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antipsyhotics for the treatment of Parkinson's disease. [PubMed: 12517232]25.Ballard C, Thomas A, Gerry S, Yu LM, Aarsland D, Merritt C, Corbett A, Davison C, Sharma N, Khan Z, Creese B, Loughlin P, Bannister C, Burns A, Win SN, Walker Z, MAIN-AD investigators. Whether the treatment has any impact on these variables is unknown. Interventions that involve training and supporting family caregivers have been found to reduce or delay nursing home placement in the general population of patients with dementia. There are no studies specifically examining the prevention of BPSD, although some strategies have been shown to reduce the risk of cognitive decline and the development of dementia. Both a dietary intervention combining a Mediterranean diet with the Dietary Approach to Systolic Hypertension (DASH) and pharmacological treatment of hypertension results in a decreased risk for incident dementia and physical exercise improves cognitive function in patients with existing dementia. Use of Benzodiazepines in Alzheimer's Disease: A Systematic Review of Literature. Behavioral and psychological symptoms of dementia (BPSD) include a range of neuropsychiatric disturbances such as agitation, aggression, depression, and apathy. Unlike BPSD, symptoms related to delirium will resolve, albeit sometimes gradually, once the underlying cause is corrected. Patients who have pain, urinary retention, constipation, or other causes of discomfort yet cannot communicate their experience may become agitated, but once the cause is corrected, the behavioral disturbances improve. Presentations of psychiatric conditions, such as schizophrenia, bipolar disorder, major depressive disorder, and post-traumatic stress disorder, may be quite similar to BPSD. An excellent first step is initiating routine (not as-needed) acetaminophen, with a maximum recommended dose of 3 grams/day in the frail elderly. 2018 Mar 30;3:CD007726. Most hospitals and some nursing homes use one of these instruments, and family caregivers can also be trained to use them. Review psychiatric history and substance use: Caregivers should be questioned about the past medical history of psychiatric disorders, especially psychotic, mood, anxiety, and post-traumatic stress disorders, and whether the patient could be using alcohol, cannabis, non-prescribed medications, or illicit drugs. Patients receiving antipsychotic medications require monitoring for adverse motor effects, and periodic (every 3 to 6 months) attempts should be made to taper and discontinue the medication. Neuropsychiatric symptoms as predictors of progression to severe Alzheimer's dementia and death: the Cache County Dementia Progression Study. The primary focus of clinical trials has been on symptoms of agitation, aggression, and psychosis since these are typically the most problematic and distressing manifestations of BPSD. Empiric treatment of pain: Painful conditions are present in at least 49% of patients with dementia, but only 20 to 40% of patients with dementia receive analgesics, compared to 60 to 80% of similar patients without dementia; this is believed to relate to both under-reporting by patients and under-recognition by clinicians.[9] Since untreated pain has a strong relationship with BPSD, an 8-week multicenter cluster randomized controlled trial examined the effect of a stepwise protocol for empiric treatment of pain in patients with dementia-related agitation. Valproate preparations for agitation in dementia. In the case of psychotic or mood disorders, the presentation is generally episodic rather than continuous, which is typical for BPSD. Patients with primary CNS neoplasms have a high frequency of behavioral and psychological disturbance, most commonly apathy, anger, and disinhibition. Donepezil for the treatment of agitation in Alzheimer's disease. Transdermal buprenorphine may be the safest alternative in this regard and also is relatively unaffected by renal insufficiency, which is common in older adults.[15] Antipsychotics: Second-generation antipsychotics (primarily risperidone, olanzapine, quetiapine, and aripiprazole) are the mainstay of treatment for agitation and aggression, although, in a systematic review of 16 meta-analyses of randomized, controlled trials of these agents, the effect sizes (differences between treatment and placebo) were typically quite small for risperidone, olanzapine, and aripiprazole, ranging between 0.15 to 0.30 in most studies, and quetiapine generally did not differ from placebo. Are they risking their health or safety by refusing basic hygiene, food, or fluids? [PMC free article: PMC5584541] [PubMed: 24697702]13.Scales K, Zimmerman S, Miller SJ. [PubMed: 16347247].Mega MS, Cummings JL, Fiorello T, Gornbein J. [PMC free article: PMC4757608] [PubMed: 23861916]16. Tampi RR, Tampi DJ, Balachandran S, Srinivasan S. Prevalence of Analgesic Use and Pain in People with and without Dementia or Cognitive Impairment in Aged Care Facilities: A Systematic Review and Meta-Analysis. Trials of antipsychotic tapering should take place every 3 to 6 months (sooner if adverse effects emerge). There may be a temporal relationship with events such as a change in environment (e.g., moving from home to nursing facility), or symptoms might worsen in the evenings, following family visits, or when providing personal care. Review Medications Clinicians should ask caregivers about any changes in medications in the weeks preceding the onset or worsening of BPSD. [PMC free article: PMC6539264] [PubMed: 31132836]11. Broday H, Arasaratnam C. [PMC free article: PMC5546647] [PubMed: 28815009] [PubMed: 1328305]20. Porsteinsson AP, Dreyl LT, Pollock BG, Devanand DP, Frangakis C, Ismail Z, Marano C, Meinert CL, Mintzer JE, Munro CA, Pelton G, Rabins PV, Rosenberg PB, Schneider LS, Shade DM, Weintraub D, Yesavage J, Lyketsos CG, CIAD Research Group. Wandering and repetitive vocalizations rarely respond to pharmacotherapy and are best addressed with non-pharmacological measures. The relations among caregiver stress, "sundowning" symptoms, and cognitive decline in Alzheimer's disease. Doses can be increased in small increments every two weeks if there is an insufficient improvement, based on prospective ratings from caregivers. Am J Psychiatry. 2019 Jun 10;9(3):47-54. [PMC free article: PMC8407230] [PubMed: 29605970]19. Seitz DP, Adunuri N, Gill SS, Gruneir A, Herrmann N, Rochon P. Patients receiving antidepressants had higher rates of adverse events and study drop-out.[33] In elderly patients without dementia, there was a greater response rate to a combination of citalopram (average dose 34 mg daily) and methylphenidate (average dose 16 mg daily) than to either medication alone, without an increase in adverse effects (25677354), but whether the combination would be effective in patients with dementia is unknown, and benefits of citalopram doses below the currently recommended maximum of 20 mg daily cannot be determined from this study.[34] SSRIs are the antidepressant treatment of choice, with citalopram and sertraline favored due to fewer drug-drug interactions than paroxetine, fluoxetine, or fluoxetine, which inhibit cytochrome p450 enzymes.Apathy: Methylphenidate may improve apathy, cognition, and functioning modestly, with minimal risk for adverse effects, but studies of cholinesterase inhibitors, memantine, and antidepressants have not demonstrated a benefit for apathy.[35] In the ADMET trial of methylphenidate, patients did not meet exclusion criteria if they had cardiovascular conditions but were excluded if they had agitation at baseline; there were no differences from placebo on any cardiac outcomes, but patients receiving methylphenidate did have greater weight loss, and two methylphenidate patients developed hallucinations or delusions, versus none on placebo (not statistically significant).[36] The response to methylphenidate usually occurs within several days, so a good dosing strategy is to begin the immediate-release formulation at 2.5 or 5 mg twice daily (morning and early afternoon) and titrate up by 2.5 or 5 mg every week. Ther Adv Drug Saf. A Systematic Review and Meta-Analysis of Nonpharmacological Interventions for Moderate to Severe Dementia. Severe agitation or aggressive symptoms usually require immediate initiation of antipsychotic therapy to bring symptoms under control, but this should not obviate the need to implement other interventions concurrently or to attempt discontinuation when the patient stabilizes. Duloxetine, gabapentin, or pregabalin can be helpful if there is a concern for neuropathic pain, although they are associated with an increase in falls. Ther Adv Chronic Dis. Pharmacological interventions for apathy in Alzheimer's disease. Antidepressants for agitation and psychosis in dementia. For depression, pharmacotherapy should begin with citalopram or sertraline, with consideration of adding methylphenidate if there is a limited response after an adequate trial of the antidepressant. History is the key to differentiating BPSD from delirium: in delirium, the onset of symptoms occurs over days to 1 to 2 weeks, while in BPSD, symptoms gradually worsen over several weeks to months. Psychiatr Clin North Am. 2018 Mar;41(1):127-139. 2012 Sep;169(9):946-53. [PubMed: 30246461]38.van den Berg JF, Kruiithof HC, Kok RM, Verwijk E, Spaans HP, J Alzheimer's Dis. Gerontologist. 2015;10(3):194-203. Patients with dementia are susceptible to the CNS effects of medications, and not all culprit medications are easily recognized. Other essential elements of the history include the onset (i.e., acute, sub-acute, or chronic/progressive), frequency, timing, and trajectory of the disturbances, and any relationship to environmental changes or medication changes. [PMC free article: PMC6494556] [PubMed: 29727467]36.Rosenberg PB, Lactôt KL, Dreyl LT, Herrmann N, Scherer RW, Bachman DL, Mintzer JE, ADMET Investigators Safety and efficacy of methylphenidate for apathy in Alzheimer's disease: a randomized, placebo-controlled trial. Safety and effectiveness of cannabinoids for the treatment of neuropsychiatric symptoms in dementia: a systematic review. Pending transfer; patients who are dangerous to self or others require monitoring with one-on-one observation, and treatment with antipsychotic medications will usually be necessary, following a risk/benefit discussion with their surrogates or guardians. Treat discomfort: Before any BPSD-specific interventions, all patients should be assessed and treated for causes of discomfort (e.g., pain, constipation, urinary retention, is the environment too warm/cold/loud), as described above, and treated appropriately. Non-Pharmacological Interventions for BPSD The next step in management is implementing non-pharmacological interventions, which may be sufficient alone for mild BPSD, and should always accompany any pharmacotherapy. [PubMed: 17914039]24.Trinh NH, Hoblyn J, Mohanty S, Yaffe K. Topical therapies such as transdermal lidocaine, diclofenac gel, or methyl salicylate cream are safe. J Am Med Dir Assoc. This activity reviews the evaluation and management of BPSD and highlights the role of the interprofessional team in improving care for patients with this condition. Both are based on structured interviews with caregivers and have seen extensive use in research, with similar performance in detecting global changes. Effect of citalopram on agitation in Alzheimer disease: the CIAD randomized clinical trial. [PubMed: 26393847]22.Wang LY, Shofor JB, Rohde K, Hart KL, Hoff DJ, McFall YH, Raskind MA, Peskind ER. Citalopram should be started at 10 mg daily and sertraline at 25 mg daily. They predict more rapid cognitive decline and earlier mortality and are associated with increased hospital length of stay, hospital complications, earlier nursing home placement, and increased rates of psychiatric and cardiovascular disorders in family caregivers.[40] Studies have not explicitly reported on injuries to patients and caregivers as a result of BPSD, but agitation and aggression would presumably increase the risk. [PubMed: 25114079]33.Dudas R, Malouf R, McCreery J, Dening T. Although the quality of evidence is low, antipsychotic discontinuation often does not result in increased behavioral disturbances in residents of nursing homes with dementia: cluster randomised controlled trial. 2019 Sep;34(9):1336-1345. 2002;(2):CD002852. Another priority is identifying delirium, which by definition is caused by a medical condition, medication, or non-prescribed CNS-active substance intoxication or withdrawal because this will require prompt medical evaluation and treatment (see Differential Diagnosis section). The Cohen-Mansfield Agitation Inventory (CMAI) specifically evaluates agitated behaviors only, dividing them into four categories depending upon whether they are physical, verbal, aggressive, or non-aggressive.While the NPI, BEHAVE-AD, and CMAI are gold standards for evaluating BPSD, they are time-consuming, and a reasonable alternative in clinical practice is to ask caregivers to very specifically describe a problematic symptom, quantify its frequency, and assess the degree of distress it causes. After eight weeks, agitation was reduced by 17% in the intervention group (an effect comparable to that seen with risperidone, the antipsychotic most commonly used for BPSD), without any adverse effects on cognition or physical functioning, suggesting that treatment of pain did not achieve benefit for BPSD simply by sedating patients.[14] This study supports the empiric treatment of known or potential pain as a first step in addressing BPSD. Visual hallucinations may be prominent in delirium, whereas delusions are more common in patients with BPSD. [PMC free article: PMC4086818] [PubMed: 24549548]21.Cummings JL, Lyketsos CG, Peskind ER, Porsteinsson AP, Mintzer JE, Scharre DW, De La Gandara JE, Agronin M, Davis CS, Nguyen U, Shin P, Tariot PN, Siffert J. Due to their potential to worsen motor symptoms, clinicians should avoid using antipsychotics other than quetiapine, pimavanserin, and clozapine in Lewy body dementia and dementia associated with Parkinson's disease. Create a Baseline Since BPSD can fluctuate and their assessment is subjective, establishing a clear baseline for assessing the effects of treatment is critically important. [PMC free article: PMC6579119] [PubMed: 28826872]4.GBD 2016 Dementia Collaborators. J Am Geriatr Soc. Dementia refers to a collection of symptoms stemming from a broad array of etiologies precipitating in functionally impairing cognitive decline, 2.3%, mainly due to cerebrovascular disease and infections). 2017 Sep - Oct;65(5):515-529. 2015 Jun;172(6):561-9. Objectives: Review environmental, psychosocial, and medical factors that may contribute to behavioral and psychological symptoms of dementia. [PMC free article: PMC8516950] [PubMed: 30293233]27.Tampi RR, Tampi DJ. They can be effective if a localized source of pain is suspected. Finally, prazosin or dextromethorphan-quinidine are potential therapies. Cochrane Database Syst Rev. After the delusions consist of paranoid themes, as in Capgras syndrome and Othello syndrome. Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial. General Approach to Pharmacotherapy for BPSD Given the limited overall benefits of pharmacotherapy, a systematic approach to implementing and evaluating BPSD is critical. 2014 May;62(5):797-804. Patients with delirium frequently have changes in the level of consciousness, such as periods of somnolence or extended periods of wakefulness, which are typically less prominent in BPSD. In general, non-pharmacological approaches are well-tolerated, but rare cases of worsening agitation have occurred with music therapy. [PMC free article: PMC4994396] [PubMed: 27583123]17.Tampi RR, Tampi DJ, Young JJ, Balachandran S, Hoq RA, Manikarra G. Lancet Neurol. 2018 May 04;5:CD012197. 2017;14(1):61-75. N Engl J Med. Characterize Symptoms Caregivers should be prompted to describe what they are seeing, rather than using generic terms such as "agitation" or "depression," which can have different meanings to different observers. Patients were started on routine acetaminophen (3 g daily) if they were not receiving analgesics. Unless patients are endangering themselves or others, interventions should begin only after establishing a baseline by identifying and quantifying target symptoms, as described above.Choose an appropriate setting: The first step in management is to decide on the proper setting for treatment and address safety issues. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. 2015 Mar 02;35(0):369. [PMC free article: PMC6535742] [PubMed: 31205674]32.Tan MS, Yu JT, Tan CC, Wang HF, Meng XF, Wang C, Jiang T, Zhu XC, Tan L. Hallucinations are not as prevalent as delusions with estimates as low as 7% at baseline.[7] Furthermore, additional symptoms leading to subsequent hospital admissions include agitation, aggression, wandering, apathy, disinhibition, sleep disturbances, and depression. Physical Examination The physical examination may document the problematic symptoms, although these are often intermittent. BMJ. Acute or subacute onset of symptoms should prompt basic studies (typically, complete blood count, electrolytes, evaluation of liver and kidney function, urinalysis, thyroid function tests, toxicology screen, and head CT) to evaluate for causes of delirium. 2009 Sep;17(9):744-51. Some of these include armodafinil, bright light therapy to reduce circadian disturbances, massage, multisensory stimulation, and reminiscence therapy, in which patients are engaged in reviewing their past via conversation, photographs, or music.[13] Some interventions with anecdotal effectiveness for agitation include giving patients simple tasks to perform, such as folding laundry or using busy quilts (lap quilts with attached interesting objects such as zippers, Velcro, beads, ties, etc.) and weighted blankets (similar to those used to calm children with pervasive developmental disorders). 2015 May 19;18(10):py005. 2016 Sep;7(5):229-45. For patients whose BPSD occurs primarily during personal care, a randomized, multi-site crossover study showed that training caregivers to deliver a protocol called Bathing without a Battle (available online) reduced agitation, bathing time, and antipsychotic use.[12]Other non-pharmacological approaches: While non-pharmacological interventions other than caregiver training and music therapy have not been consistently effective for overall BPSD in randomized, controlled trials, they may benefit individual patients, and unlike medications, rarely have adverse effects. The primary outcome measure was a change in scores on the Cohen-Mansfield Agitation Inventory; changes in cognitive and physical functioning were also assessed. JAMA. For example, a symptom might be described as "pushing me away when I try to give her a shower," and then quantified by the percentage of showering time that this occurs (e.g., 75% of the time) and the level of distress it causes for the caregiver (e.g., 7 on a scale of 0 to 10). Neurology. If this was insufficient, they were stepped up to low-dose morphine (up to 20 mg daily), buprenorphine transdermal patch (up to 10 mcg hourly), or pregabalin (up to 300 mg daily). Patients with BPSD can also have superimposed delirium as a cause for an abrupt worsening of their usual symptoms. It's wise to heed the geropsychiatry maxim "start low, go slow, but go as high as you need to go" when treating mild to moderate BPSD with SSRIs because too-rapid titration can worsen agitation. BPSD correlates with more rapid progression of dementia and earlier mortality; whether the treatment has any impact on these variables is unknown.[39]BPSD substantially contributes to the overall burden of dementia on patients, caregivers, and society. Still, patients will have a history of these disorders before the onset of their dementia. [PubMed: 12076456]31.Hillen JB, Soulsby N, Alderman C, Caughey GE, Int J Geriatr Psychiatry. 2015 Sep 22;29:314(12):1242-54. Noninvasive brain stimulation for behavioural and psychological symptoms of dementia: A systematic review and meta-analysis. [PMC free article: PMC6291454] [PubMed: 30497964]5.Kales HC, Gitlin LN, Lyketsos CG. Target symptoms and their baseline frequency/severity should undergo an assessment before starting the medication, and patients should be followed up two to three weeks later for response and tolerability. Antipsychotic use in dementia: a systematic review of benefits and risks from meta-analyses. According to the revised McGeer criteria, diagnostic evaluation and empiric therapy should be limited to patients who present with fever, dysuria, suprapubic pain, or new/increased urinary frequency, urgency, or incontinence, although other authors have suggested that culture and treatment could be initiated on the basis of an acute mental status change together with both change in the character of the urine and positive dipstick for either leukocyte esterase or nitrite.[8] Establish Priorities The first priority is characterizing the severity and nature of the symptoms – patients who are endangering themselves or others with aggressive behaviors or refusal of basic care will warrant more intensive management such as hospitalization. Because pain is present in 40 to 56% of patients with dementia and the presence of pain is associated with increased BPSD, the past medical history should have a review for painful conditions (e.g., neuropathy, osteoarthritis, peripheral vascular disease), and caregivers should be asked about both the patient's self-report about pain and nonverbal signs of pain, because patients with dementia may demonstrate nonverbal signs of pain even though they do not report it.[9]The Pain Assessment in Advanced Dementia (PAINAD) or Face, Legs, Activity, Cry, Consolability (FLACC) scales are both reliable and valid tools for objectively evaluating and tracking pain. Diagnosis and management of urinary tract infection in older adults. 2003 Jan 08;28(2):210-6. 2016 Mar;17(2):217-27. 2019 May;16(5):325-335. Determinants of behavioral and psychological symptoms of dementia: A scoping review of the evidence. 2015;43(2):589-603. Efficacy and adverse effects of ginkgo biloba for cognitive impairment and dementia: a systematic review and meta-analysis. Therefore, the history should begin with an assessment of safety; has the patient been aggressive toward others, and if so, has this caused injury? Eur J Health Econ. If there is no benefit but also no adverse effects, citalopram dosing should increase to 20 mg and sertraline to 50 mg. [PMC free article: PMC3137923] [PubMed: 21765198]15.Hirst A, Knight C, Hirst M, Dunlop W, Akehurst R. The NPI evaluates delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/emotional lability, aberrant motor behavior, sleep disturbances, and disorders of appetite/eating; for each domain, caregivers are asked to rate frequency, severity, and the degree of distress it causes, over a time period specified by the interviewer. Electroconvulsive Therapy for Agitation and Aggression in Dementia: A Systematic Review. Patients with suspected delirium should have a thorough medical evaluation, beginning with history and physical and followed by targeted laboratory testing and imaging based on these findings; typically, comprehensive metabolic panel, CBC, urinalysis, cardiac enzymes, chest X-ray, and toxicology screens are performed routinely, with neuroimaging, lumbar puncture, blood gases, and EEG reserved for select cases. Instead, a biopsychosocial model has been proposed that attributes neuropsychiatric symptoms to interactions between an individual's biology, prior experiences, and current environment. Sertraline may be further increased to a maximum dose of 200 mg daily. The goal of the physical examination is to confirm historical data and identify alternative or contributing psychiatric or general medical conditions. Behavioral disturbances often occur in the evening, a phenomenon is known as "sundowning." Some studies suggest that this phenomenon affects up to two-thirds of patients with dementia.[6] One of the most common psychiatric sequelae observed in this demographic is delusions. [PubMed: 8559361]8.Rowe TA, Iuthani-Mehta M. [PMC free article: PMC8985413] [PubMed: 22419314]29.Defrancesco M, Marksteiner J, Fleischacker WJ, Blasko L. 2014 Nov;29(7):565-74. 2013 Aug;74(8):810-6. [PMC free article: PMC4707529] [PubMed: 25731881]6.Gallagher-Thompson D, Brooks JO, Bliwis D, Leader J, Yesavage JA. 2019 Jan;18(1):88-106. World J Psychiatry. [Level 5]Review Questions1.Alaves GS, Carvalho AF, de Amorim D, Carvalho L, Sudo FK, Siqueira-Neto JI, Oertel-Knochel V, Jurcoane A, Knochel C, Boecker H, Laks J, Pantel J. Despite the lack of high-quality evidence for effectiveness, many clinicians will trial quetiapine in patients with Lewy body dementia or Parkinson's disease. 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S. and Europe for pseudobulbar affect, was studied in a single randomized trial, with modest benefit for agitation but significant adverse effects, especially falls.[21] Prazosin (average dose of about 6 mg daily) was beneficial for BPSD without adverse effects on blood pressure in a single study with 22 participants.[22] Medications that have no clinically meaningful efficacy for agitation or aggression include cholinesterase inhibitors, memantine, valproate, and benzodiazepines.[23][24][25][26][27] An exception to the negative findings regarding cholinesterase inhibitors in the dementia population as a whole is the possible benefit for patients with Lewy body dementia and dementia associated with Parkinson's disease, in which a small effect size of 0.2 was found, albeit at the cost of an increase in motor symptoms.[28] Both valproate and benzodiazepines have correlated with accelerating cognitive decline in patients with dementia.[26][29] Haloperidol is ineffective for BPSD in general but can be useful for aggression.[30] Cannabinoids (dronabinol, purified delta-9-tetrahydrocannabinol, and nabiximol) have been evaluated in a systematic review, in which the best randomized controlled trial evidence did not support benefit for a reduction in either symptoms or caregiver burden, although differences in adverse events were minimal.[31] Among other complementary and alternative therapies; the only ginkgo at a dose of 240 mg/d has shown consistent benefit for BPSD in randomized, controlled trials, although these studies were of low to moderate quality.[32] Pharmacologic Interventions for Depression and Apathy While depression and apathy are the most common BPSD, fewer studies have examined outcomes of pharmacotherapy. Depression: A meta-analysis of 10 studies of various antidepressants for treatment of depression in dementia showed no difference from placebo on the primary outcome measure (scores on depression rating scales) for antidepressants as a group or any individual agent; although there was a benefit for SSRIs (but not other antidepressants) regarding numbers of responders and remitters, the quality of this evidence was lower. Although opioids can also contribute to falls and fractures, tramadol has a stronger association than most other opioids. [PubMed: 29412841]41.Rakesh G, Szabo ST, Alexopoulos GS, Zannas AS, Lyketsos CG. Target symptoms and their baseline frequency/severity should undergo an assessment before starting the medication, and patients should be followed up two to three weeks later for response and tolerability. Antipsychotic use in dementia: a systematic review of benefits and risks from meta-analyses. 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