

RESEARCH

Open Access

groups [2]. This population often has a higher burden of chronic health conditions, functional limitations, and social isolation, all of which contribute to the complexity of depression management [2]. In particular, older people with depression commonly have a high prevalence of cardiovascular and metabolic diseases, potentially leading to cardiometabolic multimorbidity (CMM) [3, 4].

CMM, defined as the coexistence of two or more cardiometabolic diseases (CMDs) such as heart failure, stroke, and type 2 diabetes, is one of the most common multimorbidity profiles and a growing public health concern [5, 6]. While individual CMDs are well-established comorbidities of depression, current research increasingly examined whether the cumulative burden of multiple CMDs is associated with depression. Recent studies found that individuals with existing CMM are at an increased risk of experiencing subsequent depression [7–10], and suggested an additive dose–response relationship between the number of CMDs and the risk of depression [7, 8]. Notably, emerging research suggests a bidirectional relationship between CMM and depression, where CMM not only increases the risk of depression, but depression itself appears to contribute to the development of CMM [11–15]. For example, Qiao et al. observed that people with depression were more likely to develop CMM over time than people without depression, with the effect being strongest when stroke was part of the cardiometabolic disease cluster [11]. In addition, Wang et al. found a dose–response relationship between the severity of depressive symptoms and incident CMM, indicating that an increase in depressive symptoms lead to a higher likelihood of developing CMM [12]. The bidirectional approach was adopted by Zhou et al., who observed that depression and CMM independently act as risk factors for one another, with lifestyle behaviors such as physical inactivity and poor diet potentially mediating this effect [16].

Despite these advancements in understanding the association between CMM and depression, there remains a notable gap in research concerning the oldest-old population. Most studies have focused on populations of middle or older age, leaving uncertainty regarding whether similar patterns hold true-

(ac)-6l-b5u9o8(ns hold).50)TJ 0 0 1 rg /GS1 gs 0 Tw (1JW[78s).5(a)TJ .084 Tw 0 -1.224 016110

Cardiometabolic disease index

The NRW80+ survey assessed multimorbidity with an index covering 19 chronic diseases with binary response options, with interviewers asking for each of these diseases whether the participant currently receives treatment for it [20]. We selected all cardiovascular and metabolic diseases for construction of an additive cardiometabolic disease index: myocardial infarction, heart failure, hypertension, stroke, diabetes, and kidney disease. Additionally, we included obesity in the CMD index, defined as a Body-Mass-Index (BMI) ≥ 30 . Obesity was considered as a metabolic disease as it is associated with metabolic dysregulation and systemic inflammation, and an increased risk for other CMDs [21]. Consequently, the disease index

Non-responder analysis

We examined potential differences between study participant included in the final analysis ($N = 1,583$) and study participants excluded in final analysis due to missing data ($N = 280$). Across all missing data ($N = 280$), women in the age groups 85–89 years and 90 years and older had more missing values compared to other age groups (See Supplementary Table A2, Additional File 1). Study participants with a higher socioeconomic index were more

1.10–2.28) for three or more CMDs compared to no CMD. The OR for the continuous CMD index was 1.24 (95%-CI: 1.10–1.39). We also observed similar sex trends (See Supplementary Table A6, Additional File 1).

population. Effective implementation of integrated care could be guided by established models, such as collaborative care approaches, which emphasize multidisciplinary coordination between general practitioners, cardiologists, geriatricians, mental health specialists, and social care providers, and which have shown promising results in jointly managing CMDs and depression in older people [33–35]. A first step toward improved care might include the systematic implementation of routine screening for depressive symptoms in patients with CMM in primary and specialist care settings, ensuring early detection and intervention to prevent adverse effects on treatment adherence and prognosis. Similarly, to reduce morbidity and disability arising from cardiometabolic conditions, health professionals should proactively monitor CMDs in individuals with depression and adopt a comprehensive care strategy that jointly addresses shared risk factors, such as inflammation, physical inactivity, and social isolation. Future research should explore how integrated care models can be tailored to the unique needs of the oldest-old population to enhance feasibility and effectiveness.

Furthermore, preventive lifestyle factors may mitigate the link between CMM and depression. Especially physical activity and social support play key roles in older people, as both inactivity and loneliness independently increase the risk of developing CMM [36, 37] and depressive symptoms [38]. Additionally, Herbolsheimer et al. observed that old people who felt socially isolated performed less out-of-home physical activity, which in turn was associated with a greater risk for depression [39]. People with at least one CMD were half as likely to be hospitalised for a mental disorder when being physically active compared to those being inactive [40]. In people with both CMM and depression, being physically active was associated with 6.81 additional life years [41]. However, a study among Chilean adults found the strongest association with cardiometabolic risk factors among subjects that have depressive symptoms but are physically active [42]. Future high-quality research on physical activity and social support as potential protective factors of both CMM and depression is needed.

Several limitations of our study should be acknowledged. First, our results are based on cross-sectional data, which preclude us from drawing conclusions about causality of associations. Second, we rely on self-reported data, which introduces the potential for misclassification, e.g., due to recall or social desirability bias. Additionally, CMDs (except obesity) were defined as self-reported treatment status, which could potentially lead to an underestimation of disease prevalence. This limitation could result in a more conservative estimate that attenuates rather than strengthens the observed associations between CMM and depressive symptoms. In 9.4% of

cases, proxies answered on behalf of participants, which helped include individuals who might otherwise be unable to participate, thereby improving the representativeness of this often underrepresented population. However, proxy reporting may introduce bias if variables are systematically misreported, though sensitivity analyses showed no difference in results with or without proxies.

The overall response rate of 26.5% may introduce selection bias, as it can be assumed that people with high depressive symptoms or severe multimorbidity tended to be less likely to participate. However, sociodemographic factors were not significantly related to the likelihood of nonresponse [18]. Additionally, we applied adjustment weighting to account for non-respondents [23]. Item non-response (i.e., missing values) for the CMD-index could have also biased our estimates, as those with missing values were more likely female, older than 85 years, had a higher depressive symptom score, and a lower socioeconomic status. This might have led to an underestimation of the association between CMM and depressive symptoms. However, the fact that missing values were not missing at random ruled out multiple imputation of missing values.

On the other hand, the main strength of this study is the use of a comprehensive representative sample of oldest-old people, who were often underrepresented in previous research in this area. Additionally, depressive symptoms were assessed using a screening instrument specifically developed for people at old age, and we treated depressive symptoms as a continuous outcome to preserve maximum variability for analyses. Furthermore, sensitivity analyses corroborated the robustness of the main results.

Conclusions

The main finding of this study is the extension of the positive association between CMM and depression to oldest-old people. Additionally, we found a significant additive dose-repose relationship, indicating increased depressive symptomatology in people with higher CMD burden. Given that nearly half of the study participants experienced CMM, with almost a third showing signs of a depressive mood, our findings highlight the profound public health challenge presented by the co-morbidity of CMM and depression in aging populations. A holistic approach to preventing and managing depressive symptoms in oldest-old people is essential, focusing on targeted preventive and therapeutic measures for CMM, rather than solely addressing individual CMDs. However, sustainable improvements in care will require not only individualized interventions but also structural adaptations, including policies that facilitate integrated, multidisciplinary health care.

Future prospective studies based on various data types, such as clinical or routine data, considering oldest-old populations are needed. Longitudinal cohort studies could help establish causal relationships, biomarker analyses may shed light on biological mechanisms, and intervention trials could assess the effectiveness of integrated treatment approaches. Additionally, efforts to disentangle underlying mechanisms are necessary, to eventually derive clinically relevant recommendations for the aligned treatment of depression and CMM.

Abbreviations

BMI	Body-Mass-Index
CI	Confidence interval
CMD	Cardiometabolic disease
CMM	Cardiometabolic multimorbidity
DIA-S4	Short form of the Depression in Old Age Scale
NRW80 +	Survey on Quality of Life and Subjective Well-being of the Very Old in North Rhine-Westphalia
OR	Odds ratio
Ref.	Reference category
SD	Standard deviation
	Beta coefficient

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12889-025-22964-1>.

Supplementary Material 1.

Acknowledgements

Not applicable.

Authors' contributions

VM and UM conceptualised the research idea and study design. VM analysed and interpreted the data and primarily wrote the manuscript. VL was significantly involved in the visualisation of the data. UM and VL were major contributors in writing and editing the manuscript. All authors read and approved the final manuscript.

Funding

Open Access funding enabled and organized by Projekt DEAL. VM, VL and UM are supported by the Marga and Walter Boll Foundation, Kerpen, Germany. The NRW80 + study has been funded by the Ministry of Innovation, Science and Research, North Rhine-Westphalia.

Data availability

The data analysed during this study are openly available in GESIS, Cologne at <https://doi.org/10.4232/1.13978>, reference number ZA7558.

Declarations

Ethics approval and consent to participate

The NRW80+ survey has been approved by the ethics committee of the Medical Faculty of the University of Cologne, Germany (No. 17-169).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 16 December 2024 Accepted: 28 April 2025

Published online: 09 May 2025

a Hioal.

References

- Hajek A, Konig HH, Sutin AR, Terracciano A, Luchetti M, Stephan Y, et al. Prevalence and factors associated with probable depression among the oldest old during the Covid-19 pandemic: evidence from the large, nationally representative "Old Age in G6(c)6(eu984nig H11(ession among))TJ 0 -1.2 Td [(the y M Hajek A, K Hajek A, Konig HH, Sutin AR, and RodhiA)T Td [15pt, Zhe S.

- NRW80+) - Querschnittsbefragung Welle 1. 2022. <https://doi.org/10.4232/1.13978>.
18. Wagner M, Rietz C, Kaspar R, Janhsen A, Geithner L, Neise M, et al. Quality of life of the very old : survey on quality of life and subjective well-being of the very old in North Rhine-Westphalia (NRW80+). *Z Gerontol Geriatr*. 2018;51:193–9. <https://doi.org/10.1007/s00391-017-1217-3>.
 19. Heidenblut S, Zank S. Development of a new screening instrument for geriatric depression. The depression in old age scale (DIA-S). *Z Gerontol Geriatr*. 2010;43:170–6. <https://doi.org/10.1007/s00391-009-0067-z>.
 20. Diederichs C, Berger K, Bartels DB. The measurement of multiple chronic diseases—a systematic review on existing multimorbidity indices. *J Gerontol A Biol Sci Med Sci*. 2011;66:301–11. <https://doi.org/10.1093/gerona/glq208>.
 21. Paoletti R, Bolego C, Poli A, Cignarella A. Metabolic syndrome, inflammation and atherosclerosis. *Vasc Health Risk Manag*. 2006;2:145–52. <https://doi.org/10.2147/vhrm.2006.2.2.145>.
 22. Ganzeboom HBG, De Graaf PM, Treiman DJ. A standard international socio-economic index of occupational status. *Soc Sci Res*. 1992;21:1–56. [https://doi.org/10.1016/0049-089X\(92\)90017-B](https://doi.org/10.1016/0049-089X(92)90017-B).
 23. Brix JS, G., Stadler M. NRW80+ Methodenbericht. München: Kantar Public; 2018.
 24. R Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2021.
 25. Vancampfort D, Koyanagi A, Ward PB, Veronese N, Carvalho AF, Solmi M, et al. Perceived stress and its relationship with chronic medical conditions and multimorbidity among 229,293 community-dwelling adults in 44 low- and middle-income countries. *Am J Epidemiol*. 2017;186:979–89. <https://doi.org/10.1093/aje/kwx159>.
 26. Xie H, Li J, Zhu X, Li J, Yin J, Ma T, et al. Association between healthy lifestyle and the occurrence of cardiometabolic multimorbidity in hypertensive patients: a prospective cohort study of UK Biobank. *Cardiovasc Diabetol*. 2022;21:199. <https://doi.org/10.1186/s12933-022-01632-3>.
 27. Cabello M, Miret M, Caballero FF, Chatterji S, Naidoo N, Kowal P, et al. The