

Disparities in Prehospital Stroke Care: Neighbourhood Socioeconomic Status and Delays in Hospital Presentation

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Keywords

Stroke · Health equity · Prehospital care · Socioeconomic factors

Abstract

Introduction: Socioeconomic status (SES) is known to influence health outcomes. We investigated whether pre-hospital time metrics are associated with neighbourhood SES (nSES) in a cohort of patients with neurological symptoms suspect for stroke from two regions in the Netherlands. **Methods:** We analysed data from two prospective cohort studies. As a proxy for nSES, we used a postcode-based composite score as developed by “Statistics Netherlands” (CBS), with a range from –1 to 1. The associations between nSES and time metrics were examined through linear

regression. Logistic regression estimated the association with final stroke diagnoses and receiving reperfusion treatment. Models were fit using generalized estimating equations. All analyses were adjusted for age, sex, and original study. **Results:** The cohort included 2,854 patients (1,485 [52.0%] male, median age 73 [IQR 61–81], median baseline NIHSS score 2 [IQR 0–6]). nSES was associated with onset-to-alarm time ($\alpha\beta$ –0.26 [95% CI: –0.49 to –0.03], $p = 0.03$) and onset-to-door time ($\alpha\beta$ –0.21 [95% CI: –0.36 to –0.05], $p = 0.01$), with a respective 23% and 19% increase per 1 point shift toward a more deprived nSES. However, nSES was not associated with alarm-to-door time ($\alpha\beta$ –0.01 [95% CI: –0.07 to 0.05], $p = 0.79$), final stroke

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diagnosis (adjusted odds ratio [aOR] 0.91 [95% CI: 0.66–1.35]) or likelihood of receiving reperfusion therapy (aOR 1.16 [95% CI: 0.79–1.70]). **Conclusion:** Living in a more socioeconomically deprived neighbourhood is associated with prehospital delays for patients presenting with neurological symptoms suspect for stroke. This highlights the importance of examining barriers to timely emergency medical service activation and formulating strategies to reduce socioeconomic disparities in stroke response.

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Introduction

Socioeconomic status (SES) is a known determinant of health, influencing various aspects of stroke care [1, 2]. Previous research has demonstrated that socioeconomic disparities exist in the accessibility of reperfusion therapy for patients with ischaemic stroke [3]. Given the limited time window for reperfusion therapies for these patients, a possible explanation for this phenomenon is pre-hospital delay, which can significantly affect treatment eligibility and outcomes [4]. Additionally, although the association between SES and haemorrhagic stroke outcomes have been researched less extensively, emerging evidence suggests that the effectiveness of both regularly implemented treatments and experimental treatments may also be time-dependent [5–7]. This underscores the importance of identifying factors that contribute to delays in treatment for patients presenting with symptoms suspect for stroke.

Prehospital delay can result from various factors, including delayed symptom recognition, postponing seeking medical attention, and disparities in emergency medical service (EMS) accessibility and response. In previous studies, patients from lower neighbourhood socioeconomic status (nSES) areas were found to have a prolonged delay in hospital arrival [8, 9]. Hospital arrivals from lower income neighbourhoods were also found to be less likely to have prehospital notification, thereby potentially complicating in-hospital stroke workflows [10, 11].

Previous research was conducted in heterogeneous healthcare systems and geographic settings. Therefore, these findings may not be generalizable to all populations. In the Netherlands, all ambulance paramedics receive extensive training on EMS stroke care, which could contribute to reduced prehospital delays compared to regions with less standardized training [12]. Additionally, the majority of previous studies used retrospectively collected data and included only admitted

stroke patients as opposed to those presenting with symptoms suspect for stroke.

Breaking down onset to treatment times into interpretable intervals, such as onset-to-alarm time, could aid in identifying potentially actionable aspects of (pre-hospital) acute stroke care to limit delays. Understanding the mechanisms underlying these disparities is essential to improve stroke care and outcomes across different socioeconomic groups. This study aimed to investigate the association of nSES with factors pertaining to pre-hospital stroke care and the likelihood of receiving treatment for acute ischaemic stroke in the South-West Netherlands.

Methods

Study Design and Population

For this cohort study, we analysed data collected during two previously completed multicentre, prospective observational studies: the LPSS (Leiden Pre-hospital Stroke Study) and PRESTO (Prehospital Triage of Patients With Suspected Stroke) [13, 14]. These observational cohort studies recruited patients in the South-West of the Netherlands from 2018 to 2019. Patients were sourced from four Dutch ambulance regions that included 10 primary stroke centres and five thrombectomy-capable (or comprehensive) stroke centres, serving approximately 3.6 million people. This region is considered urbanised, with relatively short distances to stroke centres and relative proximity of primary stroke centres to thrombectomy-capable stroke centres when between hospital transport is required.

Patients met the inclusion criteria for the aforementioned studies if they were 18 years or older and were transported by EMS to one of the regional hospitals with a new neurological deficit that was suspect for acute ischaemic stroke. This suspect neurological deficit was defined as a positive Face Arms Speech Time (FAST) test or other new-onset focal neurological symptoms. Patients were eligible if they had a symptom onset within 6 h (PRESTO) or 24 h (LPSS). Detailed in- and exclusion criteria for these studies were published previously [15, 16].

As the nSES was needed to perform the analyses, patients could only be included if the ambulance pick-up location was registered when they were originally enrolled. Since the time-of-onset of the symptoms was required for the analyses, patients were excluded if this value was not available.

Covariates

Patient Characteristics

Data on the included patients' demographic characteristics, including age and sex, as well as relevant clinical characteristics (such as baseline NIHSS) was sourced from the PRESTO and LPSS datasets.

Neighbourhood Socioeconomic Status

The SES-WOA score, developed by Statistics Netherlands, was used to represent nSES. This publicly available composite score reflects the educational attainment, household income, and employment status of residents within a neighbourhood (defined by a four-digit postcode) in the Netherlands [17]. The SES-WOA score was derived through multiple correspondence analysis of Dutch census data and ranges from -1 to 1, with lower values indicating greater socioeconomic deprivation. Further details on the development of this composite score can be found online [18].

In order to visualize potential differences between the demographic and clinical characteristics of the patients by nSES, the patients were divided into nSES tertiles (labelled low, middle, and high) by dividing the cohort's SES-WOA scores into three near equal groups. These tertiles were not used in the statistical analysis described in the following sections, where the SES-WOA score was treated as a continuous variable.

Outcomes

Prehospital Time Metrics

Onset-to-alarm time is defined as the time in minutes between the onset of the neurological deficit (or last-seen-well time) and the time at which a call to EMS concerning the patient's health was registered. Onset-to-door time is the time in minutes between the onset of the neurological deficit (or last-seen-well time) and the arrival of the ambulance at the hospital for initial patient evaluation. Alarm-to-door time is defined as the time in minutes between the initial call to EMS concerning the patients' symptoms and the arrival of the ambulance at the hospital.

Final Diagnosis

The final diagnosis is defined as the diagnosis given to the patient after diagnostic workup in hospital. These diagnoses are categorized as either stroke (which included the diagnoses of ischaemic stroke and haemorrhagic stroke) or stroke mimic, which contained all other possible aetiologies.

Reperfusion Therapy

Patients that had an ischaemic stroke as their final diagnosis were considered as having received reperfusion therapy if they were administered a thrombolytic agent (regardless of occlusion location) and/or if they underwent endovascular thrombectomy for an anterior circulation large or medium vessel occlusion.

Statistical Analysis

All analyses were completed in R (version 4.4.2 "Pile of Leaves"). Baseline data of the patients included in the study will be reported according to standard statistical procedures. Conventional levels of significance (α 0.05) were used for interpretation. All analyses were adjusted for age, sex, and the study from which the patient data were sourced. To account for the potential influence of clustering of patients within postcodes, the regression analyses were estimated using generalized estimating equations methods.

Association between nSES and Prehospital Time Metrics

The association between the nSES and the prehospital time metrics was examined using linear regression. The time metrics were log-transformed to account for potential issues with the skewed distribution of the data. The analyses examining the association between the onset-to-door time and the alarm-to-door time were additionally adjusted for the average driving time between the patient pick-up location and the hospital. Results were reported as adjusted regression coefficients ($\alpha\beta$) with 95% confidence intervals.

Association between nSES and Final Diagnosis

The association between nSES and the final diagnosis was examined through binary logistic multivariable regression analysis. The association is reported as an adjusted odds ratio (aOR) with 95% confidence intervals.

Association between nSES and Receiving Reperfusion Therapy

For a subset of patients that had ischaemic stroke as their final diagnosis in hospital, the association between nSES and receiving reperfusion therapy was examined through binary logistic regression. The analysis was additionally adjusted for whether the event was classified as a "wake-up stroke," meaning that the first symptoms were noticed upon waking, thereby making the time of the start of symptom onset more challenging to determine. The association is reported as an aOR with 95% confidence intervals.

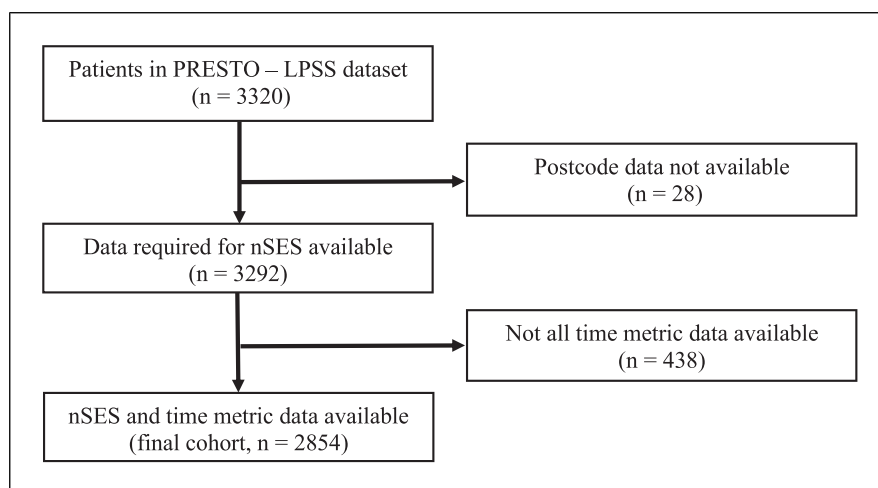


Fig. 1. Study profile.

Missing Data

Missing data were imputed through multivariate imputation by chained equations (5 sets) using the “MICE” package.

Results

A total of 2,854 of the 3,320 patients originally included in the PRESTO and LPSS studies met the criteria for inclusion in this study, as shown in Figure 1. A comparison of the baseline data of the in- and excluded patients is available in online supplementary Table 1 (for all online suppl. material, see <https://doi.org/10.1159/000551417>).

Included patients had a median age of 73 (IQR 61–81), 1,485 (52.0%) were men, and the median NIHSS score at baseline was 2 (IQR 0–6). Additional patient characteristics are reported in Table 1 and between tertile differences as well as missing values are reported in online supplementary Table 2. Significantly more patients in the lower nSES tertile had hypercholesterolemia (58.3% in the low versus 47.7% in the high tertile) and diabetes mellitus (22.7% in the low versus 17.7% in the high tertile). Patients were more likely to have a history of intracranial haemorrhage in their medical history in the high tertile (3.0%) than in the low tertile (1.8%). The tertiles had a significantly different median baseline NIHSS, as the lower tertile had a median score of 3 (IQR 1–6), while both the middle and high tertile had a median score of 2 (IQR 0–5). There was no significant difference in the distribution of the NIHSS items per nSES tertile, as shown in online supplementary Table 3.

There were 470 Dutch postcodes (out of 4,053 four-digit postcodes available in the CBS database for the

Netherlands as a whole) [17] represented in the patient cohort and the most common postcode occurred 34 times. The median nSES was 0.04 (IQR –0.15 to 0.18), with a maximum score of 0.66 and a minimum score of –0.89.

Association between nSES and Prehospital Time Metrics

The median time metrics are reported per nSES tertile in online supplementary Table 4. For illustrative purposes, we also reported the alarm-to-ambulance arrival and the arrival-to-departure time intervals. An overview of the regression analyses examining the association between nSES and the time metrics are reported in Table 2. Two-hundred and eight patients (7.3%) had a last-seen-well time that was after the time of first contact with EMS. As this was not considered possible, these values were removed and imputed through multiple imputation.

The median onset-to-alarm time was 81 min (IQR 25–257). The median onset-to-alarm time for the low nSES tertile was 94 (IQR 26–266) minutes, while the high tertile had a median of 77 (IQR 26–259) minutes. The adjusted regression coefficient (beta (β)) for the association between the nSES and onset-to-alarm time was –0.26 ([95% CI: –0.49 to –0.03], $p = 0.03$). Since the onset-to-alarm time was log-transformed prior to the analysis, this regression coefficient indicated that the onset-to-alarm time changes by a factor of 0.77 (exponent of –0.26) or 23% decrease per 1 point increase in the SES-WOA score.

The median onset-to-door time was 111 min (IQR 60–279), and the median alarm-to-door time was 40 min (IQR 33–49). The low nSES tertile had a median onset-

Table 1. Baseline and clinical patient characteristics

	Included patients (n = 2,854)
Age, median (IQR), years	73 (61–81)
Sex male, n (%)	1,485 (52.0)
Pre-stroke mRS, n (%)	
0–2, functionally independent	2,235 (78.3)
Medical history, n (%)	
Atrial fibrillation	433 (15.2)
Hypertension	1,736 (60.8)
Hypercholesterolaemia	1,539 (53.9)
Myocardial infarction	318 (11.1)
Diabetes mellitus	583 (20.4)
Intracranial haemorrhage	79 (2.8)
Peripheral artery disease	110 (3.9)
Use of VKA or DOAC	461 (16.2)
Baseline NIHSS, median (IQR)	2 (0–6)
Wake-up stroke (yes), n (%)	425 (14.9)
Diagnosis in hospital, n (%)	
Ischaemic stroke, aLVO	261 (9.1)
Ischaemic stroke, other	1,118 (39.2)
Intracerebral haemorrhage	213 (7.5)
Transient ischaemic attack	428 (15.0)
Stroke mimic	834 (29.2)
Driving time to (first) hospital, median (IQR), min	14.8 (9.3–21.2)

aLVO, anterior large vessel occlusion; DOAC, direct oral anticoagulation, ED, emergency department; mRS, modified Rankin score; NIHSS, National Institutes of Health Stroke Scale; VKA, vitamin K agonist.

Table 2. Regression analyses examining the association between prehospital care time metrics and nSES

	Unadjusted analysis (β [95% CI])	Adjusted analysis (β [95% CI]) ^a
Onset-to-alarm time	−0.21 (−0.44 to 0.02), $p = 0.07$	−0.26 (−0.49 to −0.03), $p = 0.03$
Onset-to-door time	−0.13 (−0.28 to 0.02), $p = 0.09$	−0.21 (−0.36 to −0.05), $p = 0.01$
Alarm-to-door time	0.07 (0.01 to 0.12), $p = 0.02$	−0.01 (−0.07 to 0.05), $p = 0.79$

Onset-to-door time and alarm-to-door time analyses were additionally adjusted for the average driving time to the hospital. ^aRegression analyses were adjusted for age, sex, and study.

to-door time of 120 (IQR 60–289) minutes, while the high tertile had a median of 105 (IQR 59–279) minutes. There was a significant association between nSES and the onset-to-door time ($a\beta$ −0.21 [95% CI: −0.36 to −0.05], $p = 0.01$), corresponding to a change by a factor of 0.81 (or 19%) per 1-unit increase in the SES-WOA score. There was no significant association between nSES and the alarm-to-door time in the adjusted analysis ($a\beta$ −0.01 [95% −0.07 to 0.05], $p = 0.79$).

Association between nSES and Final Diagnosis in Hospital

Two thousand and twenty patients, or 70.8%, received a stroke diagnosis after in-hospital evaluation, and the remaining diagnoses were classified as a stroke mimic. There was no significant association between nSES and a stroke diagnosis (aOR 0.91 [95% CI: 0.66–1.35]). Table 3 shows the results of the adjusted and unadjusted regression analyses.

Table 3. Regression analyses examining the association of final diagnosis and likelihood of receiving reperfusion therapy with nSES

	Unadjusted analysis (OR [95% CI])	Adjusted analysis (aOR [95% CI])
Final diagnosis	0.91 (0.66–1.25)	0.98 (0.71–1.35) ^a
Receiving reperfusion therapy	1.08 (0.76–1.55)	1.16 (0.79–1.70) ^b

^aRegression analysis was adjusted for sex, age, and study. ^bRegression analysis was adjusted for sex, age, study, and wake-up stroke.

Association between nSES and Likelihood of Receiving Reperfusion Therapy

One thousand three hundred and seventy nine (68.3%) patients with a stroke diagnosis had an ischaemic stroke. Six hundred and ten (44.2%) received an intravenous thrombolytic. An anterior circulation large vessel occlusion was found in 261 (18.9%) and 197 (14.3%) of these patients underwent endovascular thrombectomy. The demographic characteristics of the patients that received a diagnosis of ischaemic stroke are listed in online supplementary Table 5. There was no significant association between nSES and the likelihood of receiving reperfusion therapy in hospital (aOR 1.16 [95% CI: 0.79–1.70]). Table 3 shows the results of the adjusted and unadjusted regression analyses.

Discussion

In this post hoc analysis with pooled data from two prospective cohort studies, 2,854 patients with a new neurological deficit suspect for ischaemic stroke were included. We found that patients living in areas with a lower nSES had a significantly longer onset-to-alarm time and, subsequently, a longer onset-to-door time than their counterparts living in more affluent neighbourhoods.

The onset-to-alarm time was found to decrease by 23% per one-point increase in the SES-WOA score. When considering this cohort's median onset-to-alarm time of 81 min, this would imply a 19 (95% CI: 32 to 2) minutes earlier EMS notification for those living in a more affluent neighbourhood. A similar result was observed for the onset-to-door time, where a 1-point increase in the SES-WOA resulted in a 19% reduction. When considering the median onset-to-door time of 111 min, this would be a 21 (95% CI: 53–11) minute reduction in onset-to-door time.

In the Netherlands, all suspected stroke calls to EMS have high priority, regardless of symptomatology. EMS

nurses and emergency service call-centre personnel receive training in recognizing symptoms that could be related to stroke of any aetiology. We did not find that lower nSES was associated with lower rates of reperfusion therapy (intravenous thrombolytic or EVT) or alarm-to-door times among ischaemic stroke patients. This may be explained by the geographic characteristics of our study region, where access to healthcare facilities is generally well-organized and not hindered by distance or infrastructure limitations. These findings suggest that, in contrast to potential prehospital delays, paramedic and in-hospital stroke workflows remain relatively equitable across patients living in areas with different nSES.

Our study population resided in an urbanized and densely populated region in the Netherlands, with relatively short median driving times to the closest hospital (14.8 min [IQR 9.3–21.3]), meaning that it is less likely that urbanicity and rural-urban differences in help-seeking behaviour played a significant role in the disparity observed. Additionally, we found no significant association between nSES and receiving a stroke diagnosis, nor significant nSES-based differences in the type of stroke symptoms on the NIHSS (online suppl. Table 3). This implies that it is unlikely that potential differences in symptomatology prompted patients to delay notifying EMS of their symptoms. There was, however, a significant difference in the NIHSS scores observed upon in-hospital examination between nSES tertiles, suggesting that patients in the lowest nSES tertile tended to have more severe strokes. Although this raises the additional concern that patients in the lower tertile alarm later despite having more severe symptoms, it appears that this difference is relatively minor and might not have clinical relevance (online suppl. Table 2). There were no noteworthy differences in EMS response times between tertiles, which suggests that this difference in stroke severity did not significantly affect workflow (online suppl. Table 4).

Delays in seeking medical attention are thought to result from a gap in knowledge of stroke symptoms, with

the understanding that certain symptoms are associated with stroke resulting in more timely hospital arrivals [19]. We did not have data on patients' understanding of their symptoms at onset, nor if these differ across neighbourhoods. However, previous research in a Dutch stroke patient population found that recognition of certain symptoms (such as one-sided weakness) as being suspect for stroke was associated with shorter onset-to-alarm times. However, it did not always result in adequate interpretation of the urgency of the situation [19]. This is also reflected in a study using a subset of patients included in our analyses, which found that only 48% notified EMS primarily, resulting in longer onset-to-hospital times [20].

Financial concerns may also contribute. Despite mandatory health insurance in the Netherlands, patients can face fixed out-of-pocket costs for ambulance services and specialist hospital care, a barrier common to many international healthcare systems that implement co-payments for emergency and hospital services. Although we were able to compare the prevalence of many important stroke risk factors per nSES tertile, we were not able to examine all potential lifestyle attributes and comorbidities that relate to stroke risk awareness. This could influence the generalizability of the results. We did find that certain predisposing factors, such as hypercholesterolaemia and diabetes mellitus were more prevalent among the lowest nSES tertile, as can be seen in appendix (Table 2).

The results of this study highlight the need to increase the awareness of both stroke symptoms and their urgency to the general public. It has proven to be a major challenge to develop campaigns that not only increase awareness of stroke symptoms but also emphasize, to both potential patients and bystanders, the critical need to contact EMS immediately when symptoms arise [21]. Focusing additional resources, which consider potential neighbourhood, cultural and educational differences, as well as language barriers, on more socioeconomically deprived areas might improve both disparities as well as overall onset-to-alarm times.

When interpreting the results of this study, it is important to consider that the SES-WOA score ranges from -1 to 1. The effect estimates that are reported in this study reflect the change in the outcome per one-point shift on this scale, which represents a considerable difference in neighbourhood affluence. However, the SES-WOA scores for the population included in the analyses do encapsulate a one-point difference, as the values ranged from -0.89 to 0.66. Additionally, nSES was determined by the patients' location at the time of the EMS

encounter, which may not be the patient's primary residence. Nevertheless, there is evidence that most strokes occur, while the patient is at home [22], and all postcodes included in this study contained residential areas.

Comparing studies on the impact of SES on health outcomes can be challenging. This can partly be attributed to variations in the proxies used to measure SES that are healthcare system based (such as health insurance plan enrolment) or more one-dimensional (such as level of education) [1]. Using a composite measure, like the one for nSES used in this study, also has limitations, as it is a generalized proxy that could be influenced by intra-neighbourhood variability in SES. However, it can allow for a more comprehensive understanding by considering multiple factors, and has the additional benefit of helping to identify underserved neighbourhoods.

This study highlights the significant association between nSES and the time from stroke symptom onset to alarming EMS. It adds to the body of existing literature by demonstrating that disparities persist even in healthcare systems with universal coverage and relatively easy geographical access to stroke centres. Our findings suggest that patients from more deprived neighbourhoods have a delay in seeking emergency medical services, which could potentially contribute to less favourable stroke outcomes. Addressing these disparities requires targeted public health interventions, improved stroke education, and enhanced access to healthcare resources in underserved communities. This emphasizes the importance of exploring the underlying barriers to timely EMS activation and developing strategies to bridge the gap in stroke response times across different socioeconomic groups.

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Statement of Ethics

The Medical Ethics Review Committee (MERC) of the Erasmus MC, University Medical Center in Rotterdam, the Netherlands (MEC-2024-0788), reviewed the study protocol and confirmed that it did not fall under the scope of the Medical Research Involving Human Subjects Act (WMO). The study was completed in accordance with the Helsinki Declaration. Because this study met the local exceptions of informed consent regulations, the requirement for informed consent was waived (MEC-2024-0788).

Conflict of Interest Statement

B.A.S., N.S.R., E.L.L.M.S., J.O.G., R.M.W., L.M.H.K., H.K., and I.W. report no relevant disclosures. M.J.H.W. is a DSMB member for the TRIDENT study. A.L. reports funding to institution from Medtronic, Cerenovus, Dutch Heart Foundation, Brain Foundation Netherlands, and ZonMw (planning phase) and from Dutch Heart Foundation, Brain Foundation Netherlands, Stryker, Penumbra, Boehringer Ingelheim, Medtronic, Thrombolytic Science LLC, Health Holland Top Sector-LSH, GE HealthCare, Siemens Healthineers, and Philips Healthcare (past 36 months). They also serve on the advisory board for the ESCAPE MeVO study and is a member of the Research Committee, European Society of Radiology. N.D.K. reports grants to institution from Dutch Brain Foundation, Dutch Innovation Funds, and Health Holland and serves on the advisory board for the PRESTO 2 study. B.R. reports lecture payment from Medtronic Inc. (paid to institution) and serves as Chair of the Working Group for the Dutch Guideline for Ischaemic and

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Author Contributions

B.A.S., N.S.R., D.W.J.D., and B.R.: conception and design of the study. B.A.S. and N.S.R.: statistical analysis. D.W.J.D. and B.R.: supervision of statistical analysis. H.K., M.J.H.W., I.W., E.L.L.M.S., A.L., L.M.H.K., and N.D.K.: role in acquisition of data. B.A.S., N.S.R., H.K., M.J.H.W., I.R.W., E.L.L.M.S., A.L., J.O.G., R.M.W., L.M.H.K., N.D.K., D.W.J.D., and B.R. provided critical review and revision of the manuscript for intellectual content and took responsibility for the final decision to submit for publication.

Data Availability Statement

The data presented in this article are not publicly available due to privacy reasons but can be made available in pseudonymised format upon reasonable request. Data access requests should be submitted to the PRESTO and LPSS Steering Committees via email (presto@erasmusmc.nl).

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