DANISH MEDICAL JOURNAL

Original Article

Unexpected high-risk neoplasias among routine skin specimens

Karen Marie Egsgaard[1, 2], Steen Jensen[1] & Tomasz Piotr Tabor[1, 3]

1) Department of Pathology, Regional Hospital Viborg, Central Denmark Region, 2) Department of Clinical Genetics, Aalborg University Hospital, 3) Department of Clinical Pathology, Hospital Lillebælt, Vejle Hospital, Denmark

Dan Med J 2026;73(5):A09250776. doi: 10.61409/A09250776

ABSTRACT

INTRODUCTION. Turnaround time (TAT) for routine skin specimens may be prolonged at times, delaying diagnosis and treatment in cases with a unexpected high-risk neoplasia. This quality improvement study assessed the prevalence, types and characteristics of such cases.

METHODS. This was a descriptive study of all routine skin specimens submitted by general practitioners (GPs) and private dermatologists in 2022-2023 at the Department of Pathology, Viborg Regional Hospital, Denmark. From Systematized Nomenclature of Medicine (SNOMED) codes, various premalignant and malignant neoplasias were identified; melanocytic and soft tissue neoplasms were included.

RESULTS. Among 33,280 routine specimens, 77 (0.23%) were a high-risk premalignant or malignant neoplasia: 66 melanocytic (54 melanomas, 0.16%) and 11 sarcomas. Superficial spreading melanoma (n = 36) and the in situ variant (n = 10) were the most frequent high-risk neoplasia in lesions clinically assessed as benign. Among melanocytic lesions, 61% had involved/unassessable margins, and 67% of melanomas had a depth ≥ 1.0 mm. The mean TAT was 64 calendar days. Mean age: 64.1 years, with a notable proportion aged 41-50 years. Referrals: GPs 73%, dermatologists 26%, surgeons 1%. Procedures: excision 58%, curettage 25%, biopsy 10%, unspecified 7%. Suspicious shape/colour features were noted in 36% of melanocytic lesions. 7.5% had prior melanoma.

CONCLUSIONS. Unexpected high-risk neoplasia are rare (0.23%) but often advanced, highlighting the need for improved clinical assessment and a short TAT for routine skin specimens. The results serve as a reference for future AI-based screening.

FUNDING. None.

TRIAL REGISTRATION. Not relevant.

Malignant skin neoplasms, including melanomas, lymphomas, sarcomas, neuroendocrine tumours such as Merkel cell carcinoma and cutaneous metastasis, can be challenging to identify clinically [1]. Even lesions believed to be benign can hide a serious malignant neoplasia, validating the practice of routine histopathologic examination of all removed skin lesions [2]. Therefore, some cases of malignant neoplasms are inevitably sent through a routine pathway for skin specimens to undergo histopathological examination. In Denmark, the political target turnaround time (TAT) for routine skin specimens is ten working days. TAT for histopathological examination may be prolonged during periods of staffing shortages, financial constraints or increased specimen volume [3]. In such periods, delayed histopathological diagnosis and treatment initiation may worsen patient outcomes in cases of unexpected high-risk neoplasm among routine skin specimens.

Presently, only one paper has evaluated the prevalence of melanomas among routine skin specimens: a Danish

national registry study by Nervil et al., which found a prevalence of 0.50% melanomas in routine specimens referred from private dermatologists or general practitioners (GPs) for histopathological evaluation [3].

The main aim of this descriptive study was to determine the prevalence and types of unexpected high-risk neoplasias in routine skin specimens submitted by GPs and private dermatologists.

High-risk neoplasia was defined as malignant neoplasms for which delayed histopathological diagnosis could worsen treatment options and prognosis. Premalignant melanocytic lesions were also considered 'high-risk' due to their clinical similarity to malignant melanocytic neoplasms and their potential to progress into invasive neoplasia during the waiting period.

Furthermore, we identified characteristics of the cases with unexpected high-risk neoplasia, including tumour depth, resection margin status, TAT at the pathology department, age and gender distribution, referring physician, procedure type, macroscopic features at the gross inspection at the pathology department (asymmetry, border, colour and diameter), previous pathology history and clinical information from the physician.

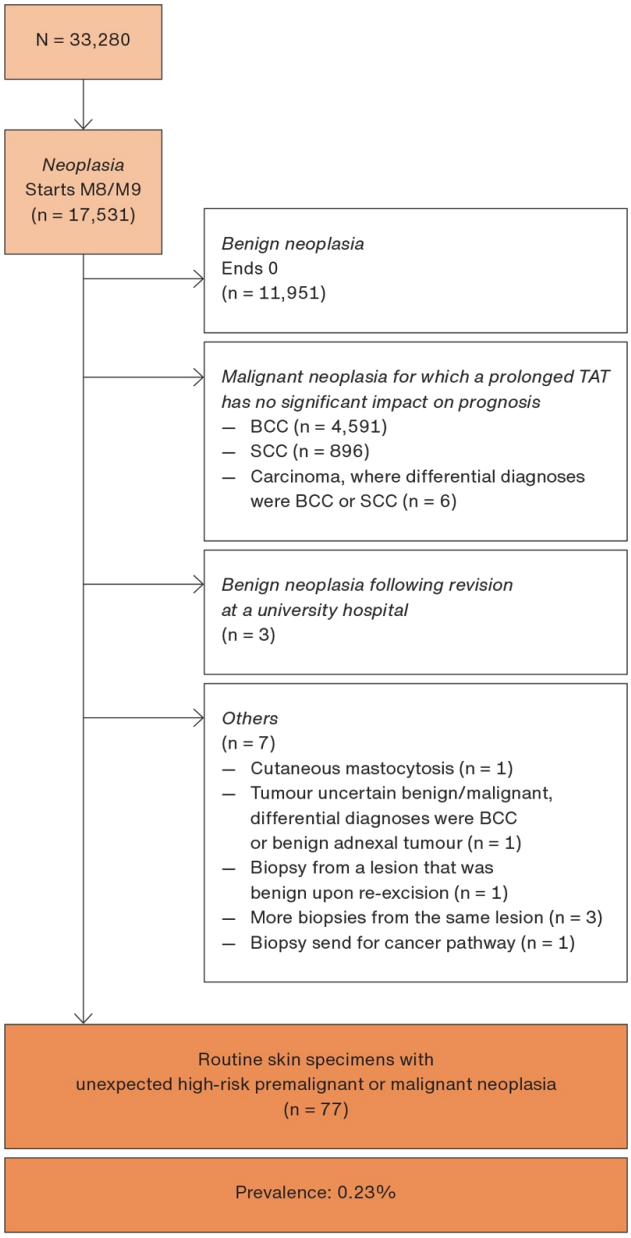
Based on the characteristics of lesions with unexpected high-risk neoplasia, we examined whether these cases exhibited features that would allow them to be identified and prioritised for fast-track diagnostics.

Methods

Data in our pathology system were extracted from a total of 33,280 routine skin specimens submitted within a routine pathway to the Department of Pathology, Viborg Regional Hospital, from 1 January 2022 to 31 December 2023. The department receives routine skin specimens from GPs, private dermatologists and private surgeons in the Central Denmark Region, which serves approximately 600,000 residents. Routine skin specimens are processed chronologically and undergo examination outside the "Urgent" and "Cancer" pathways. They include inflammatory skin lesions, non-melanocytic skin cancer and skin lesions removed with no suspicion of malignancy.

Excel was used to sort the Systematized Nomenclature of Medicine (SNOMED) codes assigned to each routine skin specimen, identifying all neoplastic lesions. From these, we excluded: 1) all benign neoplasias, 2) malignant neoplasias with a low prognostic impact from diagnostic delay, e.g., basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) and 3) cases reclassified as benign following review at a university hospital (**Figure 1**).

FIGURE 1 Flow chart of the included routine skin specimens received 2022-2023 at the Department of Pathology, Viborg Regional Hospital, Denmark.



BCC = basal cell carcinoma; SCC = squamous cell carcinoma; TAT = turnaround time.

A total of 77 routine skin specimens with a high risk of premalignant or malignant neoplasias met the inclusion criteria.

Atypical fibroxanthomas were included, since eight out of nine cases were sampled via curettage or biopsy, precluding assessment of the depth and extent of the lesion, which could be pleomorphic dermal sarcoma [4, 5].

Melanocytic in situ lesions, including superficial spreading melanoma in situ and lentigo maligna, were included because of their clinical resemblance with invasive melanoma.

We included in the study any skin specimens initially submitted within a routine pathway but subsequently

reprioritised as fast-track – either due to macroscopic suspicion of malignancy at grossing by the biomedical laboratory scientist or during microscopic assessment by the pathologist.

In total, 4,591 specimens with BCC and 896 specimens with SCC were excluded. Although SCC is a malignant neoplasia with a five-year metastasis rate of 5.2-13.7% depending on anatomical location, these cases were excluded because the majority of SCCs submitted as routine skin specimens are considered adequately treated by excision or are already under dermatological follow-up [6]. Only a minimal number of SCCs may metastasise during the TAT for histopathological evaluation, e.g., in cases where the diagnosis was not clinically suspected, and the lesion was not completely excised.

One specimen with the diagnosis "mastocytosis" was excluded because there was no clinical information or follow-up investigations suggesting a systemic variant. Therefore, it was classified as cutaneous mastocytosis, which is amenable to dermatological treatment without impacting life expectancy [7].

One specimen was excluded due to a registration error, as it was mistakenly registered for the routine pathway but processed through the cancer pathway.

Trial registration: not relevant.

Results

From a total of 33,280 routine skin specimens, 77 had a high-risk premalignant or malignant neoplasia, corresponding to a prevalence of 0.23% (95% CI: 0.18; 0.28%).

Among the 77 included routine specimens, 66 were premalignant or malignant melanocytic neoplasias and 11 were soft tissue neoplasias (**Table 1**). A total of 54 cases of melanoma were reported, with a prevalence of 0.16% (95% CI: 0.12; 0.21%). Most commonly, high-risk skin neoplasms that appeared benign on clinical examination were superficial spreading melanoma (n = 36) and superficial spreading melanoma in situ (n = 10). No lymphomas or neuroendocrine tumours, e.g., Merkel cell carcinoma, were identified (Table 1).

TABLE 1 Type and number of high-risk premalignant and malignant neoplasia among routine skin specimens.

Diagnose	SNOMED code	n
Melanocytic neoplasias		
Superficial spreading melanoma	M87433	36
Superficial spreading melanoma in situ	M87412	10
Nodular melanoma	M87213	8
Malignant melanoma	M87203	4
Malignant melanoma, metastasis	M87206	2
Lentigo maligna	M87422	2
Desmoplastic malignant melanoma	M874A3	1
Malignant melanoma, uncertain primary or metastatic	M87209	1
Malignant melanoma, observation procedure	M8720X	1
Melanocytic tumour, uncertain benign or malignant	M87201	1
Soft tissue neoplasias		
Atypical fibroxanthoma	M88311	9
Dermatofibrosarcoma protuberens	M88321	1
Leiomyosarcoma	M88903	1
Total		77

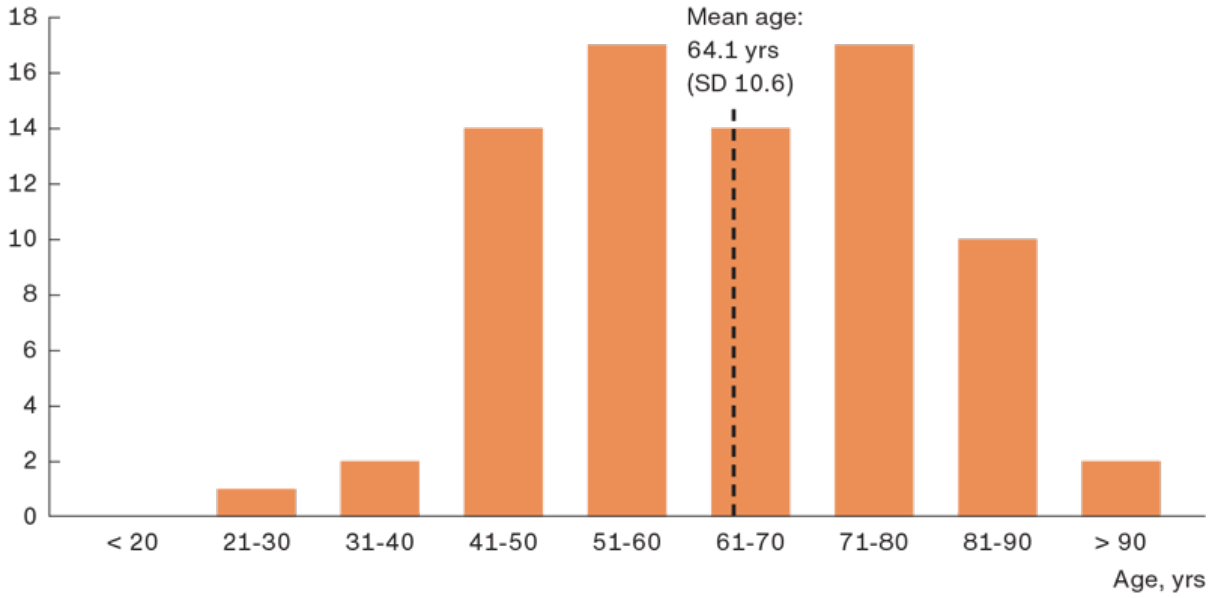
SNOMED = Systematized Nomenclature of Medicine.

Among the 66 melanocytic cases, 40 (61%) had resection margins that were involved or unassessable. Of the melanomas with a measurable depth (n = 45), 30 (67%) had a depth ≥ 1.0 mm, which is the threshold for consideration of sentinel node examination according to the national guidelines of the Danish Multidisciplinary Cancer Group [8].

The average TAT was 64 calendar days (range: 12-120 days). Only four cases were reported within the ten-working-day target period.

The mean patient age was 64.1 years (SD: 10.6 years), with a relatively high proportion aged 41-50 years (**Figure 2**). 58% of the neoplasms were from females.

FIGURE 2 Age distribution of routine skin specimens with an unexpected high-risk neoplasia.



Referrals were mostly submitted by GPs (73%), followed by dermatologists (26%) and private surgeons (1%). There was no significant difference in the proportion of routine specimens referred by GPs that were diagnosed with a high-risk neoplasia compared with the background cohort, as assessed using a pooled two-proportion z-test ($z = 0.699$).

According to the clinical information provided, lesions with a high-risk neoplasia were most often assessed clinically as basal cell carcinoma, nevus or seborrheic keratosis. Additionally, the referring clinicians suspected haemangioma, fibroma, wart, pyogenic granuloma or inclusion cyst. Only one requisition mentioned a prior patient history of melanoma. No requisitions included information on family history.

Procedure types were: excision (58%), curettage (25%), biopsy (10%) and unspecified (7%). Surprisingly, 75% of curettages with a high-risk neoplasia were submitted by dermatologists.

Among the 66 skin specimens with melanocytic neoplasias, macroscopic examination at grossing by a biomedical laboratory scientist reported suspicion of malignancy based on shape/border in seven (11%) and colour in 23 (35%) cases. Overall, 36% met at least one suspicious shape- and/or colour-related feature (**Figure 3**).

FIGURE 3 Suspicious shape or colour of the 66 routine skin specimens with an unexpected high-risk melanocytic premalignant or malignant neoplasm reported at the macroscopic examination at the pathology department.

	Suspicion of malignancy	n (%)
Shape	**A**symmetry	7 (11)
	Border irregular or indistinct	
Colour	**C**olour variation or dark	23 (35)
Shape **or/and** colour		**24 (36)**

Diameter was not included in the analysis, as it was inconsistently recorded – in some cases referring to the diameter of the lesion itself and in others to the diameter of the entire specimen.

In six (8%) cases, the referring clinician reported at least one of the ABCDE criteria used for clinical melanoma detection in the requisition.

Five out of 66 patients (7.5%) with high-risk melanocytic lesions had a previous pathology history of melanoma.

Discussion

This descriptive study found a 0.23% prevalence of unexpected high-risk premalignant and malignant neoplasias in routine skin specimens, with melanoma accounting for 0.16% (95% CI: 0.12; 0.21%). This prevalence of melanomas is significantly lower than the 0.50% (95% CI: 0.49; 0.50%) prevalence reported in the national registry study by Nervil et al. 2025 [3]. This discrepancy may be explained by differences in the distribution of referring physicians, i.e. GPs versus dermatologists. Large regional variation in access to primary care is also a likely explanation, as this study cohort resided in a region with fewer GPs and dermatologists per capita and had one of the longest waiting times for a dermatologist in Denmark (29 weeks as per January 2024) [9, 10]. Delays or avoidance of consultation may reduce the number of routine specimens submitted. Longer waiting times may result in more advanced tumours at first examination, making them less likely to be assessed as benign and therefore less likely to be submitted to the routine pathway.

In this study, we revealed characteristics of the 77 routine specimens that contained an unexpected high-risk neoplasia. Except for the referral distribution, the characteristics of the cohort of 33,280 routine specimens are unknown, and it remains unclear how the included specimens differ from those of the background cohort.

In 36% of high-risk melanocytic cases, the biomedical laboratory scientist reported a suspicious shape and/or colour at the macroscopic examination. Although shape and colour are a part of the ABCDE criteria – a validated clinical tool for macroscopic melanoma diagnosis [11, 12] – their applicability may be limited for gross evaluation of excised, formalin-fixed lesions in the pathology department. Fixation causes shrinkage and colour loss, affecting C (colour) and D (diameter). The ABCDE criteria are validated for complete in-situ skin lesions, but specimens are often incomplete or fragmented after curettage, biopsy or incomplete excision, affecting A (asymmetry) and B (border). Furthermore, patient-reported changes are often inconsistently described on the

requisition forms, affecting E (evolution). Many benign specimens may exhibit suspicious features under the ABCD criteria, risking unnecessary up-prioritisation of a substantial number of specimens and exacerbating resource shortages. Caution is required when applying the ABCD(E) criteria for triage at the macroscopic examination in the pathology apartment, although critical assessment remains essential, particularly for darkly pigmented lesions with asymmetry or colour variegation, including blue-white veil, which should always be fast-tracked.

The ABCDE criteria remain crucial in clinical triage, as most unexpected malignancies were melanocytic, underscoring the need for improved pre-excisional assessment. The nationwide Dermloop Project, to be rolled out in 2025-2026, may improve this by providing rapid dermoscopic assessments and recommendations from hospital dermatologists to GPs through an app. Although the pilot project did not reduce the number of routine specimens submitted for histopathological examination, the implementation may still help to refine pre-excisional triage and reduce unnecessary removal of benign skin lesions [13].

In five melanocytic cases (7.5%) the patient had a prior history of melanoma, but pathology history for routine specimens is not routinely checked at grossing; implementing this would require additional resources with uncertain benefit.

Future studies could include a pilot project in which all routine specimens over 1-2 months are fast-tracked if they show suspicious ABCDE features or if the patient has a prior history of melanoma, to assess ABCDE sensitivity for pathology triage. In the future, digital pathology with AI may support triage by, e.g. identifying lesions with mitotic activity in combination with pigment deposition and prioritising these early in the routine workflow.

Conclusions

Unexpected premalignant and malignant neoplasms were identified in 0.23% of routine skin specimens submitted to the Department of Pathology, Viborg, by GPs, private dermatologists and private surgeons in the Central Denmark Region; melanomas accounted for 0.16%. In these cases, there is a high risk of stage progression or metastasis during the prolonged TAT for histopathological diagnosis, which may potentially have serious consequences for the patient's treatment options and prognosis. Skin lesions clinically assessed as benign but found to be a high-risk neoplasia upon histopathological examination are most often melanocytic, particularly superficial spreading melanoma and the in-situ variant. Among the high-risk melanocytic lesions, 61% had involved/unassessable resection margins, and 67% of the melanomas had a depth ≥ 1.0 mm, indicating an advanced stage. 36% of the unexpected high-risk melanocytic lesions exhibited suspicious features in shape and/or colour at the macroscopic examination at the pathology department. Further studies are needed to determine whether this can be applied in triage of excised, formalin-fixed routine skin specimens.

The prevalence established serve as a reference for evaluating AI as a potential future screening tool in digital pathology systems.

The results of this study highlight the importance of accurate clinical assessment prior to excision, e.g., via dermoscopy, by GPs in the new national project Dermloop, and the need to submit all removed skin lesions for histopathological evaluation.

To ensure high patient safety, short TAT for routine skin specimens must be economically and organisationally prioritised.

Correspondence *Karen Marie Egsgaard*. E-mail: kmegsgaard@gmail.com

Accepted 13 January 2026

Published 17 April 2026

Conflicts of interest none. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. These are available together with the article at ugeskriftet.dk/dmj

Acknowledgements Rita Bruskin for helping with the design and initiation of the project.

References can be found with the article at ugeskriftet.dk/dmj

Cite this as Dan Med J 2026;73(5):A09250776

doi 10.61409/A09250776

REFERENCES

1. Urbancek S, Fedorcova P, Tomkova J, Sutka R. Misdiagnosis of melanoma: a 7-year single-center analysis. J Pigment Disord. 2015;2(9):1-4. https://doi.org/10.4172/2376-0427.1000208
2. Izikson L, Sober AJ, Mihm MC, Zembowicz A. Prevalence of melanoma clinically resembling seborrheic keratosis: analysis of 9204 cases. Arch Dermatol. 2002;138(12):1562-1566. https://doi.org/10.1001/archderm.138.12.1562
3. Nervil GG, Vestergaard T, Klausen S, et al. Impact of skin biopsy practices: a comprehensive nationwide study on skin cancer and melanoma biopsies. J Eur Acad Dermatol Venereol. 2025;39(7):1267-1277. https://doi.org/10.1111/jdv.20371
4. Dummer R, Luzar B, Miller K. Pleomorphic dermal sarcoma. In: Cree IA, Goldman-Lévy G, Lokuhetty D, et al., eds. WHO classification of tumours: skin tumours. 5th ed. International Agency for Research on Cancer, 2025:623-624
5. Beer TW, Calonje JE. Atypical fibroxanthoma. In: Cree IA, Goldman-Lévy G, Lokuhetty D, et al., eds. WHO classification of tumours: skin tumours. 5th ed. International Agency for Research on Cancer, 2025:620
6. Calonje E, Brenn T, Lazar AJ, et al., eds. Tumors of the surface epithelium. In: McKee's pathology of the skin: with clinical correlations. 5th ed. Elsevier, 2020:1200
7. Comenero I, Alvarez-Twose I, Torrelo A, et al. Mastocytosis. In: Cree IA, Goldman-Lévy G, Lokuhetty D, et al., eds. WHO classification of tumours: skin tumours. 5th ed. International Agency for Research on Cancer, 2025:335-338
8. Danske Multidisciplinære Cancer Grupper. Sentinel node biopsi procedure for melanom. Kliniske retningslinjer. Danske Multidisciplinære Cancer Grupper, 2025. www.dmcg.dk/Kliniske-retningslinjer/kliniske-retningslinjer-opdelt-paa-dmcg/melanom/kirurgisk-behandling/sentinel-node-biopsi-procedure-for-melanom/ (13 Sep 2025)
9. Hansen NN. Patienter venter næsten dobbelt så længe på at komme til hudlæge og psykiater som for syv år siden. DR, 12 May 12 2024. www.dr.dk/nyheder/indland/patienter-venter-naesten-dobbelt-saa-laenge-paa-komme-til-hudlaege-og-psykiater-som (30 Aug 2025)
10. PLO. PLO Analyse. Antallet af patienter hos de praktiserende læger stiger fortsat. laeger.dk. PLO, 2018. https://laeger.dk/media/o2bppmxq/plo_analyse_-_antallet_af_patienter_stiger_fortsat_hos_de_praktiserende_laeger.pdf (1 Mar 2025)
11. Danske Multidisciplinære Cancer Grupper. Kutant melanom (modermærkekræft). Klinisk undersøgelse – anamnese og objektiv undersøgelse. Kliniske retningslinjer. Danske Multidisciplinære Cancer Grupper, 2022. www.dmcg.dk/kliniske-retningslinjer/kliniske-retningslinjer-opdelt-paa-dmcg/melanom/diagnostik/kutant-melanom-modermarkekraft-klinisk-undersogelse--anamnese-og-objektiv-undersogelse/ (1 Mar 2025)
12. Friedman RJ, Rigel DS. The clinical features of malignant melanoma. Dermatol Clin. 1985;3(2):271-283
13. Moltsen M. Graverende fejl i grundlaget for offentlig millioninvestering i hudkræft-app. Onkol Tidsskr. 23 Jun 2025. https://onkologisktidsskrift.dk/behandlinger/hudkraeft/3762-graverende-fejl-i-grundlaget-for-offentlig-millioninvestering-i-hudkraeft-app.html (9 Nov 2025)