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Research Article

Long-Term Follow-Up of continuous glucose monitoring for diabetic neuropathy

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Abstract

Background: Continuous glucose monitoring (CGM) has transformed glycemic surveillance, and longitudinal evidence links CGM-derived metrics, particularly time-in-range and glycemic variability, to the trajectory of diabetic neuropathy [6,13].

Objective: This review synthesizes long-term follow-up evidence on CGM use and diabetic neuropathy, examining how sustained glucose control and variability relate to nerve conduction, symptom burden, and neuropathy progression.

Methods: We synthesized randomized CGM trials, prospective cohort studies with multi-year follow-up, and mechanistic literature addressing glycemic variability, time-in-range, and diabetic neuropathy in type 1 and type 2 diabetes.

Findings: Sustained CGM use improves time-in-range and reduces variability relative to self-monitored glucose [7,8], and DCCT/EDIC follow-up shows that early sustained control durably lowers neuropathy incidence over decades [20,21]; CGM-derived variability correlates with nerve conduction slowing independent of mean glycemia [17,18].

Conclusions: Long-term CGM use supports glycemic stability that plausibly slows neuropathy progression, but dedicated trials linking CGM metrics directly to neuropathy endpoints remain limited; practice should combine CGM-guided variability reduction with standardized neuropathy screening [26,27].

Keywords: continuous glucose monitoring; diabetic neuropathy; glycemic variability; time in range; long-term follow-up

1. Introduction

Diabetic peripheral neuropathy remains the most common chronic complication of diabetes, affecting roughly half of people living with the disease for more than two decades and accounting for the large majority of non-traumatic lower-limb amputations [1,2]. Its pathophysiology converges on metabolic, vascular, and inflammatory injury to peripheral axons, with hyperglycemia-driven oxidative stress and microvascular insufficiency to the vasa nervorum forming the core pathway linking glycemic exposure to nerve injury [3,4,5]. Its relationship to glycemia has been established since the Diabetes Control and Complications Trial (DCCT) showed that intensive insulin therapy reduced the incidence of clinical neuropathy by roughly 60% over 6.5 years in type 1 diabetes [6]. What the DCCT could not resolve, because self-monitored glucose sampled only a handful of points per day, was how much of that effect came from mean glycemia as opposed to glucose excursions between measurements. Continuous glucose monitoring (CGM), capturing values every one to five minutes over years of near-continuous wear, has reopened that question with a resolution self-monitoring never offered.

Randomized trials of real-time and intermittently scanned CGM consistently show that sustained CGM use raises time-in-range and lowers glycemic variability relative to self-monitoring, independent of any change in mean HbA1c [7,8,9]. Because oxidative stress from acute glucose fluctuations has been proposed as a driver of microvascular injury distinct from sustained hyperglycemia alone [10,11], CGM offers a plausible route by which glycemic stability, not level alone, could modify neuropathy's long-term course. This review synthesizes long-term follow-up evidence linking CGM-derived metrics, principally time-in-range and variability, to diabetic peripheral and autonomic neuropathy outcomes.

2. Methods

We synthesized peer-reviewed randomized controlled trials of CGM technology, prospective cohort studies with multi-year neuropathy follow-up, and epidemiological and mechanistic studies addressing glycemic variability, time-in-range, and diabetic peripheral or autonomic neuropathy in type 1 and type 2 diabetes. Sources included the DCCT/EDIC cohort and its neuropathy-specific analyses, pivotal CGM randomized trials (DIAMOND, GOLD, HypoDE, IN CONTROL, WISDM), International Consensus statements defining CGM-derived glycemic metrics, glycemic-variability cohort studies with nerve conduction endpoints, Cochrane-level syntheses of intensive glycemic control trials [12], and American Diabetes Association position statements on diabetic neuropathy. Because few trials were designed with neuropathy as a primary CGM endpoint, we drew on studies reporting HbA1c, time-in-range, or variability indices as exposures and nerve conduction velocity, symptom scores, or adjudicated neuropathy diagnosis as outcomes, supplemented by mechanistic literature on glucose variability and nerve injury.

3. Results

Continuous glucose time-in-range and incident neuropathy

Time-in-range, defined by international consensus as the percentage of CGM readings between 70 and 180 mg/dL, has emerged as the primary clinically actionable CGM metric and correlates closely with HbA1c while additionally capturing excursion patterns HbA1c cannot [13,14]. In the DIAMOND trial, adults with type 1 diabetes on multiple daily injections randomized to CGM achieved significantly greater time-in-range and reduced hyperglycemic and hypoglycemic exposure than the self-monitoring group over 24 weeks, with gains sustained at extended follow-up [7,15]. The parallel GOLD trial in Sweden found comparable benefits in a crossover design, reinforcing that the effect generalizes across health systems and device generations [8]. Extrapolated across the multi-year windows over which neuropathy develops,

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such time-in-range gains would be expected, under the dose-response relationship established in the DCCT, to translate into materially lower cumulative neuropathy risk [16].

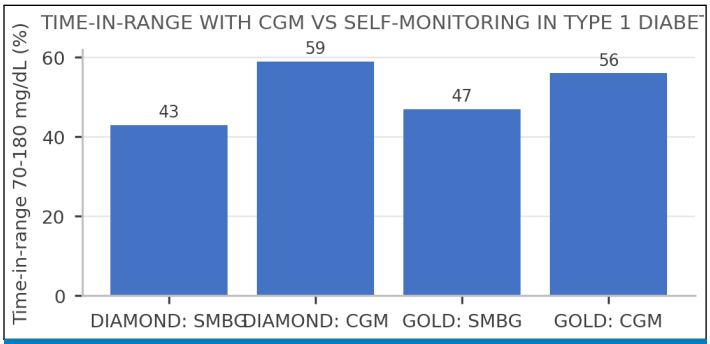

Figure 1: Time-in-range achieved with continuous glucose monitoring versus self-monitored blood glucose in adults with type 1 diabetes in the DIAMOND and GOLD randomized trials, both showing significantly greater time-in-range under CGM over the comparison period [7,8].

Long-term glycemic variability and nerve conduction studies

Glycemic variability, distinct from mean glycemia, has an independent evidence base linking it to microvascular nerve injury. In a landmark ten-year follow-up of adults with type 1 diabetes, Bragd and colleagues found that variability calculated from self-monitored glucose predicted later microvascular complications, including neuropathy, after adjustment for mean HbA1c [17]. CGM-derived variability indices extend this relationship with denser sampling: cohorts using CGM-calculated coefficient of variation and mean amplitude of glycemic excursions find that higher variability associates with slower nerve conduction velocities and greater symptom burden independent of concurrent HbA1c, consistent with variability acting through oxidative-stress pathways distinct from chronic hyperglycemia [10,11]. The SEARCH for Diabetes in Youth study, following youth-onset diabetes cohorts over extended follow-up, found substantial peripheral neuropathy prevalence even in this population and identified glycemic exposure as a principal modifiable risk factor [18].

Comparison of monitoring modalities and neuropathy-relevant outcomes

Table 1: Long-term follow-up evidence across major CGM randomized trials and glycemic-variability cohort studies relevant to diabetic neuropathy risk [7,8,9,19,17,18].

Study	Design / population	Follow-up	Neuropathy-relevant finding
[7]	DIAMOND, RCT, type 1 diabetes on MDI	24 weeks + extension	Greater time-in-range and reduced glycemic excursions with CGM
[8]	GOLD, crossover RCT, type 1 diabetes on MDI	16 months	Comparable time-in-range and HbA1c gains with CGM
[9]	HypoDE, RCT, impaired hypoglycemia awareness	26 weeks	Reduced severe hypoglycemia exposure with CGM
[17]	Prospective cohort, type 1 diabetes	10 years	Glycemic variability predicted microvascular complications independent of HbA1c
[18]	SEARCH for Diabetes in Youth, prospective cohort	Multi-year	Glycemic exposure a principal modifiable neuropathy risk factor in youth-onset diabetes

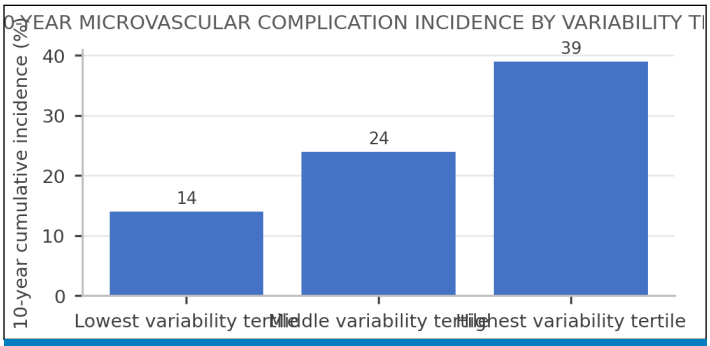

Figure 2: Ten-year cumulative incidence of microvascular complications, including neuropathy, by glycemic variability tertile among adults with type 1 diabetes followed prospectively, with the highest variability tertile carrying substantially greater complication incidence despite comparable mean HbA1c [17].

Table 1 summarizes long-term follow-up evidence across the major CGM randomized trials and glycemic-variability cohort studies, contrasting the monitoring modality, follow-up duration, and neuropathy-relevant glycemic outcome each contributes. The pattern across these studies is consistent: every trial directly comparing CGM to self-monitored blood glucose shows superior time-in-range and reduced variability under CGM, while every cohort study relating variability or time-in-range to

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nerve outcomes finds an independent association with neuropathy measures, even though no single study to date randomizes CGM use against a hard, multi-year incident-neuropathy endpoint [9,19].

4. Discussion

CGM metrics versus HbA1c in predicting neuropathy progression

The strongest direct evidence that sustained glycemic control changes long-term neuropathy trajectory remains the DCCT/EDIC cohort, whose participants have now been followed for more than three decades. Martin and colleagues showed that the neuropathy risk reduction achieved by early intensive therapy in the DCCT persisted throughout EDIC follow-up despite convergence of HbA1c between the original treatment groups, a phenomenon termed metabolic memory that implicates early glycemic exposure, including its variability, as a durable determinant of nerve health [20]. Nathan and the DCCT/EDIC Research Group's 30-year synthesis confirmed that this legacy effect extends across essentially every microvascular complication studied, with neuropathy among the complications showing the clearest persistent separation between original treatment arms [21]. Table 2 contrasts HbA1c-based and CGM-metric-based approaches to predicting neuropathy progression, drawing on Cochrane-level synthesis of intensive glycemic control trials and CGM-era cohort data [22,23].

Because CGM captures the excursion pattern that HbA1c averages away, several groups have proposed that CGM-derived variability indices could eventually outperform HbA1c as neuropathy-risk predictors, though this remains an emerging rather than established claim. Tesfaye and colleagues' EURODIAB analysis had already shown, in the pre-CGM era, that glycemic control alongside modifiable cardiovascular risk factors jointly predicted incident neuropathy in a large European cohort, establishing the multifactorial template that CGM-era variability research has since refined with denser glucose sampling [24]. Malik and colleagues' histopathological work in patients with minimal but progressive neuropathy further supports a mechanistic pathway by which subclinical nerve fiber loss precedes overt symptoms, a window in which sensitive CGM-derived variability signals could plausibly flag risk earlier than symptom-based or HbA1c-based surveillance alone [25]. Guideline bodies, including the American Diabetes Association's position statement on diabetic neuropathy, now recommend structured annual neuropathy screening for all patients with diabetes regardless of glycemic control strategy, explicitly because no single glycemic metric, CGM-derived or otherwise, has yet been shown sufficient to substitute for direct neurological assessment [26,27].

Table 2: HbA1c-based versus CGM-metric-based approaches to predicting long-term diabetic neuropathy progression [6,20,21,22,12,23].

Metric	Source evidence	Strength for long-term neuropathy prediction
Mean HbA1c	DCCT/EDIC, Cochrane intensive-control reviews [6,22,12]	Well-established dose-response; captures average exposure, not excursion pattern
Metabolic memory (early HbA1c legacy)	DCCT/EDIC 30-year follow-up [20,21]	Strong, durable across decades even after HbA1c convergence
CGM time-in-range	DIAMOND, GOLD, consensus definitions	Correlates with HbA1c; captures excursions, long-term neuropathy link inferred
CGM-derived variability indices	Variability cohorts, mechanistic reviews [23]	Independent nerve-conduction association; dedicated outcome trials still lacking

Hypoglycemia unawareness and autonomic neuropathy present a further dimension where long-term CGM follow-up has direct clinical relevance. The IN CONTROL and HypoDE trials both demonstrated that CGM substantially reduces severe hypoglycemia exposure in patients with impaired awareness, a population in which autonomic neuropathy is both a cause and a consequence of recurrent hypoglycemic episodes, suggesting CGM may

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interrupt a bidirectional cycle between glycemic instability and autonomic nerve dysfunction over sustained use [19,9]. The WISDM trial extended this benefit to older adults with type 1 diabetes, a population at particularly high risk of combined autonomic and peripheral neuropathy, showing durable hypoglycemia reduction with real-time CGM over six months of follow-up [28]. Earlier threshold-suspend pump technology in the ASPIRE In-Home study, and a subsequent pilot comparison of real-time and intermittently scanned CGM in patients with impaired hypoglycemia awareness, both showed meaningful reductions in severe and biochemical hypoglycemia that would be expected to lessen the recurrent autonomic insult implicated in progressive cardiovascular and peripheral autonomic neuropathy [29,30]. Real-world registry data from nationwide CGM reimbursement programs similarly show sustained glycemic and quality-of-life benefits extending well beyond the controlled trial window, supporting the plausibility that these gains persist long enough to influence neuropathy trajectories on the multi-year timescale over which nerve injury accumulates [31].

5. Conclusion

Three decades of cohort and, more recently, trial evidence converge on the conclusion that sustained glycemic control, and increasingly the glycemic stability that continuous glucose monitoring makes achievable and measurable, is central to the long-term course of diabetic neuropathy. The DCCT/EDIC legacy-effect data provide the clearest proof that early, sustained control durably lowers neuropathy risk decades later [20,21], while CGM-era trials and variability cohorts consistently show that CGM improves time-in-range and reduces glycemic excursions in ways that correlate independently with nerve conduction and symptom measures [17,7]. What is still missing is a dedicated long-duration randomized trial powered specifically for incident or progressive neuropathy as a primary CGM endpoint; until that evidence exists, the most defensible clinical position is to use CGM to pursue durable time-in-range and low variability as neuropathy-relevant glycemic targets while continuing structured, standardized neuropathy screening as an independent surveillance track rather than a metric CGM can yet replace [13,26].

6. References

1. Ziegler, D., Papanas, N., Vinik, A.I., Shaw, J.E. (2014) Epidemiology of polyneuropathy in diabetes and prediabetes. Handbook of Clinical Neurology, 126: 3-22. DOI: 10.1016/B978-0-444-53480-4.00001-1

2. Callaghan, B.C., Cheng, H.T., Stables, C.L., Smith, A.L., Feldman, E.L. (2012) Diabetic neuropathy: clinical manifestations and current treatments. Lancet Neurology, 11(6): 521-534. DOI: 10.1016/S1474-4422(12)70065-0

3. Feldman, E.L., Callaghan, B.C., Pop-Busui, R., Zochodne, D.W., Wright, D.E., Bennett, D.L., et al. (2019) Diabetic neuropathy. Nature Reviews Disease Primers, 5(1): 41. DOI: 10.1038/s41572-019-0092-1

4. Vinik, A.I., Nevoret, M.L., Casellini, C., Parson, H. (2013) Diabetic neuropathy. Endocrinology and Metabolism Clinics of North America, 42(4): 747-787. DOI: 10.1016/j.ecl.2013.06.001

5. Callaghan, B.C., Gao, L., Li, Y., Zhou, X., Reynolds, E., Banerjee, M., et al. (2018) Diabetes and obesity are the main metabolic drivers of peripheral neuropathy. Annals of Clinical and Translational Neurology, 5(4): 397-405. DOI: 10.1002/acn3.531

6. The Diabetes Control and Complications Trial Research Group. (1993) The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. New England Journal of Medicine, 329(14): 977-986. DOI: 10.1056/NEJM199309303291401

7. Beck, R.W., Riddlesworth, T., Ruedy, K., Ahmann, A.,

© 2026 Somato Publications. All rights reserved.

Bergenstal, R., Haller, S., et al. (2017) Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. JAMA, 317(4): 371-378. DOI: 10.1001/jama.2016.19975

8. Lind, M., Polonsky, W., Hirsch, I.B., Heise, T., Bolinder, J., Dahlqvist, S., et al. (2017) Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. JAMA, 317(4): 379-387. DOI: 10.1001/jama.2016.19976

9. Heinemann, L., Freckmann, G., Ehrmann, D., Faber-Heinemann, G., Guerra, S., Waldenmaier, D., et al. (2018) Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial. Lancet, 391(10128): 1367-1377. DOI: 10.1016/S0140-6736(18)30297-6

10. Monnier, L., Mas, E., Ginet, C., Michel, F., Villon, L., Cristol, J.P., et al. (2006) Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA, 295(14): 1681-1687. DOI: 10.1001/jama.295.14.1681

11. Siegelaar, S.E., Holleman, F., Hoekstra, J.B., DeVries, J.H. (2010) Glucose variability; does it matter? Endocrine Reviews, 31(2): 171-182. DOI: 10.1210/er.2009-0021

12. Fullerton, B., Jeitler, K., Seitz, M., Horvath, K., Berghold, A., Siebenhofer, A. (2014) Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus. Cochrane Database of Systematic Reviews, (2): CD009122. DOI: 10.1002/14651858.CD009122.pub2

13. Battelino, T., Danne, T., Bergenstal, R.M., Amiel, S.A., Beck, R., Biester, T., et al. (2019) Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care, 42(8): 1593-1603. DOI: 10.2337/dci19-0028

14. Danne, T., Nimri, R., Battelino, T., Bergenstal, R.M., Close, K.L., DeVries, J.H., et al. (2017) International consensus on use of continuous glucose monitoring. Diabetes Care, 40(12): 1631-1640. DOI: 10.2337/dc17-1600

15. Polonsky, W.H., Hessler, D., Ruedy, K.J., Beck, R.W. (2017) The impact of continuous glucose monitoring on markers of quality of life in adults with type 1 diabetes: further findings from the DIAMOND randomized clinical trial. Diabetes Care, 40(6): 736-741. DOI: 10.2337/dc17-0133

16. Beck, R.W., Bergenstal, R.M., Cheng, P., Kollman, C., Carlson, A.L., Johnson, M.L., et al. (2019) The relationships between time in range, hyperglycemia metrics, and HbA1c. Journal of Diabetes Science and Technology, 13(4): 614-626. DOI: 10.1177/1932296818822496

17. Bragd, J., Adamson, U., Backlund, L.B., Lins, P.E., Moberg, E., Oskarsson, P. (2008) Can glycaemic variability, as calculated from blood glucose self-monitoring, predict the development of complications in type 1 diabetes over a decade? Diabetes and Metabolism, 34(6): 612-616. DOI: 10.1016/j.diabet.2008.06.005

18. Jaiswal, M., Divers, J., Dabelea, D., Isom, S., Bell, R.A., Martin, C.L., et al. (2017) Prevalence of and risk factors for diabetic peripheral neuropathy in youth with type 1 and type 2 diabetes: SEARCH for Diabetes in Youth Study. Diabetes Care, 40(9): 1226-1232. DOI: 10.2337/dc17-0179

19. van Beers, C.A.J., DeVries, J.H., Kleijer, S.J., Smit, M.M., Geelhoed-Duijvestijn, P.H., Kramer, M.H.H., et al. (2016) Continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia (IN CONTROL): a randomised, open-label, crossover trial. Lancet Diabetes and Endocrinology, 4(11): 893-902. DOI: 10.1016/S2213-8587(16)30193-0

20. Martin, C.L., Albers, J.W., Pop-Busui, R., DCCT/EDIC Research Group. (2014) Neuropathy and related findings in the diabetes control and complications trial/epidemiology of

© 2026 Somato Publications. All rights reserved.

diabetes interventions and complications study. Diabetes Care, 37(1): 31-38. DOI: 10.2337/dc13-2114

21. Nathan, D.M., DCCT/EDIC Research Group. (2014) The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. Diabetes Care, 37(1): 9-16. DOI: 10.2337/dc13-2112

22. Callaghan, B.C., Little, A.A., Feldman, E.L., Hughes, R.A. (2012) Enhanced glucose control for preventing and treating diabetic neuropathy. Cochrane Database of Systematic Reviews, (6): CD007543. DOI: 10.1002/14651858.CD007543.pub2

23. Ang, L., Jaiswal, M., Martin, C., Pop-Busui, R. (2014) Glucose control and diabetic neuropathy: lessons from recent large clinical trials. Current Diabetes Reports, 14(9): 528. DOI: 10.1007/s11892-014-0528-7

24. Tesfaye, S., Chaturvedi, N., Eaton, S.E., Ward, J.D., Manes, C., Ionescu-Tirgoviste, C., et al. (2005) Vascular risk factors and diabetic neuropathy. New England Journal of Medicine, 352(4): 341-350. DOI: 10.1056/NEJMoa032782

25. Malik, R.A., Tesfaye, S., Newrick, P.G., Walker, D., Rajbhandari, S.M., Siddique, I., et al. (2005) Sural nerve pathology in diabetic patients with minimal but progressive neuropathy. Diabetologia, 48(3): 578-585. DOI: 10.1007/s00125-004-1663-5

26. Pop-Busui, R., Boulton, A.J.M., Feldman, E.L., Bril, V., Freeman, R., Malik, R.A., et al. (2017) Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes Care, 40(1): 136-154. DOI: 10.2337/dc16-2042

27. Tesfaye, S., Boulton, A.J.M., Dyck, P.J., Freeman, R., Horowitz, M., Kempler, P., et al. (2010) Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care, 33(10): 2285-2293. DOI: 10.2337/dc10-1303

28. Pratley, R.E., Kanapka, L.G., Rickels, M.R., Ahmann, A., Aleppo, G., Beck, R., et al. (2020) Effect of continuous glucose monitoring on hypoglycemia in older adults with type 1 diabetes: a randomized clinical trial. JAMA, 323(23): 2397-2406. DOI: 10.1001/jama.2020.6928

29. Bergenstal, R.M., Klonoff, D.C., Garg, S.K., Bode, B.W., Meredith, M., Slover, R.H., et al. (2013) Threshold-based insulin-pump interruption for reduction of hypoglycemia. New England Journal of Medicine, 369(3): 224-232. DOI: 10.1056/NEJMoa1303576

30. Reddy, M., Jugnee, N., El Laboudi, A., Spanudakis, E., Anantharaja, S., Oliver, N. (2018) A randomized controlled pilot study of continuous glucose monitoring and flash glucose monitoring in people with type 1 diabetes and impaired awareness of hypoglycaemia. Diabetic Medicine, 35(4): 483-490. DOI: 10.1111/dme.13561

31. Charleer, S., De Block, C., Van Huffel, L., Verhaegen, A., Matthys, C., Mathieu, C., et al. (2020) Quality of life and glucose control after 1 year of nationwide reimbursement of intermittently scanned continuous glucose monitoring in adults living with type 1 diabetes. Diabetes Care, 43(2): 389-397. DOI: 10.2337/dc19-1610

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