Animal-Assisted Interventions in Intensive Care Delirium: A Literature Review

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ABSTRACT

Critical illness has lasting consequences on the mind and the body. Acute sequelae include a decline in cognitive function known as delirium. Increased interest in improving outcomes for intensive care unit survivors without a high incidence of delirium has initiated a focus on an array of nonpharmacologic interventions in many countries. One such intervention is animalassisted intervention. As the role of animals in human healing is being recognized,

he inception of critical care dates to the 1850s after the Crimean War, whereas modern critical care began with the iron lung and negative-pressure ventilation during the polio epidemic in 1952.¹ With advancements in technology and more clinical research in this specialty, critical care has evolved since then, especially in these first 2 decades of the twenty-first century, {AQ2} during which mortality has improved exponentially among patients experiencing a critical illness and being admitted to intensive care units (ICUs).² Favorable outcomes among ICU survivors have engendered a growing array of problems that can persist for many years after dis-charge from the hospital. These problems have been unified under the term *post-inten*sive care syndrome, which can include physical impairment or a dwindling mental health status.^{3,4} Survivors of critical illness can also experience a decline in cognitive processes

{AQ1} need is increasing for formal and professionally directed therapies. This review ascertains the effect of interaction with animals on critically ill patients. Emerging evidence indicates that animal-assisted intervention improves the efficacy of critical care regarding primary symptoms and secondary factors of delirium.

Key words: animal-assisted intervention, animal-assisted therapy, delirium, intensive care, post-ICU syndrome

known as delirium. The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition, defines delirium as "a global and reduced ability to direct, focus, sustain, and shift attention, reduced orientation to the environment and a deficit in the memory, orientation, and perception," which tends to fluctuate while a patient is awake.^{5,6}

The pathophysiology of delirium is not well recognized despite extensive literature describing it. Nevertheless, a few hypotheses link this confusional state to systemic inflammatory processes that occur during critical

The author declares no conflicts of interest.

DOI: https://doi.org/10.4037/aacnacc2021708

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illness and to an imbalance between serotonin and dopamine signaling, an increase in cortisol level, and a reduction of somatostatin level.7 Neuroimaging identifies potential mechanisms behind delirium: changes to white matter integrity, a decrease in brain volume, and abnormal functional connectivity in brain regions.7 A case-control study demonstrated higher expression of HLA-DR and CD68, interleukin-6, and glial fibrillary acidic protein in participants with delirium than in age-matched controls.⁷ {AQ3}{AQ4} A possible answer to all this conjecture may be a disturbance in coagulation and inflammation cascades that leads to microvascular dysfunction and thrombosis in the brain. In addition, disturbances in the sleep-wake cycle and sleep patterns, mechanical ventilation, sedatives, pain, and sepsis can contribute to delirium.

The incidence of delirium varies. International studies have demonstrated an incidence ranging from 22% to 83% among critically ill patients.9 Incidence has been reported at 21.8% among mechanically ventilated patients in ICUs in Pakistan, in contrast to 65% in the United Kingdom.^{10,11} Delirium is a potentially modifiable sequela of critical illness, and patients in an ICU should be screened for it regularly. {AQ5} The Diagnostic and Statistical Manual of Mental Disorders, 5th edition, is the gold standard for diagnosing delirium. Because expert psychiatrists are not available around the clock, tools such as the Confusion Assessment Method for the ICU, Intensive Care Delirium Screening Checklist, and Nursing Delirium Screening Scale have been established for assessing delirium in patients in an ICU.¹²

Successful screening for and awareness of risk factors contributing to delirium are vital for better outcomes when managing this condition. Prolonged duration of delirium in an ICU confers a poor prognosis, and removing the underlying pathology can reverse its adverse effects.¹³⁻¹⁵ Antipsychotics and sedatives have slightly reduced the onset of delirium, but no pharmacologic treatment has reduced mortality or length of hospital stay.¹⁶⁻ ¹⁹ The Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption guidelines from the Society of Critical Care Medicine,²⁰ and a statement from the National Institute of Health and Care Excellence,²¹ recommend several nonpharmacologic interventions to

prevent delirium among critically ill or mechanically ventilated patients. In addition to adequate fluid intake, early mobilization, and range-of-motion exercises, therapies that use animals to promote cognitively stimulating activity are increasingly being introduced in critical care units. Many ICU clinicians are becoming interested in this area of health care. This article explores the evidence of animals' impact on the health of critically ill patients, particularly during recovery from post–intensive care syndrome and delirium associated with a traumatic critical care experience.

History of Animal-Assisted Intervention

The term animal-assisted intervention (AAI) is relatively modern, but knowledge about using animals to help heal the sick precedes present-day medicine. The earliest records of using pets to rehabilitate people are from Belgium.²² Following the same principle, {AQ6} the York Retreat in Germany included animals as part of treatment strategies for melancholia among patients who had mental illness and experienced homelessness. In the 1940s, the American Red Cross established a farm where veterans could recuperate while taking care of animals. Although Dr Boris Levinson is considered to be the first researcher on AAI, Dr Sigmund Freud is considered to be the pioneer of the therapeutic importance of AAI.²² The term *pet therapy* marked the beginning of social workers' and medical professionals' understanding of the therapeutic benefits of human-animal interaction and highlights a paradigm shift in practice that considered animals to be healers in therapy, rather than tools. {AQ7}

AAI-Related Terminology

As the AAI specialty has evolved, extensive work has been done to define and delineate the various types of AAIs, {**AQ8**} to investigate desired results within a controlled environment, and to demonstrate the effectiveness of AAI in the daily lives of health care practitioners and patients. Given the need for a clear definition in order to establish the efficacy of AAI, international bodies have defined AAI as a goal-oriented and structured process that intentionally comprises animalhuman interactions to provide therapeutic advantages to humans.²³

Animal-assisted therapy (AAT), a subgroup of AAI, is a planned, problem-specific, and structured intervention delivered by health care professionals, and it includes documenting the measure of effect throughout the process.²³ As a rule, expertly trained personnel with an active license, degree, or equivalent should deliver AAT. It mainly targets enhancing the cognitive, physical, and behavioral functioning of the human recipient. Hence, the professional providing AAT should understand the behavior, health, and needs of, and stress indicators in, the animals involved. Animal-assisted coaching works on the principle of AAT, with coaching professionals administering interventions.^{23,24}

Animal-assisted activity (AAA) refers to informal interaction between a human and an animal for educational, motivational, or recreational purposes.²⁴ For AAA, introductory training and assessment of the participant is enough to allow visitation; however, AAA teams can work directly with health care professionals to achieve specific documentation goals. Animal-assisted education is a part of AAA but is a specific intervention delivered by educational professionals with a degree in general or special education. When delivered by specialist educators, animal-assisted education is considered to be a therapeutic and goal-oriented intervention. Professionals delivering animal-assisted education should have basic knowledge about the needs and health of, and stress indicators in, the animals involved.24

Effects of AAI on Human Physiology

Conventional wisdom proclaims that an animal companion can alleviate suffering and can motivate an individual toward a positive outlook on their self and their illness. Only during the past 2 decades, however, has the therapeutic role of animals in medicine become the focus of dedicated research. Various studies have demonstrated positive cognitive feedback in humans, particularly the geriatric population, in whom AAI can alleviate agitation as a consequence of loneliness.²⁵⁻²⁷ Several observational case series have demonstrated that animal interactions increased positive social behaviors, increased weight gain, reduced mood disturbances and agitation, and resulted in longer conversations with therapists.²⁸⁻³⁰ Many nursing

researchers have qualitatively observed that animals relieve loneliness and boredom, promote social interactions, add variety to the lives of such individuals, {AQ9} act as a surrogate for human interaction, disrupt antisocial behaviors, provide a cardiovascular mortality benefit, and improve overall quality of life.³¹⁻³⁴

Apart from psychological well-being, numerous studies have shown that animals positively affect the physiological health of individuals or a target population. Allen et al³⁵ studied the effects of the presence of pets, friends, and spouses while a person encounters a stressor and found that people with pets have a lower heart rate and blood pressure than non-pet owners. They also recover faster.³⁵ Similarly, participants in 2 unblinded controlled trials exhibited lower blood pressure and heart rate during acute anxiety attacks that occurred in the presence of an animal.^{35,36} A retrospective chart survey exhibited a lower resting blood pressure in the presence of an animal.³⁷ Additionally, a randomized controlled trial determined that spending only a short time with a therapy dog can reduce neurohormone levels, decrease anxiety, and improve hemodynamic measures in patients with advanced heart failure.38 An American Heart Association statement identified 31 relevant studies concluding that pet ownership improves outcomes related to cardiovascular mortality, obesity, autonomic function, hyperlipidemia, and physical activity.34

Role of Animals in ICUs

Many studies recognize delirium as the primary cause for late recovery and loss of cognition among critical patients.³⁹⁻⁴⁷ Critically ill patients usually have difficulty maintaining intact cognition after recovery, as some distressing symptoms persist; {AQ10} therefore the introduction of animals can be beneficial to patients. Animals can distract them and alleviate distress through neurohormonal feedback. {AO11} During AAI sessions, which are typically 15 to 30 minutes long, patients can observe, touch, hold, and pet the animals. In an advanced form of AAI, patients can work with animals during specific therapy activities to exercise range of motion and practice fine motor coordination, which can improve reality orientation and increase attention span, remove a sense of

isolation, reduce stress and anxiety, increase communication, and enhance the patient's overall ICU experience. Snipelisky and Burton⁴⁸ found that AAI positively impacts motivation and provides increased energy for recovery. Figure 1 suggests integrated measures that can overlap in an ICU, allowing faster recovery from the effects of delirium. Figure 2 shows a proposed algorithm that includes AAI/AAT in managing delirium. {AQ12}

Several studies have investigated a proposed mechanism for mitigating the effects of the ICU through the use of animals. All of them confirm that the interaction of humans and animals during a stressful period can reduce levels of cortisol, norepinephrine, and epinephrine, which are key enzymes implicated in the pathophysiology of delirium.49,50 Oxytocin also seems to play some part in improving social interaction, behavior, and mood. It reduces the cortisol level in humans and animals alike,⁵¹ when administered in the brain it reduces blood pressure and heart rate,⁵² and it increases the pain threshold and has an anti-inflammatory effect. Thus, decreasing these neurotransmitters and managing the host factor can play important roles in lessening distress during an ICU stay. {AQ13}

Disadvantages of AAI

Potential risks attributed to AAI are allergic reactions, physical trauma such as scratches and bites, and transmission of zoonotic disease. Several studies confer a higher incidence of zoonotic infection associated with the presence of an animal in health care facilities.^{52,53} {AQ14} Likewise, animals can become infected via human contact and in turn can carry bacteria such as Salmonella, Streptococcus, methicillin-resistant Staphylococcus aureus, and Mycobacterium tuberculosis.⁵³ {AQ15} The American Journal of Infection Control has published guidelines that restrict animals from ICU visitation, although the recommendations are based on limited epidemiologic studies.⁵⁴ The Centers for Disease Control and Prevention, however, report a minimal risk of zoonotic transmission from service animals.55 Table 1 identifies benefits and risks of animals in an ICU setting.

AAI Policies and Guidelines

Weighing the risks and benefits of AAI/ AAT is requisite before starting these programs in any setting. Potential adverse consequences such as zoonosis, scratches, bites, allergies, and phobias should be addressed through proper guidelines and standard operating procedures. Table 2 describes proposed roles for personnel involved in an AAI program. In general, the director of the ICU should liaise with the ICU team that is using AAI. In turn, the ICU team should keep in touch with the AAI group leader to schedule visits, maintain paperwork and consent forms, and provide support for the AAI team. A responsible hospital authority should ensure that personnel providing AAI are trained and certified in animal handling. The hospital will need to work closely with infection control staff to develop policies regarding visitation times and designated locations, animal and handler screening and immunizations, patient suitability, and management of patient-animal contact.56

Animal, Handler, and Hospital Staff Training

An essential part of an AAI program is training the animals. Many organizations offer certification in animal obedience and therapy training. One of the most recognized therapy-animal organizations is Pet Partners, founded in the United States in 1977.57 In addition to training 15000 animals annually, it offers an education program for animal handlers that focuses on learning behaviors that denote stress in pets, ensuring the animals' safety, and implementing infection control measures. It is also important to engage hospital staff in an AAI program. They should be educated regarding the benefits of AAI and policies guiding the visits. The right of staff and patients to refuse AAI must be respected.

Conclusion

Currently, a paucity of literature exists on delirium, ICU care, and the role of animals in supporting critically ill patients. Despite more than 4 decades of research, work is still preliminary on human-animal bonds during critical illness. These preliminary findings are compounded by small sample sizes, flawed methods, and a lack of adequate blinding and controls. Thus far, only modest benefit has

been reported for the use of animals in improving humans' mental and physical health. Investigations of the impact of AAI on physical health must be prospective trials with robust methods that can expand knowledge of animals' true effect on human physiology. New uses for animals should be piloted in the future in order to establish AAI's effects on delirium. By creating a humanized environment in ICUs and implementing nonpharmacologic AAIs, I believe that patients will no longer need to wait to be released from a hospital before they can engage in activities with animals that may facilitate their recovery. Animal-assisted interventions reduce distress and help patients achieve a positive perspective toward their recovery.

REFERENCES

- 1. Vincent JL, Singer M, Marini JJ, et al. Thirty years of critical care medicine. *Crit Care*. 2010;14(3):311.
- Linnen DT, Escobar GJ, Hu X, Scruth E, Liu V, Stephens C. Statistical modeling and aggregate-weighted scoring systems in prediction of mortality and ICU transfer: a systematic review. J Hosp Med. 2019;14(3):161-169. doi:10.12788/jhm.3151
- Needham DM, Davidson J, Cohen H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. *Crit Care Med.* 2012;40(2):502-509.
- Elliott D, Davidson JE, Harvey MA, et al. Exploring the scope of post-intensive care syndrome therapy and care: engagement of non-critical care providers and survivors in a second stakeholders meeting. *Crit Care Med.* 2014;42(12):2518-2526.
- Van Rompaey B, Elseviers MM, Van Drom W, Fromont V, Jorens PG. The effect of earplugs during the night on the onset of delirium and sleep perception: a randomized controlled trial in intensive care patients. *Crit Care*. 2012;16(3):R73.
- Chanques G, Ely EW, Garnier O, et al. The 2014 updated version of the Confusion Assessment Method for the Intensive Care Unit compared to the 5th version of the Diagnostic and Statistical Manual of Mental Disorders and other current methods used by intensivists. *Ann Intensive Care*. 2018;8(1):33. doi:10.1186/ s13613-018-0377-7
- Munster BC, Aronica E, Zwinderman AH, Eikelenboom P, Cunningham C, Rooij SE. Neuroinflammation in delirium: a postmortem case-control study. *Rejuvenation Res.* 2011;14(6):615-622.
- 8. Kress JP. The complex interplay between delirium, sepsis and sedation. *Crit Care*. 2010;14(3):164.
- Vasilevskis EE, Han JH, Hughes CG, Ely EW. Epidemiology and risk factors for delirium across hospital settings. Best Pract Res Clin Anaesthesiol. 2012;26(3):277-287.
- Ashraf A, Hashmi M, Raza A, Salim B, Faisal Khan M. Incidence, risk factors and outcome of delirium in a surgical intensive care unit of a tertiary care hospital. *Qatar Med J.* 2019;2019(2):62.
- Page VJ, Navarange S, Gama S, McAuley DF. Routine delirium monitoring in a UK critical care unit. *Crit Care*. 2009;13(1):R16.
- 12. Krewulak KD, Rosgen BK, Ely EW, Stelfox HT, Fiest KM. The CAM-ICU-7 and ICDSC as measures of delirium

severity in critically ill adult patients. *PLoS One.* 2020;15(11):e0242378. doi:10.1371/journal. pone.0242378

- Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. *BMJ*. 2015;350:h2538.
- Girard TD, Jackson JC, Pandharipande PP, et al. Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med.* 2010;38(7):1513-1520.
- Pandharipande PP, Girard TD, Jackson JC, et al. Longterm cognitive impairment after critical illness. N Engl J Med. 2013;369(14):1306-1316.
- Riker RR, Shehabi Y, Bokesch PM, et al; SEDCOM (Safety and Efficacy of Dexmedetomidine Compared with Midazolam) Study Group. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA. 2009;301(5):489-499.
- Wang HR, Woo YS, Bahk WM. Atypical antipsychotics in the treatment of delirium. *Psychiatry Clin Neurosci*. 2013;67(5):323-331.
- Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after onpump cardiac surgery in the elderly: a randomized trial. *Anesthesiology*. 2012;116(5):987-997.
- Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. *Anaesth Intensive Care*. 2007;35(5):714-719.
- Pisani MA, Devlin JW, Skrobik Y. Pain and delirium in critical illness: an exploration of key 2018 SCCM PADIS guideline evidence gaps. *Semin Respir Crit Care Med*. 2019;40(5):604-613. doi:10.1055/s-0039-1698809
- National Institute for Health and Care Excellence. Quality Statement 2: Interventions to Prevent Delirium. Quality standard QS63. National Institute for Health and Care Excellence; 2014.
- Connor K, Miller J. Animal-assisted therapy: an indepth look. *Dimens Crit Care Nurs*. 2000;19(3):20-26.
- Fine A, Tedeschi P, Elvove E. Forward thinking: the evolving field of human-animal interactions. In: Fine A, editor. Handbook on Animal-Assisted Therapy: Foundations and Guidelines for Animal-Assisted Interventions. 4th ed. Academic Press; 2015:21-35.
- Muñoz Lasa S, Ferriero G, Brigatti E, Valero R, Franchignoni F. Animal-assisted interventions in internal and rehabilitation medicine: a review of the recent literature. *Panminerva Med.* 2011;53(2):129-136.
- Overgaauw PAM, Vinke CM, Hagen MAEV, Lipman LJA. A One Health perspective on the human-companion animal relationship with emphasis on zoonotic aspects. *Int J Environ Res Public Health*. 2020;17(11):3789.
- Thodberg K, Sørensen LU, Christensen JW, et al. Therapeutic effects of dog visits in nursing homes for the elderly. *Psychogeriatrics*. 2016;16(5):289-297.
- Dembicki D, Anderson J. Pet ownership may be a factor in improved health of the elderly. J Nutr Elder. 1996;15(3):15-31.
- Colombo G, Buono MD, Smania K, Raviola R, De Leo D. Pet therapy and institutionalized elderly: a study on 144 cognitively unimpaired subjects. *Arch Gerontol Geriatr.* 2006;42(2):207-216.
- Richeson NE. Effects of animal-assisted therapy on agitated behaviors and social interactions of older adults with dementia. *Am J Alzheimers Dis Other Demen*. 2003;18(6):353-358.
- Moretti F, De Ronchi D, Bernabei V, et al. Pet therapy in elderly patients with mental illness. *Psychogeriatrics*. 2011;11(2):125-129.
- Fick KM. The influence of an animal on social interactions of nursing home residents in a group setting. *Am J Occup Ther*. 1993;47(6):529-534.

- Brickel CM. The therapeutic roles of cat mascots with a hospital-based geriatric population: a staff survey. *Ger*ontologist. 1979;19(4):368-372.
- Fritz CL, Farver TB, Kass PH, Hart LA. Association with companion animals and the expression of noncognitive symptoms in Alzheimer's patients. J Nerv Ment Dis. 1995;183(7):459-463.
- Levine GN, Allen K, Braun LT, et al. Pet ownership and cardiovascular risk: a scientific statement from the American Heart Association. *Circulation*. 2013;127(23):2353-2363. doi:10.1161/ CIR.0b013e31829201e1
- Allen K, Blascovich J, Mendes WB. Cardiovascular reactivity and the presence of pets, friends, and spouses: the truth about cats and dogs. *Psychosom Med.* 2002;64(5):727-739. doi:10.1097/01. psy.0000024236.11538.41
- Mueller MK, Gee NR, Bures RM. Human-animal interaction as a social determinant of health: descriptive findings from the health and retirement study. *BMC Public Health*. 2018;18(1):305.
- Parslow RA, Jorm AF. Pet ownership and risk factors for cardiovascular disease: another look. *Med J Aust.* 2003;179(9):466-468.
- Cole KM, Gawlinski A, Steers N, Kotlerman J. Animalassisted therapy in patients hospitalized with heart failure. Am J Crit Care. 2007;16(6):575-588.
- Mehta S, Cook D, Devlin JW, et al; SLEAP Investigators; Canadian Critical Care Trials Group. Prevalence, risk factors, and outcomes of delirium in mechanically ventilated adults. *Crit Care Med.* 2015;43(3):557-566.
- Shehabi Y, Riker RR, Bokesch PM, et al. Delirium duration and mortality in lightly sedated, mechanically ventilated intensive care patients. *Crit Care Med.* 2010;38(12):2311-2318.
- Pandharipande P, Cotton BA, Shintani A, et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. J Trauma. 2008;65(1):34-41.
- Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. *BMJ*. 2015;350:h2538.
- Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc. 2001;49(5):516-522.
- Schulman-Marcus J, Mookherjee S, Rice L, Lyubarova R. New approaches for the treatment of delirium: a case for robotic pets. *Am J Med.* 2019;132(7):781-782. doi:10.1016/j.amjmed.2018.12.039
- Costa DK, White MR, Ginier E, et al. Identifying barriers to delivering the awakening and breathing coordination, delirium, and early exercise/mobility bundle to minimize adverse outcomes for mechanically ventilated patients: a systematic review. *Chest.* 2017;152(2):304-311. doi:10.1016/j.chest.2017.03.054
- Mehta S, Burry L, Cook D, et al. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. *JAMA*. 2012; 308(19):1985-1992.
- Kulkarni AP, Agarwal V. Extubation failure in intensive care unit: predictors and management. *Indian J Crit Care Med.* 2008;12(1):1-9.
- Snipelisky D, Burton MC. Canine-assisted therapy in the inpatient setting. *South Med J.* 2014;107(4):265-273.
- Barker SB, Knisely JS, McCain NL, Best AM. Measuring stress and immune response in healthcare professionals following interaction with a therapy dog: a pilot study. *Psychol Rep.* 2005;96(3 pt 1):713-729.
- Viau R, Arsenault-Lapierre G, Fecteau S, Champagne N, Walker CD, Lupien S. Effect of service dogs on salivary cortisol secretion in autistic children. *Psychoneu*roendocrinology. 2010;35(8):1187-1193.

- Marshall-Pescini S, Schaebs FS, Gaugg A, Meinert A, Deschner T, Range F. The role of oxytocin in the dogowner relationship. *Animals (Basel)*. 2019;9(10):792.
- Petersson M, Hulting A, Andersson R, Uvnäs-Moberg K. Long-term changes in gastrin, cholecystokinin and insulin in response to oxytocin treatment. *Neuroendocrinology*. 1999;69(3):202-208.
- Khan MA, Farrag N. Animal-assisted activity and infection control implications in a healthcare setting. J Hosp Infect. 2000;46(1):4-11.
- Boyle SF, Corrigan VK, Buechner-Maxwell V, Pierce BJ. Evaluation of risk of zoonotic pathogen transmission in a university-based animal assisted intervention (AAI) program. *Front Vet Sci.* 2019 June;6:167. doi:10.3389/ fvets.2019.00167
- 55. Sehulster LM, Chinn RY, Ardunio MJ, et al. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Centers for Disease Control and Prevention; 2003. Updated July 2019. www.cdc.gov/infectioncontrol/guidelines/environmental-guidelines-P.pdf
- Miller J. Animal-assisted interventions: impact on patient outcomes and satisfaction. *Nurs Manage*. 2020;51(4):16-23. doi:10.1097/01. NUMA.0000657240.17744.1b
- 57. Pet Partners. Therapy pets and animal-assisted activities. https://petpartners.org {AQ16}

AUTHOR QUERIES

The following queries are indicated on your galley pages by a highlighted {AQ1} or {AQ2} and so on embedded in the text. Please respond to each query directly on the galley whenever possible, indicating how the galley is to be altered. Other comments or longer changes can be marked on this query sheet and returned with the galleys. Be sure to respond to each query; if OK, mark OK."

AQ1: In the abstract, in the wording "As the role of animals in human healing is being recognized," please specify *who* is recognizing the role of animals in human healing so that this wording can be made active.

AQ2: Previous sentence OK as edited?

AQ3: In "higher expression of HLA-DR and CD68, interleukin-6, and glial fibrillary acidic protein," are HLA-DR, CD68, interleukin-6, and glial fibrillary acidic protein referring to genes?

AQ4: Added "participants with delirium" to specify the group being compared against "age-matched controls": "higher expression . . . in **participants with delirium** than in agematched controls." Does this edit appropriately identify the comparator group?

AQ5: Do edits retain your intended meaning? ("Delirium is a potentially modifiable sequela of critical illness, and patients in an ICU should be screened for it regularly.") AQ6: In "Following the same principle, the York Retreat in Germany included . . . ," to what does "the same principle" refer? the principle described in the earliest reports from Belgium? Consider specifying here to avoid ambiguity.

AQ7: Do edits retain your intended meaning? ("the beginning of social workers"... healers in therapy, rather than tools.")

AQ8: In "As the AAI specialty has evolved, extensive work has been done," please specify *who* has done this work, so that the wording can be made active (eg, "researchers have worked extensively to define and delineate . . .")

AQ9: Can you clarify who you mean by "such individuals"? Lonely people? Geriatric people?

AQ10: Do edits retain your intended meaning? ("Critically ill patients usually have difficulty maintaining intact cognition after recovery, as some distressing symptoms persist")

AQ11: Edits to previous sentence OK?

AQ12: Is Figure 2 reprinted from ref 20? Do we need permission?

AQ13: Edits to previous sentence OK?

AQ14: Please note that references 52 and 53 were duplicates. Thus ref. 53 has been deleted and references have been renumbered in the text and the references list. Please check.

AQ15: Edits to previous sentence OK?

AQ16: In reference 57, are you intending to cite the Pet Partners homepage (per the URL provided)? If you mean to cite a page on the Pet Partners site called "Therapy pets and animal-assisted activities," please provide a direct URL to that page.

Table 1: Potential Risks and Benefits of Animal-Assisted Intervention/Animal-Assisted Therapy in Critical Care

Potential Benefits	Potential Risks
Increased attention/cognition	Injury to self and others
Increased physical exercise	Damage to fragile equipment
Improved cardiovascular and neurohormonal responses and survival	Zoonotic infections/vector transmission
Improved social interactions	Cost
Decreased loneliness	Accommodation and hospital space
Decreased anxiety and fear of the intensive care unit environment Increased motivation to heal	Health burden
	1

Table 2: Proposed Roles of Involved Personnel for an AAT/AAITherapy Program

Role	Responsibilities
Program director	Policy-making with the health care team and stakeholders Training for AAT/AAI interventions and adopting a protocol Coordinating visits of loved ones along with the animals for confidence Ongoing program evaluation
ICU team	Coordinating timing and appropriateness for AAT/AAI Making adequate arrangements for the animal transport in and out of the ICU Assessing patient interests and benefits for the interventions Foreseeing infection-related issues
Risk quantification	Overseeing mechanisms for prevention of patient injury Overseeing mechanisms for management of animal injury Ensuring patient privacy
Infection control	Ensuring protocols are in place that detail: How to protect patients from zoonotic and fomite infections Mandatory hand-washing hands before and after every interaction with animals (patients, family, staff, and handlers) Cleaning animal toys after use Mandatory annual veterinary examinations and vaccinations Prohibiting animals with open wounds, parasites, and illness

Abbreviations: AAI, animal-assisted intervention; AAT, animal-assisted therapy; ICU, intensive care unit.

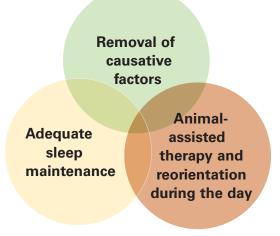


Figure 1: Proposed overlap of treatment modalities for delirium in the intensive care unit.

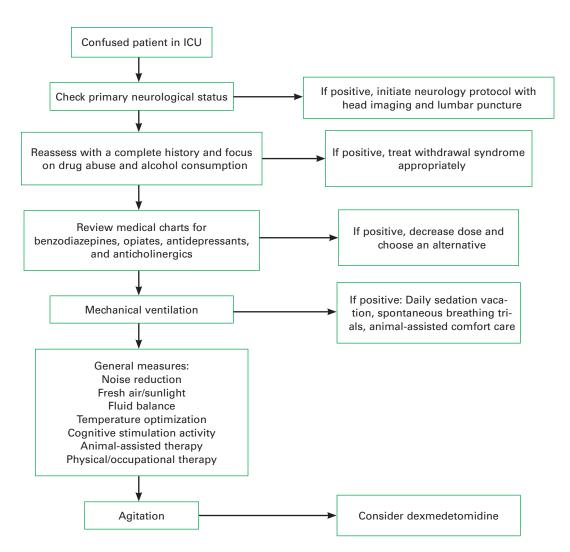


Figure 2: Algorithm for management of delirium.²⁰