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ROADMAP

**Outcome Prioritisation in Alzheimer's Disease:
Understanding the Ethical Landscape**

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- Summary of recent paper: understanding the ethical landscape of outcome prioritisation in AD
- Focus on three areas of particular relevance in the context of this session, i.e. relating to the use of RWD / RWE

- *‘Health outcome prioritisation in Alzheimer’s disease: Understanding the ethical landscape’*
- Written from November 2017 to September 2018 as a deliverable for ROADMAP WP8 under Ethical, Legal, and Social Issues
- Adapted to a peer reviewed journal article, submitted in October 2018, now awaiting outcome of peer review
- Aim is to understand and enumerate the considerations that are relevant for achieving a fair and just prioritisation of health outcomes

- Semi-systematic, in that we selected literature as in a systematic review, but the analysis was ethical / philosophical
- Full details of search criteria are available, but the process resulted in 129 documents from preceding decade
- Analysis revealed nine key areas of ethical relevance, can be grouped into three categories pertaining to methodology

- Nine key themes of relevance emerged from the analysis (the three highlighted in green are the ones we will focus on specifically)
 - Public health and distributive justice
 - *Tension between individual / societal benefits in approaches to AD treatment*
 - Scarcity of resources
 - *Resources are finite, so 'to prioritise is inevitably to say no to somebody'*
 - Heterogeneity and changing circumstances
 - *Resource availability not constant and AD is a heterogeneous condition*
 - Gaps in knowledge of treatment effects
 - *Determining fair prioritisation of outcomes depends on what needs to be known to make a decision*
 - Values and circumstances
 - *Fairness consists in patients being able to make their own choices, but this must be balanced against clinical expertise*
 - Conflicting priorities
 - *Tensions: short vs long term goals, palliation vs delay, how to prioritise management of comorbidities*
 - Communication, autonomy and coercion
 - *AD can impede communication of wishes and preferences, so how to protect self-determination as disease progresses*
 - Caregiver issues
 - *Prioritising needs of caregivers as well as people with AD and ensure preferences of former not confused with those of the latter*
 - Disclosure of risk
 - *How to assess the value of early risk detection given impact on life and uncertainty of progression to later stages?*

The nine themes can be grouped into three further categories with particular methodological implications for research

- The importance of ensuring the adequacy of the procedures according to which finite resources are allocated:
 - *Broadly speaking this is a question about justice, asking how we justify who should get what and in what quantities*
 - *Philosophical tools derived from understanding competing theories of justice are essential in negotiating these dilemmas*

- The need to identify the right outcomes to be measured, i.e. those that are most meaningful and important to stakeholders:
 - *Being able to do this requires engagement with all such stakeholders, and patients in particular*
 - *Tools such as interviews, focus groups, surveys, are ideal for this and as such the social sciences play an invaluable role*

- First two are relevant for other conditions but third is dementia-specific, namely need to mitigate impaired communication of wishes
 - *Because AD impairs ability to clearly convey wishes, risk is that prioritization does not reflect their preferences*
 - *Both sets of tools – philosophical and social scientific – are vital here, i) for providing the theoretical framework according to which discussion of the balance between individual and societal goods can meaningfully take place, and ii) for soliciting as comprehensive data as possible about preferences from individuals with AD and their carers prior to advanced decline*

- What counts as fair prioritisation of outcomes depends partly on what needs to be known to make a prioritisation decision.
 - *Whether an intervention is or is not desirable can only be judged according to its outcome*
 - *But interventions – esp. pharmaceutical ones - may have trade-offs between desirable effects and undesirable side-effects*
 - *So weighing these is still less straightforward where comorbidities requiring different types of treatment are present*

- Despite being the apparent ‘gold standard, RCTs have limitations which can come to bear on ethical outcome prioritisation.
 - *Investigation of drug-drug interactions is not always comprehensive*
 - *Data often lack statistical power from inadequate sample sizes, their generalisability is limited, and are prone to bias*
 - *RCTs determine effectiveness of a single drug for a single problem, but as AD so heterogeneous this may be unhelpful for clinical practice*
 - *Likely presence of comorbidities (as above), combined with gaps in knowledge of effects limit accuracy of prescribed treatment regimes*
 - *Risk of attrition is high, since average age of AD patients is older and comorbidities limit participation*

Discussion Question:

RCTs have gaps which RWD / RWE, for example via pragmatic trials, may be able to help fill in.

However, the greater volume of more heterogeneous data you have, the more difficult it is to prioritise particular outcomes, so is RWD / RWE practically ethically useful in resource allocation decisions?

- Acting in accordance to people's preferences depends on being able to solicit those preferences, which can be problematic in AD:
 - *AD can impede communication, cognition, decision-making, social participation, independence, relationships, perceptions of self / selfhood*
 - *It is important not to assume that people with dementia cannot represent themselves, but the means for doing so become compromised*
 - *These issues become increasingly acute in later stages of the disease but become relevant from MCI onwards*
 - *And at the end of life it is especially important that the dying person's wishes are understood as explicitly as possible in advance*
 - *Given the hermeneutic, subjective, qualitative content of such wishes, RWD / RWE looks well suited to helping deliver such a goal*

- Carers are often best placed to represent interests of people with AD, but need to ensure they actually do so:
 - *By virtue of closest interaction with people with AD, carers may be able to interpret wishes that others cannot, but is this a guarantee?*
 - *Knowing what ought to be done for people with AD if their preferences are hard to discern carries a high risk of error or harm*
 - *There is evidence to suggest carers' evaluations of QoL is more negative than affected people, but there is no way to verify this*
 - *Also evidence that carers prefer rapid decline towards the end, but whether the affected people do can also not be verified*
 - *Again, given the deeply personal nature of relevant preferences, qualitative data such as RWD / RWE looks well suited to this task.*

Ethics in RWD: Communication, Autonomy, Coercion, and Caregiver Issues

Discussion Question:

RWD / RWE may be preferable to more formalised data such as RCT data for providing information about quality of life as it is better suited to conveying meaningful and detailed insights into the wishes of people with AD and their carers

This may be effective in most stages of the disease but in the final stages it only reduces, rather than completely resolves, the challenge of how and whether we know that carers genuinely do act in the interests of the people for whom they're caring once communication is severely impaired

Therefore, is RWD / RWE in reality practically ethically useful for protecting the interests of people with AD in the final stages of the disease?

- We concluded from our analysis that the emergent themes underline the difficult balance that must be struck when allocating resources, when measuring and prioritising outcomes, and when individual preferences are sought
- Given the usefulness of a combined philosophical / ethical and social scientific approach to analysing these issues we also reflected on how the tools of these disciplines can help address challenges posed by resource allocation, measuring and prioritising outcomes, and eliciting stakeholder preferences, e.g.

- Philosophy / Ethics:
 - Balance of rights and responsibilities between the individual and the state, a salient issue here, falls within the purview of (political) philosophy and ethics, as such understanding competing theories of justice is instructive for negotiating resource allocation dilemmas
- Social Science:
 - A duty of prioritisation is to optimise outcomes for people with AD, and understanding their preferences is a necessary step in discharging that duty. Finding these out can be done via interviews, focus groups, surveys, questionnaires. Tools of social science research therefore valuable in this context



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Thank you!

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