Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Dexmedetomidine

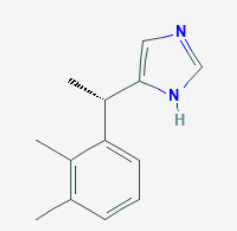
Evidence Summary

Significantly reduces postoperative delirium and cognitive dysfunction when used perioperatively, though increases bradycardia and hypotension. Administered in a medical setting and not used in healthy adults.

Neuroprotective Benefit: Cuts the incidence of postoperative delirium and cognitive dysfunction in surgery/ICU patients by ~50% but does not effectively treat delirium. Also alleviates ischemic brain injury by decreasing inflammatory markers.

Aging and related health concerns: In surgery patients, may decrease the incidence of tachycardia and preserve renal functions. The magnitude of blood pressure drop depends on genetic variants of ADRA2A.

Safety: In cardiac surgery patients, perioperative dexmedetomidine decreases mortality, POD, and POCD, though may increase bradycardia and hypotension. Numerous drug interactions are known.

Availability: given by a healthcare professional in a medical setting (i.v.)	**Dose**: For adult patients being sedated for a medical procedure, the loading infusion is typically 1 µg/kg for 10 minutes, followed by 0.2-1.0 µg/kg/hour maintenance infusion, titrated to desired effect.	**Chemical formula:** $C_{13}H_{16}N_2$ **MW**: 200.285  Source: PubChem
Half life: Elimination half-life is approximately 2 hours.	**BBB**: binds to receptors in the spinal cord	
Clinical trials: The largest meta-analysis included 23 RCTs (9,440 surgery patients).	**Observational studies**: none	

What is it? Dexmedetomidine is a sedative used for patients undergoing intensive medical care requiring a mechanical ventilator (Drugs.com). It is also used during anesthesia to get a patient ready for surgery or other medical procedures. It is a specific and selective α2-adrenergic receptor agonist that binds to presynaptic α2-receptors, inhibiting norepinephrine release from synaptic vesicles (PubChem). This action leads to an inhibition of postsynaptic adrenergic receptors, thereby inhibiting sympathetic activity. The analgesic, anxiolytic, and sedative properties of dexmedetomidine are mediated by the inhibition of α2-adrenergic receptors in the spinal cord.

Neuroprotective Benefit: Cuts the incidence of postoperative delirium and cognitive dysfunction in surgery/ICU patients by ~50% but does not effectively treat delirium. Also alleviates ischemic brain injury by decreasing inflammatory markers.

Types of evidence:

- 10 meta-analyses based on 10-58 randomized controlled trials (RCTs), mostly in patients undergoing surgery or those in the ICU; 1 meta-analysis on ischemic brain injury
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function?

No studies have tested dexmedetomidine as a treatment to prevent dementia, but numerous meta-analyses have evaluated the efficacy of dexmedetomidine in preventing postoperative delirium, a significant risk factor for dementia.

Surgery/ICU patients: DECREASED DELIRIUM INCIDENCE. In the most recent 2019 meta-analysis that included 58 RCTs, 20 RCTs (1,435 patients) examined 14 different treatments for delirium and 38 RCTs (8,168 patients total) examined 17 different treatments for prevention of delirium (Wu et al., 2019). Dexmedetomidine treatment did not show significantly better response rates compared with placebo/control when used as treatment of delirium; haloperidol plus lorazepam (OR=28.13; 95% CI, 2.38-333.08) and haloperidol alone (OR=2.37; 95% CI, 1.04-5.43) were significantly superior to placebo/control in treating delirium. For prevention of delirium, dexmedetomidine significantly decreased the occurrence of delirium compared to placebo/control (OR=0.50; 95% CI, 0.31-0.80). According to the surface under the cumulative ranking curve (SUCRA), propofol plus midazolam and dexmedetomidine were the 2 top-ranked intravenously delivered preventive interventions for delirium.

Numerous other meta-analyses have focused specifically on dexmedetomidine. In a 2019 meta-analysis examining the effects of perioperative dexmedetomidine, 23 RCTs and cohort studies were included for cardiac surgery patients (n=7,635) and 8 studies were included for non-cardiac surgery patients (n=1,805)(Peng et al., 2019). In cardiac surgery, perioperative dexmedetomidine reduced the prevalence of delirium (RR=0.50; 95% CI, 0.36 to 0.69). In noncardiac surgery, perioperative dexmedetomidine was associated with a trend toward a lower prevalence of delirium (RR=0.57; 95% CI, 0.32 to 1.01). Benefits of dexmedetomidine were not statistically significant in patients undergoing noncardiac surgery, in part due to the small number of studies.

In a 2019 meta-analysis of 25 RCTs examining the effects of dexmedetomidine (8 RCTs, n=1,425) and other treatments in ICU patients, the use of dexmedetomidine also significantly reduced delirium incidence (OR=0.36; 95% CI, 0.26 to 0.51)(Ng et al., 2019). Dexmedetomidine use was also associated with a reduced incidence of agitation (OR=0.34; 95% CI, 0.20 to 0.59).

Other older meta-analyses have consistently shown similar benefits of perioperative dexmedetomidine on delirium incidence. In a 2018 meta-analysis of 25 RCTs in ICU patients (n=4,975 patients), RR was 0.52 (95% CI, 0.39 to 0.70)(Flukiger et al., 2018); in a 2018 meta-analysis of 10 RCTs in cardiac surgery patients (n=1,387 patients), the RR was 0.46 (95% CI, 0.34 to 0.62)(Wu et al., 2018). In a 2018 meta-

analysis of 18 RCTs in adult surgical patients (n=3,309), OR was 0.41 in cardiac patients and 0.33 in non-cardiac surgical patients (Duan et al., 2018). When dexmedetomidine was administered during the postoperative period, OR was 0.30 in patients under 65 years old and 0.19 in patients 65 and above.

A 2015 meta-analysis of 18 RCTs examining the effects of perioperative dexmedetomidine (initial dose of 1.28 +/- 0.97 µg/kg, maintenance dose of 0.41 +/- 0.11 µg/kg/hr) on postoperative neurocognitive function reported that perioperative dexmedetomidine treatment was associated with significantly better neurocognitive performance in comparison with saline (mean difference in MMSE=9.10; 95% CI, 3.03 to 15.16)(Man et al., 2015). Perioperative dexmedetomidine treatment was beneficial in comparison with both saline controls and comparator anesthetics (e.g., midazolam).

Elderly surgery patients: DECREASED DELIRIUM INCIDENCE, IMPROVED MMSE. In a meta-analysis of 13 RCTs in elderly patients who had undergone general anesthesia, dexmedetomidine significantly reduced the incidence of POCD (RR=0.59; 95% CI, 0.45 to 2.95) and improved postoperative cognitive scores as measured by MMSE (mean difference, MD=1.74; 95% CI, 0.43 to 3.05) on the first postoperative day (Zhou et al., 2016) . Dexmedetomidine treatment also reduced the incidence of POCD after the first postoperative day (MD=2.73; 95% CI, 1.33 to 4.12).

Ischemic brain injury patients: POTENTIAL BENEFIT. In a meta-analysis of 19 RCTs including 879 patients with ischemic brain injury, dexmedetomidine reduced the release of inflammatory mediators and neuroendocrine hormones as well as maintained intracranial homoeostasis, alleviated ischemic brain injury, and exerted neuroprotective effects. Specifically, dexmedetomidine treatment (loading dose ranging from 0.5-1.0 µg/kg, maintenance dose ranging from 0.2-2.5 µg/kg/hr) significantly reduced a surge of TNF-α (MD=-2.34; 95% CI, -3.25 to -1.44), IL-6 (MD=-2.44; 95% CI, -3.40 to -1.47), S100-β (MD=-2.73, 95% CI, -3.65 to -1.82), NSE (MD=-1.69, 95% CI, -2.77 to -0.61), cortisol (MD=-2.48; 95% CI. -3.38 to -1.58), and glucose (MD=-1.44; 95% CI, -1.85 to -1.04); and maintained SOD levels (MD=1.36; 95% CI. 0.62 to 2.10) (Jiang et al., 2017). Dexmedetomidine attenuated the stress-related increase in mean arterial pressure, heart rate, and intracranial pressure without significant effects on cerebral oxygen metabolism.

In a clinical study including 120 patients undergoing elective surgery, dexmedetomidine (0.2 µg/kg/hr) or propofol (3-10 mg/kg/hr) + remifentanil (0.5-1.0 µg/kg/hr) were infused before surgery (Chen et al., 2018). Outcome measures included verbal learning (RAVLT score), depression score (Beck Depression Inventory), and mitochondrial membrane potential. On days 3 and 5 post-surgery, the National Institutes of Health Stroke Scale (NIHSS) scores and RAVLT scores decreased in both groups, but the

decline in the dexmedetomidine group was significantly smaller in magnitude than that in the propofol + remifentanil group. On days 1, 3 and 5 post-surgery, the mitochondrial membrane potentials of the two groups were decreased and the magnitude of decline was significantly smaller in the dexmedetomidine group compared to the propofol + remifentanil group. The mitochondrial membrane potentials of the two groups returned to preoperative levels on day 15 post-surgery. The decrease in activities of mitochondrial respiratory chain complex I-IV in the propofol + remifentanil group on day 1 post-surgery was significantly greater than that in the dexmedetomidine group. The results suggest that dexmedetomidine may improve POCD in patients by alleviating the damage to mitochondrial respiratory chain enzyme complexes I, II, III and IV and preventing the mitochondrial oxidative stress-induced neuronal damage.

Human research to suggest benefits to patients with dementia: None available.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Damaging effects of surgery/anesthesia: Trauma experienced during surgery can contribute to the development of a systemic inflammatory response (SIRS) that can cause multi-organ dysfunction or even failure (Alam et al., 2018). In the nervous system, SIRS includes the loss of blood-brain-barrier integrity, cytokine-mediated neuronal injury, microglia activation, POD, and POCD. These processes are set off as TNF-α and other proinflammatory mediators are induced via NF-kB, which together cause endothelial dysfunction and increased blood-brain-barrier permeability. Circulating lymphocytes are recruited into the neuronal tissue, and microglia and astrocytes are activated. Cytokines increase intracellular calcium levels and induce the synthesis and release of nitic oxide via inducible nitric oxide synthase from the activated microglia and astrocytes. Neuroinflammation ensues, leading to reduced hippocampal neurogenesis, impaired synaptic plasticity, loss of synaptic connections, and neuronal apoptosis. All of this, in turn, leads to neurodegenerative conditions such as POCD, POD, and increased risk of Alzheimer's disease. Elderly patients with post-operative cognitive dysfunction or delirium are up to 6 times more likely to experience permanent cognitive impairment or dementia.

Neuroprotective effects of dexmedetomidine: The neuroprotective effects of dexmedetomidine are thought to be mediated by several molecular mechanisms, including increased expression of the neurotrophic factor BDNF (Bilotta et al., 2017; Wang et al., 2018) and decreased levels of inflammatory markers (IL-1β, IL-18, NLRP3 inflammasome, and its downstream target caspase-1)(Li et al., 2018).

Anesthesia/surgery model: Numerous rodent studies have shown neuroprotective benefits of perioperative dexmedetomidine. Dexmedetomidine treatment (3 or 12 µg/kg, i.p.) rescues anesthesia/surgery-associated cognitive impairment and inflammatory changes, as well as upregulates expression of BDNF, PKA, and p-CREB/CREB (Wang et al., 2018). In a rat model of POCD, dexmedetomidine treatment (12 µg/kg, i.p.) suppressed GABA-B receptors, which in turn up-regulated the cAMP/PKA/CREB signaling pathway, alleviating hippocampal inflammation caused by surgical trauma (Zhu et al., 2019). In an aging mouse model of isoflurane-induced cognitive decline, deficits in spatial learning and memory were partly prevented by dexmedetomidine treatment (50 µg/kg, i.p.) via stimulation of the JAK2/STAT3 signaling pathway involved in neuronal survival and differentiation (Si et al., 2016). In an aging rat model of isoflurane-induced cognitive impairment, dexmedetomidine treatment (1 mg/kg for 5 hours) attenuated cognitive impairment through antioxidant, anti-inflammatory, and anti-apoptotic mechanisms (e.g., decreased TNF-α, IL-1β, MDA, SOD, and caspase-3)(Wang et al., 2015).

Inflammation models: In an aged rat model of (LPS-induced) inflammation, immediate dexmedetomidine treatment (10 µg/kg, i.p., every 3 hours x 4) prevented neurocognitive deficits by preventing the increase in proinflammatory cytokines (TNF-α and IL-1β) (Yamanaka et al., 2017). Treatment with dexmedetomidine during peripheral systemic inflammation prevented subsequent hippocampal neuroinflammation, overexpression of toll-like receptor 4 (TLR-4) in microglia, and cognitive dysfunction. These effects were mediated by the α2A adrenergic receptor signaling pathway. However, treatment initiated 24 hours after inflammation (LPS) did not have any protective benefits.

In a human microglia cell culture (HMC3 cells) exposed to inflammation (LPS), dexmedetomidine prevented the release of proinflammatory cytokines including IL-1β and IL-18 in the culture medium, and the expression of NLRP3 and its downstream target, caspase-1, in the cells (Li et al., 2018). Exposure to inflammation (LPS/ATP) increased nuclear protein levels of the transcription factor c-Fos, but treatment with dexmedetomidine reversed this increase in c-Fos. c-Fos can bind to the promoter region of NLRP3 gene and positively regulate its expression. Thus, dexmedetomidine may exert anti-inflammatory effects by inhibiting c-Fos nuclear protein levels, preventing the upregulation of the NLRP3 inflammasome.

TBI model: In a rat model of traumatic brain injury, dexmedetomidine improved spatial memory, preserved neurons, inhibited microglial activation, suppressed NLRP3-mediated inflammasome activity, and decreased caspase-1 levels (Zheng et al., 2018).

Potentially damaging effects of dexmedetomidine: Dexmedetomidine treatment (300 µg/kg, i.p.) induced tau hyperphosphorylation in the hippocampus of non-transgenic mice, and in a transgenic hTau mice, dose-dependently impaired spatial memory, increased tau hyperphosphorylation (at AT8 and PHF1 epitopes), and increased insoluble tau levels (Whittington et al., 2015). Dexmedetomidine treatment did not significantly alter total tau or soluble tau levels.

APOE4 interactions: Unknown.

Aging and related health concerns: In surgery patients, may decrease the incidence of tachycardia and preserve renal functions. The magnitude of blood pressure drop depends on genetic variants of ADRA2A.

Types of evidence:

- 6 meta-analyses including up to 18 RCTs, mostly in surgery patients
- 1 clinical study examining ADRA2A variants and responses to dexmedetomidine
- Numerous laboratory studies

ADRA2A genetic variants and dexmedetomidine responses: MAGNITUDE OF BLOOD PRESSURE DROP DEPENDS ON VARIANTS. In a single-blind placebo-controlled study in 73 healthy subjects, the effects of incremental infusion of dexmedetomidine (cumulative dose, 0.4 µg/kg) were examined based on the α2-adrenergic receptor (α2A-AR) genetic variants (9 ADRA2A tagging variants and 5 inferred haplotypes)(Kurnik et al., 2011). Homozygous carriers of rs553668 and the corresponding haplotype 4, previously associated with increased α2A-AR expression, had a 2.2-fold greater decrease in systolic blood pressure after dexmedetomidine; and the maximum decrease in systolic blood pressure was 24.7±8.1 mmHg compared with 13.6±5.9 mmHg in carriers of the wild-type allele. Carriers of haplotype 3, previously associated with reduced α2A-AR expression, had a 44% smaller decrease in systolic blood pressure. Genotypes were not significantly associated with norepinephrine responses (as measured by plasma norepinephrine levels). Since common ADRA2A variants are associated with the hypotensive response to dexmedetomidine, optimal doses may vary widely across individuals.

Cardiac function in cardiac surgery patients: DECREASED TACHYCARDIA, INCREASED BRADYCARDIA. In a meta-analysis of 18 RCTs including a total of 1,730 cardiac surgery patients, the effects of dexmedetomidine (typical loading dose was 1.0 µg/kg; maintenance dose ranging from 0.1-0.7 µg/kg/hr) on hemodynamic indices were compared with control (any treatment without dexmedetomidine)(Wang

et al., 2018). Compared to control, dexmedetomidine treatment showed a pooled mean difference (MD) of -14.46 (95% CI; -24.69 to -4.23) for systolic arterial pressure, a standardized mean difference (SMD) of -1.74 for mean arterial blood pressure (95% CI; -2.80 to -0.68), -2.12 (95% CI; -3.23 to -1.00) for heart rate, and combined odds ratio (OR) of 0.22 (95% CI; 0.11 to 0.44) for tachycardia, 3.44 (95% CI; 1.95 to 5.96) for bradycardia, 0.74 (95% CI; 0.49 to 1.12) for atrial fibrillation, and 0.99 (95% CI; 0.51 to 1.90, not significant) for hypotension. Dexmedetomidine effectively reduced the incidence of ventricular tachycardia in patients who had undergone cardiac surgery and these findings also suggest that dexmedetomidine may not increase the incidence of hemodynamic complications.

There have been 2 other 2018 meta-analyses and one 2017 meta-analysis in cardiac surgery patients. The 2018 studies reported that dexmedetomidine treatment after elective cardiac surgery (induction at 1.0 µg/kg, maintenance dose at 0.1-1.5 µg/kg/hr) did not reduce the incidence of atrial fibrillation (RR=0.82; 95% CI, 0.60 to 1.10; p=0.19; 9 studies), but significantly reduced the incidence of ventricular arrhythmia (OR=0.24; 95% CI, 0.09 to 0.64; p=0.008; 4 studies) compared to the control group (Zhu et al., 2018; Ling et al., 2018). The 2017 meta-analysis reported that dexmedetomidine treatment lowered heart rate, systolic blood pressure, and incidence of tachycardia in both adult and pediatric patients, but elevated the risk of bradycardia (Gong et al., 2017).

Postoperative renal function: BENEFIT. A 2018 meta-analysis of 95 RCTs (of which 5 studied dexmedetomidine, 470 patients total) examined the effects of 13 different preoperative/intraoperative interventions on renal function after cardiac surgery (Kim et al., 2018). Dexmedetomidine treatment significantly decreased the rate of postoperative renal dysfunction and ranked third regarding protection from renal dysfunction and mortality. Atrial natriuretic peptide and B-type natriuretic peptide were ranked numbers one and two, respectively. Dexmedetomidine attenuates the surgical stress-induced sympathetic responses and results in stable hemodynamics that may contribute to better preservation of perioperative renal function. It acts on central α2 receptors in renal peritubular vasculatures and tubules, inducing vascular relaxation and diuresis by inhibiting the release of renin and arginine vasopressin. Dexmedetomidine can also protect multiple organs by attenuating ischemia/reperfusion injury and the inflammatory response.

Peripheral neuropathy: POTENTIAL BENEFIT IN RATS. In a rat model of sciatic nerve injury, dexmedetomidine treatment (0.5, 6, and 20 µg/kg, i.p.) once after injury, then at 2 and 6 weeks post-injury (given 3 times per week) significantly improved sciatic functional index and preserved the number of axons (Jeong et al., 2017). In a rat model of diabetic neuropathic pain (induced by streptozotocin), dexmedetomidine treatment (50 µg/kg, i.p.) prevented the elevated activation of microglia, increase in

proinflammatory cytokines (TNF-α, IL-1), and increase in glutamate levels and apoptotic markers (TUNEL-positive neurons, cleaved caspase 3)(Lu et al., 2017).

Safety: In cardiac surgery patients, perioperative dexmedetomidine decreases mortality, POD, and POCD, though may increase bradycardia and hypotension. Numerous drug interactions are known.

Types of evidence:

- 4 meta-analyses or systematic reviews based on numerous RCTs
- Numerous laboratory studies

Meta-analyses: DECREASED MORTALITY, INCREASED BRADYCARDIA IN SURGERY PATIENTS. Numerous meta-analyses have examined the effects of dexmedetomidine in surgery and ICU patients.

In the most recent 2019 meta-analysis assessing numerous treatments including dexmedetomidine in ICU patients, dexmedetomidine treatment was significantly less likely to increase mortality rate than placebo/control (OR=0.56; 95% CI, 0.32-0.99)(Wu et al., 2019). Dexmedetomidine and midazolam were associated with the least increase in overall mortality among all intravenously delivered preventive interventions for delirium.

In a different 2019 meta-analysis examining the effects of perioperative dexmedetomidine, 23 RCTs and cohort studies were included for cardiac surgery patients (n=7,635) and 8 studies were included for non-cardiac surgery patients (n=1,805)(Peng et al., 2019). In cardiac surgery, dexmedetomidine administration reduced postoperative 30-day mortality (RR=0.35; 95% CI, 0.24 to 0.51); durations of mechanical ventilation (mean difference [MD]=-1.56 h; 95% CI, -2.52 to -0.60), ICU stay (MD=-0.22 day; 95% CI, -0.35 to -0.08), hospital stay (MD=-0.65 day; 95% CI, -1.12 to -0.18); and the incidences of delirium (RR=0.50; 95% CI, 0.36 to 0.69), atrial fibrillation (RR=0.74, 95% CI, 0.57 to 0.97), and cardiac arrest (RR=0.34; 95% CI, 0.13 to 0.87). In noncardiac surgery, dexmedetomidine administration was associated with decreases in the durations of mechanical ventilation and hospital stay, with a trend toward a lower prevalence of delirium (RR=0.57, 95% CI, 0.32 to 1.01). The prevalence of bradycardia was increased in dexmedetomidine-treated patients undergoing cardiac surgery (RR=1.70; 95% CI, 1.19 to 2.44) and noncardiac surgery (RR=1.64; 95% CI, 1.05 to 2.58). Perioperative dexmedetomidine use did not increase the prevalence of hypotension.

In another 2019 meta-analysis of 25 RCTs examining the effects of dexmedetomidine (8 RCTs, n=1,425) and other treatments in ICU patients, dexmedetomidine treatment significantly increased the incidence of bradycardia (OR=2.18; 95%CI, 1.46 to 3.24) and hypotension (OR=1.89; 95% CI, 1.48 to 2.41)(Ng et al., 2019). The use of dexmedetomidine was also associated with a reduced incidence of agitation (OR=0.34; 95% CI, 0.20 to 0.59). In this meta-analysis, there was no evidence of an effect on mortality (OR=0.86; 95% CI, 0.66 to 1.10).

A 2018 meta-analysis that compared the effects of dexmedetomidine to standard sedatives or placebo included 25 RCTs for delirium incidence (4,975 patients total) and 3 RCTs for delirium treatment (166 patients) in ICU patients (Flukiger et al., 2018). Administration of dexmedetomidine was associated with significantly lower overall incidence of delirium when compared to placebo (RR 0.52; 95% CI 0.39-0.70), standard sedatives (RR 0.63; 95% CI 0.46-0.86), as well as to opioids (RR 0.61; 95% CI 0.44-0.83). When compared to standard sedatives, risks of bradycardia (RR=2.05; 95% CI, 1.31 to 3.22) and hypotension (RR=1.26; 95% CI, 1.04 to 1.54) were significantly higher with dexmedetomidine.

Drug interactions: Dexmedetomidine can interact with other drugs that cause drowsiness or slowed breathing, leading to dangerous side effects or even death (Drugs.com). There are a total of 712 drugs known to interact with dexmedetomidine, including 7 major drug interactions (acetaminophen/propoxyphene, aspirin/caffeine/propoxyphene, buprenorphine, buprenorphine/naloxone, propoxyphene, sodium oxybate, and tizanidine) and 705 moderate drug interactions (Drugs.com).

Sources and dosing: Dexmedetomidine is available only in a medical setting. It is manufactured by Pfizer and its brand name is Precedex™. It is administered intravenously.

For adult patients being sedated for a medical procedure, the loading infusion is typically 1.0 µg/kg for 10 minutes, followed by 0.2-1.0 µg/kg/hr maintenance infusion, titrated to desired effect (Drugs.com). For patients over 65 years old, the loading infusion is 0.5 µg/kg over 10 minutes, and dose reduction for the maintenance infusion is considered. For adult patients with impaired hepatic function, a dose reduction is considered.

In a 2018 meta-analysis of 10 RCTs including a total of 1,387 patients, dexmedetomidine doses varied; 6 trials used a loading dose of 0.4-1.0 µg/kg, followed by an infusion of 0.1-0.8 µg/kg/hr, and 4 studies used an infusion of 0.04 to 5.0 µg/kg/hr without a loading dose (Wu et al., 2018). Future studies are needed to determine the optimal dose and dosing regimen of perioperative dexmedetomidine. Because

genetic variants of ADRA2A are associated with varying degrees of the hypotensive response to dexmedetomidine, optimal doses likely vary across people (Kurnik et al., 2011).

Research underway: There are 251 ongoing clinical trials testing dexmedetomidine (ClinicalTrials.gov). A significant number of those (at least 51) are testing dexmedetomidine to prevent or treat delirium (ClinicalTrials.gov). Other trials are testing its effects in kidney disease, sleep, postoperative pain, and other conditions.

Search terms:

Pubmed, Google: dexmedetomidine

- + meta-analysis, + cognitive, + Alzheimer, + dementia, + ApoE, + diabetes, + neuropathy

Websites visited for dexmedetomidine:

- Clinicaltrials.gov
- DrugAge (0)
- Geroprotectors (0)
- Drugs.com
- WebMD.com
- PubChem
- DrugBank.ca