

Disabling stroke in persons already with a disability

Ethical dimensions and directives

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Abstract

Stroke is the second leading cause of death worldwide and a leading cause of adult disability worldwide. More than a third of individuals presenting with strokes are estimated to have a preexisting disability. Despite unprecedented advances in stroke research and clinical practice over the past decade, approaches to acute stroke care for persons with preexisting disability have received scant attention. Current standards of research and clinical practice are influenced by an underexplored range of biases that may hinder acute stroke care for persons with disability. These trends may exacerbate unequal health outcomes by rendering novel stroke therapies inaccessible to many persons with disabilities. Here, we explore the underpinnings and implications of biases involving persons with disability in stroke research and practice. Recent insights from bioethics, disability rights, and health law are explained and critically evaluated in the context of prevailing research and clinical practices. Allowing disability to drive decisions to withhold acute stroke interventions may perpetuate disparate health outcomes and undermine ethically resilient stroke care. Advocacy for inclusion of persons with disability in future stroke trials can improve equity in stroke care delivery.

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Editorial

Stroke in persons with disability: Need for ethically resilient care

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Glossary

ADA = Americans with Disabilities Act; **DAWN** = Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo; **DEFUSE 3** = Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke; **MR CLEAN** = Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke; **mRS** = modified Rankin Scale.

Stroke is the second leading cause of death worldwide and the leading cause of serious adult disability in America.^{1,2} More than 17% of the US population lives with disability. This population is disproportionately represented in ischemic stroke presentations; more than a third of patients with stroke present with a preexisting disability.^{3,4} Acute stroke intervention is currently driven by mechanical thrombectomy and IV thrombolysis. The aim of these interventions is mitigation of future disability by reperfusion, and therefore salvage, of threatened penumbral tissue. Despite unprecedented advances in stroke care and research over the past decade, approaches to acute stroke intervention for persons with disabilities have received limited attention. Increased awareness of key principles and recent findings from disabilities rights research, bioethics, and health law can highlight new insights into the specificities of stroke in persons with disability, help to improve care, and stimulate timely research in this underexplored domain.

The paucity of data and direction pertaining to this growing population has engendered wide variation in clinical practice between individuals and institutions but generally a lack of therapeutic aggression^{4,5} and reflects a concerning and critical gap in evidence-based and ethically resilient stroke care.⁵⁻⁷ These exigencies are amplified through the lens of directives from biomedical ethics, disabilities rights, and health law that emphasize inclusion of persons with disabilities in health care services and research.

Ethics, law, and disability

The Rehabilitation Act of 1973 and the Americans with Disabilities Act (ADA) provide official legal standards prohibiting limitation of health care services for people with disabilities relative to persons without a disability.^{8,9} These standards are rooted in the principles of bioethics, including justice, respect for autonomy, beneficence, and non-maleficence.¹⁰ Whereas the Rehabilitation Act devolves exclusively on federally funded institutions and programs, the ADA applies to private, state, and local government programs regardless of federal funding status. These policies define a disability as any physical or mental condition that substantially limits a major life activity such as walking, learning, or working.¹¹ In addition to prohibiting overt limitation of medical care for persons with disability, the ADA proscribes discrimination based on disparate impact. Discrimination by disparate impact occurs when seemingly neutral eligibility criteria for a treatment or service exclude persons with a disability when broadly implemented.

Despite clear legal and bioethical guidance, however, these directives frequently go overlooked. Unequal health outcomes between persons with and without disabilities across a wide range of clinical contexts have been reported. These disadvantages are often preventable and are largely independent of differences in baseline physiologic risk profiles.^{12,13} A cadre of social forces contribute to these inequities, including multiform psychological biases, stigma, economic disadvantages, exclusion from research, and suboptimal access to health services.³ Despite growing awareness of these determinants of health, attention to how these particular forces shape stroke care for persons with disability has been limited.

The heavy weight of bias

Biases in clinical decision-making affecting persons with disability include ineffectual bias, fragility bias, and catastrophe bias.¹⁴ Ineffectual bias refers to the tendency to underestimate the competence and quality of life of persons with disability. Misattributions of incompetence can result in discounting the preferences of patients with a disability in favor of substituted judgments by clinicians (i.e., paternalism).¹⁵ External observers estimating the quality of life of persons with disabilities tend to vastly underestimate relative to estimations reported by those with disability themselves, who tend to endorse good or excellent quality of life.¹⁶⁻¹⁹ These tendencies might stem from misguided preconceptions of lower life or hedonic value. In acute settings, parallel preconceptions might result in premature withdrawal of care or withholding of life-saving treatments for patients with disabilities, often stemming from covert or overt beliefs that disabled lives are not worth living and therefore not worth saving.¹⁹ This bias comes into play not only when considering preexisting disability but also in considering future disabilities.¹⁹ For example, while decompressive hemicraniectomy has been shown to reduce death and may improve functional outcome after malignant stroke, because of high rates of disability in survivors, controversy still exists about whether and when to offer it.^{20,21} Despite a high incidence of disability, however, the majority of patients who have undergone this procedure report being satisfied with life without regretting undergoing the procedure.^{19,22,23}

Fragility bias is the misperception that persons with disability are, by being disabled, more prone to perceived risks and possible harm of treatments compared to their nondisabled counterparts. Erroneous overestimation of risk due to fragility bias may skew clinician decision-making in favor of not

offering otherwise beneficial treatments to patients. This may be especially true in the context of an invasive or aggressive treatment such as thrombectomy for large vessel occlusion stroke. The cognitive tendency to be unduly pessimistic when prognostication involves someone with a preexisting disability is well described.^{24–27}

Catastrophe bias is the assumption that the subjective experience of a person with disability faced with a new medical problem is worse than it is. This presumption of magnified suffering and underestimation of resilience has been studied as a common caregiver reaction to those with a range of disabling conditions, including spinal cord injury, trauma, terminal cancer, and amputation.^{28,29} When catastrophe bias enters into clinical decision-making, it can animate self-fulfilling prophecies whereby choices, assessments, and outcomes are artificially swayed to match pessimistic expectations.¹⁴

Stroke trials and disability outcomes

Despite a robust evidence base supporting the utility of thrombectomy and thrombolysis in select patients, prestroke disability is commonly invoked as a reason to withhold these treatments from otherwise eligible patients who have preexisting disabilities.^{30–34} Although there is no clear pathophysiologic rationale for this practice, such decisions are often predicated on the absence of data pertaining to patients with disability from key trials, which tend to systematically exclude patients with disability. This is routinely operationalized in trials through the implementation of an exclusion criterion for individuals with baseline modified Rankin Scale (mRS) score greater than 1 or 2.

The mRS is the most widely used scale for quantifying disability and dependency in stroke research and practice, typically assessed as a baseline variable for trial inclusion or treatment selection and then again at 90 days after the stroke has occurred. The original scale was devised by Dr. John Rankin in 1957 and revised in 1988 as a means to assess functional outcomes in patients who have had strokes. It is an ordinal scale ranked from 0 to 5, with a separate category of 6 reserved for patients who die. In this scale, a patient with no symptoms at all is assigned a score of 0, with a spectrum of disability to 5, a patient with severe disability who is bedridden and incontinent and requires continuous care. mRS scores of 0, 1, or 2 represent grades of disability (either at baseline or 90 days after a stroke) in which a patient can live without the assistance of another person (i.e., functional independence).

Consider the case of a young patient with spinal cord injury who is unable to walk unassisted. When mRS-based guidelines that have emerged from clinical trials are implemented, such a patient would not be routinely considered for thrombectomy or thrombolysis in the event of a major stroke because of his preexisting mRS score of 3, despite a priori likelihood of benefit and sound rationale for treatment.

The importance of homogeneity in trial populations as a means of better isolating the effect of an intervention is well recognized. The competing challenge is to study a population that closely resembles the heterogeneity of clinical practice. One explanation for the practice of excluding patients with baseline disability from stroke intervention trials is the convolutions required in dichotomized mRS analyses that arise from enrollment of patients with disability; this is pragmatic and distinct from any mechanistic hypotheses about reduced benefit for this population.^{35–37} Given the simple dichotomized mRS endpoints that are routinely used to quantify favorable outcomes in stroke trials (which tend to define favorable outcome as an mRS score of <2 for thrombolysis or 3 for thrombectomy), enrolling patients with preexisting disabilities introduces practical difficulties in adjusting for different levels of premorbid disability when quantifying the utility of an intervention, especially when the good outcome is defined as functional independence (mRS score ≤ 2).^{36,38}

The road ahead

Rather than excluding patients with disabilities from stroke trials due to anticipated complexities in data analysis, it is ethically and clinically imperative that the current orthodoxy in trial design occasioning this systematic exclusion be challenged and revised. That patients with preexisting disability face higher rates of mortality and institutionalization, care costs, and accumulated disability after stroke merely augments the propriety of ensuring that this population of patients are not categorically excluded from potentially beneficial interventions.⁴ Apart from satisfying the normative demands of nondiscrimination, enrolling patients with disabilities in trials can further help to ensure more representative and generalizable samples, especially as increasing longevity drives a higher proportion of patients with stroke with increased premorbid baseline mRS score over time.³⁸ Outcome measures that capture accumulated functional dependence (such as change in mRS score from before stroke to after stroke, the modified Rankin shift,³⁴ or the weighted mRS³³) rather than the mere binary state transfer from nondependent to dependent could become standard outcomes for future studies. These outcome measures may allow more widespread inclusion of persons with disability without compromising data construct validity.³⁸

With respect to thrombolysis, data from stroke registries suggest that those with significant disability account for <10% of treated cases, despite accounting for a much larger percentage of patients who present with acute stroke.^{39,40} This disparity demands careful evaluation. The argument sometimes cited that those with preexisting disability have higher chances of sustaining unfavorable outcomes erroneously ascribes anticipated adverse outcomes to the intervention rather than to the natural history of stroke itself. Neither the Food and Drug Administration nor the American Heart Association/American Stroke Association 2018 acute stroke guideline specifies

preexisting disability as prohibitive.⁵ Multiple studies have demonstrated that preexisting disability does not portend increased risk of symptomatic intracranial hemorrhage,³⁷ the most dreaded complication of thrombolysis. Moreover, limited data suggest that treatment with thrombolysis increases the chances of returning to prestroke functional status without increased attributable risk of mortality.^{41–44}

Available data to guide thrombectomy decisions for patients with preexisting disabilities are similarly limited, likewise largely due to trial selection paradigms that have excluded patients with significant disabilities despite the absence of principled hypotheses to explain why this population would fail to benefit. Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo (DAWN) and Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke (DEFUSE 3), the 2 recent landmark trials that established endovascular thrombectomy for patients with emergent large vessel occlusions presenting up to 24 hours after stroke, excluded patients with baseline mRS scores >1 (in DAWN) or >2 (in DEFUSE 3).^{33,34} Only 13 DEFUSE 3 patients had a prestroke mRS score of 2, an inadequate sample to extrapolate favorable response.⁴⁵ Nonetheless, the 2018 American Heart Association/American Stroke Association guidelines delineate that for patients with a prestroke mRS score >1, “the use of mechanical thrombectomy with stent retrievers may be reasonable.”⁵

An analysis of the Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke (MR CLEAN) registry estimates that 11% of patients who underwent thrombectomy had prestroke functional dependence, defined as baseline mRS score ≥ 3 . After adjustment, functional dependence was not associated with less favorable outcomes, complication rates of symptomatic intracranial hemorrhage and stroke progression were similar, and a substantial portion returned to their prestroke functional status.⁴⁶ These findings are bolstered by other analyses that have found no higher procedural complication rates in those with preexisting disability, with many returning to their prestroke level of disability after thrombectomy.^{47,48} Preexisting disability is an independent risk factor for poorer clinical outcomes, and passive nonintervention may only amplify the likelihood of actualizing these risks.⁴⁹ Taken together, these considerations argue for the inclusion of patients with preexisting disability in clinical treatment paradigms.

Resource use

In weighing the utility of acute stroke interventions for persons with disabilities, some may cite perceived resource constraints and costs as prohibitive. If resources are limited, their application must be, too; therefore, treatment of individuals with a disability is practically infeasible or unjustified from a distributive justice standpoint. A lack of normative equipoise in systematically excluding patients with a disability from receiving therapies due to perceived costs

notwithstanding, such considerations merely bolster the justification for offering these interventions to this population. Those with disabilities stand to incur only costlier outcomes from stroke, including length of stay, discharge destination, mortality, and complications, if therapies are routinely withheld and preventable neurologic injury is sustained.⁴ Economic analyses further suggest that treatment with endovascular thrombectomy not only is cost-effective but also may significantly reduce health care use and attenuate longitudinal health care costs after stroke.^{6,7}

The autonomy paradox

Respect for patient autonomy, a cornerstone of modern bioethics, requires understanding patient preferences and values and allowing these ideals to inform care. When approaching stroke treatment decisions or undertaking advanced care planning, clinicians should diligently explore and understand patient or surrogate preferences, especially when it comes to potentially life-sustaining interventions. If an informed patient or surrogate chooses to forego a treatment, this should be acknowledged and respected. However, to limit this choice for patients with disabilities or to make the decision on their behalf assuming that such therapies would be undesirable simply by virtue of a disability, as some have suggested,⁵⁰ not only discriminates against those with disability but paradoxically further usurps patient autonomy by limiting their voice in guiding trajectories of care. Clinicians and scientists should be mindful of the potential for ineffectual bias, fragility bias, and catastrophe bias in clinical decision-making, advanced care planning, and trial design before prematurely narrowing the range of choices made available for those with disabilities.

Conclusions

Awareness of the cognitive vulnerabilities, social stigmas, and psychological biases surrounding disability that may covertly creep into treatment decisions and trial design is crucial. The action that follows from this awareness will ensure that these social and psychological forces do not magnify the impact of disability on this already vulnerable and growing population. The principles of beneficence, nonmaleficence, and justice find particularly acute expression in this arena, where current practices do not clearly align with biological insights or ethical ideals.⁵¹ If mitigation of lasting new deficits from acute stroke is taken as a guiding principle, then this should apply regardless of whether there is a preexisting disability. Routinely excluding patients with disability from consideration of treatments that could prevent further morbidity and mortality may exacerbate disparate health outcomes, increase long-term costs, and undermine ethically resilient stroke care. Advocacy for inclusion of persons with disability in future stroke trials can improve equity in stroke care delivery and stimulate timely research in this critically underexplored domain.

Author contributions

M.J. Young: drafting/revising the manuscript, data acquisition, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval. R.W. Regenhardt: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, study supervision. T.M. Leslie-Mazwi: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval. M.A. Stein: drafting/revising the manuscript, study concept or design, accepts responsibility for conduct of research and will give final approval.

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