FEP Medical Policy Manual

FEP 6.01.54 Dopamine Transporter Single-Photon Emission Computed Tomography

Effective Policy Date: April 1, 2021

Original Policy Date: December 2012

Related Policies:

6.01.06 - Miscellaneous (Noncardiac, Nononcologic) Applications of Fluorine 18 Fluorodeoxyglucose Positron Emission Tomography
6.01.55 - Beta-Amyloid Imaging With Positron Emission Tomography for Alzheimer Disease
7.01.63 - Deep Brain Stimulation

Dopamine Transporter Single-Photon Emission Computed Tomography

Description

Description

Dopamine transporter imaging with single-photon emission computed tomography (DaT-SPECT), using radiopharmaceutical ioflupane injection, is a neuroimaging modality being evaluated to improve the differential diagnosis of parkinsonian syndromes from nonparkinsonian tremor, as well as dementia with Lewy bodies from Alzheimer disease.

DaT-SPECT is based on the selective affinity of DaT ligands for dopamine-synthesizing neurons, which allows visualization of deficits in the nigrostriatal dopaminergic pathway.

DaT ligands include iodine 123I-2β-carbomethoxy-3β-(4-iodophenyl) tropane (^{123}I-β-CIT), which is a cocaine analogue with an affinity for both dopamine and serotonin transporters. Intravenous ^{123}I-β-CIT requires a delay between injection and scan of about 24 hours. Iodine-123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl) nortropane (^{123}I-FP-CIT)is a fluoropropyl derivate of β-CIT that is selective for brain striatal DaT but can also bind to the serotonin transporter. Intravenous ^{123}I-FP-CIT can be injected 3 to 6 hours before the scan (DaTscan). Other SPECT ligands with affinity for dopamine transporter include technetium 99m (2β((N,N-bis(2-mercaptoethyl) ethylene diamino) methyl) and 3β-(4-chlorophenyl) tropane (^{99m}Tc-TRODAT-1).[2,3,]

Binding of ligands with an affinity for DaT ligands in the striatum is, in general, reduced in PD, genetic parkinsonism, DLB, corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy. In contrast, striatal DaT ligand binding is expected to be within the normal range of Alzheimer disease, essential tremor, dystonic tremor, orthostatic tremor, drug-induced parkinsonism, and psychogenic parkinsonism.[2,]

Visualization of striatal dopamine transporter binding, through DaT-SPECT, permits assessment of presynaptic dopaminergic deficit. It is proposed that an abnormal DaT-SPECT scan supports the diagnosis of PD, DLB, or other neurodegenerative parkinsonian syndromes, while a normal DaT-SPECT scan in a symptomatic patient supports the diagnosis of a disease not affecting the nigrostriatal dopaminergic pathway.

Analysis of DaT-SPECT images can be visual, semiquantitative, or quantitative. In patients with PD, physical symptoms start after 30% to 50% of dopaminergic neurons have degenerated.[4,5,] Symptomatic patients with PD would be thus expected to have sufficient abnormality on DaT-SPECT for visual analysis to be adequate for interpretation. A variety of methods are being tested to improve the validity and reliability of ratings, including commercially available software to define the region of interest for analysis and the development of an atlas for visual interpretation. Several research centers are developing quantitative and semiquantitative classification methods for the evaluation of DaT-SPECT images.[6,7,8,9,]

Anatomic variation in the brain, including vascular lesions, may interfere with the distribution of the iodine-123 tracer and could result in an abnormal scan.[10,] Dopamine agonists and levodopa may also affect DaT expression, which could influence the ability of DaT-SPECT to monitor the progression of disease unless these agents are discontinued prior to imaging. Patients with clinically diagnosed PD or DLB, who present with a normal DaT-SPECT scan, are referred to in the literature as having "scans without evidence of dopaminergic deficit." While many of these patients are ultimately diagnosed with non-PD syndromes, a portion of patients with normal DaT-SPECT imaging are confirmed to have PD or DLB by the reference standard. In studies where clinical diagnosis is used as an endpoint, scans without evidence of dopaminergic deficit are present in 3% to 20% of PD patients.[11,] In a study of patients clinically diagnosed with DLB, van der Zande et al (2016) found that 10% of these patients had normal scans.[12,] Further research may shed light on these cases.

OBJECTIVE

The objective of this evidence review is to determine whether dopamine transporter imaging with single-photon emission computed tomography improves health outcomes in individuals with clinically uncertain Parkinson disease or clinically uncertain dementia with Lewy bodies.

POLICY STATEMENT

Dopamine transporter imaging with single-photon emission computed tomography may be considered **medically necessary** when used for individuals with:

- clinically uncertain Parkinson disease; or
- clinically uncertain dementia with Lewy bodies.

Use of dopamine transporter imaging with single-photon emission computed tomography is considered **investigational** for all other indications not included above.

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

In 2011, DaTscan™ (GE Healthcare) was approved by the U.S. Food Drug Administration (FDA) through a new drug application and is "indicated for striatal dopamine transporter visualization using single-photon emission computed tomography brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndromes. In these patients, DaTscan may be used to help differentiate ET [essential tremor] from tremor due to parkinsonian syndromes (idiopathic Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations."[13,]

FDA product code: KPS.

RATIONALE

Summary of Evidence

For individuals who have clinically uncertain Parkinson disease (PD) who receive single-photon emission computed tomography (DaT-SPECT), the published evidence includes randomized controlled trials (RCTs), cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. In populations with clinically apparent PD, studies of diagnostic accuracy have reported high sensitivity and specificity for PD. Studies of clinical validity in the target population of clinically uncertain PD are limited by gaps in study design, conduct, and relevance. Evidence on clinical utility in the target population includes an RCT showing no significant difference in outcomes over time between patients who received a DaT-SPECT scan and those who did not. The evidence is insufficient to determine the effects of technology on health outcomes.

For individuals who have clinically uncertain dementia with Lewy bodies who receive DaT-SPECT, the published evidence includes RCTs, cohort studies, and case series studies. Relevant outcomes are symptoms, functional outcomes, and treatment-related mortality and morbidity. No studies with the optimal reference standard to assess clinical validity have been performed in the target population of clinically uncertain dementia with Lewy bodies. No studies have directly evaluated the effect of DaT-SPECT on health outcomes in the target population. The evidence is insufficient to determine the effects of technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American College of Radiology

In 2019, the American College of Radiology updated the appropriateness criteria for movement disorders and neurodegenerative diseases.[40,] The College categorized Ioflupane SPECT/CT as 'may be appropriate' for initial imaging of Parkinsonian syndrome. A strength of evidence rating was not given for this statement.

The American College of Radiology (2019) updated the appropriateness criteria for dementia.[41,] The College categorized Ioflupane SPECT or SPECT/CT brain as 'may be appropriate' for initial imaging for suspected dementia with Lewy bodies.

American Academy of Neurology

The practice parameters from the American Academy of Neurology (2006; reaffirmed 2013) stated that β-CIT and IBZM (iodobenzamide) SPECT are possibly useful in distinguishing PD from essential tremor (5 class III studies).[42.] There was insufficient evidence to determine whether these modalities are useful in distinguishing PD from other forms of parkinsonism.

Society of Nuclear Medicine and Molecular Imaging

In 2011, the Society of Nuclear Medicine, now called the Society of Nuclear Medicine and Molecular Imaging, provided practice guidelines for DaT-SPECT.[43.] The guidelines stated that the main indication for DaT-SPECT is striatal DaT visualization in the evaluation of adults with suspected parkinsonian syndromes to help differentiate essential tremor from tremor due to presynaptic parkinsonian syndromes (PD, multisystem atrophy, progressive supranuclear palsy). Other indications are the early diagnosis of presynaptic parkinsonian syndromes, differentiation of presynaptic parkinsonian syndromes from parkinsonism without a presynaptic dopaminergic loss (eg, drug-induced parkinsonism, psychogenic parkinsonism), and differentiation of DLB from Alzheimer disease. The guidance stated that visual interpretation of the scan is usually sufficient for clinical evaluation, where the striatal shape, extent, symmetry, and intensity differentiate normal from abnormal. For semiquantitative analysis, each site should establish its own reference range by scanning a population of healthy controls or by calibrating its procedure with another center that has a reference database.

Movement Disorders Society

In 2015, the Movement Disorders Society (MDS) diagnostic criteria for PD are intended for use in clinical research but can be used to guide clinical diagnosis.[15.] The MDS considers the clinical expert opinion to be the criterion standard to diagnose PD and that diagnoses are usually made clinically without ancillary diagnostic testing. Methods that may become available as knowledge advances are diagnostic biochemical markers, anatomic neuroimaging, and methods to detect alpha-synuclein deposition. Normal functional neuroimaging of the presynaptic dopaminergic system, if performed, is listed as an absolute exclusion criterion for PD. MDS noted that, although dopaminergic neuroimaging can help to distinguish parkinsonism from PD mimics like essential tremor, "it does not qualify as a criterion for the differentiation of PD from other parkinsonian conditions like atypical parkinsonian syndromes." Normal functional neuroimaging of the presynaptic dopaminergic system is also listed as criteria for exclusion from diagnosis of PD in patients with early/de novo PD.[44.]

National Institute for Health and Care Excellence

In 2006, the National Institute for Health and Care Excellence (NICE) published guidance on the diagnosis and management of PD,[45.] which was updated in 2017.[46,47.] The 2006 guidance stated thatiodine 123 N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl) nortropane (^{123}I-FP-CIT) SPECT should be considered for people with tremor where essential tremor cannot be clinically differentiated from parkinsonism (based on studies with a level of evidence 1a or 1b); this recommendation is continued in 2017 guidance. Also unchanged was the recommendation that ^{123}I-FP-CIT SPECT should be available to specialists with expertise in its use and interpretation (based on the level of evidence IV, expert opinion).

The NICE updated its 2016 guidance on dementia in 2018.[48.] It recommended that ^{123}I-FP-CIT SPECT be used to help establish the diagnosis in those with suspected DLB if the diagnosis is uncertain.

Dementia of Lewy Bodies Consortium

In 2017, the Dementia of Lewy Bodies Consortium published clinical guidelines on diagnosis and management, based on American expert opinion.[49.] The guidelines stated that reduced DaT uptake in basal ganglia demonstrated by SPECT is an indicative biomarker. As such, dementia with abnormal DaT-SPECT imaging would be classified as possible DLB. The presence of another core clinical feature (fluctuating cognition, recurrent visual hallucinations, rapid-eye-movement sleep disorder, parkinsonism motor abnormalities) in

addition to dementia and abnormal DaT-SPECT imaging would allow classification as probable DLB. It was noted that patients with autopsy-confirmed DLB may have normal DaT-SPECT imaging.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

1. Elahi FM, Miller BL. A clinicopathological approach to the diagnosis of dementia. Nat Rev Neurol. Aug 2017; 13(8): 457-476. PMID 28708131
2. Kagi G, Bhatia KP, Tolosa E. The role of DAT-SPECT in movement disorders. J Neurol Neurosurg Psychiatry. Jan 2010; 81(1): 5-12. PMID 20019219
3. Levine CB, Fahrbach KR, Siderowf AD, et al. Diagnosis and Treatment of Parkinsons Disease: A Systematic Review of the Literature (Evidence Report/Technology Assessment No. 57). Rockville, MD: Agency for Healthcare Research and Quality; 2003
4. Burke RE, O'Malley K. Axon degeneration in Parkinson's disease. Exp Neurol. Aug 2013; 246: 72-83. PMID 22285449
5. Fahn S, Oakes D, Shoulson I, et al. Levodopa and the progression of Parkinson's disease. N Engl J Med. Dec 09 2004; 351(24): 2498-508. PMID 15590952
6. Prashanth R, Roy SD, Mandal PK, et al. High-Accuracy Classification of Parkinson's Disease Through Shape Analysis and Surface Fitting in 123I-Ioflupane SPECT Imaging. IEEE J Biomed Health Inform. May 2017; 21(3): 794-802. PMID 28113827
7. Skanjeti A, Castellano G, Elia BO, et al. Multicenter Semiquantitative Evaluation of (123)I-FP-CIT Brain SPECT. J Neuroimaging. Nov-Dec 2015; 25(6): 1023-9. PMID 25923060
8. Ueda J, Yoshimura H, Shimizu K, et al. Combined visual and semi-quantitative assessment of 123 I-FP-CIT SPECT for the diagnosis of dopaminergic neurodegenerative diseases. Neurol Sci. Jul 2017; 38(7): 1187-1191. PMID 28389938
9. Booij J, Dubroff J, Pryma D, et al. Diagnostic Performance of the Visual Reading of 123 I-Ioflupane SPECT Images With or Without Quantification in Patients With Movement Disorders or Dementia. J Nucl Med. Nov 2017; 58(11): 1821-1826. PMID 28473597
10. Nuvoli S, Spanu A, Piras MR, et al. 123I-ioflupane brain SPECT and 123I-MIBG cardiac planar scintigraphy combined use in uncertain parkinsonian disorders. Medicine (Baltimore). May 2017; 96(21): e6967. PMID 28538394
11. Erro R, Schneider SA, Stamelou M, et al. What do patients with scans without evidence of dopaminergic deficit (SWEDD) have? New evidence and continuing controversies. J Neurol Neurosurg Psychiatry. Mar 2016; 87(3): 319-23. PMID 25991401
12. van der Zande JJ, Booij J, Scheltens P, et al. [(123)]FP-CIT SPECT scans initially rated as normal became abnormal over time in patients with probable dementia with Lewy bodies. Eur J Nucl Med Mol Imaging. Jun 2016; 43(6): 1060-6. PMID 26830298
13. GE Healthcare. DaTscan Ioflupane I123 Injection Full Prescribing Information. n.d.; http://www3.gehealthcare.com/en/products/categories/nuclear_imaging_agents/datscan. Accessed July 31, 2019
14. Bhatia KP, Bain P, Bajaj N, et al. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. Jan 2018; 33(1): 75-87. PMID 29193359
15. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. Oct 2015; 30(12): 1591-601. PMID 26474316
16. Rizzo G, Copetti M, Arcuti S, et al. Accuracy of clinical diagnosis of Parkinson disease: A systematic review and meta-analysis. Neurology. Feb 09 2016; 86(6): 566-76. PMID 26764028
17. Scherfler C, Schwarz J, Antonini A, et al. Role of DAT-SPECT in the diagnostic work up of parkinsonism. Mov Disord. Jul 15 2007; 22(9): 1229-38. PMID 17486648
18. Tu XJ, Hwang WJ, Ma HI, et al. Determinants of generic and specific health-related quality of life in patients with Parkinson's disease. PLoS One. 2017; 12(6): e0178896. PMID 28650957
19. Marshall VL, Reininger CB, Marquardt M, et al. Parkinson's disease is overdiagnosed clinically at baseline in diagnostically uncertain cases: a 3-year European multicenter study with repeat [123I]FP-CIT SPECT. Mov Disord. Mar 15 2009; 24(4): 500-8. PMID 19117369

20. Vlaar AM, de Nijs T, Kessels AG, et al. Diagnostic value of 123I-ioflupane and 123I-iodobenzamide SPECT scans in 248 patients with parkinsonian syndromes. Eur Neurol. 2008; 59(5): 258-66. PMID 18264015
21. Kupsch AR, Bajaj N, Weiland F, et al. Impact of DaTscan SPECT imaging on clinical management, diagnosis, confidence of diagnosis, quality of life, health resource use and safety in patients with clinically uncertain parkinsonian syndromes: a prospective 1-year follow-up of an open-label controlled study. J Neurol Neurosurg Psychiatry. Jun 2012; 83(6): 620-8. PMID 22492213
22. Kupsch A, Bajaj N, Weiland F, et al. Changes in clinical management and diagnosis following DaTscan SPECT imaging in patients with clinically uncertain parkinsonian syndromes: a 12-week follow-up study. Neurodegener Dis. 2013; 11(1): 22-32. PMID 22571977
23. Hauser RA, Bajaj N, Marek K, et al. Sensitivity, specificity, positive and negative predictive values and diagnositic accuracy of DaTscan(TM) (Ioflupane I123 injection): Predicting clinical diagnosis in early clinically uncertain parkinsonian syndrome. J Neurol Stroke. May 11 2014;1(1):00003
24. Bajaj N, Hauser RA, Seibyl J, et al. Association between Hoehn and Yahr, Mini-Mental State Examination, age, and clinical syndrome predominance and diagnostic effectiveness of ioflupane I 123 injection (DaTSCAN) in subjects with clinically uncertain parkinsonian syndromes. Alzheimers Res Ther. 2014; 6(5-8): 67. PMID 25478029
25. Brigo F, Matinella A, Erro R, et al. [I]FP-CIT SPECT (DaTSCAN) may be a useful tool to differentiate between Parkinson's disease and vascular or drug-induced parkinsonisms: a meta-analysis. Eur J Neurol. Nov 2014; 21(11): 1369-e90. PMID 24779862
26. O'Brien JT, Oertel WH, McKeith IG, et al. Is ioflupane I123 injection diagnostically effective in patients with movement disorders and dementia? Pooled analysis of four clinical trials. BMJ Open. Jul 03 2014; 4(7): e005122. PMID 24993764
27. Sadasivan S, Friedman JH. Experience with DaTscan at a tertiary referral center. Parkinsonism Relat Disord. Jan 2015; 21(1): 42-5. PMID 25465746
28. Oravivattanakul S, Benchaya L, Wu G, et al. Dopamine transporter (DaT) scan utilization in a movement disorder center. Mov Disord Clin Pract. Oct 2015;3(1):31-35
29. Bega D, Gonzalez-Latapi P, Zadikoff C, et al. Is There a Role for DAT-SPECT Imaging in a Specialty Movement Disorders Practice?. Neurodegener Dis. 2015; 15(2): 81-6. PMID 25592727
30. Catafau AM, Tolosa E. Impact of dopamine transporter SPECT using 123I-Ioflupane on diagnosis and management of patients with clinically uncertain Parkinsonian syndromes. Mov Disord. Oct 2004; 19(10): 1175-82. PMID 15390019
31. Tolosa E, Borght TV, Moreno E. Accuracy of DaTSCAN (123I-Ioflupane) SPECT in diagnosis of patients with clinically uncertain parkinsonism: 2-year follow-up of an open-label study. Mov Disord. Dec 2007; 22(16): 2346-51. PMID 17914722
32. McKeith I, O'Brien J, Walker Z, et al. Sensitivity and specificity of dopamine transporter imaging with 123I-FP-CIT SPECT in dementia with Lewy bodies: a phase III, multicentre study. Lancet Neurol. Apr 2007; 6(4): 305-13. PMID 17362834
33. Galvin JE. IMPROVING THE CLINICAL DETECTION OF LEWY BODY DEMENTIA WITH THE LEWY BODY COMPOSITE RISK SCORE. Alzheimers Dement (Amst). Sep 01 2015; 1(3): 316-324. PMID 26405688
34. McCleery J, Morgan S, Bradley KM, et al. Dopamine transporter imaging for the diagnosis of dementia with Lewy bodies. Cochrane Database Syst Rev. Jan 30 2015; 1: CD010633. PMID 25632881
35. Walker RW, Walker Z. Dopamine transporter single photon emission computerized tomography in the diagnosis of dementia with Lewy bodies. Mov Disord. 2009; 24 Suppl 2: S754-9. PMID 19877236
36. Thomas AJ, Attems J, Colloby SJ, et al. Autopsy validation of 123I-FP-CIT dopaminergic neuroimaging for the diagnosis of DLB. Neurology. Jan 17 2017; 88(3): 276-283. PMID 27940650
37. Walker Z, Moreno E, Thomas A, et al. Clinical usefulness of dopamine transporter SPECT imaging with 123I-FP-CIT in patients with possible dementia with Lewy bodies: randomised study. Br J Psychiatry. Feb 2015; 206(2): 145-52. PMID 25431431
38. Walker Z, Moreno E, Thomas A, et al. Evolution of clinical features in possible DLB depending on FP-CIT SPECT result. Neurology. Sep 06 2016; 87(10): 1045-51. PMID 27511183
39. Kemp PM, Clyde K, Holmes C. Impact of 123I-FP-CIT (DaTSCAN) SPECT on the diagnosis and management of patients with dementia with Lewy bodies: a retrospective study. Nucl Med Commun. Apr 2011; 32(4): 298-302. PMID 21278615
40. Harvey HB, Watson LC, Subramaniam RM, et al. ACR Appropriateness Criteria Movement Disorders and Neurodegenerative Diseases. Available at https://acsearch.acr.org/docs/3111293/Narrative/. American College of Radiology. Accessed September 17, 2020.
41. Moonis G, Subramaniam RM, Trofimova A, et al. ACR Appropriateness Criteria Dementia. Available at https://acsearch.acr.org/docs/3111292/Narrative/. American College of Radiology. Accessed September 17, 2020.
42. Suchowersky O, Reich S, Perlmutter J, et al. Practice Parameter: diagnosis and prognosis of new onset Parkinson disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. Apr 11 2006; 66(7): 968-75. PMID 16606907
43. Djang DS, Janssen MJ, Bohnen N, et al. SNM practice guideline for dopamine transporter imaging with 123I-ioflupane SPECT 1.0. J Nucl Med. Jan 2012; 53(1): 154-63. PMID 22159160

44. Berg D, Adler CH, Bloem BR, et al. Movement disorder society criteria for clinically established early Parkinson's disease. Mov Disord. Oct 2018; 33(10): 1643-1646. PMID 30145841
45. National Institute for Health and Care Excellence (NICE). Parkinson's disease in over 20s: diagnosis and management [CG35]. 2006; https://www.nice.org.uk/guidance/cg35#diagnosing-parkinsons-disease. Accessed October 3, 2020.
46. National Institute for Health and Care Excellence (NICE). Parkinson's disease in adults [NG71]. 2017; https://www.nice.org.uk/guidance/NG71. Accessed October 2, 2020.
47. Rogers G, Davies D, Pink J, et al. Parkinson's disease: summary of updated NICE guidance. BMJ. Jul 27 2017; 358: j1951. PMID 28751362
48. National Institute for Health and Care Excellence (NICE). Dementia: assessment, management and support for people living with dementia and their carers [NG97]. 2018; https://www.nice.org.uk/guidance/ng97. Accessed October 1, 2020.
49. McKeith IG, Boeve BF, Dickson DW, et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. Jul 04 2017; 89(1): 88-100. PMID 28592453

POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2012	New policy	
December 2013	Replace policy	Updated policy with literature review. Added reference 19 and 24. No change to policy statement or summary.
December 2014	Replace policy	Policy updated with literature review; reference 6 added; policy statement unchanged.
March 2016	Replace policy	Policy updated with literature review through June 4, 2015; references 5, 7, 10-11, 13, 15, 22-25, 31, and 33 added. Clinical input reviewed. Policy statement unchanged.
December 2016	Replace policy	Policy updated with literature review; references 33, 35, 39, 41, and 45 added; reference 38 updated. Policy statement unchanged.
December 2017	Replace policy	Policy updated with literature review through July 21, 2017; Rationale revised and several references added. Policy statement unchanged.
March 2019	Replace policy	Policy updated with literature review through August 4, 2018. Change policy statements to medically necessary for clinically uncertain Parkinson disease and clinically uncertain dementia with Lewy bodies; reference 39 added; references 26 and 43 updated.
December 2019	Replace policy	Policy updated with literature review through July 17, 2019; no references added. Policy statements unchanged.
December 2020	Replace policy	Policy updated with literature review through September 9, 2020; references added. Policy statements unchanged.

Date	Action	Description
March 2021	Replace policy	Policy updated with format editing. Policy statements unchanged.