nonsteroidal anti-inflammatory drugs (NSAIDs). Ethical and practical challenges include minimizing stress during handling and ensuring compatibility with social housing.

Aquatic and exotic species: Emerging models with specialized needs

Aquatic (*e.g.*, zebrafish) and exotic species (*e.g.*, reptiles and amphibians) are increasingly used in research but require tailored anesthetic and analgesic protocols. For example, zebrafish Anesthesia typically involves tricaine methanesulfonate (MS-222), but dosing must account for water pH and temperature (Collymore *et al.,* 2014). Owing to their ectothermic physiology, reptiles demand precise temperature control during anesthesia to maintain metabolic stability. Pain assessment in these species is understudied. For example, amphibians lack validated grimace scales, necessitating reliance on behavioral proxies such as reduced mobility or appetite. The AVMA Guidelines for Euthanasia stress species-specific euthanasia protocols to minimize distress in exotic models (Leary *et al.,* 2020).

Case studies in refinement: Integrating preemptive analgesia in surgical models

Refinement of anesthetic and analgesic protocols is essential for ethical research and robust scientific outcomes. Preemptive analgesia has emerged as the gold standard for reducing postoperative pain and inflammation in laboratory animals. A landmark study by Mumtaz *et al.* (2024) in a rat uterine pain model demonstrated that, compared with traditional opioid-only regimens, combining preemptive local anesthesia (bupivacaine) with general isoflurane reduced postoperative pain behavior and inflammatory markers. This approach not only improved animal welfare but also enhanced data consistency by minimizing stress-induced physiological variability. Similarly, Miller *et al.* (2015) achieved success in mice by pairing isoflurane with buprenorphine, which reduced strain-specific stress behaviors in CBA and DBA/2 mice, underscoring the importance of tailoring protocols to genetic backgrounds.

Failures and lessons learned: Missteps in anesthetic management

Historical reliance on outdated protocols has led to preventable welfare breaches. Reimer *et al.* (2020) revealed that intraperitoneal sodium pentobarbital, elicits acute pain in rats, challenging its ethical use. In another case, Klune *et al.* (2020) reported that hypothermia during general anesthesia masked pain assessment in rats, causing undertreated postoperative pain. These failures highlight the consequences of overlooking physiological confounders and underscore the need for multimodal monitoring. A study (Miller *et al.,* 2016) demonstrated the risk of using isoflurane without complementary pain assessment tools: its sedative properties suppress rat grimace scale (RGS) responses, delaying analgesic intervention. Such cases emphasize the necessity of integrating advanced monitoring (*e.g.*, telemetry, biomarkers) with anesthesia.

Translational impact: How refined protocols improve human relevance

Refined animal protocols directly enhance translational research. For example, preemptive analgesia models validated in rodents Mumtaz *et al.* (2024) have informed clinical practices in human obstetrics, reducing opioid dependence in postcesarean sections (Bollag *et al.,* 2021). Similarly, thermoregulation strategies for rodents (Klune *et al.,* 2020) mirror human perioperative guidelines to prevent hypothermia-related complications (Bollag *et al.,* 2021).

Nonhuman primate (NHP) studies further bridge gaps: (Janus and Golde, 2014) demonstrated that refined analgesia protocols in NHPs improved postoperative recovery metrics, paralleling advancements in human pain management. These interspecies insights validate the One Health paradigm, where animal welfare refinements yield reciprocal human benefits.

Current challenges and knowledge gaps

Despite advancements in laboratory animal anesthesia and analgesia, significant challenges and knowledge gaps hinder the universal implementation of best practices.

Training and resource limitations in low-income settings

Resource disparities perpetuate animal welfare inequities. Outdated equipment (*e.g.*, lack of precision vaporizers) and limited analgesics force reliance on suboptimal protocols, like intraperitoneal sodium pentobarbital (Reimer *et al.,* 2020). Training gaps exacerbate these issues. Despite the recognized need for education and training in laboratory animal science (LAS) and ethics in Africa, access to such opportunities has historically been limited. The Pan-African network for laboratory animal science and ethics (PAN-LASE) was established to address the lack of education and training in laboratory animal science and ethics across Africa, benefiting 3,635 individuals from 28 countries in 4.5 years, strengthening ethics and welfare. Sustainability challenges persist, while cost constraints neglect basics like thermoregulation, causing preventable hypothermia (Flecknell, 2016; Mohr *et al.,* 2023; Klune *et al.,* 2020).

Solutions

- Partnerships between institutions for equipment donations and virtual training programs (ICLAS, 2023).
- Open-access guidelines tailored to low-resource settings (National Research Council 2011).

Understudied areas: Chronic pain and long-term effects of anesthesia

Chronic pain and the long-term physiological impacts of anesthesia remain understudied in laboratory animals. While acute pain models are well characterized, chronic conditions (*e.g.*, neuropathic pain in cancer models) lack validated assessment tools. For example, (Miller *et al.,* 2015) highlighted strain-specific differences in pain behaviors in mice, but similar data for chronic pain are lacking.

The long-term effects of repeated anesthesia exposure are also poorly understood. A study by (Seubert *et al.,* 2013) reported neurodevelopmental deficits in juvenile rats exposed to isoflurane; however, such outcomes are rarely monitored in routine research. Similarly, chronic opioid use in NHPs may lead to tolerance or addiction, complicating translational relevance (Janus and Golde, 2014).

Knowledge gaps

- Biomarkers for chronic pain in nonrodent species (*e.g.*, zebrafish, reptiles).
- Longitudinal studies on anesthesia-induced metabolic or immune dysfunction.

Disconnect between research innovation and routine practice

Despite innovations such as closed-loop anesthesia systems (Ching *et al.,* 2013) and the real-time RGS scoring method (Klune *et al.,* 2020), many institutions are cling to traditional protocols. For example, (Mumtaz *et al.,* 2024)'s preemptive analgesia model has yet to be widely adopted.

Root causes

- **Inertia:** Familiarity with outdated methods.
- **Funding:** High costs of advanced monitoring technologies (*e.g.*, telemetry).
- **Guideline lag:** Slow updates to institutional policies reflecting recent evidence.

Recommendation

- Mandatory continuing education for animal care staff.
- Funding incentives for adopting refined protocols (*e.g.*, National Institutes of Health's Rigor and Reproducibility initiatives).

Practical recommendations for researchers

To bridge the gap between innovation and practice, researchers must adopt actionable strategies for refining anesthesia and analgesia protocols.

Step-by-step framework for designing anesthetic-analgesic protocols (Fig 1)

Assess the model

- Define the species, strain and procedure type (*e.g.*, acute vs. chronic surgery).
- Consult species-specific guidelines (*e.g.*, Flecknell, 2016 for rodents; Janus and Golde, 2014 for NHPs).

Select anesthetics and analgesics

- Inhalants (*e.g.*, isoflurane) are prioritized for titratability in rodents (Miller *et al.,* 2015).
- Preemptive analgesia (*e.g.*, local lidocaine) should be incorporated to reduce postoperative pain (Mumtaz *et al.,* 2024).

Integrate monitoring tools

- Implement validated pain scales (*e.g.*, RGS/MGS) adjusted for anesthetic masking effects (Miller *et al.,* 2015).

Pilot and refine

- Pilot studies should be conducted to optimize dosing and monitor adverse effects (*e.g.*, hypothermia, (Klune *et al.,* 2020).

Checklists for perioperative monitoring and postprocedural care (Fig 2)

Preoperative checklist

- Preemptive analgesics (*e.g.*, meloxicam 30 minutes preincision) should be administered.
- Warming devices (heated pads, ambient temperature >24°C for rodents) were prepared.

The dose should be carefully monitored to avoid complications, as meloxicam can cause gastrointestinal

(GIT) lesions, nephrotoxicity, hepatotoxicity and variations in hematological parameters at the selected dose and duration (Bharani *et al.,* 2019).

Intraoperative checklist

· Vital signs should be monitored every 5-10 minutes.

· **Cardiorespiratory:** Heart rate, SpO_2.

· **Thermoregulation:** Core temperature (target: 36-38°C for rodents).

· The anesthetic depth was adjusted *via* closed-loop systems where available (Ching *et al.,* 2013).

Postoperative checklist

· Pain was assessed *via* multimodal tools (grimace scales and activity monitoring).

· Postoperative analgesia (*e.g.*, buprenorphine q8-12 h) was provided.

· Recovery was monitored until full ambulation and normal feeding resumed.

Advocacy for institutional training programs and ethical audits

Training programs

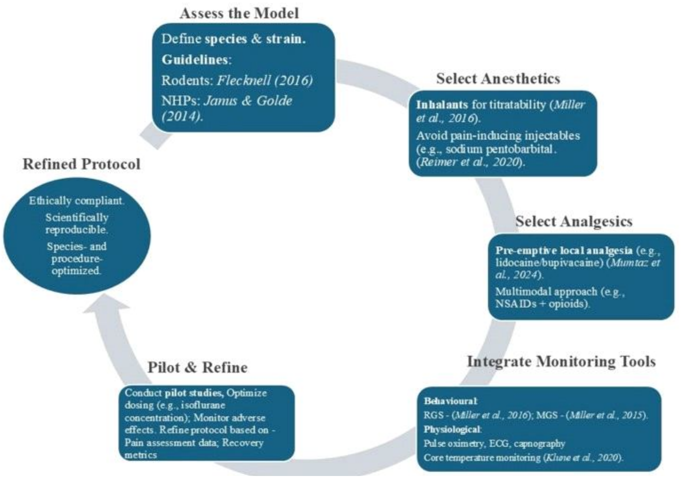
· **Hands-on workshops:** Teach staff to use advanced monitoring tools (*e.g.*, capnography, telemetry).

· **Species-specific modules:** Include exotic species (*e.g.*, zebrafish, reptiles) and NHPs.

· **Continuing education:** Partners with organizations such as AALAS or ICLAS for certification courses.

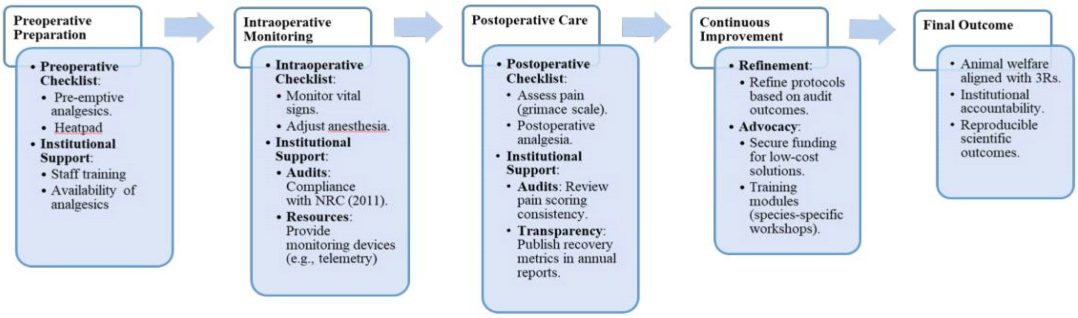
Ethical audits

· **Protocol reviews:** Ensure compliance with the Guide for the Care and Use of Laboratory Animals (NRC, 2011) and EU Directive 2010/63.



This flowchart outlines a systematic approach to protocol development, integrating species-specific guidelines (*e.g.*, rodents, NHPs), advanced monitoring tools (*e.g.*, grimace scales, telemetry) and iterative refinement to balance animal welfare, scientific rigor and compliance with the 3Rs (Replacement, Reduction, Refinement).

Fig 1: Designing ethical and effective anesthetic-Analgesic protocols: A stepwise framework for laboratory animal research.



This flowchart links procedural best practices (preemptive analgesia, multimodal monitoring, postoperative recovery) with institutional advocacy (training, audits, resource allocation) to uphold the 3Rs (replacement, reduction, refinement), ensuring animal welfare and scientific rigor in biomedical studies.

Fig 2: Integrating Perioperative Care and Institutional Accountability: A Synergistic Framework for Ethical Animal Research.

· **3Rs compliance:** Audit for Refinement metrics (*e.g.*, pain scoring consistency, mortality rates).
· **Transparency:** Publish audit outcomes in institutional annual reports to foster accountability.

Resource allocation

· Advocate for funding to upgrade equipment (*e.g.*, precision vaporizers, wireless monitors).
· Low-cost solutions (*e.g.*, warming boxes) for resource-limited settings should be developed (Mohr *et al.* 2023).

Interdisciplinary approaches: Integrating veterinary and human medicine

The convergence of veterinary and human medical research has catalyzed innovations in anesthesia and pain management, fostering bidirectional knowledge transfer that enhances both laboratory animal welfare and clinical outcomes.

Comparative anesthesia: Lessons from veterinary clinics informing laboratory protocols

Veterinary clinics routinely manage diverse species under anesthesia, offering insights applicable to laboratory settings. For example, protocols for maintaining normothermia in dogs and cats, such as forced-air warming systems, have been adapted for rodents, mitigating hypothermia-related complications during prolonged surgeries (Flecknell, 2016). Similarly, multimodal analgesia strategies, including epidural anesthesia in livestock, have inspired hybrid approaches in laboratory rodents (Mumtaz *et al.,* 2024).

A key lesson from veterinary practice is the value of species-specific pharmacokinetic data. For example, dosing regimens for alpha-2 agonists (*e.g.*, dexmedetomidine) in companion animals have been shown to be safer in nonhuman primates (NHPs), reducing cardiovascular risk (Janus and Golde, 2014). Such cross-disciplinary adaptations underscore the importance of integrating clinical veterinary expertise into laboratory protocol design.

Health collaborations: Joint ventures between researchers, clinicians and ecologists

The One Health paradigm, which recognizes the interconnectedness of human, animal and environmental health, has become a cornerstone of modern interdisciplinary research. By fostering collaboration among laboratory scientists, clinicians and ecologists, this framework addresses complex challenges such as zoonotic disease transmission, the environmental sustainability of medical practices and the refinement of translational pain management strategies. Rodent models have elucidated conserved pain pathways relevant to human conditions, such as neuropathic pain and osteoarthritis. The Rat Grimace Scale (RGS), validated in surgical models (Miller *et al.* 2015), mirrors facial pain expressions observed in humans, enabling translational biomarker discovery.

CONCLUSION

The evolution of laboratory animal anesthesia and analgesia reflects a shift toward welfare-driven, precision-based approaches. Innovations like the Rat Grimace Scale and closed-loop anesthesia systems enhance both ethics and data quality, though challenges like hypothermia and pain masking remain. To advance, the global community must harmonize welfare guidelines, invest in training and technology and support under-resourced institutions. Embracing One Health principles and embedding animal welfare into research practices will ensure that scientific progress remains ethically sound, collaborative and globally impactful.

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Disclaimers

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Informed consent

Not applicable.

Conflict of interest

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