ADVANCE RESEARCH DIRECTIVES: LEGAL AND ETHICAL ISSUES AND INSIGHTS FROM A NATIONAL SURVEY OF DEMENTIA RESEARCHERS IN AUSTRALIA

Abstract: Advance research directives (ARDs) are a means by which people can document their wishes about research participation in the event of future incapacity. The concept of ARDs emerged in literature in the 1980s and they have since been endorsed in some ethics guidelines and position statements. To date, formal legal recognition is limited. A few empirical studies have investigated the views of researchers and other stakeholders on ARDs and tested strategies to implement such directives. To further knowledge in this area, we undertook a survey of dementia researchers in Australia (n=63) to examine their views on ARDs. Recent law reform initiatives in Australia aim to provide a statutory framework for ARDs and the National Statement on Ethical Conduct in Human Research supports advance research planning, especially for participants who may experience cognitive impairment. Most of the survey respondents (>80%) thought ARDs would promote autonomy in decision-making and enable opportunities for people with cognitive impairment to be included in research. Respondents indicated concern about directives not being available when needed (71%) and that ethics committees would not accept ARDs (60%). Few respondents had used ARDs, but a majority (from 57–80%) would be willing to offer ARDs for a range of research activities, such as observing behaviour, taking measures, accessing records, and taking blood samples or scans. Nearly all respondents (92%) agreed that current dissent should override prior wishes stated in an ARD. The survey findings are contextualised with attention to ethics guidelines, laws and practices to support advance research planning.

Keywords: advance research directive; advance research planning; Australia; dementia; research; survey

I. INTRODUCTION

A. Importance of involving people with dementia in research

The ageing population and rising prevalence of dementia in many countries around the world[1] have prompted calls for greater investment in research to inform practices and policies to meet the needs of older people living with neurocognitive disability.[2] There is also increasing advocacy for the inclusion of people at all stages of dementia in research.[3] It is recognised that the needs of people with dementia change as symptoms progress and the exclusion of people with moderate to advanced dementia from research leaves significant gaps in the evidence base for effective care and supports.[4]

The exclusion of people with dementia from research is at least partially attributed to legal and ethical complexities, especially in relation to consent issues.[5] Where a prospective research participant is considered unable to give their own consent, ethics guidelines typically require consent from a legally authorised representative.[6] Laws in different jurisdictions vary in who has this authority, in what circumstances proxy decision-making can occur and the criteria for decision-making about research participation.[7] Studies have identified shortcomings in proxy decision-making for research: proxies' views often differ from what

[1] M Prince and others, 'The Global Prevalence of Dementia: A Systematic Review and Metaanalysis' (2013) 9 Alzheimers Dement 63.
[2] Alzheimer's Disease International, *From Plan to Impact: Progress Towards Targets of the Global Action Plan on Dementia* (2018); M Prince and others, 'The Burden of Disease in Older People and Implications for Health Policy and Practice' (2015) 385 Lancet 549.
[3] Alzheimer Europe, *The Ethics of Dementia Research* (2011) <https://www.alzheimer-europe.org/Ethics/Ethical-issues-in-practice/2011-Ethics-of-dementia-research> accessed 29 July 2019; E West and others, 'Operationalising Ethical Challenges in Dementia Research—A Systematic Review of Current Evidence' (2017) 46 Age Ageing 678; B Prusaczyk and others, 'Informed Consent to Research with Cognitively Impaired Adults: Transdisciplinary Challenges and Opportunities' (2017) 40 Clin Gerontologist 63.
[4] West and others (n 3); K Murphy and others, 'Articulating the Strategies for Maximizing the Inclusion of People with Dementia in Qualitative Research Studies' (2015) 14(6) Dementia 800.
[5] E Rivett, 'Research Involving People with Dementia: A Literature Review' (2017) 21 Working with Older People 107; West and others (n 3).
[6] A Thorogood and others, 'Consent Recommendations for Research and International Data Sharing Involving Persons with Dementia' (2018) 14(10) Alzheimers Dement 1334.
[7] For example, a legally authorised representative may be formally appointed into an enduring representative role or may be an informal decision-maker (eg, a close family member) and proxy decisions may only be permitted for lower risk research. C Peisah, U Vollmer-Conna and SYH Kim, 'Capacity to Consent to Research: The Evolution and Current Concepts' (2012) 4 Asia-Pac Psychiat 219.

prospective participants would want[8] and they tend to underestimate the willingness of older adults to participate in research.[9] While there is growing consensus on the importance of making decisions that reflect the will and preferences of the person with cognitive disability,[10] proxy decision-makers may have never discussed with the person their views on research participation, with the result that the proxies' own ideas, values and concerns may steer their choices.[11]

Advance research planning, including the making of an advance research directive (ARD), has been proposed as a means to overcome these difficulties. Similar to recommended processes to support effective advance care planning,[12] research planning would involve provision of relevant information to inform deliberations, reflecting on one's preferences for being involved in research during future periods of incapacity, documenting values and preferences in an ARD, and, where a suitable person is available, identifying a proxy to make decisions when necessary.[13] Such processes, if done well, could promote respect for the autonomy and self-determination of a person who wishes to plan for future incapacity, help ensure that proxy decision-making reflects the values and wishes of the person with cognitive impairment and support inclusion in research where a person has expressed their prior interest in participation.[14]

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[8] G Bravo and others, 'Does Promoting Research Advance Planning in a General Elderly Population Enhance Completion of a Research Directive and Proxies' Predictive Ability? A Randomized Controlled Trial' (2016) 7 AJOB Empir Bioeth 183; C Stocking and others, 'Speaking of Research Advance Directives: Planning for Future Research Participation' (2006) 66(9) Neurology 1361.

[9] S Kim and others, 'How Important is "Accuracy" of Surrogate Decision-Making for Research Participation?' (2013) 8(1) PLoS ONE e54790.

[10] Convention on the Rights of Persons with Disabilities (open for signature 30 March 2007, entered into force 3 May 2008) UNTS 2515, art 12.

[11] D Wendler, 'The Theory and Practice of Surrogate Decision-Making' (2017) 47 Hastings Cent Rep 29.

[12] RL Sudore and others, 'Defining Advance Care Planning for Adults: A Consensus Definition From a Multidisciplinary Delphi Panel' (2017) 53 J Pain Symptom Manag 821.

[13] AM Heesters and others, 'Power of Attorney for Research: The Need for a Clear Legal Mechanism' (2017) 10 Public Health Ethics 100; C Porteri, 'Advance Directives as a Tool to Respect Patients' Values and Preferences: Discussion on the Case of Alzheimer's Disease' (2018) 19(1) BMC Med Ethics 9.

[14] See eg, R Pierce, 'A Changing Landscape for Advance Directives in Dementia Research' (2010) 70 Soc Sci Med 623.

B. The contribution of this paper

This paper proceeds in two parts. First, we trace the evolution of the idea of ARDs, which emerged in literature in the 1980s but, until recently, 'benign neglect' stalled the development of strategies to support advance research planning.[15] We review ethical and legal frameworks, especially to analyse how ARDs are envisioned to function, for example, as a legally binding advance decision or as an expression of wishes to guide a proxy decision-maker. We summarise the limited research that has examined practical strategies to implement ARDs as well as empirical studies that have investigated the views of researchers and other stakeholders. These latter studies emphasise the need to 'better understand how researchers look upon the use of ARDs'[16] and to 'advance knowledge and solve dilemmas associated with ARD implementation'.[17]

To that end, the second part of this papers presents a survey study of dementia researchers in Australia, where there is some legal and ethical recognition of ARDs. The survey findings reveal insights from this key stakeholder group on the perceived benefits and disadvantages of ARDs, the types of research activities to address in an ARD and the factors that should override agreement expressed in an ARD. As an important caveat, we emphasise that ARDs would only be applicable in the context of research that is otherwise ethically approved and legally compliant, for example, with regulations governing clinical trials. The proposed research would need to have scientific merit and be designed to minimise risks to participants. As our focus in on ARDs, discussion of the full range of legal and ethical

[15] SYH Kim and J Karlawish, 'Ethics and Politics of Research Involving Subjects with Impaired Decision-Making Abilities' (2003) 62 Neurology 1645, 1646.
[16] K Jongsma and S van de Vathorst, 'Advance Directives in Dementia Research: The Opinions and Arguments of Clinical Researchers − An Empirical Study' (2015) 11 Res Ethics 4, 6.
[17] P Werner and S Schicktanz, 'Practical and Ethical Aspects of Advance Research Directives for Research on Healthy Aging: German and Israeli Professionals' Perspectives' (2018) 5(81) Front Med 1, 9.

requirements for research involving people with decision-making impairment is beyond the scope of this paper.

II. ADVANCE RESEARCH DIRECTIVES – ETHICAL AND LEGAL CONTEXT

A. Evolution of the Concept of ARDs

Advance directives for research were considered over two decades ago in recommendations for research involving people with cognitive impairment. A project funded by the Social Sciences and Humanities Research Council of Canada in the early 1990s resulted in recommendations for guidelines on the involvement of people with dementia in research.[18] ARDs were identified as a tool that would 'normally allow for both the designation of a substitute decision maker and specific instructions' and their 'principal merit … is that they could enable one to retain control of this aspect of life [participation in research] in the event of future incompetence.'[19] Similarly, in a major 1998 report, the United States National Bioethics Advisory Commission endorsed ARDs: 'NBAC believes that one of the ways in which individuals can be respected in their choices is to provide them opportunity to express their preferences (where they have them) regarding future research participation, within certain limits.'[20]

In regard to such limits, both reports stated it is not acceptable for an ARD to be a "blank check" but suggested that ARDs could take various forms, ranging from an expression of a desire to be involved in research and the types and levels of risks acceptable to the person, to instructions about involvement in specific research where the person had an opportunity,

[18] EW Keyserlingk and others, 'Proposed Guidelines for the Participation of Persons with Dementia as Research Subjects' (1995) 38(2) Perspect Biol Med 319, especially pages 346–347.
[19] ibid 347.
[20] National Bioethics Advisory Commission (NBAC), *Research Involving Persons with Mental Disorders that May Affect Decisionmaking Capacity* (1998). This report cites commentary on advance research decisions from the mid-1980s, see pages 71–72. Chapter 5, Recommendation 13.

prior to cognitive decline, to be informed of a study or 'class of research' and the associated risks, potential benefits and protections for participants.[21] According to NBAC, a person's stated wish to be involved in research 'should be given considerable weight by whoever has authority to authorize research participation, but it cannot by itself be considered sufficient for enrollment in a particular study.'[22] Even for an advance consent specific to particular research, NBAC stipulated that a legal representative would need to confirm participation in a study for a person lacking capacity.[23]

In contrast, the Canadian report did not envision the need for proxy endorsement of an ARD that gave advance consent for a specific study. However, a proxy could withdraw or override the advance consent in limited circumstances where 'it becomes apparent that enrollment or continued participation would seriously endanger that subject's welfare to an extent not foreseen by the subject, or even if foreseen, to an extent judged by the substitute to be socially and morally unacceptable.'[24] For an ARD expressing general preferences about future research involvement, a proxy decision-maker would interpret the ARD in relation to specific studies.

Both reports recognised that a person who makes an ARD in favour of research participation may indicate signs of objection to study activities during periods of cognitive impairment. In general, the reports called for respecting such dissent. The Canadian report considered the applicability in the research context of a "Ulysses contract", where a directive instructs that

[21] NBAC referred to this model as a 'Prospective Authorization' and suggested that the higher the risk the more specific the ARD should be to evidence that the person knew of and was willing to accept that risk. The Canadian report described a more general ARD where a person would 'indicate awareness of and consent to the general kinds of research and levels of risk they are willing to undertake once incompetent': Keyserlingk and others (n 18) 350–51.
[22] NBAC (n 20).
[23] ibid.
[24] Keyserlingk and others (n 18) 352.

advance consent overrules objections expressed during periods of incapacity. This type of self-binding directive has mainly been discussed in the context of psychiatric advance directives where a person with episodic illness gives their consent, while capable, to future treatment and instructs that dissent is to be disregarded in favour of treatment.[25] As research may not offer direct therapeutic benefits for a participant, Ulysses clauses were considered inappropriate for ARDs.[26]

NBAC called for nuance in interpreting objections, citing an example of a person with dementia in a longitudinal study who shows distress in relation to collection of a blood sample.[27] Such distress should be heeded by stopping the blood draw but would not warrant excluding the person from the ongoing study; it would be acceptable for researchers, at a later time, to check whether the person would be willing to have the research procedure. This view recognises that personal tolerances and preferences may fluctuate for a participant living with cognitive impairment.

Since these early recommendations for ARDs, other developments have occurred in the past decade. A 2009 consensus statement of the World Psychiatric Association section on old age psychiatry recommended that older people engaged in advance care planning 'should be encouraged to include a statement addressing their wishes concerning participation in

[25] See eg, T Gergel and GS Owen, 'Fluctuating Capacity and Advance Decision-Making in Bipolar Affective Disorder — Self-Binding Directives and Self-Determination' (2015) 40 Int J Law and Psychiatry 92; JK Davis, 'How to Justify Enforcing a Ulysses Contract When Ulysses is Competent to Refuse' (2008) 18(1) Kennedy Inst of Ethics J 87.
[26] Keyserlingk and others (n 18) 349.
[27] NBAC (n 20) Chapter 3, Advance Planning, Surrogate Decision Making, and Assent or Objection.

research'.[28] Alzheimer Europe endorsed ARDs in its position statements on advance directives and the participation of people with dementia in clinical trials:

> Alzheimer Europe encourages the use of advance directives to cover wishes to participate in research (or not participate as the case may be). We feel that allowing consent in this way respects people's right to self-determination and their possible desire to do something constructive which may eventually benefit others with a similar medical condition.[29]

It emphasised that researchers, medical practitioners and proxy decision-makers should respect the wishes set out in an ARD unless, for example, the person expresses dissent in relation to an activity they previously indicated as acceptable in an ARD. Moreover, Alzheimer Europe advocated that '[n]ational governments should put into place legislation recognising the legally binding character of advance directives.'[30]

An international expert panel, comprised of ten experts from Europe, Canada and Australia in areas of clinical research, ethics, law and patient advocacy, recently proposed recommendations for consent to research and data sharing involving people with dementia.[31] The panel endorsed advance research planning processes: 'One means of supporting decision-making is to allow persons to appoint a representative and/or to specify their will

[28] C Katona and others, 'World Psychiatric Association Section of Old Age Psychiatry Consensus Statement on Ethics and Capacity in Older People with Mental Disorders' (2009) 24 International Journal of Geriatric Psychiatry 1319, 1323.
[29] Alzheimer Europe, *Position Paper on the use of Advance Directives*, Clause 31 (2009), <https://www.alzheimer-europe.org/Policy-in-Practice2/Our-opinion-on/Advance-directives> accessed 9 January 2020. See also Alzheimer Europe (n 3). The statement also lists safeguards for ARDs, including that they must be made by a person with capacity to do so, the research must be ethically approved, dissent is respected and a proxy decision maker (if one exists) has a role in ensuring the actual study aligns with the person's wishes.
[30] Alzheimer Europe, *Opinion on the Participation of People with Dementia in Clinical Trials* (2009), <https://www.alzheimer-europe.org/Policy-in-Practice2/Our-opinion-on/Participation-of-people-with-dementia-in-clinical-trials#fragment1> accessed 9 January 2020.
[31] Thorogood and others (n 6). Consumer representatives provided input on draft recommendations.

and preferences in advance.'[32] Within the context of variable legal frameworks that address ARDs and proxy decision-making for research, the panel recommended that consent for longitudinal studies should specify that consent will be respected in the event a participant loses capacity, subject to the participants' dissent or an authorised representative withdrawing consent according to local law.[33] The panel recommended integrating discussions of advance planning for research participation into advance planning for medical or other personal matters; while the legal status of such an ARD may vary it would, at minimum, provide evidence of the person's wishes and preferences to guide decisions by legally authorised representatives, researchers and ethics committees.[34]

B. Ethics Guidelines

1. Australia

Australia's *National Statement on Ethical Conduct in Human Research* encourages researchers to discuss and document views on future research participation with participants who anticipate periods of cognitive impairment:

> The process of seeking the person's consent should include discussion of any possibility that his or her capacity to consent or to participate in the research may vary or be lost altogether. The participants' wishes about what should happen in that circumstance should be followed unless changed circumstances mean that acting in accordance with those wishes would be contrary to the participant's best interests.[35]

[32] ibid 1338.
[33] ibid 1339.
[34] ibid.
[35] National Health and Medical Research Council, *National Statement on Ethical Conduct in Human Research (2007)* (Australian Government 2018), 59, para 4.5.7.

A participant's documented wishes about future participation should be witnessed by a person independent of the research team, ideally someone close to the participant.[36] These provisions contemplate that an ARD could be made in relation to a specific study where details about the research procedures, risks and possible benefits are explained and the person can document their wishes about participation or withdrawal in the event of cognitive decline. The National Statement also recognises that individuals may give broad consent to future uses of data and tissue in research and provides that the 'necessarily limited information and understanding about research for which extended or unspecified consent is given can still be sufficient and adequate for the purpose of consent'.[37]

2. Other examples

In Canada, updates in 2012 to the national ethics statement for human research included provisions for ARDs. While noting that the legal status of ARDs was untested, the Statement considered that ARDs promote respect for persons and established the following principle: 'Where individuals have signed a research directive indicating their preferences about future participation in research in the event that they lose capacity or upon death, researchers and authorized third parties should be guided by these directives during the consent process.'[38] Directives could be made in advance of opportunities to take part in research, or when a participant consenting to a particular study anticipates cognitive decline; 'in the event of ambiguity or imprecision, [ARDs] should be interpreted narrowly.' [39]

[36] ibid para 4.5.8.
[37] ibid 18 para 2.2.14.
[38] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (updated 2018), Article 3.11.
[39] ibid 47.

The 2016 *International Ethical Guidelines for Health-Related Research Involving Humans* states: 'If participants have made advance directives for participation in research while fully capable of giving informed consent, the directives should be respected'.[40] The Guidelines indicate that agreement of a legally authorised representative is not necessary where an ARD authorises participation.[41] However, while the Guidelines refer to an ARD being made by a person capable of giving informed consent, they do not elaborate on whether the ARD must convey consent to a particular study where the person was advised of the risks and benefits of participation.

C. Legal Context for ARDs

1. Australia

To provide context for our survey study of dementia researchers in Australia, we discuss here the extent to which ARDs are recognised in Australian law.[42] Legally, advance directives (ADs) are recognised in all Australian states and territories, either by statute, common law or both.[43] ADs are typically understood as referring to advance decisions about healthcare treatment, however some forms prompt the person to document wishes about other health-related matters.[44] This provides an opportunity to state preferences about research

[40] Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Health-Related Research Involving Humans* (Council for International Organization of Medical Sciences 2016).
[41] The CIOMS Guidelines describe the legally authorised representative as making a decision when no ARD is available: 'When there are no advance directives for research participation for the period of incapacitation, permission of a legally authorized representative must be sought. This permission must take account of the participant's previously expressed preferences and values, if any.' ibid 63.
[42] For comprehensive analysis of Australian legal and ethical frameworks governing the involvement of people with dementia in research, see NM Ries, K Thompson and M Lowe, 'Including People with Dementia in Research: An Analysis of Australian Ethical and Legal Rules and Recommendations for Reform' (2017) 14 J Bioeth Inq 359.
[43] ibid.
[44] For forms and completion requirements across all Australian jurisdictions, see Advance Care Planning Australia, <https://www.advancecareplanning.org.au/resources/advance-care-planning-for-your-state-territory#/> accessed 17 December 2019.

participation, which could then be taken into account by authorised representatives making decisions in the future about including the person in a study.

The Australian state of Victoria explicitly recognises ARDs in legislation that took effect in 2018.[45] The *Medical Treatment Planning and Decisions Act* provides for advance directives for medical care and for research. It defines two types of directives: instructional directives, which set out an express statement of a choice and are meant to be legally binding; and values directives, which state the person's values and preferences.[46] Accordingly, an instructional ARD may document consent or refusal instructions for specific research procedures or activities, while values statements in an ARD could identify acceptable or unacceptable types of research activities or areas of research the person would like to support or would find objectionable. Advance consent to a research procedure as documented in an instructional directive is sufficient to include a person in an ethically approved study and it is not necessary to seek agreement from a proxy decision-maker.[47] For the categories of research covered by the legislation – for example, a trial of drugs, equipment or devices[48] – a researcher 'must make reasonable efforts' to find out whether a prospective participant has made a research directive,[49] such as by inquiring with an appointed proxy decision-maker or the person's family members or doctor. If there is concern that a directive no longer reflects the person's preferences and values, an application may be made to a statutory tribunal for a determination about the validity of the directive.[50] Various directive forms are available on the Victorian Health Department website; to date, an ARD form is not provided but the

[45] *Medical Treatment Planning and Decisions Act 2016* (Victoria).
[46] ibid s 6.
[47] ibid s 75; see also s 12(1).
[48] ibid s 3 for definition of 'medical research procedure'.
[49] ibid s 73(1). This duty applies to researchers who are registered health professionals and failure to do so is deemed to constitute unprofessional conduct: s 73(2).
[50] ibid ss 22–24.

advance care directive form indicates that values and preferences in relation to medical research may be documented.[51]

The Law Reform Commission in the most populous Australian state of New South Wales completed a review of guardianship legislation in 2018 and recommended a new law that would establish a statutory framework for ARDs similar to Victoria's model.[52] In particular, it was recommended that statutory reform should make it clear that a person may consent to research or express refusals or objections in an ARD.[53] The Commission also stated that '[a] precise or scientific description of the research they wish to participate [in] should not be required to give effective consent.'[54]

Statutes in other Australian jurisdictions do not set out explicit provisions for ARDs but contemplate such directions indirectly by requiring authorised representatives to consider any known values and wishes of a person when making decisions about their participation in research. The Australian Capital Territory recently updated its statutes governing powers of attorney and medical decision-making to 'remove barriers to people with impaired decision-making capacity participating in medical research.'[55] A person who wishes to plan for future research may now appoint a Medical Research Power of Attorney who, in making decisions about participation in research must give effect to the person's 'wishes, as far as they can be worked out … unless making the decision in accordance with the wishes is likely to significantly adversely affect' their interests.[56] The power of attorney appointment form

[51] See 'Advance care directive for adults' form, <https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/end-of-life-care/advance-care-planning/acp-forms> accessed 9 January 2020.
[52] New South Wales Law Reform Commission, *Review of the Guardianship Act 1987 – Report 145* (2018) < https://www.lawreform.justice.nsw.gov.au/Documents/Current-projects/Guardianship/Report/Report%20145.pdf> accessed 29 July 2019. See Chapter 11, Medical Research, for discussion of advance directives for research.
[53] ibid 184, 185, 188.
[54] ibid 187.
[55] Legislative Assembly for the Australian Capital Territory, *Powers of Attorney Amendment Bill 2015 Explanatory Statement* (2015) <https://www.legislation.act.gov.au/View/es/db_53083/20151119-62368/PDF/db_53083.PDF > accessed 29 July 2019.
[56] Powers of Attorney Act 2006 (Australian Capital Territory), s 41B(2)(a).

prompts the person to specify directions, limitations or conditions on the attorney's power.[57] If the person was taking part in research prior to the onset of incapacity, the law establishes a statutory presumption that they wish to continue to participate.[58] In the state of Queensland, guardianship legislation governs the involvement of people with impaired decisional capacity in clinical research and experimental care. The guardianship tribunal may not consent on behalf of persons with impaired capacity if they have 'indicated unwillingness to participate' in an enduring document.[59]

2. European context

A developing body of scholarly literature in Europe considers ARDs,[60] which provides a useful comparison with the Australian context. The Council of Europe's Convention on Human Rights and Biomedicine Additional Protocol concerning Biomedical Research enables inclusion in research for adults who lack capacity with the authorisation of a legal representative, who will take 'into account the person's previously expressed wishes or objections.'[61] Andorno and colleagues suggest that such wishes can be seen 'as an element that might complete the consent given by the legal representative of the incapable person, as opposed to an independent basis for' authorising their participation in a study.[62]

The EU Directive on Clinical Trials, which will come into application in 2020, provides for inclusion of 'incapacitated subjects' in a trial if the person gave 'informed consent before the onset of their incapacity' or, in the absence of such consent, on the consent of a legal

[57] See form <https://www.legislation.act.gov.au/View/af/2017-45/current/PDF/2017-45.PDF> accessed 17 December 2019.
[58] Power of Attorney Act (n 56), s 41B(3).
[59] Guardianship and Administration Act 2000 (Queensland) s 72(3)
[60] See eg, S Lötjönen, 'Medical Research on Patients with Dementia – the Role of Advance Directives in European Legal Instruments' (2006) 13 Eur J Health Law 235; R Andorno and others, 'Integrating Advance Research Directives into the European Legal Framework' (2016) 23 Eur J Health Law 49.
[61] Council of Europe, *Convention on Human Rights and Biomedicine, Additional Protocol concerning Biomedical Research* (2005), art 15(1)(iv).
[62] Andorno and others (n 60).

representative.[63] Informed consent is defined to mean 'a subject's free and voluntary expression of his or her willingness to participate in a particular clinical trial, after having been informed of all aspects of the clinical trial that are relevant to the subject's decision to participate.'[64] Where consent is sought from a legal representative, the prospective participant should take part in the consent discussion 'as far as possible'[65] and the representative must give priority to their interests.[66]

In Germany, the *Medicinal Products Act* was recently amended to permit non-therapeutic research involving participants who lack capacity to consent on the basis of an ARD that documents their wish to participate in research.[67] Analysing the interaction of the German law with the EU Clinical Trials Directive, Scholten and colleagues contend that limiting ARDs to specific studies where the research aims, activities, risks, benefits, and protections are known 'sets an unreasonably high standard for disclosure for ARDs'.[68] They argue that ARDs should also enable a person to document their preferences in relation to types of research activities, such as observations, physical measures, imaging and blood samples. A legal representative would then consider these wishes when determining whether the person should participate in a particular study.

D. Empirical Investigations

To date, ARDs have received scant attention in empirical studies to elicit stakeholder perspectives and to provide evidence for implementation. In Wales, researchers conducting a

[63] Regulation (EU) No 536/2014.
[64] ibid art 2(21). Art 29(2)(a)(i) elaborates that informed consent requires, *inter alia,* disclosure of the 'nature, objectives, benefits, implications, risks and inconveniences of the clinical trial', protections for participants and the expected duration of their involvement.
[65] ibid art 31(3).
[66] ibid preamble clause 1.
[67] M Scholten and others, 'Advance Research Directives in Germany: A Proposal for a Disclosure Standard' (2018) 31(2) GeroPsych 77.
[68] ibid 82.

randomised medical care trial among nursing home residents sought the views of residents, their relatives, staff and general practitioners on an advance consent process.[69] The researchers proposed to seek residents' consent to participate in the trial up to one year before their randomisation into the treatment or placebo arm, at which point their decisional capacity could be impaired.[70] Participants had divided views on whether the advance consent would be legally sufficient to permit ongoing participation or whether permission should be sought from an authorised decision-maker for a resident with impaired capacity. In the Netherlands, an interview study of 13 clinical dementia researchers elicited their views on arguments for and against ARDs and their perceived practical utility.[71] Most agreed ARDs would be useful to guide proxy decision-making but not as a binding consent. They also stated that the current dissent of a person with cognitive impairment, as well as disagreement by the proxy, would override wishes documented in an ARD. Most recently, scholars in Germany and Israel conducted focus groups and interviews on the ethical and practical aspects of ARDs with 16 stakeholders in those countries, including dementia researchers, experts in medical law and ethics, and policymakers.[72] Participants felt that ARDs could empower people to express their values and preferences and opined that the proxy role is important to interpret documented wishes and to safeguard the person's current interests during periods of incapacity.

In regard to implementation, two older American studies and a more recent Canadian project examined the feasibility and uptake of ARDs. Over a six-month period in 2000, all patients admitted to a US National Institutes of Health research hospital were given an opportunity to

[69] F Wood and others, 'Consent, Including Advanced Consent, of Older Adults to Research in Care Homes: A Qualitative Study of Stakeholders' Views in South Wales' (2013) 14 Trials 247.
[70] Randomisation would occur when the resident was prescribed an antibiotic, which could be anytime within a one-year window of consenting to be part of the trial.
[71] Jongsma and van de Vathorst (n 16). The interviewees were from fields of neurology, gerontology, aged care medicine, psychiatry and psychology.
[72] Werner and Schicktanz (n 17).

make an ARD and 11% (261 of 2,371 patients) did so.[73] In 2007, results were published from the first randomised controlled trial (RCT) of an ARD intervention targeted to people with dementia and their proxy decision-makers.[74] Patients and their proxies were presented with five hypothetical clinical trials involving varying risk levels and were asked to reflect separately on their views about the patient's participation. The 69 dyads then had a joint interview to discuss their views and prepare a Planning Ahead Together (PAT) document designed to instruct the proxy about future decisions. This study found that patients and their proxies were willing to discuss and document preferences for future research participation, however the experience of completing the PAT document was found not to make a difference in later enrolment decisions about an actual clinical trial and the reported ease of making those decisions. In 2016, Canadian researchers reported on their RCT to promote the uptake of advance directives for treatment and research decisions.[75] Their intervention consisting of educational sessions and personalised facilitation resulted in 80% of older adults in the experimental group making an ARD, a majority of whom documented preferences in favour of future research participation.

III. SURVEY OF DEMENTIA RESEARCHERS IN AUSTRALIA

A. Overview

We undertook a national survey of dementia researchers in Australia that investigated their views and experiences concerning the involvement of people with dementia in studies, including practices for assessing capacity to consent to research, seeking proxy consent and

[73] P Muthappan, H Forster and D Wendler, 'Research Advance Directives: Protection or Obstacle?' (2005) 162 Am J Psychiat 2389.
[74] CB Stocking and others, 'Empirical Assessment of a Research Advance Directive for Persons with Dementia and Their Proxies' (2007) 55 J Am Geriatr Soc 1609. The proxies were typically family caregivers and were not necessarily legally appointed as a decision-maker for health-related matters.
[75] G Bravo and others, 'Promoting Advance Planning for Health Care and Research Among Older Adults: A Randomized Controlled Trial' (2012) 13 BMC Med Ethics 1; G Bravo and others 'Does Promoting Research Advance Planning' (n 8).

positive and negative consequences of ethics review processes (eg, improved protections for research participants; excessive delays). A component of the survey, reported here, focused on ARDs, with the aims of determining researchers' (1) awareness of Australian ethics guidance on advance research decision-making; and (2) attitudes about ARDs, including (i) perceived benefits, disadvantages and acceptability to ethics committees; (ii) willingness to offer an ARD for various research activities; and (iii) factors that should override an ARD. The survey also aimed to determine the proportion and experiences of researchers, if any, who had proposed or used an ARD to involve participants in research during periods of decisional incapacity. Seeking the views of Australian researchers is timely in light of domestic law reform initiatives (discussed above) that aim to provide clearer frameworks for involving people in research who lack capacity to give their own consent.

B. Survey Method

1. Eligibility

Researchers in Australia were eligible to complete the survey if they had experience with the ethical aspects of conducting dementia-related studies with human participants, such as requesting ethics approvals, recruiting participants and seeking consent for participation. An initial survey question confirmed eligibility.

2. Recruitment and data collection

Researchers were identified from publicly available lists of Australian dementia grants awarded by the National Health and Medical Research Council, the Dementia Collaborative Research Centres and the Dementia Australia Research Foundation. A preliminary screen for eligibility was conducted using researchers' institutional profiles. Research collaborators of funding recipients who met the study inclusion criteria were also invited to participate. The

lead author (N.R.) sent emails to 140 researchers with an invitation to complete the online survey. Two reminder emails were sent after three and eight weeks of non-response. Data were collected between November 2017 and January 2018.

3. Measures

The survey questions were informed by current literature on ARDs and relevant Australian ethical and legal principles. The survey was pilot tested with approximately 10 dementia researchers who provided feedback on its content, organisation and flow. The following definition was provided at the start of the survey: 'An advance research directive (ARD) is a written statement of a person's wishes regarding research participation during future periods of incapacity. A person makes an ARD when they have decision-making capacity.'

(a) Researchers' awareness of Australian ethics guidance

Respondents were asked whether the National Statement on Ethical Conduct in Human Research gives guidance on advance research decisions/directives (yes/no/unsure). The Statement does not explicitly refer to ARDs, but as noted earlier, it recommends discussion and documentation of participants' preferences for future participation if cognitive decline is anticipated.

(b) Researchers' attitudes about ARDs

Perceived benefits, disadvantages and acceptability to ethics committees: Respondents were asked about their level of agreement with specific benefits and disadvantages of using ARDs in dementia research on a four-point Likert scale (strongly agree to strongly disagree). A text box allowed them to note any additional benefits or disadvantages. They were asked for their view on the likelihood that the ethics committee they deal with most often would accept an ARD as a valid expression of a person's willingness to participate in research (likely to accept; unlikely to accept; not sure).

Willingness to offer an ARD: Researchers were asked to imagine they were recruiting a person with dementia who has capacity to make research participation decisions but who may experience reduced capacity in the future. Respondents were asked to indicate their willingness to offer the person an opportunity to make an ARD for various research activities. Thirteen research activities were listed, covering varying degrees of risk and invasiveness, such as observing behaviour, accessing medical records, taking blood samples and giving experimental drugs (see Table 4). Willingness was indicated on a Likert scale (would definitely offer, would probably offer, would probably not offer, would definitely not offer, not sure/no opinion).

Factors that should override an ARD: Assuming a person with capacity made an ARD agreeing to participate in research activities during future periods of incapacity, researchers were asked what should override the ARD. They indicated their level of agreement (strongly agree to strongly disagree) with the following options: the person who made the ARD and now lacks capacity expresses objection to a research activity, such as through body language or verbalisation; a family member or carer for the person who made the ARD expresses an objection; a health practitioner for the person expresses an objection; or an ethics committee expresses an objection. They could specify in a text box anything else they thought should override the wishes stated in an ARD.

(c) Researchers' experiences with ARDs

Respondents were asked whether they had used or proposed the use of an ARD to document individuals' preferences for future research participation. While the survey included follow-up questions for those who indicated they had used an ARD, these data are not reported due to the low number of respondents who answered affirmatively to the question about previous use of ARDs.

(d) Demographic items

Respondents were asked to indicate: years of experience conducting research involving human participants, as well as years of research experience specifically with people with dementia; the population focus of their research (people with dementia living in the community, in institutional settings such as a care facility, or a mix of both); whether they have involved people with dementia as co-researchers to assist with study design, data collection, data analysis, or other research activities; discipline of research (eg, medicine, nursing); whether they have served on a human research ethics committee (HREC) and, if yes, their years of experience; the state or territory in which they carry out the majority of their research; and their gender.

4. Data analysis

Survey responses are reported using descriptive statistics, including frequencies and percentages calculated using available data for each aim. Data are pooled for some response options as indicated in each table. Quotations from respondents' comments are included to illustrate further perspectives and experiences beyond the quantitative data.

C. Results

1. Response rate and respondent characteristics

The survey was sent to 135 eligible researchers and 70 usable surveys were returned for an overall response rate of 52%. Slightly fewer respondents (n=63) completed the section on ARDs (47% response rate) and these data are reported here. The survey respondents represent an experienced sample of researchers from a range of disciplines. Over half had at least eight years of experience in dementia-related research and a sizeable minority (37%) had served on a HREC. The survey included respondents from all states and territories in Australia. Table 1 reports key demographic characteristics.

[Insert Table 1 here]

2. Awareness of National Statement guidance

A majority of respondents (66%, n=42) were unsure whether the National Statement contains guidance on advance research decisions/directives; 11% (n=7) said yes and the remainder (n=14) said the Statement does not provide such guidance.

3. Attitudes about ARDs

(a) Perceived benefits, disadvantages and acceptability of ARDs to ethics committees

A majority of respondents – 78 to 87% – agreed or strongly agreed with the possible benefits of ARDs as listed in Table 2. These benefits relate to autonomy in decision-making, informing others of a person's wishes and enabling appropriate inclusion in research.

[Insert Table 2 here]

Just over one-quarter of respondents (27%, n=17) added text box comments that elaborated on the benefits of ARDs. For the person planning for cognitive decline, making a directive would give them 'the benefit of knowing they can contribute to research after they no longer have capacity to consent'. Expanding on the importance of people making their own choices, ARDs could promote 'dignity and respect for the person with dementia' and avoid 'formal and informal "gatekeepers" speaking for the person without considering their preferences.' Further, a valid ARD could help to ensure a 'proxy does not disrespect or overrule' the person's documented wishes either in favour of or against participating in research.

Beyond the benefits for the person who makes a directive, ARDs could 'perhaps provide some formality and protection for [those] involved in facilitating recruitment or obtaining informed consent (eg, researchers, health professionals, family members)'. For researchers, ARDs would allow them 'to undertake their research with the confidence that the prior

consent of the individual has been offered'. At a societal level, the promotion of ARDs could help to raise awareness of research – 'Greater awareness of the role of research in improving the lives of people with dementia' – and 'develop a culture of inclusivity'. It was also suggested that ARDs could streamline ethics review processes: 'The processes of obtaining ethics approval and recruitment should be clearer and less time consuming for the researcher, thus reducing costs of research.'

Respondents had more divided views on the disadvantages of ARDs, as shown in Table 3. Substantial proportions had concerns about ARDs not being available when needed or that ethics committees would not accept ARDs. Few respondents perceived ARDs as less reliable than consent from a proxy decision-maker.

[Insert Table 3 here]

Just over 40% of respondents (42%, n=26) added written text box comments elaborating on potential difficulties with ARDs. Half of those (n=13) noted the importance of periodically reviewing and updating directives to record any changes in preferences, as well as the need for assent processes at the time of study activities to determine, where possible, the person's current wishes about participation. (The survey explored this issue in a later question on what should override an ARD.) Several respondents expressed concern that the practice of using ARDs could create a new form of exclusion from research if ethics committees come to expect them as evidence of a person's wishes: 'introducing this practice [ARDs] could lead to less involvement of people with dementia in research, because once it becomes accepted practice HRECs might require ARDs from all people with dementia as a blanket policy approach'.

However, when asked whether the ethics committee they deal with most often would accept an ARD as a valid expression of a person's willingness to participate in research, over half (56%, n=33) of respondents were unsure. Around a quarter (24%, n=14) believed their committee would be likely to accept an ARD while 20% (n=12) thought the opposite.

(b) Willingness to offer an ARD

As reported in Table 4, a majority of respondents – 57 to 80% – would offer participants an opportunity to make an ARD in relation to a wide range of research activities. Slightly under half (48%) would offer an ARD covering future pharmaceutical studies.

[Insert Table 4 here]

(c) Factors that should override an ARD

When asked about factors that should override an ARD, nearly all respondents (92%, n=54) agreed or strongly agreed that a participant's current objection or dissent should override prior consent stated in an ARD. Written text box comments elaborated on this point: 'An individual may still change their mind and withdraw their consent after an ARD giving consent. It is important that researchers are able to assess 'assent', *i.e.* no visible signs of disagreement or distress in participants.'

Around half of respondents (49%, n=29) thought the objection of a family member or carer should override an ARD. Slightly fewer respondents agreed that the objections of a health practitioner for the person (42%, n=25) or an ethics committee (37%, n=22) should override an ARD. Just over 20% of respondents (22%, n=13) volunteered other circumstances in which an ARD should not be followed, including: changes in ethics norms, such that research agreed to in an ARD is subsequently considered ethically or scientifically unjustified; the risks of participating in a study outweigh the potential benefits; or the validity of the ARD is

questioned, such as ‘clear and compelling evidence that the person signed under duress or when they were already impaired to the extent they would not have been aware of the decision and its consequences.’

[Insert Table 5 here]

4. Experiences with ARDs

Nearly all respondents (95%, n=55) reported they had not used or proposed the use of an ARD as a way to document a person’s preferences for research participation during future periods of incapacity. One respondent who reported use of an ARD noted s/he is part of an international research team and investigators in another country are seeking advance consent at the time of study enrolment for post-mortem brain autopsy. Another respondent reported using an ARD for a project that involved follow-up tests on people with mild cognitive impairment. These examples do not reflect the use of ARDs as contemplated in ethics statement and laws, which refer to directives as evidence of the wishes of a person who is alive but lacks decisional capacity.

D. Discussion of Survey Results

Our survey results reveal insights from dementia researchers, a group whose views and experiences are important to the continued development of legal and ethical frameworks governing research for people with impaired capacity and practical strategies to implement ARDs. Our survey respondents perceived that ARDs would be advantageous, and while ARDs seem rarely used in practice, the respondents expressed a willingness to offer them for a variety of research activities. The key findings are discussed here with suggestions for ethics guidelines, laws and practices to support future work in this area.

1. Awareness about ethics guidance

Australia's National Ethics Statement encourages researchers and participants to discuss and document preferences about involvement in studies during periods of incapacity. However, a majority of our respondents were unsure about the existence of ethical guidance on advance research decisions/directives. Updating the National Statement to refer explicitly to ARDs would provide clearer direction to researchers, ethics committees, participants and proxy decision-makers. The recent study of German-Israeli professionals found that knowledge and familiarity with ARDs was higher in Germany than Israel due to public debate over law reforms to provide for ARDs.[76] In contrast, the ARD term was unfamiliar to many Israeli professionals, since such directives are not mentioned in local laws and policies. Explicit rules for ARDs would be beneficial to provide a solid ethical and legal foundation, augmented by awareness campaigns and resources to support their use, including education for researchers and ethics committees.

2. Attitudes about ARDs

(a) Perceived benefits, disadvantages and acceptability to ethics committees

Our survey findings reveal positive views about ARDs among Australian dementia researchers. The respondents perceived that ARDs would promote individuals' decision-making autonomy, provide helpful evidence of a prospective participant's preferences to guide proxy decision-makers, researchers, ethics committees, and support inclusion in research for people with dementia. These findings resonate with similar benefits highlighted in recent studies of dementia researchers and other stakeholders in other countries.[77] A previous study of proxy decision-makers for people with dementia found that those who strive to 'honor patients' historical values' look for evidence of those values 'whether

[76] Werner and Schicktanz (n 17) 6.
[77] See Jongsma and van de Vathorst (n 16); Werner and Schicktanz (n 17).

expressed in past conversations or behaviors, or embodied in patients' character traits'.[78] For example, in making a choice about her father taking part in a study, one daughter reflected on what he would want: '[W]ould he believe in promoting science and moving forward with knowledge …? Yes. Would he tolerate small amounts of discomfort for a greater benefit? Yes.'[79] ARDs could strengthen this decision-making process by providing written evidence of the person's wishes and reducing speculation about their preferences and recourse to a generic 'best interests' standard.

The most prevalent downside of ARDs cited by our respondents was the practical concern that the time lag between making and needing the directive might mean it cannot be located. This problem could be overcome in the context of dementia research registries and longitudinal studies that recruit participants at pre- or early symptomatic phases.[80] In these circumstances, researchers could engage participants in advance research planning and maintain copies of ARDs to inform future decisions when necessary. To the extent that research planning is incorporated into a process of advance care planning – as done in a Canadian study[81] – the importance of sharing documents with key others and storing copies in an accessible and known location would need to be emphasised,[82] including adding ARDs to electronic health records.

Many researchers were concerned about ethics committees not accepting an ARD as valid evidence of willingness to take part in research. Clear ethical and legal rules for making and using ARDs are important to minimise uncertainty about their status; new legislation in the

[78] E Overton and others, 'Alternative Decision-Makers' Perspectives on Assent and Dissent for Dementia Research' (2013) 21 Am J Geriat Psychiat 346, 351.
[79] ibid.
[80] MM Nuno and others, 'Attitudes Toward Clinical Trials Across the Alzheimers Disease Spectrum' (2017) 9 Alzheimer's Research & Therapy 81.
[81] Bravo and others, 'Does Promoting Research Advance Planning' (n 8).
[82] A recent expert consensus panel on the outcomes of successful advance care planning stressed the importance of directive documents being accessible when needed: RL Sudore and others, 'Outcomes That Define Successful Advance Care Planning: A Delphi Panel Consensus' (2018) 55 J Pain Symptom Manag 245.

Australian state of Victoria, summarised earlier, provides one model. Contrariwise, several respondents worried that ethics committees might come to expect or require ARDs as evidence of agreement to research for participants with cognitive impairment, a drawback that Muthappan and colleagues identified in a prior study of the uptake of ARDs among people admitted to a clinical research hospital.[83] This would be an unintended and undesired outcome of promoting ARDs and training for ethics committees would need to discourage such blanket approaches. Moreover, ARDs should only be referred to in cases where the prospective participant does not have current capacity to consent.

(b) Willingness to offer an ARD

Our results indicate that many researchers would be willing to offer ARDs to prospective participants. As discussed earlier, some sources recommend that ARDs should prompt people to articulate their preferences according to different types of research activities and the levels of risk or burden that may be involved. Our study provides insights into the research activities that researchers believe would be suitable to cover in an ARD. In a separate survey study, we asked people aged 60 years and older attending hospital outpatient clinics (n=174) whether they would want to be included in these same research activities if they had dementia-related cognitive impairment.[84]

The views of researchers were largely consistent with those of older adults, with some exceptions. A majority of researchers stated they would offer an ARD for a wide variety of

[83] Muthappan and others (n 73). All patients admitted to an NIH research hospital were given an opportunity to make an advance research directive. During the six month study period, 11% of the patients (261 of 2,371) completed an ARD. Of these, just 13% said they would not want to be involved in any research during future periods of incapacity. The authors noted that many people might be willing to be involved in research but not formalise their preferences in a written directive. Thus 'proposals to require a formal research advance directive could exclude many impaired adults whose competent preferences supported research participation' (2390).
[84] N Ries, E Mansfield and R Sanson-Fisher, 'Planning Ahead for Dementia Research Participation: Insights from a Survey of Older Australians and Implications for Ethics, Law and Practice' (2019) 16(3) J Bioeth Inq 415.

research activities and older adults indicated they would be willing to participate in a range of research activities if they had dementia. Interestingly, while some literature on ethical issues in dementia raises privacy concerns about wearable devices,[85] our respondents' willingness to offer an ARD was highest for research that would involve wearing a device that tracks behavioural or physiological data. A large majority of our outpatient survey respondents (92%) said they would be willing to be included in this research activity during future periods of dementia-related incapacity.

The researchers' willingness to offer an ARD dropped to just over 60% for the activity of taking blood or other biological samples for genetic or non-genetic research. In contrast, previous studies of the views of older people, including those with a dementia diagnosis, on future research participation during periods of decisional incapacity show that 80 to 90% would be agreeable to blood draws for research.[86] Our outpatient survey found a similarly high level of agreement of over 90% for blood draws for both genetic and non-genetic studies. The extensive debates over the ethics of biobanking and genomics research[87] may influence researchers to hold more conservative views on ARDs for future blood draws than those held by members of the public.

Our survey results add to existing studies that indicate greater hesitance about involving people with impaired capacity in experimental drug studies. Just under half of our researcher respondents (48%) would offer an ARD to a person to express their preferences about future pharmacological research. In our outpatient survey, willingness to be involved in drug studies

[85] F Meiland and others, 'Technologies to Support Community-Dwelling Persons With Dementia: A Position Paper on Issues Regarding Development, Usability, Effectiveness and Cost-Effectiveness, Deployment, and Ethics' (2017) 4(1) JMIR Rehabil Assist Technol e1.
[86] Bravo and others, 'Does Promoting Research Advance Planning' (n 8); J Karlawish, 'Older Adults' Attitudes Toward Enrollment of Noncompetent Subjects Participating in Alzheimer's Research' (2009) 166(2) Am J Psychiat 182.
[87] See eg, C Grady and others, 'Broad Consent for Research with Biological Samples: Workshop Conclusions' (2015) 15 (9) Am J Bioethics 34; T Caulfield and B Murdoch, 'Genes, Cells, and Biobanks: Yes, There's Still a Consent Problem' (2017) 15(7) PLoS Biol e2002654.

during future periods of incapacity attracted the lowest level of agreement: 60% compared to over 90% for all the other listed research activities. In a Canadian trial of an advance research planning intervention, around 65% of older people expressed willingness to be included in a pharmaceutical study if they had severe dementia.[88] Older Americans involved in a longitudinal study on cognitive ageing also reported a lower level of interest in taking part in dementia drug trials compared to other research activities.[89] These findings suggest a need to ensure that recruitment strategies provide accurate information about risks and the safety protections for participants in drug studies.[90]

(c) Overriding an ARD

The survey findings reveal researchers' awareness of the need to balance respect for the precedent autonomy of people who express preferences in ARDs with adequate protections if they are later involved in research when their cognitive abilities are impaired. Most notably, the results demonstrate the importance that researchers place on eliciting and respecting the present-day preferences of a person with cognitive impairment, with over 90% stating that current dissent should override agreement previously documented in an ARD. As discussed earlier, other sources reveal a similar emphasis on seeking assent and respecting dissent. All but one dementia researcher in Jongsma and van de Vathorst's Dutch study said that current dissent should override an ARD.[91] Bravo and colleagues' study in Canada found that nearly 80% of surveyed researchers seek the assent of an older person with cognitive impairment before undertaking a study activity.[92] A US study that examined key informants' views on

[88] Bravo and others, 'Does Promoting Research Advance Planning' (n 8).
[89] M Calamia, JPK Bernstein and JN Keller, 'I'd Do Anything for Research, But I Won't Do That: Interest in Pharmacological Interventions in Older Adults Enrolled in a Longitudinal Aging Study' (2016) 11(7) *PLoS ONE* e0159664.
[90] KN Fargo and others, 'The Crisis in Recruitment for Clinical Trials in Alzheimer's and Dementia: An Action Plan for Solutions' (2016) 12(11) Alzheimers Dement 1113.
[91] Jongsma and van de Vathorst (n 16).
[92] Bravo and others, 'Does Promoting Research Advance Planning' (n 8).

assent and dissent in dementia research emphasised 'the primacy of respecting an individual's objection to participating in research'.[93]

A majority of our respondents indicated an ARD would be more reliable than seeking consent from a proxy decision-maker, consistent with empirical studies that show discordant views between individuals and their proxies about research participation.[94] Yet, half of the respondents thought an objection of a family member or carer should override wishes stated in an ARD. Similarly, Dutch researchers would want consent to research as documented in an ARD confirmed by a decision-maker for the person who lacks capacity.[95] A Welsh study of an advance decision-making process in a nursing home found mixed views on this issue, with facility staff preferring to seek permission from an authorised decision-maker and local GPs believing this to be unnecessary if the resident had given advance consent.[96] Residents and family members had mixed views on whether relatives should be consulted and what should happen if they disagreed with the resident's prior consent to research participation. A point of consensus in the German-Israeli study of professional stakeholders was that 'the role of the proxy remains very important as a safeguard … the proxy needs to balance the patient's [current] welfare and … wishes' stated in an ARD.[97]

The characterisation of autonomy offered by Werner and Schicktanz helps to reconcile the apparent tension between respect for the person who made an ARD and the role of proxies. They describe autonomy 'as being relational, processual, and as self-expression through the support and interpretation of others'.[98] In other words, the proxy, in their relationship with the person with reduced cognitive capacity, could use supported and shared decision-making

[93] BS Black and others, 'Seeking Assent and Respecting Dissent in Dementia Research' (2010) 18(1) Am J Geriat Psychiat 77.
[94] Bravo and others, 'Does Promoting Research Advance Planning' (n 8) .
[95] Jongsma and van de Vathorst (n 16).
[96] Wood and others (n 69).
[97] Werner and Schicktanz (n 17) 5.
[98] Werner and Schicktanz (n 17) 3.

processes to enable the person to articulate their current wishes for as long as possible.[99] Using this approach, neither the ARD nor the proxy alone speak for the participant; rather, her or his contemporary preferences are elicited to guide, but not necessarily dictate, decision-making.

A rule that current dissent must be followed may not, however, take adequate account of the nuances that proxy decision-makers encounter, a point raised some years ago in the NBAC report on research involving people with impaired capacity. Overton and colleagues' study of assent and dissent in dementia research found that some decision-makers would override indications of dissent in situations of 'minor inconveniences or discomforts' where they believed that taking part in the research was consistent with the person's long-held values. For example, if the person with dementia expressed boredom or mild discomfort with a research activity, some decision-makers would encourage them to persist and take part. Black and colleagues suggested that signs of dissent must be respected if they are sustained after efforts to address a participant's concerns.[100]

3. Practical experience with ARDs – a gap to address in future work

Almost no one in our respondent group of experienced dementia researchers had used an ARD. In addition to clearer legal and ethical rules for such directives, there is a need for evidence-informed resources and training to support advance research planning. Further studies are needed that involve key stakeholders, including people with conditions that affect cognition, research participants, proxy decision-makers, researchers and ethics committees.

[99] Findings from a current European research project on supported decision-making in clinical dementia research will be valuable to inform practical strategies in this context: J Haberstroh, F Oswald and J Pantel, 'ENSURE Project: Supported Decision-Making and Capacity Assessment in Clinical Dementia Research' (2017) 1 Innovation in Aging 729. An Australian team has recently produced guidance on supported decision-making for people living with dementia, however it does not focus specifically on decision-making to participate in research: see Cognitive Decline Partnership Centre, *Supported Decision-Making* (2018) <http://sydney.edu.au/medicine/cdpc/resources/supported-decision-making.php> accessed 29 July 2019.
[100] Black and others (n 93).

As a follow-up to this survey study, we are conducting qualitative interviews with a subset of respondents for in-depth exploration of their views on topics including: the content to include in an ARD template, including information to support research literacy (eg, what it means to be a participant, explaining the difference between medical care and research) and how to capture values and instructional statements; whether, and if so when, an ARD should operate as a standalone consent; the use of ARDs by proxy decision-makers; and suggestions for the legal and ethical governance of ARDs.

Well-designed intervention studies are needed to investigate the processes and outcomes of advance research planning strategies. Previous American and Canadian trials used a dyadic approach involving older people and their family carers or proxies, with differing approaches to ARD documentation. The American study asked participants to express their preferences in relation to five hypothetical clinical trials involving varying levels of risk: blood draw for an Alzheimer disease test; blood draw for genetic marker; experimental oral medication; lumbar puncture for Alzheimer disease marker; and intracranial stem cell implant.[101] The Canadian study used a basic ARD template that offered several choices about future research participation: no participation regardless of benefits or risks; consent to research that might offer personal benefits; consent to research with no personal benefits but that might benefit others; or both of the latter options.[102] The template included space for people to note any special interests in or objections to particular areas of research. We agree with Scholten and others' recent suggestion to develop an ARD covering types of research activities,[103] and a template based on the categories used in our survey could be developed. This would allow consideration of a range of research activities, including observations of behaviour, bloods draws for genetic and non-genetic studies, imaging procedures, and physical and

[101] Stocking and others (n 74).
[102] Bravo and others, 'Does Promoting Research Advance Planning' (n 8)
[103] Scholten and others (n 67).

psychological therapy interventions. Preferences for future uses of biosamples and records could also be documented, as recommended by a recent expert panel on consent to dementia research and data sharing.[104]

The impact that ARDs would have on increasing or decreasing research participation remains to be seen, however several study findings suggest they could support inclusion and ameliorate the underrepresentation of people with cognitive impairment in research. In the Canadian RCT study a majority of older people documented preferences in favour of future research participation.[105] An earlier study by Muthappan and others also found that 87% of people who made an ARD expressed willingness to take part in future research.[106] Our outpatient survey revealed strongly positive attitudes among people aged 60 and older in being involved in research during future periods of incapacity and a large majority (79%) expressed interest in making an ARD if they had the opportunity to do so.

E. Limitations of the Survey

The results are limited by the sample size, however the respondents represent an experienced group of dementia researchers with nearly 40% having served on a human research ethics committee. The survey instrument used fixed choice questions and provided optional text boxes for respondents to add comments. Many of them did so, however this method does not allow for detailed exploration of their attitudes and experiences. As noted above, a follow-up interview study will provide additional qualitative data on ARD content and advance research planning processes.

[104] AM Hake and others, 'Concise Informed Consent to Increase Data and Biospecimen Access May Accelerate Innovative Alzheimer's Disease Treatments' (2017) 3 Alzheimers Dement (N Y) 536; A Thorogood, SC Deschenes and BM Knoppers, 'Substitute Consent to Data Sharing: A Way Forward for International Dementia Research?' (2017) 4 J Law Biosci 133.
[105] Bravo and others, 'Does Promoting Research Advance Planning' (n 8).
[106] Muthappan and others (n 73).

IV. CONCLUSION

Effective healthcare and supports for people with dementia depend on high-quality research that involves participants at varying stages of cognitive impairment. The regulation of research involving people with decisional incapacity is increasingly under scrutiny, especially to the extent that laws reinforce exclusion from research and contribute to 'evidence-biased medicine'.[107] ARDs have long been proposed as a way for people to communicate their values and preferences for research participation yet their legal recognition lags behind. Promoting the rights of people with cognitive disabilities means that '[a]dvance decision-making, such as representation agreements and personal planning documents, should be encouraged and facilitated.'[108]

Dementia researchers are a key group to involve in such facilitation and our survey study contributes to a nascent body of empirical research on ARDs. The results showed that Australian dementia researchers perceived a number of advantages to using ARDs and, although few respondents had used ARDs in practice, a majority of respondents indicated they would be willing to offer ARDs for a range of research activities. These results suggest dementia researchers would be receptive to implementing advance research planning processes, which would be enabled by improved clarity and awareness of ethical and legal rules.

In the context of dementia research, ARDs could enable people at early stages of a diagnosis to document their preferences for being involved in research activities as their symptoms

[107] V Shepherd, 'Research Involving Adults Lacking Capacity to Consent: The Impact of Research Regulation on "Evidence Biased' Medicine"' (2016) 17(55) BMC Med Ethics <https://bmcmedethics.biomedcentral.com/articles/10.1186/s12910-016-0138-9> accessed 9 Jan 2020. See also A Thorogood and others, 'Canadian Consent and Capacity Regulation: Undermining Dementia Research and Human Rights?' (2018) 12(1) McGill JL & Health 67; J Cohen-Mansfield, 'Who is Informed and Who Uninformed? Addressing the Legal Barriers to Progress in Dementia Research and Care' (2019) 8(17) Israel J Health Policy Research <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6381665/> accessed 9 Jan 2020.
[108] J Dute, 'Should Substituted Decision-Making Be Abolished?' (2015) 22 Eur J Health Law 315, 318.

progress. The lessons learned from the extensive research and experience with advance care planning can be used to inform strategies to support research planning.[109] In particular, any kind of advance planning should be understood not as a one-time completion of a directive but as an ongoing process of reflection and communication with key others, including proxy decision-makers.[110] A written directive provides valuable evidence of a person's values, wishes and preferences and should be periodically reviewed and updated as necessary for as long as the person is able to do so, including with supportive communication and decision-making strategies.

Table 1: Demographic characteristics (n=63)

Characteristic	Response	% (n)
Years of research experience	1–7 years	26% (15)
	8–15 years	34% (20)
	> 15 years	40% (23)
Years of experience conducting research with people with dementia	1–7 years	45% (26)
	8–15 years	19% (11)
	> 15 years	36% (21)
Population focus of research	People with dementia in community settings	27% (15)
	People with dementia in institutional settings	14% (8)
	Mix of both	59% (33)
Experience involving people with dementia as co-researchers	Yes	46% (29)
	No	54% (34)
Discipline of research	Other*	22% (13)
	Psychology	21% (12)
	Medicine	17% (10)
	Nursing	17% (10)
	Neuroscience	14% (8)
	Allied health	9% (5)
	**Other areas specified were health services research, pharmacy, palliative care, social sciences and arts.*	
Experience serving on a human research ethics committee	Yes	37% (36)
	No	63% (21)
Gender	Female	71% (41)
	Male	22% (13)
	Other/prefer not to say	7% (4)

[109] See eg, G Jimenez, 'Overview of Systematic Reviews of Advance Care Planning: Summary of Evidence and Global Lessons' (2018) 56(3) J Pain Symptom Manag 436; J Bryant and others, 'Effectiveness of Interventions to Increase Participation in Advance Care Planning for People with a Diagnosis of Dementia: A Systematic Review' (2018) 33(3) Palliative Med 262; R Piers and others, 'Advance Care Planning in Dementia: Recommendations for Healthcare Professionals' (2018) 17(1) BMC Palliat Care 88; J Gilessen 'Preconditions for Successful Advance Care Planning in Nursing Homes: A Systematic Review' (2017) 66 Int J Nurs Stud 47.
[110] Sudore and others, 'Defining Advance Care Planning for Adults' (n 12).

Note: Demographic questions were divided between the start and end of the survey; complete demographic data is not available for respondents who did not finish the survey. Frequencies may not add to 63 due to missing data. Percentages are calculated based on number of responses to the specific question.

Table 2: Benefits of advance research directives in dementia research (n=63)

Respondents' agreement with benefits of ARDs	% (n) agree / strongly agree
Enable people to make their own choices about future research participation	87% (55)
Help other decision-makers know the wishes of the person with impaired capacity	87% (55)
Help researchers know the wishes of a person with impaired capacity	84% (53)
Help to include people with impaired capacity in research	81% (51)
Provide HRECs with evidence of the wishes of a person with impaired capacity	78% (49)

Table 3: Disadvantages of advance research directives in dementia research (n=62)

Respondents' agreement with disadvantages of ARDs	%(n) agree /strongly agree
Time lag between person making ARD and losing capacity may mean directive is not available when needed (eg, has been misplaced)	71% (44)
HRECs might not accept ARD as valid evidence of consent	60% (37)
ARD would not adequately protect the interests of person with impaired capacity	42% (26)
ARD are not as reliable as seeking consent from a substitute decision maker for the person with impaired capacity	11% (7)

Table 4: For what activities would researchers offer an ARD to participants? (n=60)

Research activity	Would definitely or probably offer
Putting a device on the body (example: bracelet) that keeps track of information about the person such as their activity level	80% (48)
Testing cognitive abilities (example: assessing memory)	75% (45)
Observation of behaviour	73% (44)
Surveys or interviews	72% (43)
Taking physical measures (example: weight, blood pressure)	72% (43)
Accessing personal records, such as medical records or test results	70% (42)
Accessing previously collected body tissues, blood or other body fluids	63% (38)
Taking a sample of blood or other biospecimen for genetic research (example: to identify genetic risk factors for dementia)	63% (38)
Taking x-rays or scans	62% (37)
Taking a sample of blood or other biospecimen for non-genetic studies (example: for a study investigating a link between infection and dementia risk)	62% (37)
Giving physical therapy (example: massage or other non-invasive therapies)	62% (37)
Giving psychological therapy (example: counselling for anxiety or depression)	57% (34)
Giving experimental medicines	48% (29)

Table 5: Overriding an ARD (n=59)

If a person made an ARD agreeing to participate in research during periods of incapacity, which of the following do you think should override the wishes stated in the ARD?	Agree	Neutral	Disagree
The participant who made the ARD and now lacks capacity expresses an objection to a research activity (eg, through body language or verbalisation)	92% (54)	2% (1)	7% (4)
A family member or carer for the person who made the ARD expresses an objection	49% (29)	24% (14)	27% (16)
A health practitioner for the person who made the ARD expresses an objection	42% (25)	22% (13)	36% (21)
A human research ethics committee expresses an objection	37% (22)	36% (21)	27% (16)

Note: Data are pooled for 'strongly agree' and 'agree' responses and for 'strongly disagree' and 'disagree'