Decision-making capacity for research in schizophrenia

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Abstract

This thesis is a story of a journey into understanding the phenomenon of decision-making capacity for research (DMC-R) in inpatients with schizophrenia and seeing if there are possibilities to enhance it.

It starts with the legal background to the concept of decision-making capacity, the regulation for research participations, and the research already done in the area. It finds a variety of conceptual questions, such as the nature of the DMC-R test itself, the role of insight in DMC-R, and whether the 'therapeutic misconception' really is as central as some have made it out to be.

It tells of my study setting out to measure DMC-R in inpatients in schizophrenia and the associated symptoms with a direct comparison with decision-making capacity for treatment (DMC-T). Half had DMC-R (51%, 95%CI 40-62%) and a third had DMC-T (31%, 95%CI 21-43%), this difference was statistically significant, $p<0.01$. Thought disorder was most associated with lacking DMC-R (OR 5.72, 95%CI 2.01-16.31, $p=0.001$) whereas lack of insight was most associated with lacking DMC-T (OR 26.34, 95%CI 3.60-192.66, $p=0.001$).

Knowing that previous studies doing similar have methodological issues with selection bias it reports the nature of participants and crucially non-participants in the study. It finds that women were far less likely to be recruited than men into the study (OR, 2.36, 95%CI 1.46-3.82, $p<0.001$) and explores reasons for this.

It investigates whether the central measure that I use in the study, the clinician's expert 'judgement standard' of DMC-R is reliable by using an expert-panel evaluation of a range

of actors in the research consent world, finding that group reliability is fair (pairwise kappa=0.68 ('substantial') between my assessments and that of the panel decision).

To explore how research works in practice and the suitability and any means to enhance DMC-R it has a qualitative sub-study exploring the views of clinicians, patients, and carers. It finds that within the process of research consent there are a series of tensions, with clinicians torn between their duty of care and respect for the 'wishes and feelings' of the patient. Patients on the other hand simply want to have the power to make the choice, and are more focussed on experiential reasons for participation in research, than the clinicians who prioritise altruism and academic endeavour. Depending on one's role in the process of research consent one is either assessing or asserting decision-making authority.

It unites all these strands of research to develop a new conceptual model of DMC-R, the 'salience model'. This model incorporates my evidence that DMC is not just time and decision specific, but also *person specific*; the weight given to individual factors within the decision will vary by the individual. It makes policy recommendations for enhancing DMC-R and supporting research in the future.

‘Was aus Liebe getan wird, geschieht immer Jenseits von Gut und Böse.’

What is done out of love always takes place beyond good and evil.

Friedrich Nietzsche

Beyond Good and Evil, Aphorism 153

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Chapter 1. Introduction

Schizophrenia and decision-making capacity for research

Schizophrenia is a common psychiatric condition, with 400,000 people thought to be affected in the UK [1] and costs to society estimated at £36,000 to the public sector per year per person [2]. Current optimal treatment still leads to a high burden of disability [3], and there is an urgent need for more biomedical research [4].

When acutely unwell the main symptoms of schizophrenia comprise delusions, hallucinations, and thought disorder [5]. These symptoms are often classified as *positive symptoms*. For the purpose of this work a delusion is defined as 'belief that is firmly held on inadequate grounds, that is not affected by rational argument or evidence to the contrary, and that is not a conventional belief that the person might be expected to hold given their educational, cultural, and religious background' [5], a hallucination defined as 'a false perception which is not a sensory distortion or a misinterpretation' [6]. Thought disorder is more difficult to define as it comprises a range of disturbances in the form of thought but prominently in schizophrenia these can include 'distorted connections between successive thoughts' [6] and 'loss of the normal structure of thinking' [5].

In addition, there are symptoms classified as *negative symptoms*, normally as a feature of the chronic syndrome and include amotivation or apathy [5]. Patients can also experience neurocognitive deficits [5] as a result of their illness.

There is ample evidence, which I systematically review in detail in Chapter 3 p.40, that the symptoms of schizophrenia can have substantial deleterious effects on both

decision-making capacity for treatment (DMC-T) and decision-making capacity for research (DMC-R). While the evidence suggests that different symptoms can have differential impact on different decisions, there are substantial methodological limitations to the work that has already been done and no previous work has directly compared DMC-R with DMC-T.

Patients with schizophrenia can often be perceived by bioethicists as vulnerable [7], with Research Ethics Committees (RECs) and legislation seen to be there by the UK Government (Department of Health) to protect them from research and researchers [8]. A top priority for RECs and researchers is to ensure that participants' consent to research participation is valid [9]. Participation in research normally requires consent with DMC-R. While there are regulations and procedures to enable recruitment when people lack DMC-R, these are complex (see Chapter 2 – Research when DMC-R is lacking p.22) and may act as barriers to involvement or ethical approval in the first place [10].

This thesis explores the nature of DMC-R in people who have schizophrenia, how it may be enhanced, and the process of research consent in England and Wales (E&W). There were two main ethical and conceptual drivers behind this work, which I name here as the 'moral imperative' and the 'research paradox':

The 'moral imperative'

Schizophrenia's common association with impairments in DMC-R (see my systematic review – Chapter 3 p.40) may impact either researchers' or Research Ethics Committees' decisions about the recruitment of research participants with schizophrenia. There is evidence that, in other disorders, participants felt likely to lack DMC-R are routinely excluded from participation [11, 12].

Equal access to participation in research is a statutory requirement, made available to all NHS patients regardless of disability [13-15]. However, there is a risk that the legislative framework around protection of research participants and its application or assumptions regarding the research consent capability of groups vulnerable to lacking DMC-R may lead to basic rights of autonomy and freedom to participate in research being impinged. Therefore, I submit that there is moral imperative to *both* adequately protect people from the consequences of a decision made when decision-making capacity (DMC) is lacking but also to ensure autonomy is respected and DMC maximised. This means that involvement in research must not be blocked due to assumptions or prejudices regarding the characteristics of the group (in contravention of The Declaration of Helsinki para 13 [16], and Royal College of Psychiatrists – ethics of psychiatric research, para 3 [17]). Given the central role of DMC-R in consent to research, understanding lack of DMC-R in people with schizophrenia, the associated symptoms, the extent loss is decision-specific, and how the individual context might affect DMC-R, is of critical importance.

The 'research paradox'

There is an indisputable need for more research in schizophrenia [4], especially with participants who are detained in hospital, severely unwell, or with chronic illness and prominent negative symptoms – people for whom there is evidence of systemic exclusion from research studies [18, 19]. They are missing from community research [20] or worse are systematically excluded from medical research through study ineligibility [21]. This exclusion leads to a reduced evidence base for understanding the prevention, diagnosis, and treatment of people with schizophrenia when acutely unwell. In practice, the end result can be 'trials of treatment' led by one's doctor when unwell in hospital: pragmatic

n of 1 trials of different treatments extrapolated from the evidence, without the framework or governance of a research trial.

Thus, I submit that there is a 'research paradox':

> 'Protection of people with schizophrenia from involvement in regulated 'research trials' when unwell risks leading to unregulated 'treatment trials' due to a limited treatment evidence base.'

When acutely unwell patients with schizophrenia may be subject to compulsory treatment under the powers of the Mental Health Act 1983 (MHA) therefore not only are these unregulated 'trials', but may be forced 'trials' without any role for patient consent. While clearly there is a need for adequate protections to be in place, and ethics of research involving human participants will mean that there will always be a certain degree of 'research paradox', we should aim to ensure that the degree of protection is appropriate to the context. This means that we need a clear and precise understanding of the scope of the need to protect and regulate human research for specific people in specific situations. Again, given the central role of DMC-R in consent to research, understanding the lack of DMC-R in people with schizophrenia is of critical importance.

Thesis structure, context, and scope

For the purpose of my thesis I focus on the legislative framework in E&W, where my work took place, and any reference to the Courts or law should be assumed to refer to E&W unless stated otherwise. Although I consider research and concepts from different legal jurisdictions, I use the E&W 'judgement standard' definition of DMC defined by the Mental Capacity Act 2005 (as explained in Chapter 2 p. 17). The medico-legal assessment of DMC is my primary focus and my methods will be primarily empirical.

Throughout the thesis references to 'schizophrenia' should be taken to include in scope schizophrenia (as defined by the ICD-10, f20), and other non-affective psychotic illnesses as defined by f22 (persistent delusional disorders), f23 (acute and transient psychotic disorders), f24 (induced delusional disorder), f25 (schizoaffective disorder), f28 (other nonorganic psychotic disorders), and f29 (unspecified nonorganic psychosis) [22]. At times, for clarity, I refer to the expanded definition of schizophrenia and related non-affective psychoses.

For my thesis, I am primarily interested in inpatients being treated for schizophrenia, however further detailed understanding of the concept and phenomenon of DMC-R can have application to all research involving people who undergo an assessment of their DMC-R (see Chapter 9 – 'Salience model' and contested assessments p.231).

In Chapter 2 p.17, I explore the concept of DMC, the regulations and law around research, and conceptual challenges around DMC-R generally and research into schizophrenia, and how these differ from those of DMC-T.

In Chapter 3 p.40, I systematically review the current evidence in DMC-R and DMC-R. I present the limitations of current research in the field and the methodological considerations that research in this field should adopt.

In Chapter 4 p.64, I present the central hypotheses and aims of my thesis, and link these along with the methodological considerations raised in Chapter 3 to my quantitative study designs and methods.

In Chapter 5 p.102, I report the main results from the quantitative study – a comparison of the proportions and symptom/socio-demographic associations of DMC-R and DMC-T.

In Chapter 6 p.123, I report the results from the recruitment selection bias sub-study – an analysis of non-participation and non-approach of people who were eligible to participate in the study and the features associated with each.

In Chapter 7 p.143, I report the results from the reliability sub-study of DMC-R, which evaluates the reliability and external validity of my assessment of DMC-R within the quantitative study.

In Chapter 8 p.154, I report on the study design and results from the qualitative sub-study and how it impacts on DMC-R and research governance.

In Chapter 9 p.199, I develop the conceptual work in the introduction based on the results of the research study and develop a conceptual model of DMC-R named the 'salience model'.

In Chapter 10 p.235, I consider interventions to enhance DMC-R and I summarise my conclusions from the work with reference to the main aims and hypotheses. I conclude with a set of policy recommendations.

Chapter 2. Decision-making capacity for research and decision-making capacity for treatment

What is decision-making capacity?

Decision-making capacity (DMC) is the ability to make a decision which has legal authority when consent is formalised, such as decisions around medical treatment or research. DMC is a legal concept and the final arbiter or 'gold standard' is a decision by the Court. However, psychopathological symptoms are what lead to impairment of DMC and, when finding that DMC is lacking in an individual, these symptoms must be observed to impact on DMC. Thus, DMC is a legal construct underpinned by psychopathology.

It is often argued by bioethicists that a criterion for having autonomy is that one must have the ability to make a *rational* decision (for discussions on this topic see for example [23-27]). Here, DMC is the legal construct of *rational* decision-making ability and its presence operates as the gatekeeper to respect for autonomy in law: Many jurisdictions have laws that can empower an individual acting on behalf of the state to intervene and act as surrogate decision-maker when DMC is lacking. Confirmation that DMC is present ensures that the decisions made by the individual remain their responsibility and intervention by others prohibited, ensuring their autonomy is respected.

This most obviously occurs in the context of treatment, when someone lacking DMC-T, perhaps due to the effects of their mental illness is unable to make treatment decisions and thus the doctors, acting on behalf of the state, assess and act on their 'best interests'. The process of assessment of 'best interests' includes considering the decision the person would have made were they able to make the decision with DMC (see [28] for the process of assessing 'best interests' when considered by the Supreme Court). In

this context, the prevailing concern is to protect the individual from the consequences of a decision that they are not able to make, or are making differently than they otherwise would, due to illness. In contrast, DMC can be used to ensure that decisions made, remain the responsibility of the individual. Using another treatment example, if an individual consents to a surgical intervention and has full understanding of the likely risks and benefits, with DMC-T, then the consequences of this decision are theirs, and theirs alone (providing the surgeon performed their duties with due diligence).

Different legislative regions have separate legal definitions for the abilities which are jointly necessary for DMC. In E&W the legal test is defined by the Mental Capacity Act 2005 (MCA) at sections 2 and 3:

> '2. (1) For the purposes of this Act, a person lacks capacity in relation to a matter if at the material time he is unable to make a decision for himself in relation to the matter because of an impairment of, or a disturbance in the functioning of, the mind or brain.
>
> …
>
> 3. (1) For the purposes of section 2, a person is unable to make a decision for himself if he is unable—
>
> (a) to understand the information relevant to the decision,
>
> (b) to retain that information,
>
> (c) to use or weigh that information as part of the process of making the decision, or

(d) to communicate his decision (whether by talking, using sign language or any other means).

…

(3) The fact that a person is able to retain the information relevant to a decision for a short period only does not prevent him from being regarded as able to make the decision.

(4) The information relevant to a decision includes information about the reasonably foreseeable consequences of—

(a) deciding one way or another, or

(b) failing to make the decision.'

Therefore, there is a requirement for an individual to have the ability to: 'understand' the information relevant to a decision; 'retain' it; 'use or weigh' the information to arrive at a decision; and 'communicate' that decision (this is also known as the 'functional test'). Any deficit or inability to perform any of these abilities must be due to the 'impairment of, or a disturbance in the functioning of, the mind or brain' (this is also known as 'the diagnostic threshold') such as resulting directly from the psychopathology of schizophrenia. The MCA is silent on the definition of these terms, although they have been considered extensively in case law, which the MCA in effect codified. The Code of Practice also, perhaps deliberately, leaves it open to interpretation [29].

Many US states use a similar model – the 'four factor model' of 'understanding', 'appreciation', 'reasoning', and 'expressing a choice' [30-32]. The four abilities of the

MCA are viewed as largely synonymous with the US four factors, with 'use or weigh' incorporating 'appreciation' and 'reasoning' [33].

Assessments of DMC for legal and medical consent are made by clinicians or the court based on the relevant legal test. Such assessments are, ultimately, the 'gold standard' of DMC assessment and, although the court is the final arbitrator, the assessment process itself is delegated mainly to clinicians.

DMC is defined as being decision-specific: Different factors will affect the ability to make different decisions and the presence or absence of DMC for one type of decision does not necessarily imply the status of DMC for other decisions; the same individual may lack DMC for one decision but not another [25]. Decision-specificity is recognised in the MCA test in the following ways:

- The information to be understood and retained is different and tailored for each decision [34].

- The act of 'using or weighing' involves considering this information within the context of its 'reasonably foreseeable consequences' which will vary by decision.

Some specific decisions have tests which are variants of these, based in case law, which are similar to but different from the MCA test on a number of features, these include testamentary capacity, capacity to consent to sexual intercourse, etc. They are mentioned for completeness but will not be explored further here.

DMC is a complex construct: The underlying abilities, e.g. 'understanding' or 'reasoning', can be measured as dimensional or categorical (such as by applying a cut-off). However, in clinical and legal practice a decision must be made that the person has, or lacks, the ability for DMC, making it a binary judgement. DMC can be measured

therefore as either a binary categorical outcome, or on the abilities that are legally defined on continua as follows:

Continuous outcomes

- 'Dimensional scores': use of structured tools to psychometrically assess performance within individual domains of abilities deemed core to DMC (such as the 'four factor model') to return dimensional (continua) scores for each domain.

Categorical outcomes

- 'Judgement standard': clinical or court assessment of DMC returning a binary judgement. This assessment may be framed by legal criteria such as the MCA in the UK or 'four factor model' in the US.

- 'Cut-off standard': applying a cut-off or scoring algorithm to 'dimensional scores'.

Each approach has both advantages and limitations: The 'cut-off standard' and 'dimensional scores' are primarily for research use, and allow for a more detailed exploration of symptoms contributing to DMC vulnerability than the 'judgement standard' permits. **The 'judgement standard' is *the* standard of DMC in clinical and legal practice, although it may be guided by the other two tools. For the purposes of this work the 'judgement standard' defined by the MCA is the standard I shall use as a synonym to DMC**.

A highly influential study, the MacArthur Treatment Competence study [30-32], developed a set of tools for assessing DMC-T using 'dimensional scores' based on the 'four factor model'. These were subsequently condensed into the MacArthur Competence Assessment Tool for Treatment (MacCAT-T) [35] and then adapted for

decisions regarding Clinical Research (MacCAT-CR) [36]. These tools led to an explosion of research into DMC, with many studies measuring DMC using 'dimensional scores'.

Research consent and DMC-R

Regulations around research with human participants are enshrined in domestic law through the common law of consent and sections 30-34 of the MCA. Both have been influenced and guided primarily by the World Medical Association Declaration of Helsinki [16] and also the United Nations Educational, Scientific and Cultural Organisation (UNESCO) Universal Declaration on Bioethics and Human Rights [37].

These declarations dictate that participation in human research requires the consent of participants with DMC-R, and that refusal or objection in an individual regardless of DMC-R must be respected. Research may occur with participants lacking DMC-R, but only with special conditions and permissions attached. Importantly, when DMC-R is lacking, informed consent must be sought from a 'legally authorised representative' and objection from them must also be respected (see below for the incorporation in E&W domestic law). Research with human participants must be reviewed and approved by a Research Ethics Committee (REC) ([16] para 23). In E&W, the review and governance of health research falls under the remit of the Health Research Authority.

Research when DMC-R is lacking

As explained, it is possible to recruit human participants to research studies when DMC-R is lacking. The relevant domestic legislation that applies depends on whether

the study is a Clinical Trial of an Investigational Medical Product (CTIMP) and all other studies (non-CTIMP). The reason for the dichotomy is that their origin in law differs: CTIMP studies are regulated by EU directives incorporated into domestic law through the use of statutory instruments (The Medicines for Human Use (Clinical Trials) Regulations 2004/1031 [38] (the clinical trials regulations 2004) as amended by The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006/1928 [39] and The Medicines for Human Use (Clinical Trials) Amendment (No. 2) Regulations 2006/2984 [40] (see also [10] and [41]). All other studies are regulated by the MCA; Both are influenced by the provisions of the Declaration of Helskinki (paras 25 and 28-29) on the role of consultees and 'legally authorised representatives' when they lack DMC-R.

For the purposes of participation of those lacking DMC-R there are substantial similarities:

In non-CTIMP studies, in order to recruit an individual lacking DMC-R, the researchers must consult a 'consultee' of the patient. Sections 32(2) and 32(3) of the MCA provide for the law regarding researchers (R) in selecting a consultee for (P) the person lacking DMC:

> '(2) R must take reasonable steps to identify a person who—
>
> (a) otherwise than in a professional capacity or for remuneration, is engaged in caring for P or is interested in P's welfare, and
>
> (b) is prepared to be consulted by R under this section.
>
> (3) If R is unable to identify such a person he must, in accordance with guidance issued by the appropriate authority, nominate a person who—

(a) is prepared to be consulted by R under this section, but

(b) has no connection with the project.'

This consultee is therefore selected on the basis of the guidance of the patient if possible and can be someone such as a relative, carer of the individual. Crucially professionals involved in the person's care (such as a nurse, doctor, or paid carer) cannot perform the consultee role. The researcher must ask the consultee 'for advice about whether the person who lacks capacity should take part in the project, and what they think the person's feelings and wishes would be, if they had capacity to decide whether to take part' [29]. Should the consultee or the participant object to participation, then they cannot be recruited to the study.

In CTIMP studies, in order to recruit an individual lacking DMC-R to the study, the researchers must contact a 'personal legal representative' (PLR) of the patient. The process is similar to that of non-CTIMP studies with two important differences: paid professionals can perform the PLR role, and in exception to all other E&W law they in fact *consent* on behalf of an adult participant (see [10] for further exploration of the legal issues and their interpretation by RECs).

These systems for authorising participation in research when DMC-R is lacking are not without their critics (see for example [42] in which the consultee process is criticised for protecting researchers but not being sufficient to protect the interests of people lacking DMC). To my knowledge there is no work looking at barriers to participation in research in schizophrenia specifically through the need for consultee assent or PLR consent. However, there have been studies aiming to recruit in nursing home [43] and general hospital settings [44] in which potential participants suffered from dementia and semi-consciousness and confusion respectively. In these studies, the potential participants'

DMC-R was lacking and in attempting to gain consultee approval they found substantial barriers due to an inability to contact relatives. When relatives were contacted they often refused.

Therefore, there is a legitimate concern that the current regulations around recruiting people into research studies who lack DMC-R may act as a selection bias, in effect discriminating against participation into research and thus breaching the Declaration of Helsinki's own provisions through their adoption (The Declaration of Helsinki para 13 [16]). This legal framework needs to be explored further regarding issues specific to schizophrenia and its suitability and acceptability.

Conceptual issues in DMC-R and research involving participants with schizophrenia

Formulations of DMC-R

Central to any work on DMC-R requires a formulation as to what actually comprises DMC-R. To my knowledge the precise nature of DMC-R has never been the subject of exploration by the court, unlike DMC-T and the aforementioned decisions that have established tests under case law.

Current online guidance from the HRA [45] does not make its own recommendations of the assessment of DMC, rather linking to other guidance [46] which are silent on the assessment of DMC-R. Guidance from the Department of Health and Welsh Assembly is also silent on the test [47] and there is also limited guidance in the REC manual (although it has not been updated since the MCA came into force) [9]. Therefore, there is a need for consideration as to how to frame a decision to participate in research using the 'functional test' of the MCA.

The MacCAT-CR formulation

Although there exist a number of structured tools available for the assessment of DMC (for reviews of these see [48, 49]), I will focus here on the MacCAT-CR which is the most commonly used and studied tool (see Chapter 3 p.40).

The MacCAT-CR is a semi-structured interview, designed according to the framework of the US model of 'understanding', 'appreciation', 'reasoning', and 'expressing a choice'.

It is an adaptation of the MacCAT-T, which assesses DMC-T and was developed by the same authors based on the work of the MacArthur Competence Study [30-32]. The tool returns scores on each of the four abilities, but does not apply cut-offs or a threshold at which these abilities are deemed to be present or absent. The aim of the authors in its design was to measure the abilities psychometrically and in isolation [50]. The MacCAT-CR is purported to be adaptable to different types of research and research methodologies, although it was designed using a randomised-control trial (RCT) as its research paradigm [36], and the specific features of studies of this nature compared to other research types are notable throughout its construction. Areas of particular interest for this work are the construction of MacCAT-CR 'understanding', 'appreciation', and 'reasoning'.

MacCAT-CR 'understanding'

The MacCAT-CR's construction of 'understanding' requires the disclosure and assessment of understanding of the following topics related to the research project: 'Nature of project', 'Primary purpose is research, not individualized care', 'Effect of research methods on individualized care', 'Benefits of participation', 'Risks/Discomforts of participation', and 'Ability to withdraw/received ordinary care'. These are non-specific research features, however with observational or non-therapeutic research, the '[e]ffect of research methods on individualized care' and benefits/risks sections may, depending on the research project, be of limited relevance. The problem here is that rather than being arguably entirely irrelevant, they are relatively unimportant compared to other features (i.e. a research project that involves no change to normal care, but research interviews about childhood experiences, where the risks and benefits are negligible) and there is an associated risk of an over-emphasis on these areas. This could be detrimental to understanding of the true key issues when the person whose DMC-R is

being assessed has limited ability to process new information and thus is distracted by superfluous information.

MacCAT-CR 'appreciation' and the 'therapeutic misconception'

The 'therapeutic misconception' (TM) was first used by Appelbaum in the 1980s [51], to describe an incorrect belief or strong expectation that, when participating in research study, the procedures of the study will work towards their individual therapeutic benefit rather than for the benefit of the research study itself. Although to date there still remains no 'widely accepted definition' of TM [52-54], Appelbaum viewed participation in medical research as a conflict between two drivers: that of the clinical interests of the patient, and that of the need to obtain unbiased research data.

The different agendas of researcher and patient may converge at times, but Appelbaum considered that even within participation in an RCT they are divergent: Although participation in an RCT may allow access to a potentially beneficial new drug, the expectation of the participant may be that the doctor will fix the randomisation so that they will not truly be randomised. This rather extreme formulation may be better characterised as an 'optimism bias' (the cognitive bias that future outcomes for oneself are likely to be positive, see for example [55] for evidence for the phenomenon and a discussion surrounding it).

There has been a substantial body of research into TM and while this area is not uncontroversial, it certainly has been influential. Many studies and conceptual work have explored and supported it as having a core role in research consent, with TM necessary to be overcome for valid consent (see for example [53, 56-61]). However, Kim has been a strong dissenting voice with his work [52, 54, 62] suggesting that rather than TM being

as ubiquitous as has been claimed [63], its apparent prevalence may be due to problems its measurement due to linguistics rather than a true *misconception* of the study information [64]. He found that when the benefits of participation in a research study were explored with participants, they commonly misinterpreted the questions [64] and provided answers which implied but did not necessarily mean TM.

Whether or not TM has the prevalence and impact that it has been purported to have, it has influenced the conceptualization of DMC-R. Kimmelman noted that its prevalence as a concept exploded in early 2000s [53] and I would link this to the time of publication of the MacCAT-CR. The MacCAT-CR 'appreciation' component was clearly designed to target the TM. In the MacCAT-CR manual exploring the concept of appreciation in research Appelbaum focuses on TM [36] and recently Dunn in a review article on TM also confirmed that it 'most closely targets' TM [58].

The MacCAT-CR splits 'appreciation' into three components [36]:

1. 'Subject believes that his or her personal benefits are not the primary objective of the study' (explained as 'Appreciation that the purpose of inviting them to participate in the study is not to optimize their care or well-being. Rather, the goal is to generate new knowledge').

2. 'Subject believes that there is a reasonable possibility that being in the experimental condition may be less personally beneficial' (explained as 'Appreciation that methods actually involved in the study may take precedence of individualized care (e.g., use of placebos, randomized assignment, medication protocols, double-blind procedures, etc.)').

3. 'Subject believes that a personal decision to decline/withdraw will be honored' (explained as 'Appreciation they have an actual ability to decline to participate or

to withdraw at a later time, and still received ordinary clinical care and not otherwise be penalized').

As can be seen the first and second components of appreciation, as formulated by the MacCAT-CR, measure TM. Given that most research into DMC-R has used the MacCAT-CR (as we shall see in the next chapter, Chapter 3 p.40) accordingly TM has since featured centre stage in what is deemed important for valid consent in empirical studies of DMC-R [58, 65].

MacCAT-CR 'reasoning'

The construction of 'reasoning' within the MacCAT-CR assesses the domains of 'Consequential and comparative reasoning', 'generating consequences', and 'logical consistency of choice'. These are perhaps the most conceptually problematic components of the MacCAT tools in general. 'Consequential reasoning' requires the individual to apportion consequences to decision choices, whereas 'comparative reasoning' requires the individual to compare two choices. 'Generating consequences' requires the generation of real day to day life impact of a choice made, that is a reasonable construction of their impact (i.e. not based on a delusional belief). Crucially, this reasoning process, although informed by the disclosed risks and benefits during the 'understanding' section, does not apportion a priority or ranking to them, or indeed specifically require that these are the issues that must be considered. Are there within DMC risks and benefits that *must* be considered or 'used or weighed' in order to have DMC? This needs to be investigated and I explore it further in Chapter 9 p.199.

MacCAT-CR summary

It is important to reflect on the limitations of the MacCAT-CR: it is a psychometric tool designed to measure abilities known to be related to DMC-R, not DMC-R itself and not to be used a substitute for the 'judgement standard'. The structure of the MacCAT-CR may create situations in which the formulation of DMC-R under the MacCAT-CR and the MCA may conflict. I explore this further in the context of worked examples in Chapter 9 – Applying cut-offs to MacCAT scores and the 'trump error' p.199. Given that its assessment of 'appreciation' almost exclusively focuses on TM it may not measure adequately all elements of 'appreciation' necessary to have DMC-R using the MCA model (see my development of 'appreciation' in Chapter 4 – DMC-R p.83 and exploration of conceptual models of DMC-R 'use or weigh' based on my results in Chapter 9 – Delving deeper into 'use and weigh' under the MCA p.225).

Earlier in this chapter I have reported that previous work using both the 'judgment standard' and 'dimensional scores' using the 'four factor' model of DMC-T has considered 'appreciation' and 'reasoning' largely synonymous with 'use or weigh' under the MCA [33]. I argue here, there is reason to be sceptical regarding the degree of synonymy between the MacCAT-CR's formulation of 'appreciation' and 'use or weigh' under the MCA for DMC-R.

Formulating an MCA model of DMC-R

What needs to be understood – valid consent vs DMC-R

Studies use patient information sheets to explain the information needed to be understood by the participant. A review of the guidance of content regarding participant

information sheets [66] suggests that they are performing two roles for the REC: that of explaining to participants what they may reasonably expect should they participate in research, and that of the information that they need in order to 'base an informed decision'. This is as expected given their separate requirements for providing both sufficient information for valid informed consent and the essential information to be understood in order to have DMC. Therefore, the scope of the information to satisfy 'understanding' for DMC-R may be substantially more circumscribed than that in the information sheet. The guidance pithily explains:

> 'The content of your Participant Information Sheet (PIS) should describe clearly what a potential participant should expect if they agreed to take part in your study. You should simply provide sufficient and appropriate information on which they can base an informed decision.' [66]

But later clarifies:

> **'**Participant Information Sheet - What's involved
>
> This section should introduce more detailed information that will allow potential participants to make a decision: to agree to take part in your research or to decline.
> It should provide clear information on the essential elements of the study, such as:
>
> • The condition or treatment under study;

• For studies involving therapeutic interventions, clarity on which elements of your study are research and which constitute standard care;

• Alternatives to participation (particularly important in therapeutic trials involving patients);

• What will happen to participants during and after the research study;

• The potential benefits and risks / inconveniences or restrictions they might expect;' [66]

The latter section would seem to lay out the essential information that one might consider would comprise DMC-R. It is interesting to note here that the condition or treatment under study forms part of this, but not the intended benefit to the research itself. However, it is also important to note that:

'The level of detail should be appropriate to the nature and burden of the study.

For example:

• You can explain a questionnaire study may be summarised on the front of the questionnaire itself, and completion of the questionnaire would be regarded as consent:

Whilst

> • The Participant Information Sheet for a Clinical Trial of an Investigational Medicinal Product (CTIMP) will need to be significantly more detailed.
>
> …
>
> Consent arrangements must match the study's burden and risk/benefit profiles as well as the complexity of the protocol. ' [66]

As evidenced here, the RECs seem to be taking a risk based (proportionate) approach to valid consent as they are in effect clearer and more robust consent procedures for more risky research, which would also imply more robust DMC-R assessment procedures. However, I would argue that while more information is being provided for the more risky or complex research, and there is a requirement for more robust consent, neither written guidance helps us with a clear definition of the information to be understood. Rather it would appear that unless covered by the individual REC when reviewing the research application, this decision is left up to the person obtaining consent to decide. In effect this is similar to what occurs in assessments of DMC-T, although again many cases regarding DMC-T have been considered by the courts meaning more explicit guidance has been laid down.

Insight in research

Insight is a clinical concept which does not feature explicitly in the legal tests for DMC (although it is arguably subsumed within 'appreciation'). Insight has been defined as having 'three dimensions: (a) awareness of illness, (b) the capacity to relabel psychotic experiences as abnormal, and (c) treatment compliance' [67]. We know that lacking

insight into one's illness is very strongly associated with lacking DMC-T and to a lesser extent DMC-R (as my systematic review will demonstrate in Chapter 3 p.40). Is it possible for a person to validly consent to participation in a research project if they do not believe themselves to have the condition being studied? Is insight into one's illness necessary in order to be able to 'use or weigh' within DMC-R?

Focussing on DMC-T to begin, the relation between insight and DMC-T poses particular conceptual difficulties [68] because a key component of a person's autonomy is the right to refuse treatment when one has DMC-T. In effect, this means that the individual, whose decision-making is unimpaired, has the right for their disagreement with their clinician concerning the nature or treatment of their illness to be respected. Yet lack of insight is a clinical phenomenon which comprises non-acknowledgement of illness [67], due to a *specific pathological process of the illness itself*, and which often manifests itself as treatment refusal. A judgement as to whether treatment refusal stems from the personal preferences and beliefs of someone with DMC-T or from lack of insight depends, primarily, on the judgement of the clinician [68]. In the context of a person with a severe mental illness who is refusing treatment, there are understandable legal concerns if treatment refusal is equated with lack of DMC-T. At the same time, lack of insight is a common and core element of psychosis [67], which can, have a substantial impact on DMC-T. These conceptual complexities are a natural corollary of mapping a medico-legal test onto clinical concepts.

The role of insight in research decisions poses an entirely different challenge. With therapeutic research, one could argue that the role of insight in DMC-R will be as in DMC-T as both consider the risks and benefits of a therapeutic intervention. There will also be additional considerations regarding the research paradigm and TM may feature. With non-therapeutic research this may differ. Given that there is no direct therapeutic benefit, is insight into one's illness, or indeed recognition that one has the illness being studied, necessary to be able to 'use or weigh'?

Therefore, the role of insight in DMC-R remains unknown. Given that there is a high prevalence of people with schizophrenia lacking in insight [69] understanding the role of insight in DMC-R is central to both the 'moral imperative' and tackling the 'research paradox'.

Can DMC-R in schizophrenia be enhanced?

Given the 'moral imperative' behind this work, and the aforementioned problems of the research regulations when people lack DMC-R, a priority is to explore methods of supporting or enhancing DMC-R in people with vulnerabilities in it. Treaties such as the UN Convention on the Rights of Persons with Disabilities [70] (which the UK has ratified) require that nation states take a supported decision-making approach to people with mental disorder even if severe; however, there is little research on how this might be realised in relation to clinical research.

Previous work in the field of enhancing DMC-R for people with a range of disorders has mainly concentrated on interventions aimed at supporting understanding; there have been several reviews of interventions in DMC [71-73], with one focussing specifically on DMC-R, Flory 2004 [73] (for a conceptual overview of the field see [74]).

Flory characterised in his review different types of interventions as '(1) multimedia, (2) enhanced consent form, (3) extended discussion, (4) test/feedback, and (5) miscellaneous.' [73]. All interventions were aimed around improving 'understanding' and their outcomes were based on 'understanding' scores: Multimedia interventions presented information in different forms to facilitate understanding, enhanced consent forms simplified the information and how it was presented, extended discussion involved further discussion and education regarding the study with a neutral educator or member of the study team, and in test/feedback participants were tested on study information and incorrect answers fed back to them. All of these, in effect, are educational interventions based on clarity and repetition of information. Although the results from Flory are not strictly generalizable to this work as a range of diagnoses are considered, and he reported several limitations to the methods used to study them, he found that there was limited benefit for all interventions with the exception of extended discussion.

Following Flory's review, specifically in the field of schizophrenia, studies have found empirical support for the effect of interventions enhancing 'understanding' either through the use of multimedia [75, 76] or computerised presentation of simple information [77].

To my knowledge, there have been no interventions to date designed specifically around the ability to 'use or weigh', as seen all studied so far have targeted 'understanding' (see also [74]). Therefore, as part of this work, it is logical given the mixed evidence to explore further neurocognitive interventions to support 'understanding' in the inpatient setting, there is a need to explore the possibility of enhancing DMC-R through supporting the ability to 'use or weigh'.

Prominent features of schizophrenia can be paranoia and persecutory beliefs [5]. Requests to take part in human research would seem instinctively to be fear or *paranoia* inducing (using here the lay definition of paranoia). There is a central role of trust in any consent setting (for an exploration of the area see [78]), therefore I hypothesise one method to support 'use or weigh' may involve supporting or enhancing 'trust'.

An intervention to enhance cognitive function (working and verbal memory) would provisionally involve presenting information to participants in 'chunks' (categorizing and grouping information to reduce the sets of information that needs to be attended to) and to present information through different perceptual pathways such as in simple diagrams or icons rather than written or spoken words. This intervention would support the 'understanding' component of DMC-R. The intervention could take the form of a manual to guide the presentation of information to people with psychosis and design of participant materials in those with neurocognitive deficits.

An intervention to ameliorate the psychopathology, in particular 'trust', would provisionally involve other people being present to help support decision-making, as selected by patients being a 'person whom the patient trusts'. They would be invited to

take part in the consent for research process at an early stage, with the aim to ameliorating consequences of the positive psychopathology, such as suspiciousness or paranoia (supporting the ability to 'use or weigh'). The intervention could take the form of a manual guiding the consent process with supported decision-makers present.

Summary

In this chapter I have described the legal and conceptual framework around DMC-R in schizophrenia, the questions and controversies regarding the formulation of DMC-R in this setting, and the evidence around enhancing DMC-R and my hypotheses around interventions. In the following chapter I review the current evidence surrounding DMC-R and DMC-T in schizophrenia and its limitations with a view of developing the framework for my investigation.

Chapter 3. A systematic review of decision-making capacity for treatment and research in schizophrenia and other related non-affective psychoses.

Review objective

The objective of my review was to explore proportions and clinical associations of DMC in people with schizophrenia using the three standards of 'dimensional scores', 'cut-off standard', and the 'judgement standard'.

My research questions were:

1) What proportion of people with schizophrenia have DMC for specified civil decisions (such as treatment or participation in research) in specified settings (e.g. inpatient, outpatient)?

2) What are the associations with DMC for civil decisions? I pre-specified associations of interest as: positive symptoms, negative symptoms, general symptoms of psychosis, neurocognitive symptoms, affective symptoms, awareness of illness (insight) and socio-demographic variables (age, sex, ethnicity, and educational level).

To my knowledge there have been two previous systematic reviews into DMC in schizophrenia, rather than in conjunction with other diagnoses such as dementia or bipolar affective disorder [79, 80]. However, both these reviews focused primarily on comparing dimensional DMC scores in those diagnosed with schizophrenia and in 'normal controls', finding that people with schizophrenia did less well.

Methods

Eligibility Criteria

I included studies published in English which assessed the DMC of samples of people over the age of 18 diagnosed with schizophrenia or related non-affective psychotic illness as defined by ICD-10: f20-f29 [22] (excluding f21 'schizotypal disorder' which can be considered to be a personality disorder and has only some of the features of schizophrenia [5]) or 295, 297, 298 DSM-IV [81]. I included studies measuring DMC or domains of DMC using the three approaches described in Chapter 2 – What is decision-making capacity? p.17: the 'judgement standard'; 'cut-off standard'; or 'dimensional scores'. I excluded non-civil assessments of DMC (such as fitness to plead).

Search

I used OVID to search Embase, Ovid MEDLINE (R), and PsycINFO. My search string was chosen following several trial iterations of searches to maximise the sensitivity of the search, given that 'capacity' has multiple homonyms. My final search string was a title and abstract search of: (capacity or competence or competency or 'decision making' or 'decision-making') AND (schizophrenia or psychosis or 'mental illness' or 'mental disorder' or psychotic). The search was completed on 16/02/2015, with results exported to Endnote X7. The citation search was performed on 17/07/2015, with all steps in both searches performed by myself.

References reporting data from the same study were excluded unless the samples were mutually exclusive. Exclusion occurred at the data extraction stage and following correspondence with the authors. In these cases the reference best suited to the review

was selected by myself for retention within the final selection. In addition, if multiple references reported complementary analyses of the same sample they were treated as one reference in the final analysis.

Data collection and data items

I extracted all data using a data extraction form which specified: population studied and associated demographics; nature of decision for which DMC was assessed (whether it was for a decision related to the present disorder, such as treatment for schizophrenia rather than treatment for another unrelated medical condition, and, in the case of DMC-R, whether it was for hypothetical or real study involvement); outcome of the DMC assessment (proportions from studies using 'judgement standard' and 'cut-off standard'); effect sizes for any associations between DMC and variables of interest. Only summary data, rather than data on individual items of tools was extracted from studies. The only exception was item G12 on the Positive and Negative Syndrome Scale (PANSS) [82] 'lack of judgement and insight', which I chose to include, given that this was the primary measure of insight used in several studies.

Statistical analysis

Confidence intervals (95%) were calculated for proportions of DMC following 'judgement standard' or 'cut-off standard' using the Wilson score interval. Odds ratios and correlation coefficients were converted into effect sizes (ES) for my principal summary measure. Given that some studies were able to detect very small ES, I modified the Cohen criteria [83] to: >0 to $\leq$0.3 small ES, $\geq$0.3 medium ES, and $\geq$0.5 large ES.

I aimed to meta-analyse the proportions of people with DMC as measured by the 'judgement standard'. For studies to be eligible for the meta-analysis for DMC, they needed to test DMC for similar decisions (e.g. DMC-T for treatment of the present disorder) within a homogenous setting (e.g. solely inpatients or outpatients) and without other factors likely to bias the result as decided by myself (e.g. not systematically excluding detained or severely unwell people). Meta-analysis of proportions was performed using Stata 14 (StataCorp, Texas). Given the residual heterogeneity between studies, a random effects model was used.

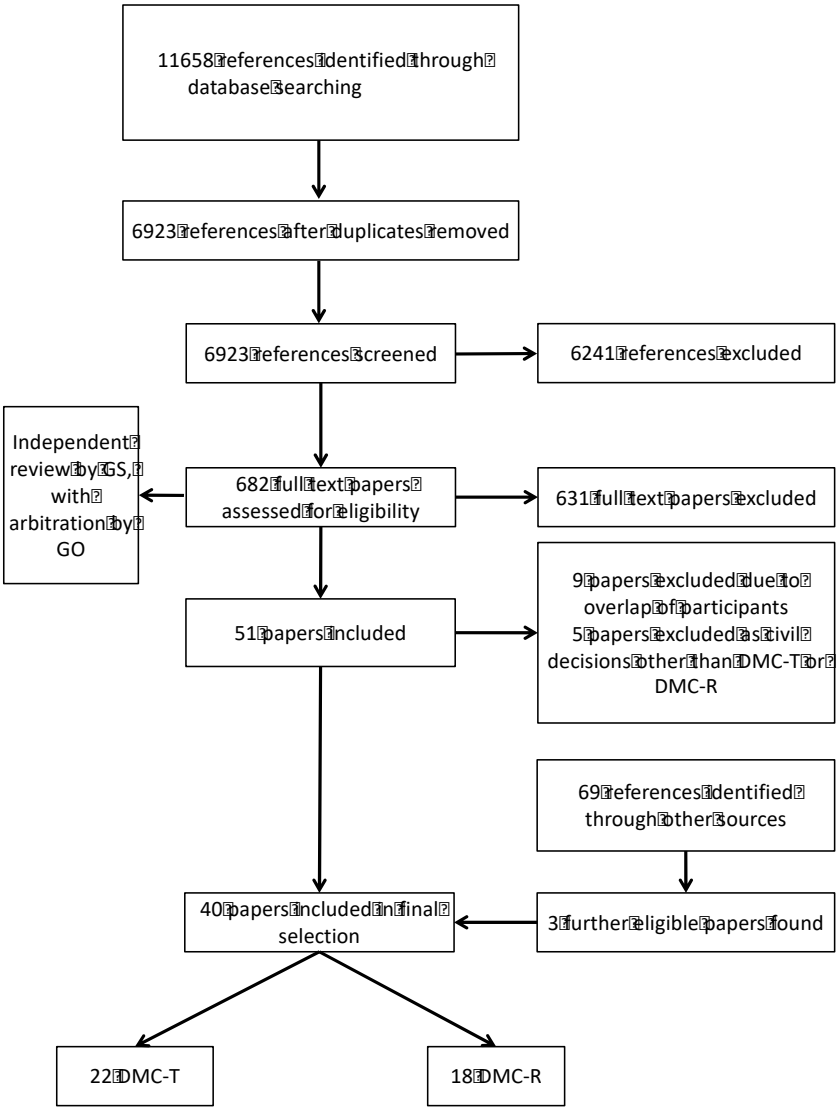
Risk of bias assessment

To my knowledge there has been no prior attempt to appraise quality in DMC studies. I considered certain factors to be important based on my clinical experience when reviewing studies on DMC. These included: 1) the exact nature of the decision for which DMC is being assessed (whether it was real, hypothetical, related to the present disorder – schizophrenia or wholly unrelated), as this may impact on effect of symptoms of schizophrenia on DMC (for example, whether insight into illness is relevant to the decision, whether the decision was cognitively demanding, etc.); 2) homogenous setting of recruitment (either all inpatients or outpatients and thus controlling for hidden confounders in these settings); 3) ability to recruit people with a range of severity of illness within a specified setting, given that this would likely impact on DMC (for example, were people deemed to be 'too unwell' systematically excluded from the sample). I developed a risk of bias assessment based on these which demonstrated critical risk of bias for the majority of studies. As I wanted to provide an overview of the literature, I decided to exclude a risk of bias assessment from my review, but I comment further on the quality of research in the discussion.

Results

Of 11658 references screened from titles, 682 references went to full text review, and 40 met my inclusion criteria (see Figure 1 below) [30-33, 35, 75, 77, 84-122]. A clinician with expertise in the field (GS) performed an independent review of all 682 references applying the inclusion and exclusion criteria. Inter-rater reliability between myself and GS was high (K=0.80). Disagreements were resolved following discussion between myself and GS, while any unresolved disputes went to GO, my PhD supervisor, as final arbiter (n=3).

Figure 1 – PRISMA flow chart



Heterogeneity between studies was high, with considerable variation in study design, population, measurements and the nature of decision for which DMC was assessed (see Table 1 p.46). Many studies reported only partial data for the outcomes of interest, while the studies assessing DMC using a 'judgement standard' rarely presented any associations with my pre-specified variables of interest. Results from all studies and characteristics are available in Appendix 2 – Table 29 p.254. Most studies assessed psychopathology using either the PANSS or Brief Psychiatric Rating Scale (BPRS) [123]. Many studies used a range of diverse individual neurocognitive sub-tests from various test batteries (such as the Wechsler Adult Intelligence Scale - III (WAIS-III [124]) without a summary score provided. These individual results were not extracted, given the difficulties in direct comparison between studies.

Given the limited numbers of studies investigating decisions other than DMC-T and DMC-R (n=5), I limited my review to treatment and research (n=40). These five studies considered DMC for organ donation [122], making a psychiatric advance directive [119-121], and DMC to manage one's own finances [125].

Table 1 – Main characteristics of studies

DMC-T or DMC-R	Standard used	Decision related to schizophrenia	Population setting	Decision to be made by participant	Format of assessment	Associations reported	Other Features	Title
DMC-T	Expert Judgement	Related	Mixed	Current psychiatric treatment with medication.	Clinical assessment under the critera of the MCA and structured using the MacCAT-T.		Mixed inpatients and outpatients under forensic services	Skipworth 2013
			Inpatients	Treatment in hospital with ECT.	Clinical assessment (no further details).		Inpatients requiring ECT.	Bean 1994
					Clinical assessment (no further details).		Patients who received ECT without consent.	Chiu 2014
				Current psychiatric treatment.	Clinical assessment (no further details).		Referred to the Court for determination of lack of competency to refuse or consent to treatment forensic population.	Veliz 1987
				Current admission and psychiatric treatment.	Clinical assessment under the criteria of the legal precursor to the MCA and structured according to this.			Bellhouse 2003
				Current psychiatric treatment with medication.	Clinical assessment under the criteria of the legal precursor to the MCA and structured and structured using the MacCAT-T.			Cairns 2005
				Either current admission or psychiatric treatment in hospital.	Clinical assessment under the criteria of the MCA and structured using the MacCAT-T.	SAI, BPRS.		Owen 2009/11
		Unrelated	N/A	Physical health treatment in a medical hospital.	Clinical assessment using criteria based on early precursors to the four factor model, unstructured.		Medically unwell in a physical health hospital referred for determination of DMC-T for medical treatment.	Weinstock 1984
		Unclear	Mixed	Routine blood test.	Clinical assessment under the criteria of the legal precursor to the MCA and structured according to this.		Decision for a blood test - unclear degree related.	Wong 2000
	Cut-off	Related	Inpatients	Current psychiatric treatment.	SSICA.	Socio-demographics.	Guardian also needed to agree in order to participate in study.	Di 2013
				Current admission and psychiatric treatment.	Tool assessing early precursors to the four factor model.		No detained patients.	Norko 1990
		Unrelated	Outpatients	Hypothetical medical vignette involving a toe amputation or femoral bypass in non-healing toe ulcer.	ACCT.		≥ 60 years old.	Moye 2008

Table 1 (continued 2/4)

DMC-T or DMC-R	Standard used	Decision related to schizophrenia	Population setting	Decision to be made by participant	Format of assessment	Associations reported	Other Features	Title
DMC-T	Four Factor Scores	Related	Outpatients	Current psychiatric treatment with atypical antipsychotic medication.	MacCAT-T.	PANSS, BPRS, DRS, socio-demographics.	Outpatients, although most living at community assisted living facilities. ≥ 40 years old.	Palmer 2004
				Current psychiatric treatment.	MacCAT-T.	SUMD, PANSS, BDI, socio-demographics.	No treatment changes for the past month.	Capdevielle 2009
				Current psychiatric treatment with antipsychotic medication.	MacCAT-T.	PANSS, BDI, socio-demographics.	No treatment changes for the past month.	Raffard 2013
			Inpatients	Current psychiatric treatment.	MacCAT-T precursors	BPRS, VCF, socio-demographics.	Clinicians requested really unwell people to not be recruited.	Grisso 1995
					MacCAT-T.	BPRS, socio-demographics.		Grisso 1997
					MacCAT-T.		Within two weeks of admission when clinician has determined them able to cooperate.	Koren 2005
				Maintenance antipsychotic treatment following discharge from hospital.	MacCAT-T.	G12 PANSS insight, PANSS, MADRS, socio-demographics.	Before discharge from hospital.	Wong 2005
	Cut-off & Expert Judgement	Related	Inpatients	Current psychiatric treatment with medication.	Clinical assessment under the criteria of the four factor model, unstructured, MacCAT-T.	Socio-demographics.	No detained patients.	Vollmann 2003

Table 1 (continued 3/4)

DMC-T or DMC-R	Standard used	Decision related to schizophrenia	Population setting	Decision to be made by participant	Format of assessment	Associations reported	Other Features	Title
DMC-R	Cut-off	Related	Outpatients	RCT of adjunctive therapy to usual antipsychotic regimen.	mESC.	BPRS, MMSE.	Already recruited to the parent study (deemed to have DMC-R).	Fischer 2013
			Mixed	RCT of atypical antipsychotic medication.	MacCAT-CR.	BIQ, PANSS, HAM-D, neurocognitive Z score, DRS, socio-demographics.	Mixed outpatient and inpatients, including board and care homes. Aged ≥50.	Dunn 2007
	Four Factor Scores	Related	Outpatients	fMRI study of decision-making capacity.	MacCAT-CR.		Outpatient study recruiting from board and care homes.	Eyler 2005
			Mixed	RCT of antipsychotic medication.	MacCAT-CR.	BPRS, RBANS.		Carpenter 2000
				CATIE study (naturalistic antipsychotic treatment study).	MacCAT-CR.	PANSS, neurocognitive Z score, socio-demographics.	Mixed inpatients and outpatients already recruited to the CATIE study (having suboptimal antipsychotic treatment) and passing a MacCAT-CR based DMC-R threshold (U ≥ 16).	Stroup 2005
				Observational study of tardive dyskinesia and other side effects of atypical antipsychotic medications.	MacCAT-CR.	BIQ, PANSS, HAM-D, neurocognitive Z score, socio-demographics.	Mixed inpatients and outpatients, some in board and care homes. Aged ≥ 40.	Palmer 2006
			Inpatients	RCT of antipsychotic medication.	MacCAT-CR.	BPRS, VCF.	Long stay patients on a research ward with schizophrenia.	Kovnick 2003
		Unclear	Outpatients	RCT of cognitive enhancement medication.	MacCAT-CR.	PANSS, MMSE, socio-demographics.	Aged ≥60.	Palmer 2005
					MacCAT-CR.		Recruited before medication free period as an inpatient for treatment of schizophrenia. Only data on correlations is effect of interventions.	Moser 2005
					MacCAT-CR.		Only data on correlations is effect of interventions.	Moser 2006
				fMRI study of decision-making capacity.	MacCAT-CR.	PANSS, socio-demographics.	Outpatient study recruiting from board and care homes.	Eyler 2007
			Mixed	RCT of cognitive enhancement medication.	MacCAT-CR, ESC.	RBANS.		Moser 2002

Table 1 (continued 4/4)

DMC-T or DMC-R	Standard used	Decision related to schizophrenia	Population setting	Decision to be made by participant	Format of assessment	Associations reported	Other Features	Title
DMC-R	Four Factor Scores	Unclear	Inpatients	RCT of cognitive enhancement medication.	MacCAT-CR, Clinical assessment of audio-tapes of MacCAT-CR but no absolute scores reported.	G12 PANSS insight, PANSS, CGI, MMSE.	Members of a hospital based therapeutic community. Stable patients.	Lan 2013
		Unrelated	Mixed	RCT for an antibiotic for sore throat vs an established treatment.	MacCAT-CR.	PANSS, MMSE, socio-demographics.		Candilis 2006/08
		Two studies one related one not	Inpatients	Two studies: 1) RCT of antipsychotic medication; 2) Ketamine PET scan study.	MacCAT-CR.			Cohen 2004
		Not reported	Inpatients	Hypothetical clinical trial – no further information.	Clinical assessment (no further details or absolute scores reported), MacCAT-CR.	FAB, ACE.	Voluntary inpatients admitted for > 6 months.	Linder 2012
	Four Factor Scores & Expert Judgement	Unclear	Outpatients	RCT of cognitive enhancement medication.	MacCAT-CR, clinical assessment based on reviewing the MacCAT-CR records using the criteria of the four factor model.	PANSS, HAM-D, RBANS, socio-demographics.	Outpatients aged >40.	Jeste 2009

Legend: ACCT, Assessment of Capacity to Consent to Treatment Interview, ACE, Addenbrooke's Cognitive Exam, BDI, Beck Depression Inventory, BIQ, Birchwood Insight Questionnaire, BPRS, Brief Psychiatric Rating Scale, CGI, Clinical Global Impression, DRS, Mattis Dementia Rating Scale, ESC, Evaluation to Sign Consent, FAB, Frontal Assessment Battery, HAM-D, Hamilton Depression Rating Scale, MacCAT-CR, MacArthur Competence Assessment Tool for Clinical Research, MacCAT-T, MacArthur Competence Assessment Tool for Treatment, MADRS, Montgomery-Åsberg Depression Rating Scale, mESC, Modified Evaluation to Sign Consent, MMSE, Mini-Mental State Exam, PANSS, Positive and Negative Syndrome Scale, RBANS, Repeatable Battery for the Assessment of Neuropsychological Status, SAI, Schedule for the Assessment of Insight, SSICA, Semi-structured inventory for competence assessment, SUMD, Scale to assess Unawareness of Mental Disorder, VCF, Verbal Cognitive Functioning.
NB – many studies also reported on individual neurocognitive sub-tests from various test batteries, these are not presented in this table.

Performance on different standards of DMC

Proportion of DMC-T in studies using 'judgement standard' and 'cut-off standard'

Ten studies reported the proportion of DMC-T amongst participants when using the 'judgement standard' [33, 84-87, 89-93, 117], while three studies used the 'cut-off standard' [88, 110, 111]. Characteristics and results from all studies providing data on 'judgement standard' or 'cut-off standard' of assessment are presented in Table 2 p.51 (Chiu 2014 and Norko 1990 are excluded and considered separately below).

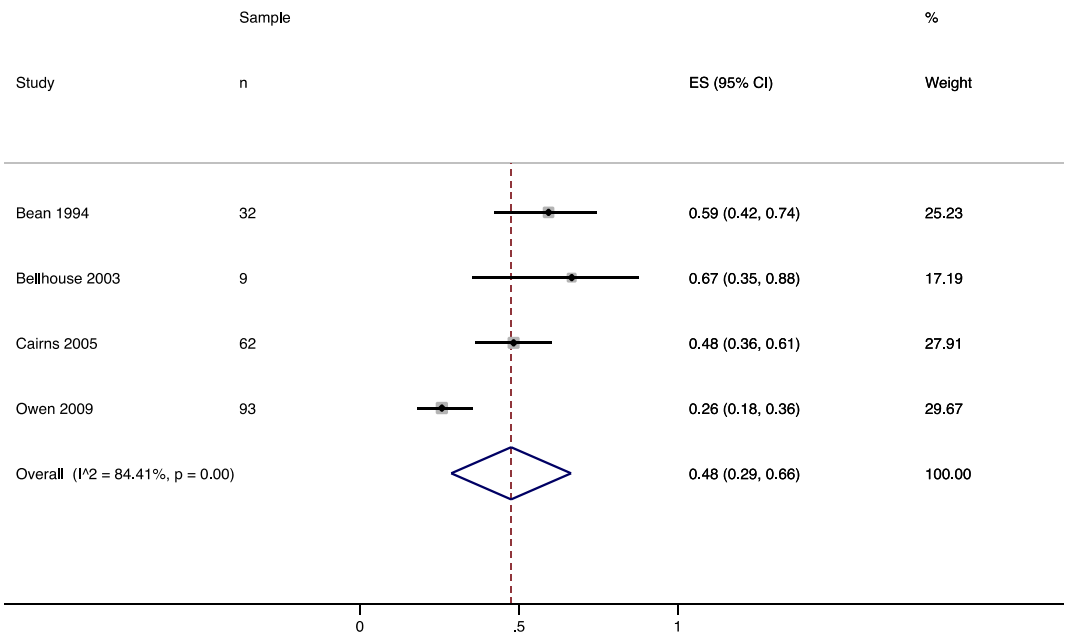
The range of proportions of DMC-T reported by all studies is large (11-100%) and there is significant heterogeneity between studies: six studies recruited from inpatient settings [33, 85, 86, 90, 91, 93, 110, 117], one from outpatients [88], two from mixed inpatients and outpatient settings [89, 92], and one from a general medical hospital setting [87]. Seven studies assessed DMC-T for a decision that was related to the disorder (hospital admission or treatment for schizophrenia) [33, 85, 86, 90-93, 110, 117]; two assessed DMC-T for medical treatment unrelated to schizophrenia [87, 88]; and one assessed DMC-T for treatment with an unclear relationship to schizophrenia [89]. Two studies assessed DMC-T as a naturalistic study in which people were recruited following concerns regarding a lack of DMC-T having been raised [86, 87].

Table 2 – Summary of DMC-T studies with a binary outcome of DMC-T

Study	DMC Standard	Decision assessed	Setting	Other relevant features	Total study N	n with DMC-T	Proportion with DMC-T (95%CI)
Weinstock 1984	Clinical	Unrelated medical treatment	N/A	Medically unwell in a physical health hospital referred for determination of DMC-T for medical treatment	N=2	n=2	1 (0.34-1)
Veliz 1987	Clinical	Related psychiatric treatment	Inpatients	Referred to the Court for determination of lack of competency to refuse or consent to treatment forensic population	N=35	n=4	0.11 (0.05-0.26)
Bean 1994	Clinical	Related psychiatric treatment	Inpatients	Inpatients requiring ECT	N=32	n=19	0.59 (0.42-0.75)
Wong 2000	Clinical	Blood test - unclear degree related	Mixed		N=21	n=19	0.90 (0.71-0.97)
Bellhouse 2003	Clinical	Related psychiatric treatment	Inpatients		N=9	n=6	0.67 (0.35-0.88)
Vollmann 2003	Clinical	Related psychiatric treatment	Inpatients	No detained patients.	N=43	n=35	0.81 (0.67-0.90)
Moye 2008	Threshold	Unrelated medical treatment	Outpatients	> 60 years old.	N=20	n=4	0.2 (0.08-0.42)
Cairns 2005	Clinical	Related psychiatric treatment	Inpatients		N=62	n=30	0.48 (0.36-0.61)
Owen 2009/11	Clinical	Related psychiatric treatment	Inpatients		N=93	n=24	0.26 (0.18-0.36)
Di 2013	Threshold	Related psychiatric treatment	Inpatients	Guardian also needed to agree in order to participate in study.	N=192	n=138	0.72 (0.65-0.78)
Skipworth 2013	Clinical	Related psychiatric treatment	Mixed	Mixed inpatients and outpatients under forensic services	N=97	n=63	0.65 (0.55-0.74)

It was only within the set of studies recruiting from inpatient settings that there were two or more studies sufficiently comparable with each other in terms of recruitment setting and nature of decision for which DMC-T was assessed in order to be eligible to undergo meta-analysis [33, 85, 90, 93, 110, 117]. These studies assessed DMC-T for psychiatric admission and/or treatment in hospital with medication or ECT; three were UK based and used the MCA legal standard. The range of people with DMC-T was 26-67%. A meta-analysis of proportions using a random effects model indicated high heterogeneity (I^2 – 84.41%) and a pooled proportion of 48% (95%CI 29-66%) with DMC-T (see Figure 2 below).

Figure 2 – Meta-analysis of proportions of DMC-T



Of the two studies considered separately: Norko 1990 [111] , used a range of 'cut-offs' based on combinations of 'dimensional scores', and found that DMC varied between 45-80%, depending on the precise cut-off used. Chiu 2014 [84] reported the characteristics of people given Electro-Convulsive Therapy (ECT) without consent,

dichotomising the groups into people without DMC-T given ECT and people with DMC-T given ECT despite objecting. In those having ECT without consent, n=13, 76% (95%CI 53-90%) lacked DMC-T.

Proportion of DMC-R from 'judgement standard' and 'cut-off standard'

One study [95] tested DMC-R concerning a hypothetical decision related to schizophrenia in a mixed population of inpatients and outpatients. It used three 'cut-off standards', 'least'; 'intermediate'; and 'most', (the 'Dunn standard') and found that 92%, 81%, 43% met their standards for each of these respectively. Another study used a 'judgement standard' to test DMC-R amongst older outpatients [75] and found that 47% of those undergoing 'routine consent' had DMC-R.

'Dimensional scores' and DMC-T/DMC-R

Five studies reported 'dimensional scores' from MacCAT-T sub-scales [35, 106-108, 112], and thirteen studies reported 'dimensional scores' from MacCAT-CR sub-scales [75, 77, 94-105]. These were all reported as arithmetic means and standard deviations. One study provided 'dimensional scores' from the precursor tools to the MacCATs [30-32]. Given that the data are consistently reported as highly skewed, a formal statistical comparison between the studies cannot be made, while study heterogeneity already renders comparison of questionable usefulness.

Associations

Most associations were reported as correlations with 'dimensional scores' based on the 'four factor model'. These are summarised and presented along with associations with the 'judgement standard' in Table 3 p.55.

Associations with DMC-T

With the exception of insight, neurocognition, and socio-economic status (which includes a measure of years of education) most studies found no associations with DMC-T measured using either 'dimensional scores' or the 'judgement standard'. There was no heterogeneity between direction of associations when they were found by studies.

There was strong evidence for a negative association between lack of insight and DMC-T (medium to large ES), and positive association between better neurocognitive performance and DMC-T (medium ES). These associations covered a range of different dimensions with no discernible pattern for individual abilities such as 'understanding'.

The lack of any association with most socio-demographic variables (age, gender, race) is notable. There was a positive association in one study with higher socio-economic status and DMC-T, and weak evidence for a positive association for more years of education and DMC-T, especially with 'understanding' (small to large ES).

Table 3 – Associations with DMC-T and DMC-R

	Associated with lack of DMC / worse performance on dimension scores			No association	Associated with presence of DMC / better performance on dimension scores		
Effect Size (cohen's d)	L	M	S		S	M	L
	≥ 0.5	< 0.5	< 0.3	0	< 0.3	< 0.5	≥ 0.5
Lack of insight	P A R	U A R C P*	U A R	U U A R CC			
PANSS Total	UU	U A R UU A	R	AA RR CC U A R CC			
PANSS General	U U A R	U A C	UU A R C	U AA RR CC P* UU A RR C			
PANSS +VE		U A R	U A	UUU AAAA RRRR CCC P* UUUUUU AAA RRRR CCCC			
PANSS –VE	U U A	UU U A R	UU A R C	U AAAA RRRR CCC P* UUU AA RRR CCC			
BPRS	U A	P U R		UU AAA RRR CC P U A R C			
Affective symptoms				UUU AAA RRR CC P* UU A R C			
Higher neurocognitive performance				AA P AA RRRR CCCCC	U A RR	UU RR C P**P* UUU AA	UUUUU AAA RR
Older age			R	PP UUUUU AAAAA RRRRR CCCC P* UUUUUU AAAA RRR CCC			
Male gender				PP UU AA RR CC UUU AA RR C			
Black and minority ethnicity			A R	UU AA RR CC UU A R C			
Higher socio-economic status				A	R	U	
More years of education				P UU AAAAA RRRR CCCC P* UUU A RR CCC	R U A RR	UU UA	P U A

Associations with DMC-T in red, DMC-R in black. Each letter symbolises an individual study finding an association, with horizontal position on the table representing direction of association and effect size. Individual letters represent the DMC standard the association was found with: P, association with binary outcome of DMC; U, association with 'understanding'; A, association with 'appreciation'; R, association with 'reasoning'; C, association with 'expressing a choice'. * Dunn 2007 used three standards as their binary outcome so the 'most' standard was selected as this required scoring in 'understanding', 'appreciation', and 'reasoning', rather than the other two standards which just required scores in 'understanding'. Dunn also used two presented data on two summary summary neurocognitive scores (DRS and a neurocognitive z score), the neurocognitive z score is presented here. ** Linder 2012 presented data on two summary neurocognitive scores (FAB positive association of medium ES, ACE no association), the FAB score is reported here.

With regards to symptoms of psychosis and DMC-T, there was some evidence for a negative association of PANSS total symptoms and PANSS negative symptoms with 'understanding' (medium to large ES). There was little evidence for a possible negative association of PANSS positive and PANSS general symptoms with dimension scores; overall, the majority of studies did not find any associations. One study reported on associations with BPRS factors. These are not included in the summary table [30-32] but are in Appendix 2 – Table 29 p.254 and did not differ from the general pattern of the findings of associations of psychotic symptoms with DMC-T. No associations were found with affective symptoms.

Associations with DMC-R

The associations with DMC-R were similar to DMC-T with a few notable exceptions. Again, there was no heterogeneity between direction of associations when they were found by studies. As with DMC-T, other than one multi-centre study [94], which reported negative associations between DMC-R and both 'non-white' ethnicity (small ES) and age and 'reasoning' (small ES), all studies found no associations with socio-demographics and DMC-R. Again, there was weak evidence for a positive association for more years of education and DMC-R (small to large ES).

There was evidence for a positive association of better neurocognitive performance and DMC-R, which was much stronger than for DMC-T (small to large ES). By contrast, the associations with insight and DMC-R were fewer and of smaller ES than with DMC-T (small to medium ES)

There was a range of negative associations with DMC-R and measures of psychotic symptoms (PANSS scores and BPRS – small to large ES), which appears stronger than

with DMC-T, and perhaps not as specific to 'understanding'. Unlike DMC-T, there was also evidence for a negative association between PANSS general and PANSS negative symptoms with dimension scores. Two studies reported on associations with BPRS factors [100, 103] (again not included in the summary table but are included in Appendix 2 – Table 29 p.254). These results did not substantially differ from the general pattern of the findings of associations of psychotic symptoms with DMC-R.

Discussion

DMC-T versus DMC-R in schizophrenia

Following meta-analysis, DMC-T, when measured by the 'judgement standard' was present in 48% of people receiving inpatient treatment for schizophrenia. The range of the proportion with DMC-T was wide (26-67%). Heterogeneity between both samples and different decisions for which DMC was assessed was high. Outside of the analysis of DMC-T restricted to inpatient populations, it is difficult to draw any other distinct conclusions, using either 'judgement standards' or 'cut-off standards', beyond the finding that there is a wide range of DMC-T and DMC-R proportions in different samples of people with schizophrenia.

There was little evidence that socio-demographic factors had an impact on DMC-T or DMC-R. The lack of association between DMC and basic demographics is both a reassuring and an important finding, given that DMC measurement outcomes should not, in principle, be influenced by age, gender, or ethnicity. It runs counter to common misconceptions or presumptions that might be made regarding a lack of decision-making capacity with certain demographic characteristics such as age. Nevertheless, there was some weak evidence of an association with greater years of education.

While there was strong evidence of an association between greater insight and DMC-T, evidence of a similar association with DMC-R was much weaker. As discussed in Chapter 2 p.17 the role of insight in DMC-T has been well established but its role in DMC-R remains unclear and is an area of interest for this study.

The finding of associations between total symptoms (measured as PANSS total score or BPRS), negative symptoms and dimension scores is as we might expect, although it is curious that evidence is less convincing for DMC-T than DMC-R. The lack of association between positive symptoms and dimension scores in DMC-T and DMC-R is an interesting finding, which runs counter to anecdotal clinical experience and requires further investigation. These findings may be due to few participants with severe positive symptoms of psychosis being recruited for studies - many studies systematically excluded severely unwell people, either directly (through requiring vetting from the treating clinician), or indirectly (through recruiting in stable outpatient settings or setting a threshold of 'understanding' or DMC for involvement in the primary study itself). Another possibility is that severe positive symptoms themselves (such as persecutory delusional beliefs) may result in participation refusal.

Given that studies investigating DMC are vulnerable to this selection bias, I consider it important that studies are designed to recruit from homogenous settings or disorders and minimise selection bias for participants with severe illness or lacking DMC-R for the study itself. A few studies have tackled this by collecting data on non-participants [33, 92, 93, 117], but none have presented data on the symptom profile of non-participants in order to investigate further the lack of reported associations with DMC and positive symptoms.

There was evidence that better neurocognitive performance was positively associated with DMC-T. The evidence for this association in DMC-R was stronger, where better

neurocognitive performance was highly positively associated with 'understanding' and, to a lesser extent, with 'appreciation' and 'reasoning'. This could suggest that a decision about participation in research presents a greater cognitive burden than DMC-T. If this is the case, it has implications for how information should be presented to potential participants. There is already evidence that educational and multimedia interventions can improve DMC-R in people with psychosis, mainly through enhancing 'understanding' (as discussed in Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37). An alternative possibility is that, whereas a DMC-R testing paradigm is likely to present new information, within a DMC-T study, 'understanding' may already have been supported through treatment discussions in years of clinical interactions.

Methodological limitations

Sample size between studies varied considerably, with the exception of one outlier study with n=1447, the range was n=2 to 192 with a median of 37.5, interquartile range 42. The majority of studies did not provide information on sampling frames and recruitment rates. Although some provided information on non-participants [33, 92, 93, 117], this was for people of all diagnoses and hence could not be used specifically to refer to people with schizophrenia.

Inappropriate statistical analyses were often employed in source publications. Within the DMC-T studies there were many studies with substantial biases or study specific features, such as the assessment of DMC-T for unrelated medical treatment or the restriction of sampling to those referred for a secondary opinion of DMC-T or those refusing treatment (see Table 1 p.46 and Appendix 2 – Table 29 p.254).

The review was limited by significant heterogeneity between studies, with differences between the outcome tools used, the decisions in relation to which DMC was assessed

and the sampled populations. For the analysis of DMC proportions, such differences were managed through stratifications using narrow inclusion criteria. For the analysis of factors associated with DMC, given the extensive differences between all studies, stratification of analysis was not possible and all studies were therefore considered. Accordingly, due to possible confounders, I would recommend that these results are interpreted with caution.

The decision-specificity of DMC is an important source of the heterogeneity within the literature. Even for clearly defined decisions around, for example, treatment for schizophrenia, the precise nature of the decision, such as Electro-Convulsive Therapy versus antipsychotic treatment with clozapine, may lend itself to different vulnerabilities in the different abilities that make up DMC. While cognitively demanding decisions may require better performance on 'understanding' and 'reasoning', there is limited ability to compare the dimensional measures accordingly between studies.

The nature of the decision in relation to which DMC-R was tested requires special comment. It is important to point out that many of the DMC-R studies tested decisions relating to research which could not be considered as schizophrenia-specific, but which concerned a generic treatment, aimed at a general population. Several tested DMC-R concerning a trial of an experimental drug which may help cognitive deficits, both in schizophrenia and in normal ageing. This decision, therefore, related to non-schizophrenia specific therapeutic research, where the salience of the decision to their present symptoms would vary substantially between participants and where the role of insight and other factors was unclear and not homogenous. The contribution of these studies to understanding DMC-R in schizophrenia in relation to therapeutic research for schizophrenia is thus unclear. Decisions around research participation for therapeutic or non-therapeutic research may also pose different challenges, given the different

risk/benefit profiles for the individual, and may therefore further complicate direct comparison between studies.

As a consequence, there remains a need to unpick which what abilities are global, impacting decision-making in general, and which are specific to the particular decision in hand. I hypothesise that lack of insight into one's illness would be relatively circumscribed to decisions around treatment or life consequences of the functional deficits of the illness through impact on 'appreciation', compared to symptoms such as 'thought disorder' which may affect decision making more generally through impact on 'understanding'.

The effect of publication bias on this review is unclear. Funnel plots are difficult to do with this data but as most studies report simple proportions and/or multiple association analysis there are no strong reasons to suspect publication bias.

Categorical versus dimensional measures of DMC

The majority of studies I found used 'dimensional scores' for their measurements of DMC. The 'judgment standard' when used was used in isolation or guided by tools using 'dimensional scores'.

Dimensional measures of DMC take an overly siloed view of the DMC construct, and it is likely these abilities are not independent of each other. It is clear from my work that poor performance on different individual measures can impact others (if there are profound deficits on 'understanding', then there will be resultant deficits on 'appreciation' or 'use or weigh'; conversely in people with low insight this can be a total barrier to discussing the nature of their illness, even in abstract, and result in serious doubts about

their resultant 'understanding'). This creates a hierarchical element to dimensional measures of DMC, in that sufficient performance on one ability is pre-requisite to performance on other abilities.

Dimensional measures can in some situations be relatively insensitive to deficits that categorical measures can detect. Some elements of psychopathology can be highly circumscribed, and have marked impact on DMC as measured by a categorical standard, but relatively less impact on dimensional measures. For example, an isolated delusional belief that participation within a research study will cure the participant of all illness may result in partially reduced scores on 'appreciation' and 'reasoning' when assessed using the framework of the MacCAT-CR, but a clear lack of DMC-R when using a 'judgement standard'. I will explore this in detail in Chapter 9 p.199. Given the limitations to using dimensional measures in isolation, I recommend that future research employ both dimensional and judgement measures of DMC.

Conclusions

I found that a significant proportion of people with schizophrenia, even on inpatient wards, have DMC, that DMC is associated with clinically relevant variables, such as insight and neurocognitive performance, and that DMC is not related to socio-demographic factors.

There have been many studies investigating DMC in schizophrenia in the past two decades. To my knowledge, this is the most methodologically rigorous attempt to synthesise the findings from these studies, and one that was not limited to one standard of assessment of DMC or one type of decision for which DMC was assessed such as DMC-T or DMC-R. This review is the first to overview the field and draw broad

conclusions regarding the proportion and associations of DMC in schizophrenia and compare and contrast these for DMC-T and DMC-R. It is clear, however, that the complexity of the DMC construct resulting from its decision-specificity and the dimensional and categorical approaches to measuring it renders the literature diverse. Arguably it is in disarray.

Chapter 4. Methods

The decision specificity of DMC renders research in this area complex. I have found from systematic review evidence that different psychopathology affects different decisions differently: insight has the largest effect on DMC-T, whereas neurocognitive deficits have the most impact on DMC-R [126]. However, no study has ever compared the impact of psychopathology on two different types of decision concomitantly, a necessary feature to control for differing study designs. Few studies to date have investigated DMC-R in an inpatient setting with severely unwell participants, and none of these used an 'judgement standard' measure.

Do some symptoms affect only certain decisions or do some affect general decision-making? This is required to further our understanding of the role of insight in both DMC-T and DMC-R and otherwise the time and decision-specific nature of DMC may lead to study-specificity. In order to develop the understanding of DMC in schizophrenia there is a need for a comparative study of DMC-R and DMC-T, using both dimensional and categorical measures, and provide data on non-participants and sampling-frames. This will enable understanding of symptom specificity on different decisions.

In order to develop an intervention to enhance DMC-R, there is a need for data on the proportion of people with DMC-R in inpatients with psychosis, and the effect sizes of psychopathology and neurocognitive deficits in order to select the best target for an intervention to enhance DMC-R. I need qualitative data on the acceptability of any intervention in order to balance the largest potential effect size with acceptability and feasibility of any intervention using the qualitative data collected. We know that there are possible conceptual problems with the MCA model of DMC-R (especially the role of

insight in the ability to ‘use or weigh’) and the acceptability and effectiveness of consultee decision-making and these issues also need to be explored.

Aims and hypotheses

My goal was to clarify the nature and extent of the DMC-R problem and work toward developing an intervention to support decision-making about biomedical research in inpatients with schizophrenia and to contribute to refining existing guidance.

Hypotheses

1. DMC-R does not share the same proportion or symptom associations as DMC-T in adults who are admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

2. It may be possible to improve a person's DMC-R if we support their cognitive function or trust.

Aims

1. To describe the proportion of people with DMC-R in adults admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

Previous research in the UK using the framework of the MCA has investigated DMC-T in inpatient samples with psychosis [33, 89, 90, 93, 127, 128]. No similar work has been done with DMC-R. This study aimed to investigate the proportion of people with DMC-R in an inpatient sample with psychosis.

2. To determine how the symptoms of psychosis impact on DMC-R compared to DMC-T in this population.

Most international research into DMC-R in psychosis has been done in outpatient samples using the MacCAT-CR. This has demonstrated reduced scores (less DMC-R) in patients with greater neurocognitive deficits, e.g. working memory as described in Chapter 3 p.40. In contrast, lack of insight has the largest effect size on DMC-T.

There is evidence that in outpatients with psychosis, DMC-R can be enhanced through simple educational measures targeting 'understanding' through use of repetition or multimedia (see Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37). Whether other domains of DMC such as the ability to 'use or weigh' can be enhanced remains unclear, as is the appropriate target for an intervention: enhancing cognitive function in psychosis (supporting 'understanding'), or ameliorating consequences of the psychopathology, such as suspiciousness using a model based around trust (supporting 'use or weigh'). To resolve this, I aimed to collect data on neurocognitive deficits and psychopathology to find the associations with DMC-R compared with DMC-T.

The contexts in which DMC-T and DMC-R are assessed in practice are very different. DMC-T is often assessed when a doctor believes that the patient would benefit from treatment that they are refusing, to protect a person from an unwise decision if made without DMC [129]. In research, refusal automatically bars participation and the capacity assessment is there to ensure true and valid voluntariness. Is the nature of these decision-making capacities intrinsically different or are they made different by the different contexts in which they are assessed? To address this question there needs to be systematic comparison of DMC-T and DMC-R in individual participants.

3. To investigate the suitability of interventions to enhance DMC-R and explore views on the current framework around consent for research.

If a participant is judged to lack DMC-R but wishes to participate, agreement for participation must be sought by the investigator from a third party (consultee/PLR) [10]. Refusal by the consultee/PLR blocks recruitment to the study, regardless of the participant's wishes (see Chapter 2 – Research when DMC-R is lacking p.22). How do participants view this, and the current legal and ethical framework surrounding consent for research participation? What issues/considerations are likely to come up for consultee/PLR if they were to be involved in an intervention to support DMC-R? What do they think about being involved in supporting biomedical research? These data will be used to design a possible intervention, ensuring it is acceptable to patients and their consultee/PLR.

Study design considerations

As I have explored in Chapter 1 p.11, Chapter 2 p.17, and Chapter 3 p.40 there is a need for future studies to incorporate into their design:

a) **Measuring DMC using both categorical and continuous outcomes.**
b) **Minimising selection bias into the study due to severity of illness, detention in hospital, or lacking DMC for the present study.**
c) **Collecting detailed data on non-participants to measure and characterise selection bias.**
d) **Comparing and contrast two DMC decisions in the same individual in order to explore the symptom specificity of DMC and draw meaningful and unbiased conclusions on the differences between DMC-R and DMC-T**
e) **Assessing the reliability of assessments of DMC-R.**

Therefore, I designed a cross-sectional study, the 'quantitative study' to address aims 1 and 2, with the methodology addressing design considerations a, b, and d. In addition, there is a 'recruitment selection bias sub-study' to address design consideration c, a 'reliability sub-study' to address design consideration e, and a 'qualitative sub-study' to address aim 3.

Given that the nature of qualitative research is that analysis feeds directly back into decisions about recruitment and topics explored, and hence methods, there cannot be as clear a delineation between methods and results for this sub-study as with other sections. Therefore, I will present here the methods used for all the quantitative sections of my study procedures with the results and discussion for each in their own chapters (Chapter 5 p.102, Chapter 6 p.123, and Chapter 7 p.143), but will consider the methods

for the qualitative sub-study with their results and analysis in Chapter 8 p.154, the qualitative sub-study results chapter.

Quantitative study

To address aims 1 and 2:

1. To describe the proportion of people with DMC-R in adults admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

2. To determine how the symptoms of psychosis impact on DMC-R compared to DMC-T in this population.

And study design considerations a, b, and d:

a) **Measuring DMC using both categorical and continuous outcomes.**
b) **Minimising selection bias into the study due to severity of illness, detention in hospital, or lacking DMC for the present study.**
d) **Comparing and contrast two DMC decisions in the same individual in order to explore the symptom specificity of DMC and draw meaningful and unbiased conclusions on the differences between DMC-R and DMC-T.**

Methods

Participants

Diagnosis and admission purpose

Many mental illnesses can have psychotic presentations, such as psychotic depression, organic psychosis such as within Parkinson's disease, as a result of intoxication with substances, post-partum psychosis etc. I aimed to study schizophrenia and related non-affective psychoses in order to focus on the core symptoms of *schizophreniform* psychotic illnesses of interest (delusions, hallucinations, thought disorder, negative symptoms, neurocognitive symptoms, and lack of insight), again for clarity within this thesis I shall use the term 'schizophrenia' to refer to all these disorders. I set the scope of diagnosis deliberately narrow in order to gain a homogenous sample in order to perform the correlational analysis between predictor variables and the outcomes of assessment of DMC-R and DMC-R and manage possible confounds (severe affective symptoms in affective disorders such as depression, or underlying neurological illness such as in organic brain disease). Bipolar affective disorder and related affective psychoses such as psychotic depression were excluded given that these disorders have separate and distinctive putative mechanisms that impact on DMC independent to that of schizophrenia (see for example Owen 2013 for a discussion of the mechanisms of affective symptoms impacting on DMC-T in severe depression [130]).

Within the psychosis population substance misuse, especially with psychotogenic drugs such as cannabis is very common (around 50% used cannabis at presentation in a first episode sample with a similar catchment area to this work [131]). Substances such as cannabis can also induce a brief but self-terminating psychotic episode due to its psychogenic effects. To exclude substance misuse from the sample would be to both render the study ungeneralisable to the psychosis population, and severely impact on recruitment. Therefore, substance use was not an exclusion criterion, other than in patients acutely intoxicated with substances, or where there was a clear and isolated substance induced psychosis.

Therefore the eligibility for inclusion in the study was a diagnosis of schizophrenia or related non-affective psychotic illness as defined by ICD-10: f20-f29 [22] (excluding f21 'schizotypal disorder' which can be considered to be a personality disorder and has only some of the features of schizophrenia [5]) or 295, 297, 298 DSM-IV [81], primary purpose of admission into hospital for the assessment and/or treatment of symptoms of psychosis. I included schizo-affective disorder, f25, within my sample given that although there are prominent affective symptoms within the syndrome, the core symptoms of interest for my study are also present.

Assessment of diagnosis

I decided to assess diagnosis, and therefore ensure eligibility to the study, via case note review rather than structured clinical assessment. Given that study involvement would take a substantial amount of time and participation, to have required a structured clinical assessment to confirm eligibility would have reduced the participation in other components of the study and would have acted as both a barrier and selection bias to participation. I therefore decided to confirm diagnosis from case note review.

Psychiatric diagnoses can be fluid, changing over time. There are several options available when selecting a defined diagnosis, either the diagnosis specified in the relevant section of the electronic medical record (EMR), or the assessments performed by the treating team (these may be historic, community based assessments, or follow assessment after acute admission) and these diagnoses may be contradictory or unclear. Therefore, I adopted the following procedure: I reviewed case notes including the current treating team's stated diagnosis in the notes. I am a trained psychiatrist (Specialist Registrar) and approved under section 12(2) of the MHA as having specialist knowledge and experience in the diagnosis and management of mental disorder and

with extensive clinical experience working in this setting. Should the current and (if recorded) previous treating team considered that the person clearly had an eligible diagnosis then this was subject to OPCRIT confirmation (OPCRIT – OPerational CRITeria – is a reliable and valid computerised method of assigning psychiatric diagnosis using operational criteria of the ICD-10 [22, 132]). Should the current and (if recorded) previous treating team clearly confirmed a diagnosis incompatible with eligibility to my study then they were excluded. Should there be inconsistency between current and previous treating team regarding diagnoses, with a confliction between eligible and ineligible diagnoses, then my clinical judgement and OPCRIT confirmation was applied to give support to my clinical judgement. In essence, my own clinical judgement was used to arbitrate where there were conflicting diagnoses prior to OPCRIT confirmation.

Admission for assessment and/or treatment

There are a variety of reasons for admission or ongoing admission in a psychiatric hospital that include:

1. A person with a known psychotic illness has a relapse of the illness and is admitted for assessment and treatment.

2. A person has a suspected psychotic illness but this is not confirmed and is admitted for assessment of this illness.

3. A person has a known psychotic illness which is symptomatic but may not be experiencing an acute deterioration, and who is admitted for related treatment optimisation, such as an inpatient trial of clozapine.

4. A person with a known psychotic illness admitted for the assessment and/or treatment of unrelated psychiatric disorder, such as depression or anxiety not associated with active psychotic phenomena.

5. A person with a known psychotic illness admitted in hospital whose treatment is now optimised but is residing in hospital while awaiting a suitable discharge location or care provision in the community.

Assessment and treatment in hospital of a psychotic relapse may involve treatment with medication, however it is not limited to this and may concentrate on clarifying the variables in the patient's relationships or environment that have predisposed and precipitated relapse. Treatment would then focus on changing those variables.

I required a sample of people acutely unwell with schizophrenia, and therefore I defined the criteria for the admission purpose as 'admission for assessment and/or treatment' of schizophrenia to exclude those who were well from a psychosis perspective but admitted for other reasons. A limitation of this approach is that there was the possibility of people without a known psychotic illness being admitted for the assessment of psychosis, but ultimately being diagnosed as not having a psychotic illness. For example: a person could present with what appear to be psychotic symptoms that following the course of assessment are re-evaluated as non-psychotic and related to an abnormal personality. If approached for involvement in my study at the start of the assessment period they could be recruited and contribute to the study data, even though ultimately through re-diagnosis they would become ineligible for participation. This scenario is, however, relatively rare.

Wards

I aimed to recruit from inpatient wards in South London and Maudsley NHS Foundation Trust (SLaM). Within SLaM there are four general hospital sites (Bethlem, Ladywell, Lambeth, and Maudsley) with around 10-20 general adult wards depending on service-configuration. There are several types of wards catering for different patient populations: 1) triage wards – acute admission wards that are for short term assessment and treatment prior to discharge to the community or referral to another inpatient ward; 2) 'general adult wards' – wards for general adult patients either directly admitted from the community or via another ward; 3) Psychiatric Intensive Care Units (PICUs) – wards for intensive treatment of the most severely unwell and agitated patients; 4) rehabilitation wards – for long term treatment and intensive rehabilitation of severe mental illness; 5) forensic wards – for mentally disordered offenders; 6) Specialist units – such as for the treatment of early onset psychosis or other specialist areas of general adult psychiatry.

As I aimed to recruit severely unwell and acutely admitted patients with schizophrenia I selected the triage wards initially for the main recruitment sites. Three of the hospital sites (Ladywell, Lambeth, and Bethlem) all had triage units in operation at the start of the study, however the Bethlem site only provided triage for male patients. To avoid selection bias towards male participants, triage wards on the Lambeth and Ladywell sites were selected as the initial recruitment sites. I chose to exclude PICUs, rehabilitation, forensic, and specialist wards from the study to ensure that the sample frame was representative of the general inpatient psychiatric population. Thus, I was limited to a maximum of 14 wards eligible for recruitment on the four hospital sites. Subsequently based on recruitment rates into the study, the other general adult wards on the Ladywell and Lambeth sites were opened for recruitment.

Only the general adult wards on the Ladywell and Lambeth sites were chosen as the triage wards on those sites as these wards reflect general inpatient populations, are linked, share sites and were willing research collaborators. This decision was also taken in order to reduce the number of case notes that would need to be reviewed in the recruitment selection bias sub-study due to the internal transfer of patients between wards (see Recruitment selection bias sub-study p.90).

Inclusion and exclusion criteria

Inclusion and exclusion criteria of patient participants were selected to ensure the broadest sample of inpatients with schizophrenia.

Inclusion criteria:

- Adults aged over 18.
- Fluency in English to a level able to undergo a diagnostic clinical interview.
- Clinical diagnosis of schizophrenia or related non-affective psychotic illness as defined by ICD-10: f20-f29 [22] (excluding f21 'schizotypal disorder').
- Primary purpose of admission into hospital for the assessment and/or treatment of symptoms of psychosis.

Exclusion criteria:

- Current intoxication.

- Previous recruitment into a bioresource study.

First approach and recruitment strategy

Research governance requires that the first approach for participation in research is performed by individuals other than the research team, and that the researchers cannot have access to confidential medical information (which includes patient names) without prior consent except in exceptional circumstances and through authorisation under section 251 of the NHS Act 2006 [133].

In SLaM there are systems in place to support recruitment for research and facilitate first approach. These include the National Institute for Health Research Biomedical Research Centre (NIHR BRC) Clinical Record Interactive Search (CRIS) and Consent for Contact (C4C). CRIS comprises a database of anonymised individual electronic case records for SLaM patients that can be used to search for potentially eligible cases. C4C is a process in which patients can give prior consent for researchers to have access to their EMR to review eligibility and approach them directly to discuss participation in research as described below. The Mental Health Research Network also has a team of Clinical Studies Officers (CSOs) who are part of the Trust's clinical team with the purpose of discussing research with patients and are able to perform first approach.

I used two main methods to select and approach participants for recruitment:

Selection through CRIS and direct approach in those who have granted C4C.

I used CRIS to automatically select anonymised patient records that on first screening would appear to meet the eligibility criteria. I reviewed the anonymised individual case information gained from CRIS to ensure that the case did in fact meet eligibility criteria. In those who had already consented to C4C I asked CRIS administrators to 'reverse search' them in order to provide me with patient identifiable information, the SLaM ID, and then to approach the patient to discuss involvement in the study. Prior to directly approaching the patients I liaised with the ward staff to ensure there were no concerns regarding approaching the patient and approached them to discuss involvement in the study.

Recruitment using selection and first approach by the CSOs.

CSOs had access to the ward list on wards in which I was recruiting. Following liaising with the ward staff to ensure there were no concerns regarding approaching the patient, they made first approach to ask if they would like to discuss participation in the Study. Prior to doing this they ensured that the patients had not already dissented to C4C or previously been approached for the Study (recorded in the EMR). If the patient expressed a desire to talk to me to discuss involvement in the study their details were passed on to me for me to approach and I liaised with the ward staff to ensure there were no concerns regarding approaching the patient and approached them to discuss involvement in the study.

Other methods

Occasionally first approach was performed by the ward staff who knew my study and recruitment criteria, including other research workers. Similar procedures operated as above. This was initially anticipated to be a form of first approach, but ultimately was negligible recruitment pathway to involvement in my study given the work pressures these staff faced.

Recording research approach

All contacts with patients regarding the study either in terms of first approach by clinical staff/CSOs or discussion with researchers were recorded in the EMR along with the date, time, type and outcome of approach. At closure of recruitment all cases that were eligible for recruitment were re-searched in CRIS in order to record recruitment data in an anonymised fashion (see Recruitment selection bias sub-study p.90).

Recruitment strategy

Recruitment took place in a consecutive fashion, aiming to approach all eligible patient participants no earlier than 24-48 hours after admission on a case-by-case basis guided by ward staff, but as soon as possible after this. If the patient was transferred to another ward within SlaM before I was able to see them, then I attempted to see them on the ward they were transferred to providing this was a ward in which I was actively recruiting from. All study interviews were performed by myself. Participants were offered £10 as compensation for their time. I recruited over an 18 months period from June 2015 to December 2016.

Each participant underwent a structured clinical interview split into two 45-minute sessions which was audio-recorded. Interviews were often split over several days at the participant's request. The sequence of testing prioritised the collection of variables in order of importance to the main outcomes of the study and natural flow of the interviews, collecting data on DMC-R and DMC-T first, then followed by the symptom assessments and neurocognitive testing last. I had a brief run in period of recruitment (around 10 patient participants) to ensure that all study materials and protocols were appropriate and effective prior to the start of consecutive recruitment.

Informed Consent

Following first approach I invited participants to discuss participation in the study. I provided participant information materials, discussed the study, and offered them time to consider participation. If there was any reluctance or objection to take part in the study then they were not recruited. If this occurred during the study they were withdrawn. Any patients with whom I had clinical involvement with during the current admission (including the admission process) were excluded from being recruited into the study to ensure no confusion or lack of clarity on behalf of the patients as to my role when recruiting as researcher rather than as clinician, and to minimize any perception of undue influence or coercion on behalf of the patients. During the period of recruitment my main clinical work was limited to on-call duties, normally covering a hospital site I was not recruiting from, and the occasional Electro-Convulsive Therapy Clinic session. Therefore, this exclusion had very limited impact on the study.

The potential issues in gaining capable consent to take part in studies on DMC have already been considered by researchers in this field such as Saks with parallels drawn

to a ‘catch-22’ scenario [134] (how can DMC-R be studied if lacking DMC-R prevents participation in studies on DMC-R). For Saks, simply excluding participants from research and reducing its representativeness is a ‘violation of justice’ given that she sees the justification for research activity based on the benefits to that group. She concluded that research that is 'scientifically valid, minimal risk, and otherwise ethically appropriate, […] there is no added ‘‘harm’’ against which individuals need be protected, so the right to be treated as an autonomous agent and the dignity thereby afforded take precedence’ [134].

There is direct application to my study which was also very low risk (asking people to take part in interviews on how they make decisions about research) but highly informative. Therefore, I presumed DMC to consent to the study (as per the first principle of the MCA), but this assumption was rebutted if it was obvious to me or the clinical team that the participant lacked DMC to consent to the study. The Mental Health, Ethics and Law research group at the Institute of Psychiatry, Psychology and Neuroscience, Kings College London has experience recruiting in this field using similar methods [33, 93, 127], and this approach was reviewed and supported by the Camberwell and St Giles REC during my application for ethical approval for the study.

Consultee approval was sought in patient participants who lacked DMC to consent, or who lose DMC to consent to the study once recruited, following the regulations on recruitment to research studies of people who lack DMC-R (see the MCA Code of Practice [29]). Consultee approval was gained over the ‘phone or through face-to-face meeting at the research sites. I asked the participant to select the person they would like the researchers to contact for the purposes of seeking consultee approval. If they were unable to specify a choice, then I attempted to contact first-degree relatives and unpaid carers in that order, using contact details from the patient's EMR. If no-one was willing or available to perform the consultee role, then the ward consultant or ward

manager was approached to act as nominated consultee. This followed national guidance on the selection of consultees in research [135].

Measures

Outcome variables

DMC-R

Studies of DMC-R comprise a study assessing DMC-R (in this case the present study), and a 'parent study' (the study that is explained to participants and for which their DMC is assessed). I desired a research paradigm for non-therapeutic research as I considered that a decision regarding therapeutic research in schizophrenia (such as a randomised controlled trial of an antipsychotic) would have a strong overlap with decisions regarding current treatment, and thus would not elucidate factors specific to DMC-R alone.

I selected the NIHR BioResource as the 'parent study', given that it is a real non-therapeutic research study recruiting in inpatient settings [136]. The NIHR BioResource is a biobank study collecting biological (blood and/or saliva) samples and linking them to medical data. BioResource resource also includes re-contacting participants in the future based on phenotype or genotype, 'broad consent' for future research, and that participation will have no therapeutic benefit to the participant (*viz a viz* TM [51]). As discussed in Chapter 2 – Formulating an MCA model of DMC-R p.31 there is only limited guidance from the REC in terms of what information is necessary to be understood in order to have DMC-R, and it is left to the judgement of the person gaining consent.

MacCAT tools have been used to structure and complement the assessment of DMC using the 'judgement standard' by enhancing the consistency of information disclosure between participants and prompting exhaustive exploration of all issues (see [33] and the guidance in [25, 137]). I decided to structure my assessment of DMC-R using the MacCAT-CR [36] and thus I adapted the tool for BioResource research as follows:

I consulted with experts in the field and my study's Service User and Carer Advisory Group and distilled the key information about BioResource research that an individual would need to consider in order to provide valid *informed* consent. Notably the MacCAT-CR is formulated around an RCT with a focus on TM and, as discussed in Chapter 2 – MacCAT-CR 'appreciation' and the 'therapeutic misconception' p.28, I considered that 'appreciation' in BioResource research would not be limited by TM as it is in the MacCAT-CR. Therefore, I expanded 'appreciation' to key elements of BioResource research that I considered necessary to be appreciated (again in consultation with experts in the field and my study's Service User and Carer Advisory Group). There were some elements of appreciation within the original MacCAT-CR that are generic, such as believing involvement in research is entirely voluntary and this was retained in the modified MacCAT-CR. In addition, one element of TM (personal benefits are not the primary objective of the study) is relevant to BioResource research and was modified accordingly; unlike RCTs on which the MacCAT-CR is based, there is also no substantive personal benefit from taking part in BioResource research either.

In reviewing the issues involved in consent to BioResource research, future re-contact based on genotype/phenotype and 'broad consent' to future research were considered essential. These both have distinct implications for the research subject to appreciate: 'broad consent' requires the subject to appreciate that involvement in research forms an agreement in which the researchers may use the data for a range of projects (some not

designed at time of consent), while future re-contact based on genotype/phenotype provides for an ongoing research relationship.

The final components of appreciation comprised:

1) Subject believes that they will not benefit or suffer from being involved in the research (his or her personal benefits are not the primary objective of the study);

2) Subject believes that the BioResource will be used for a range of research projects that the subject themselves does not decide on;

3) Subject believes that they may be contacted in the future if eligible for other studies based on genotype/phenotype;

4) Subject believes that involvement in research is entirely voluntary (regardless of legal status, a decision to withdraw will be respected).

A fifth component of appreciation, 'overall appreciation', was also included to investigate if this was a useful assessment given the unknowns regarding the formulation of appreciation, however in practice it did not contribute to supporting the assessment of DMC-R as it mirrored my assessment of 'use or weigh' and therefore I did not use it in my analyses.

During the run in period of the study the MacCAT-CR modified for BioResource research was refined following participant interviews. The final modified MacCAT-CR is presented in Appendix 3 p.266.

I examined DMC-R through semi-structured interview aided by the modified MacCAT-CR and using the legal framework for the assessment of capacity under the MCA, dichotomised into a binary outcome. I also subdivided the groups further into 'definitely has DMC-R', 'definitely lacks DMC-R' and an additional group 'marginal capacity' in the middle that would form the main target of any intervention. During this assessment, I made use of the modified MacCAT-CR to help formulate my decisions regarding abilities on the 'functional test' under the MCA. Where necessarily I explored relevant issues that were raised during the interview which were not covered by the modified MacCAT-CR or where it was necessary to formulate an opinion as to the abilities on the 'functional test'. Hence, my interview was semi-structured according to the modified MacCAT-CR but not constrained to it.

As I have already mentioned, I am a trained psychiatrist (Specialist Registrar) and approved under section 12(2) of the MHA as having specialist knowledge and experience in the diagnosis and management of mental disorder. Clinical psychiatric training in E&W incorporates training in the assessment of DMC using the expert 'judgment standard' framed by the MCA. There is extensive clinical and legal guidance for its assessment of which I am familiar by virtue of my training and expertise in the field (see for example, the Royal College of Psychiatrists' Higher Training Curriculum [138], MCA Code of Practice [29], and professional guidance such as [139] (on which I am acknowledged as a contributor). I drew on this expertise and experience when making my assessments of DMC. I was mindful during these assessments that I was conducting them in a research setting, not a therapeutic one or one serving the needs of the justice system.

When studied in DMC-T, the assessment of DMC using the 'judgement standard' by clinically trained professionals has been found to be highly reliable (see for example [140]), however I also performed a reliability assessment of my assessment of DMC-R in this study as described in methods – Reliability sub-study p.95 and Chapter 7 p.143.

Fieldnotes and reflections were taken during the assessments focusing on clinical features compromising DMC-R, and in my judgement if there was the potential to enhance DMC-R, and what this would take. I explained to participants that we wanted to explore how people decided about participating in the BioResource, but would not be recruiting them to the study.

DMC-T

I used a similar approach to measuring DMC-T as with DMC-R. Here the decision was framed around 'admission and treatment' in hospital (conjunctively), informed by relevant information about the patient's diagnosis, symptoms, purpose and reasons for admission, and recommended treatment from the case notes and discussion with the clinical team. I structured the interview using the MacCAT-T [35], similar in structure to the MacCAT-CR. There was no need to modify the MacCAT-T at this stage given that it generically written and designed to be easily customised for each and every assessment of DMC-T based on the specifics of the case. Accordingly, when recruiting into the study it was customised for each participant interview.

Predictor Variables

I collected basic demographics from participants, clinical diagnosis under ICD-10 [22] was obtained from case note review as described above. The EMR was searched for the participant's consent status at time of admission (agreement to the admission, DMC-T at time of admission, and use of the MHA), closest DMC-T assessment from the clinical team to the DMC-T assessment in the study, MHA status at time of interview, and the clinical team's assessment of illness severity using HoNOS [141].

Participants underwent the following assessments:

1. The PANSS [82] was administered returning scores on the positive, negative, and general sub-scales (this includes a measure of insight PANSS item G12). Several factors on the PANSS are associated with 'trust' e.g. 'hostility', 'suspiciousness'. Results from these factors were pooled into a standardised 'trust' score to be used as a proxy measure of 'trust' (P6 Suspiciousness/persecution; P7 Hostility; N3 Poor rapport; G2 Anxiety; G4 Tension; G8 Uncooperativeness; G16 Active social avoidance).

2. Assessment of affective symptoms using the Young's Mania Rating Scale (YMRS) [142], and Hamilton Depression Index (HAM-D) [143].

3. Assessment of illness severity using HoNOS at time of assessment) [141] and the Clinical Global Impression - Severity Scale (CGI-S) [144].

4. Assessment of compliance with research using Part C of the Schedule for Assessment of Insight - Expanded (modified SAI-E) [145], which I modified for agreement to participate in a biomedical research project (see Appendix 4 p.279).

5. I developed a Neurocognitive Assessment Battery (NAB) for the study that included: a series of individual subtests derived from published Neurocognitive Assessment Batteries such as the Wechsler Adult Intelligence Scale-III (WAIS-III) [146] and WAIS-IV [147], and the Wechsler Memory Scale-III (WMS-III) [148] and WMS-IV [149]. This included the following tests: Category Fluency[150] (executive function and semantic memory), Digit Span [146] (working memory), Digit-Symbol Substitution Test [146] (processing speed and working memory),

Letter Number Sequencing [146] (working memory), Story Memory Test [151] (verbal memory), Token Test [152] (receptive language dysfunction), and Trail Making Test A and B [153] (visual attention and task switching). These tests were selected for the NAB for brevity of assessment and to focus on deficits in verbal and working memory present in schizophrenia [99, 154]. The standardised result from each test based on population normative data was pooled into an overall mean NAB z-score [94, 124, 148, 155-157]. When designing the NAB I consulted with Professor Barton Palmer, a neuro-psychologist who has used neurocognitive assessments in studies on DMC and published extensively in the area (see for example his review on the subject [155]).

Recruitment selection bias sub-study

To address aims 1 and 2:

1. To describe the proportion of people with DMC-R in adults admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

2. To determine how the symptoms of psychosis impact on DMC-R compared to DMC-T in this population.

And study design consideration c:

c) **Collecting detailed data on non-participants to measure and characterise selection bias.**

Methods

CRIS enables anonymised data to be collected from individual case records. For the purposes of the recruitment selection bias sub-study, I used CRIS to extract data on the characteristics of participants and non-participants in the study, including those who were approached and not approached by the research team to discuss participation. I used these data to compare the approached and non-approached groups, and recruited and non-recruited groups to investigate if there were any systematic differences between the groups and hence any approach or recruitment selection bias.

Selection of ward episodes

I used CRIS to select all inpatient admissions from the wards in which first approach and recruitment took place, delineated by the dates of which each individual ward was used as a site for recruitment. Individual patients through their admission journey often changed ward or were transferred out to other sites and back again, with some of these wards not being sites for recruitment for the study. For each inpatient episode, the series of wards that the patient traversed through were joined together.

Standardising data extraction

The first point at which the patient was admitted to a ward which was open as a site for recruitment was used as the date at which they were 'first at risk of recruitment' (irrespective of their later movements in hospital). The recruitment strategy of the main study was designed to approach patients as soon as possible after they were admitted to a ward open as a site for recruitment. Therefore, this was the time point in the inpatient admission selected for the extraction of clinical data. Many patients had multiple inpatient admission episodes during the recruitment period, these were each included, with their own individual date 'first at risk of recruitment'. The analysis was based not on individual cases, but rather individual admission episodes.

Eligibility

I used the same eligibility criteria as with the main arm of the study to evaluate and select ward episodes in order to select those who were eligible for recruitment. Patients whose age was over 65 at the point of 'first at risk of recruitment' were excluded from the

dataset. I manually reviewed the case notes from each ward episode, using the same criteria as I applied during the recruitment of the main arm of the study, to evaluate if the patient was eligible for recruitment into the study in terms of 'primary purpose of admission into hospital for the assessment and/or treatment of symptoms of psychosis' and removed those who were not. In terms of language proficiency, where it was clearly documented that an interpreter was necessary for clinical interview, I excluded these cases.

I did not exclude those with comments regarding risk to staff/on close observations/or around sexual disinhibition. As although in practice these acted as barriers to recruitment, I wanted to ensure these were measured and evaluated as potential biases to recruitment.

Research approach outcome

During the study outcome of research approach by CSOs, nursing staff, and myself (when permitted though C4C authorisation) including consent to participate was recorded in the EMR. These outcomes were extracted and each linked to an individual admission episode in order to allocate the outcome of each admission episode with regards to participation in the study. Some patients had prior refusal of participation in the study through C4C and this was recorded as a research outcome. However, some patients had prior refusal recorded, but nevertheless were still approached to participate and these were treated in the analysis as if they did not have prior refusal. Some patients had been approached on a prior admission and these were categorised accordingly as having been previously approached. I used these data to generate a research recruitment flow chart and to dichotomise the potentially eligible participants as approached vs not-approached, and participants vs non-participants.

Socio-demographic and basic clinical data extracted

I extracted gender and ethnicity for each ward episode. The primary diagnosis recorded in the EMR set closest in time to the date of 'first at risk of recruitment' was extracted, along with the legal framework of their admission at this date (such as detention under section 2 or 3 of the MHA, or informally admitted). If they were converted from a short-term section, such as a section 136 to a section 2 on the same day the longer-term section was extracted as the relevant legal framework. The recorded HoNOS score that was assessed closest in time to the date 'first at risk of recruitment' within two weeks of that date was extracted.

Complex symptomatic data extracted

I used 'TextHunting Apps' [158] designed by the CRIS team to extract data from the case notes regarding the presence of absence of symptoms that form components of the PANSS, HAM-D, and YMRS for the fourteen days from and including 'first at risk of recruitment'. These apps use natural language processing to extract data on the symptom profile of cases based on unstructured clinical records (such as contemporaneous case notes). They scan the records for key words associated with symptoms in clinical entries and then return a value for the entry as either reporting the presence or absence of a symptom during the entry, and unknown if the statement is ambiguous. If there are no entries within a scope specified to the app then a null value is returned. There have been several apps designed for a range of symptoms. As I was interested in the core symptoms of psychosis and affective symptoms as possible confounds, and limited to the range of apps already designed by the CRIS team I selected symptoms relating to the individual sub-scale items of the PANSS positive scale (delusions, formal thought disorder, hallucinations, agitation, grandiosity, persecutory

ideation, and hostility) and formed a mean average positive score from these, and core symptoms of manic and depressive episodes (low mood, anergia, anhedonia, elevated mood, pressured speech, insomnia, abnormal energy levels).

Reliability sub-study

To address aims 1 and 2:

1. To describe the proportion of people with DMC-R in adults admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

2. To determine how the symptoms of psychosis impact on DMC-R compared to DMC-T in this population.

And study design consideration e:

e) Assessing the external validity and reliability of assessments of DMC-R.

Methods

In previous research into both DMC-R and DMC-T expert panel methods have been used to evaluate the reliability of assessments of DMC (see for example [140, 159]). The 'expert panel' method involves using a range of experts in the field to judge transcripts or videos of DMC assessments and judging the case for the presence of absence of DMC based on the 'judgement standard'. Analysis and comparison of the judge's ratings allows for calculation of kappa statistics of inter-rater reliability of the assessment of DMC, and also the extraction of 'difficult cases' for which there is most disagreement for further, more detailed, exploration of the phenomenon of DMC at a meeting of the panel.

A criticism that could be raised toward the quantitative study is that the assessments of DMC-R were performed by me alone. Therefore, it is possible that the proportions of and associated symptoms found with DMC, despite the use of validated tools with high inter-rater reliability and my clinical training, are still limited to my subjective assessment. To be clear, it could be asserted that the proportion of people with DMC-R found by my study is in fact the proportion of people with DMC-R under the 'Ben Spencer standard'. The use of an expert panel reliability exercise is to evaluate the strength of this assertion by using a panel of independent judges who may in their work be required to perform similar assessments of DMC-R.

A second criticism that could be raised, is that the assessment of DMC could vary by the specific training and background of the assessor of DMC. For example, the reliability between clinicians assessing DMC may not be a result of the stability of the DMC construct, but rather reliability of the training of the clinicians in their evaluation of DMC due to factors independent of DMC itself – such as a risk sensitive DMC model in the context of DMC-T (see [160] for a study investigating risk-sensitivity of DMC-T assessments).

I decided to closely follow the method used by Kim in his 2011 study [159]. His method, as I shall explain here and later in this chapter (see Reliability sub-study analysis p.100) collects both continuous and categorical data which allows for a more detailed analysis of individual judges' DMC thresholds. In comparison, other studies have focused on categorical data alone (see for example [140]).

Selection of expert panel and transcripts

I aimed to select a broad range of people with differing perspectives in the research process in the expert panel. Previous work on reliability in DMC assessments has used expert panels that were homogenous with regards to background and training. A possible criticism of the use of a panel comprised solely of one professional group is that the consistency of rater opinion may derive from the professional training rather than external reliability of the DMC phenomenon [161]. Therefore, I aimed to select a panel that would not just evaluate the reliability of DMC-R assessment, but in addition through the use of experts from differing backgrounds would also evaluate DMC-R assessment across backgrounds and thus evaluate the trans-professional nature of DMC-R assessment.

I selected a panel accordingly: two consultant psychiatrists with specialist expertise in the assessment of DMC and use of the MacCAT tools, a REC chair with experience of granting ethical approval to studies in which the participants may lack DMC-R, an academic and service-user with a research interest in DMC assessment, and an academic psychologist with expertise and experience in consenting to the BioResource study.

The first ten DMC-R interviews from participants during the run in period were excluded. The following 50 consecutive DMC-R interviews, following the modified MacCAT-CR structure, were transcribed by a professional transcriber. Cairns 2005 [140] found that a vignette improved inter-rater reliability of DMC-T so a vignette describing core details of the case was provided with each transcript

Evaluation criteria

I instructed members of the expert panel to independently review each transcript and to 'judge each interview as to whether in your expert opinion, taking into account your professional knowledge and experience, and the information in the vignette and transcript, whether the individual being interviewed had DMC-R for BioResource research using the standard of the Mental Capacity Act 2005'. They were instructed to rate on a scale of 1-4 whether they considered the participant had DMC-R (1, definitely has DMC-R; 2, probably has DMC-R; 3, probably does not have DMC-R; 4, definitely does not have DMC-R). This allowed for dichotomisation of DMC-R as a binary outcome, but also allowed for a continuous measure of DMC-R allowing for the calculation of mean DMC-R scores by each judge [159]. Each judge also rated each case based on the ease of assessment of DMC on a scale of 1-5 (1, very easy; 3, average; 5, very hard).

Expert panel meeting

The expert panel of judges was convened to a meeting to discuss the cases for which the judging panel was most split (3:3 or 2:4 disagreement – including the DMC-R assessment by myself in the panel). At this meeting, specific features of the case were discussed that led to disagreement and themes developed.

Quantitative analyses

All quantitative analyses were performed using Stata 14 (StataCorp, Texas).

Quantitative study analysis

The proportion of people with DMC-R and DMC-T was calculated with 95% CIs. The extent to which DMC-R overlaps with DMC-T was assessed using a chi-squared test of proportions. Measures of symptoms were converted into z scores based on the sample mean and standard distribution to facilitate direct comparison. Where the distribution of scores was skewed the score was trichotomised into high, medium, low, based on the sample range. Univariate analysis: logistic regression analysis was performed for the binary DMC-R and DMC-T outcome variable using the predictor variables. Effect sizes are expressed as odds ratios and 95% CIs. Within the neurocognitive measures the number of missing items was very high (>70% cases missing at least one item) and I was interested in the core symptoms of psychosis, such as hallucinations and delusions. Therefore, I did not impute and I performed a 'complete case' analysis and selected individual measures from the neurocognitive assessment battery with the both most data and measuring abilities of interest (working memory – digit span, short term memory – Logical Memory 1). To enable direct comparison between the PANSS and neurocognitive items I further restricted the analysis of these to those cases with data for all measures 'restricted dataset'.

Recruitment selection bias sub-study analysis

Basic descriptive statistics on socio-demographic data and clinical data including complex symptomatic data were calculated for participant and non-participants. I

compared at the time ‘first at risk of recruitment’ the illness severity scores (student's t-test), recorded consent status (chi-squared test), socio-demographics, and complex symptom scores between the participants and the non-participants, and those who were approached and not approached (student's t-test and chi-squared tests). Logistic regression analysis was used to compare the associations of these factors with those approached vs not-approached, and participants vs non-participants. The ‘TextHunter App’ data was only used in the non-approach and non-participation analysis due to the very high null/unknown rate in the data (all ‘TextHunter’ variables used in this study returned null or unknown for the vast majority of cases so absolute scores are difficult to interpret).

Reliability sub-study analysis

The analysis follows closely to that of Kim 2011 [159]. Basic descriptive statistics on the socio-demographic and clinical data of those participants contributing to the reliability study were calculated. Average DMC-R scores for each judge on the panel is presented and compared using ANOVA. Kappa statistics were calculated for the dichotomous outcome of the rating of DMC-R for each pair of judges in the panel, including pairing with my assessment of DMC-R and mean difference in average DMC-R score between judges and paired t-test statistic for these. Group kappa statistic was calculated for the panel, and group decision of the panel was dichotomised based on DMC-R being present if the majority of judges consider DMC-R to be present (three or more). Kappa statistic between the group decision and my DMC-R assessment was calculated. Intra-class correlation statistics were calculated to investigate whether controlling for variability in the thresholds of DMC-R of each judge increased the reliability of DMC-R assessment.

Ethical approval

This study was approved by the Camberwell and St Giles Ethics committee, reference 15/LO/0427. Final study information and consent materials are in Appendix 8 p.305.

The use of CRIS for research is covered by a database approval from Oxfordshire REC C (08/H0606/71+5) granted September 2008. CRIS has a rigorous security model developed with service users and the SLaM Caldicott Guardian. All projects using CRIS require approval from the CRIS oversight committee. The use of CRIS in this project was approved by the committee (project ref 14-116).

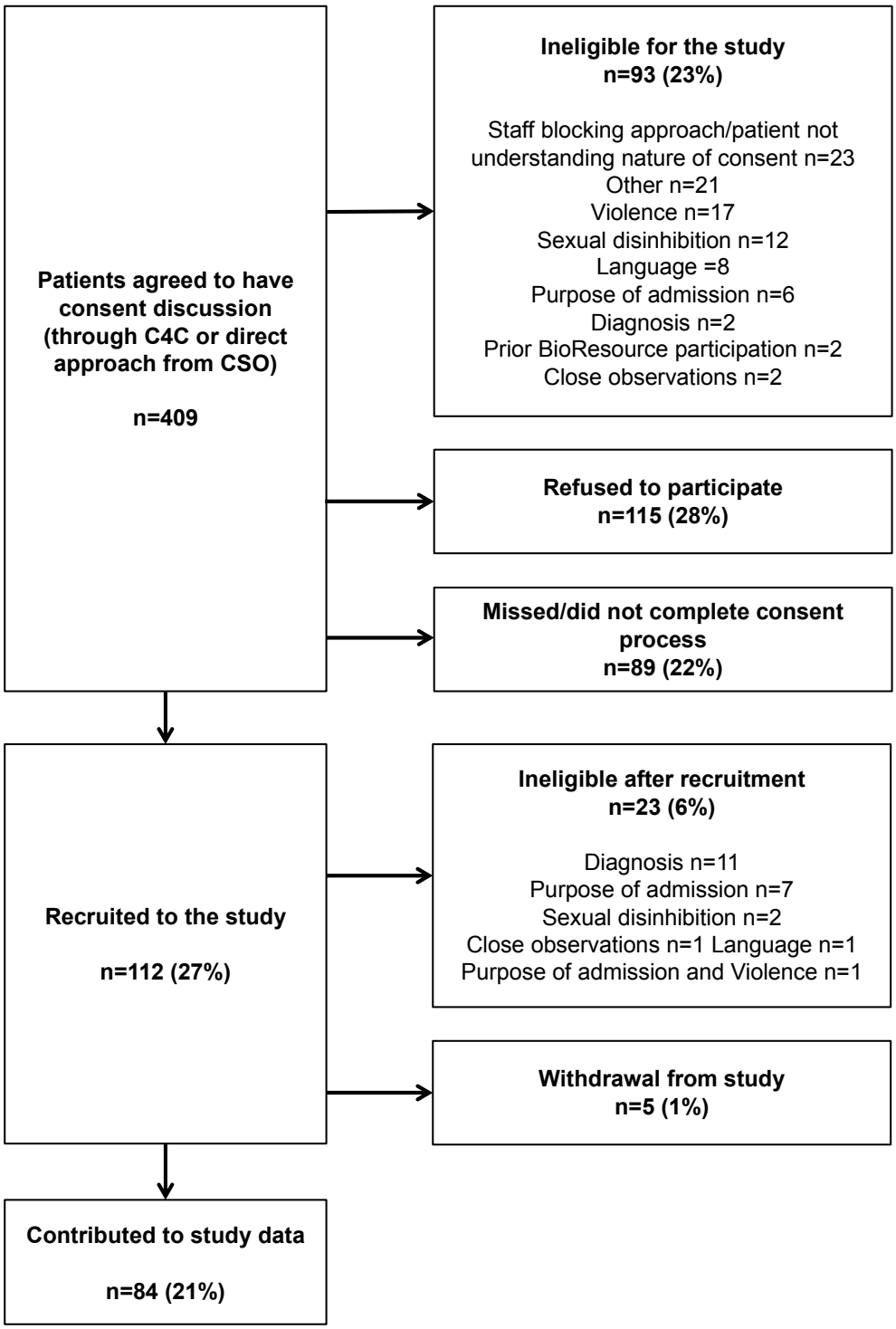
To ensure anonymity of participants all case numbers presented here have been anonymised from the individual study ID participants that were allocated at recruitment to the study.

Chapter 5. Quantitative study – A comparison of the proportions and symptom/socio-demographic associations of decision-making capacity for research and decision-making capacity for treatment

Study sample

84 participants completed the DMC-R assessments. Consultee approval to consent to the study was obtained in three participants, with one subsequently regaining DMC-R for the present study. The recruitment flow chart to the study is presented in Figure 3 p103. This presents the patients who had granted permission for a consent discussion with myself to take place, either through a priori consent via C4C or following discussion with a CSO. Usually, until consent for participation was gained for the study I was unable to review the notes (if first approach was performed by the CSO rather than through C4C) and therefore final decisions regarding eligibility could only be made following recruitment into the study. Often it was clear prior to the consent discussion that the patient would be ineligible following discussion with staff, such as due to risk of aggression, n=17, or sexual disinhibition, n=12. In total of those who had provided permission for consent discussions, n=84, 21% were recruited and contributed to study data. Of the five withdrawals that took place, n=1 participant requested deletion of study data after first interview, the other n=4 did not complete the research interviews sufficiently to form a judgement regarding DMC-R which was used as the bare minimum data required in order to contribute to the study dataset. More detailed exploration regarding participation and selection bias using the CRIS dataset is provided in Chapter 6 p123.

Figure 3 – Recruitment flow chart to the quantitative study



Basic socio-demographics and measures on the symptom scores of the sample are provided in Table 4 p105. The sample was predominantly male (n=73, 75% male), middle aged (mean age 38.40 (12.21) years), diagnosed with schizophrenia (n=61, 73%), and detained under the MHA (n=63, 75%). Half had participated in research before, n=38, 45%. The median time from admission to recruitment was 11 days (IQR 17). The majority reported maximum agreement on desire to participate in research as measured by the modified SAI-E, n=50, 61%, had the maximum agreement score.

Table 4 – Descriptive socio-demographics and symptom scales of participants

Socio-demographics		
Age (n=84)		38.40 (12.21)
Gender (n=84)	Number female	21 (25%)
Ethnicity (n=80)		
	White British	21 (25%)
	Black African	21 (25%)
	Black Caribbean	17 (20%)
	Mixed	12 (14%)
	Non-white other	5 (6%)
	White other	4 (5%)
Education (n=84)		
	GCSE or below	37 (44%)
	A-Level or above	47 (56%)
Current employment (n=84)		
	Employed	11 (13%)
	Unemployed	73 (87%)
Previous involvement in research (n=84)		
	Other research - prior involvement	38 (45%)
	No prior research discussions	46 (55%)
Days from admission to recruitment (n=84)		11 (17)*
Clinical variables		
Primary diagnosis (n=84)		
	f20 - schizophrenia	61 (73%)
	f25 - schizoaffective disorder	14 (17%)
	f22 - persistent delusional disorder	4 (5%)
	Other (f23, f28, f29)	5 (5%)

Table 4 (continued)

MHA status at time of Interview (n=84)		
	Informal	21 (25%)
	Section 2	36 (43%)
	Section 3	27 (32%)
Clinician's DMC-T assessment	DMC-T lacking	45 (58%)
	DMC-T present	33 (42%)
PANSS Scores		
	Total score (n=64)	68.66 (15.33)
	Positive symptom score (n=78)	20.77 (6.47)
	Negative symptom score (n=78)	12 (12)*
	General symptom score (n=69)	33.13 (6.88)
Insight	Item G12 Insight (n=77)	4.44 (1.63)
Trust score (n=73)	(Maximum range 7 - 49)	14.12 (4.08)
Global Illness severity		
	CGI (n=84)	4.08 (0.88)
	Study HoNOS (n=81)	12.70 (5.89)
	Clinician's HoNOS (n=68)	13.76 (5.23)
Affective symptoms		
	YMRS (n=65)	12.06 (7.27)
	HAMD 17 (n=65)	5 (6)*
Neurocognition	Neurocognitive Z score (n=25)	-1.28 (0.98)
Research agreement	SAI-E BioResource involvement (n=82)	7 (2)*

Results are presented as means and standard deviations unless specified. * Median and interquartile range.

Measures of DMC-R and DMC-T

Half of participants had DMC-R (51%, 95%CI 40-62%), compared with a third who had DMC-T (31%, 95%CI 21-43%). This difference was highly statistically significant, $p<0.01$. Table 5 below shows the distribution of people having DMC-R versus DMC-T. While in most cases participants either lacked or had both DMC-R and DMC-T (n=59, 74%) there were dissociations: n=18, 23% had DMC-R but lacked DMC-T, and n=3, 4% lacked DMC-R but had DMC-T. N=13, 15%, were found to have 'marginal' DMC-R, of these n=8, 62%, lacked DMC-R.

Table 5 – Presence of DMC-R vs DMC-T

		DMC-T	
		Present	Absent
DMC-R	Present	22 (28%)	18 (23%)
	Absent	3 (4%)	37 (46%)

DMC-R differed from DMC-T in terms of the performance on the individual criteria of the 'functional test' under the MCA (see Table 6 p.108): lacking the abilities of 'understanding' and 'retention' was commoner in DMC-R than DMC-T. Conversely lacking the ability to 'use or weigh' was commoner in DMC-T than DMC-R. Very few people lacked the ability to 'communicate a decision' for either DMC-R and DMC-T.

When assessed by the ward clinician close to the date of the assessment of DMC-T by the present study, the proportion of people with DMC-T was n=33, 42%, the difference between this and that of the study was not statistically significant (p=0.1494).

Table 6 – DMC-R and DMC-T MCA outcomes

DMC-R (n=84)		**DMC-T (n=80)**	
Lacking	41 (49%)	Lacking	55 (69%)
Present	43 (51%)	Present	25 (31%
Proportion with DMC-R 0.51 (95%CI 0.40-0.62)		Proportion with DMC-T 0.31 (95%CI 0.21-0.43)	
Chi-Squared test of proportions DMC-R vs DMC-T p=0.0096			

Marginal DMC-R	
DMC-R marginal	13 (15%)
DMC-R not marginal	71 (85%)

DMC-R MCA Understanding (n=84)		**DMC-T MCA Understanding (n=80)**	
Lacking	23 (27%)	Lacking	8 (10%)
Present	61 (73%)	Present	72 (90%)
Chi-Squared test of proportions Understanding DMC-R vs DMC-T p=0.0045			

DMC-R MCA Retention (n=84)		**DMC-T MCA Retention (n=80)**	
Lacking	24 (29%)	Lacking	8 (10%)
Present	60 (71%)	Present	72 (90%)
Chi-Squared test of proportions Retention DMC-R vs DMC-T p=0.0027			

DMC-R MCA Use or Weigh (n=84)		**DMC-T MCA Use or Weigh (n=80)**	
Lacking	41 (49%)	Lacking	55 (69%)
Present	43 (51%)	Present	25 (31%)
Chi-Squared test of proportions Use or Weigh DMC-R vs DMC-T p=0.0096			

DMC-R MCA Communicating a decision (n=84)		**DMC-T MCA Communicating a decision (n=80)**	
Lacking	2 (2%)	Lacking	1 (1%)
Present	82 (98%)	Present	79 (99%)
Chi-Squared test of proportions Communicating a choice DMC-R vs DMC-T p=0.5890			

Associations with DMC-R and DMC-T – socio-demographics

Associations between socio-demographic variables and DMC-R and DMC-T are presented in Table 7 p.111. There were no associations with age, gender, ethnicity, previous involvement in research, and current employment with either DMC-R or DMC-T. Highest educational attainment (A-Level or above) was associated with having DMC-R (OR 0.31 95%CI 0.12-0.75, p=0.010), however there were no associations with highest educational attainment and DMC-T.

Associations with DMC-R and DMC-T – clinical factors and symptoms

Associations between clinical factors and symptoms and DMC-R and DMC-T are presented in Table 8 p.114. Diagnostic subtype was not associated with lacking either DMC-R or DMC-T with the exception of delusional disorder, in which all cases had DMC-R but lacked DMC-T (n=4). Detention in hospital under section 3 of the MHA was associated with lacking both DMC-R and DMC-T (ORs 4.64, 4.89).

Measures of total psychotic symptom burden or overall illness severity (PANSS Total Score, CGI, and HoNOS) were associated with worse DMC-R and DMC-T. There were no associations with HAM-D 17 and lacking either DMC-R or DMC-T. Manic symptoms were associated with lacking both DMC-R and DMC-T with similar effect sizes (ORs 3.00, 3.74). There was no association with research agreement when measured by the modified SAI-E and either DMC-R or DMC-T.

The restricted dataset did not differ significantly from the full dataset on age (mean 39.93 (12.56) vs 38.40 (12.21)), sex (number female n=13, 28% vs 21, 25%) and education A-Level and above (n=30, 65% vs 47, 56%) (see Chapter 4 – Quantitative study analysis

p.99 for the explanation use of the 'restricted' and 'unrestricted' datasets and its limitations later in this chapter: Power and missing data p.120). Using the restricted dataset PANSS positive symptoms were associated with both lacking DMC-R and DMC-T (ORs 4.00, 3.88) although PANSS negative symptoms were not associated with lacking either DMC-R or DMC-T, significance was just missed for DMC-R (OR 2.33, 95%CI 0.91-5.98, p=0.079). Of the individual key symptoms of psychosis, as measured by PANSS individual items, hallucinations were not associated with lacking either DMC-R or DMC-T; delusions were associated with lacking both DMC-R and DMC-T (ORs 2.13, 3.67) but thought disorder was only associated with lacking DMC-R (OR 5.72, 95%CI 2.01-16.31, p=0.001). Worse digit span performance was not associated with lacking either DMC-R or DMC-T, but worse Logical Memory 1 performance was associated with lacking DMC-R (OR 2.68, 95%CI 1.43-5.02, p=0.002). Lack of insight had the largest effect on lacking DMC-T (OR 26.34, 95%CI 3.60-192.66, p=0.001) but narrowly missed significance with lacking DMC-R (OR1.86, 95%CI 0.91-3.79, p=0.089). The 'trust score' was not significantly associated with either DMC-R or DMC-T. When the dataset was unrestricted, thought disorder was associated with lacking DMC-T (OR 2.12. 95%CI 1.22-3.68, p=0.008) and lack of insight was associated with lacking DMC-R, (OR 2.76, 95%CI 1.55-4.90, p=0.001).

Table 7 – ORs of socio-demographic predictor variables on lacking DMC-R and DMC-T

(n DMC-R, n DMC-T)	DMC-R			DMC-T		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Age (n=84, 80)						
Years	1.03	0.99-1.07	0.116	1.04	0.99-1.08	0.100
Gender (n=84, 80)						
Male	1			1		
Female	0.56	0.20-1.54	0.260	0.80	0.27-2.33	0.676
Ethnicity (n=80, 76)						
White British	1			1		
Black African	0.56	0.17-1.91	0.356	0.64	0.17-2.38	0.508
Black Caribbean	0.67	0.18-2.41	0.537	0.94	0.23-3.92	0.936
Mixed	0.54	0.13-2.25	0.394	1.14	0.22-5.87	0.873
Non-white other	1.13	0.15-8.21	0.908	1.71	0.16-18.73	0.659
White other	2.25	0.20-25.37	0.512	*		
Involvement in research (n=84, 80)						
No prior involvement in research	1			1		
Previous involvement in research	1.09	0.46-2.58	0.843	1.14	0.44-2.95	0.786

*All participants of white other ethnicity lacked DMC-T

Table 7 (continued 2/3)

(n DMC-R, n DMC-T)	DMC-R			DMC-T		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Education (n=84, 80)						
GCSE or below	1			1		
A-Level or above	**0.31**	**0.12-0.75**	**0.010**	0.63	0.24-1.66	0.348
Current Employment (n=84, 80)						
Unemployed	1					
Employed	0.86	0.24-3.06	0.811	2.25	0.45-11.28	0.324
Diagnosis (n=84, 80)						
Schizophrenia	1			1		
Schizoaffective disorder	0.85	0.27-2.71	0.782	0.61	0.17-2.20	0.454
Delusional disorder	**			**		
Other	0.21	0.02-2.01	0.176	0.66	0.10-4.29	0.662
MHA status at time of interview (n=84, 80)						
Informal	1			1		
Section 2	0.92	0.30-2.79	0.881	2.67	0.83-8.54	0.099
Section 3	**4.64**	**1.36-15.90**	**0.015**	**4.89**	**1.30-18.38**	**0.019**

** All participants with delusional disorder (n=4) had DMC-R and lacked DMC-T

Table 7 (continued 3/3)

(n DMC-R, n DMC-T)	DMC-R			DMC-T		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Days until recruited (n=84)						
Days until recruited	1.01	0.99-1.03	0.282	1.00	0.98-1.02	0.832
Clinicians DMC-T assessment (n=78,75)						
DMC-T present	1			1		
DMC-T lacking	**3.79**	**1.46-9.86**	**0.006**	**6.20**	**2.11-18.25**	**0.001**
Research agreement (n=82, 78)						
SAI-E BioResource involvement	0.83	0.66-1.04	0.106	0.80	0.59-1.08	0.144

Table 8 – ORs of symptom predictor variables on lacking DMC-R and DMC-T

(n DMC-R, n DMC-T)	DMC-R			DMC-T		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Global severity assessments						
CGI score (n=84, 80)	**6.59**	**2.93-14.81**	**<0.001**	**3.73**	**1.88-7.40**	**<0.001**
Study HoNOS (n=81, 77)	**2.50**	**1.48-4.23**	**0.001**	**1.82**	**1.07-3.09**	**0.026**
Clinician's HoNOS (n=68, 64)	1.38	0.84-2.27	0.203	0.78	0.45-1.36	0.377
Affective symptoms						
HAMD 17 T* score (n=65, 65)	0.31	0.07-1.35	0.119	0.48	0.16-1.48	0.203
YMRS Score (n=65, 65)	**3.00**	**1.53-5.88**	**0.001**	**3.74**	**1.69-8.31**	**0.001**
Psychosis and neurocognitive symptom measures - full dataset						
PANSS Total symptom (n=64,64)	**4.97**	**2.19-11.29**	**<0.001**	**1.88**	**1.06-3.36**	**0.032**
PANSS Positive symptom (n=78,75)	**4.29**	**2.17-8.47**	**<0.001**	**3.18**	**1.65-6.15**	**0.001**
PANSS Negative symptom T* score (n=78,75)	1.93	0.98-3.83	0.059	0.91	0.46-1.80	0.777
PANSS General symptom (n=69,69)	**2.59**	**1.42-4.72**	**0.002**	**1.83**	**1.06-3.16**	**0.031**
Trust Score (n=73,72)	1.41	0.87-2.28	0.161	1.52	0.90-2.58	0.119
Delusions (n=81,78)	**2.34**	**1.40-3.93**	**0.001**	**3.20**	**1.78-5.76**	**<0.001**
Thought disorder (n=83,79)	**6.19**	**2.87-13.36**	**<0.001**	**2.12**	**1.22-3.68**	**0.008**
Hallucinations T* score (n=80,76)	1.23	0.65-2.34	0.518	1.26	0.61-2.60	0.532
Insight (n=77,76)	**2.76**	**1.55-4.90**	**0.001**	**36.68**	**6.43-209.20**	**<0.001**

All symptom measures have been converted into z scores based on the sample mean and standard deviation to facilitate direct comparison unless indicated. * T score – trichotomized by sample range into low 1, medium 2, high 3 score due to skewed distribution.

Table 8 (continued 2/3)

(n DMC-R and DMC-T)	DMC-R			DMC-T		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Psychosis and neurocognitive symptom measures - full dataset						
Digit span (n=58)	1.58	0.78-3.19	0.201	1.37	0.70-2.71	0.360
Letter number sequencing (n=46)	**2.30**	**1.01-5.24**	**0.047**	**2.78**	**1.12-6.88**	**0.027**
Logical Memory 1 recall (n=53)	**2.57**	**1.44-4.58**	**0.001**	1.24	0.77-2.01	0.373
Logical Memory 2 recall (n=46)	**3.11**	**1.10-8.78**	**0.032**	1.82	0.62-5.35	0.274
Logical Memory 1 thematic recall (n=53)	**1.93**	**1.15-3.26**	**0.013**	1.15	0.72-1.84	0.566
Logical Memory 2 thematic recall (n=46)	**2.15**	**1.18-3.94**	**0.013**	1.59	0.90-2.81	0.107
Trail making test A (n=55)	**1.25**	**1.03-1.51**	**0.021**	1.01	0.85-1.20	0.881
Trail making test B (n=37)	1.21	0.98-1.50	0.083	1.11	0.89-1.38	0.350
Letter fluency (FAS) (n=49)	1.69	0.98-2.93	0.060	1.52	0.90-2.54	0.114
Category fluency (n=43)	1.55	0.97-2.46	0.066	1.25	0.79-1.98	0.347
Digit symbol substitution (n=48)	2.15	0.90-5.11	0.084	1.20	0.54-2.65	0.652

Table 8 (continued 3/3)

	DMC-R			DMC-T		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Psychosis and neurocognitive symptom measures - restricted dataset n=46						
PANSS Total symptom	**8.99**	**2.60-31.13**	**0.001**	**2.36**	**1.08-5.15**	**0.031**
PANSS Positive symptom	**4.00**	**1.70-9.41**	**0.002**	**3.88**	**1.44-10.42**	**0.007**
PANSS Negative symptom T* score	2.33	0.91-5.98	0.079	0.89	0.36-2.22	0.805
Trust Score	1.76	0.87-3.57	0.116	1.85	0.84-4.03	0.124
Delusions	**2.13**	**1.09-4.16**	**0.026**	**3.67**	**1.62-8.32**	**0.002**
Thought disorder	**5.72**	**2.01-16.31**	**0.001**	1.82	0.85-3.90	0.125
Hallucinations T* score	1.41	0.55-3.60	0.473	1.47	0.52-4.13	0.466
Insight	1.86	0.91-3.79	0.089	**26.34**	**3.60-192.66**	**0.001**
Digit span	1.67	0.76-3.67	0.202	1.94	0.89-4.27	0.098
Logical Memory 1 recall	**2.68**	**1.43-5.02**	**0.002**	1.38	0.81-2.34	0.232

Discussion

Main findings

I have shown that DMC-R is different from DMC-T in terms of proportion of people in which is it present while unwell in hospital and the associated symptoms with lacking DMC. When unwell, around half of people with schizophrenia recruited to my study had DMC-R, more than those with DMC-T. Symptoms that had the largest effect on DMC-R were related to disorganised thinking and poor short-term memory (thought disorder and logical memory 1). By contrast, the largest and most significant effect on DMC-T was lack of insight.

Consistent with other work, I did not find an association with socio-demographic variables and either DMC-R and DMC-T, with the exception of an effect of greater years of education and having DMC-R. Out of the core symptoms of psychosis, hallucinations and delusions, only delusions had an effect on DMC-R and DMC-T, whereas hallucinations had no effect. On measures of total psychotic symptom burden or overall illness severity higher scores were associated with worse DMC-R and DMC-T.

Insight

The findings of a central role of insight with DMC-T is consistent with previous work [126]. The association with DMC-R just missed significance on the restricted dataset, but was significantly associated on the unrestricted dataset. I deliberately selected a parent study which I believed would not require insight into one's own illness. One explanation could be that lack of insight is associated with a reduction of meta-cognitive ability [162] and

thus would impact on decision-making in general. However, it is possible that even in decisions regarding non-therapeutic research, there remains a role for insight in decision-making. The conceptual relationship between insight and DMC-R is explored further in Chapter 9 p.199.

Thought disorder and understanding

The cases that lacked DMC-R but had DMC-T bear special consideration. On review of each case, my field notes report that in two out of three of the cases the main issue in lacking DMC-R was lack of 'understanding' due to thought disorder, but that this was both not severe enough to impact 'understanding' in DMC-T, and that participants were protected from the effects of the thought disorder due to prior knowledge. DMC-R required the ability to understand and processing novel information, but this was not necessarily the case in DMC-T and may explain the strong effect of short term memory performance and thought disorder on DMC-R rather than DMC-T. There is already a rich literature around the utility of educational interventions to support 'understanding' for research participation in schizophrenia (see Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37) and my findings both support this and the importance of decisional support tools around 'understanding' in research participation discussions. The different patterns of relationships between clinical variables and DMC are discussed further in Chapter 9 p.199.

MCA criteria measures of DMC

The 'functional test' of the MCA is inherently hierarchical, with 'use or weigh' at the top of the hierarchy: In order to be able to 'use or weigh' one needs to be able to

'understand', 'retain', and arguably 'communicate a decision'. In order to 'retain' on first needs to be able to 'understand'. The proportions lacking the ability to 'use or weigh' for DMC-R and DMC-T are identical to the proportions lacking DMC-R and DMC-T (see Table 6 p.108). This is unsurprising given this hierarchy. If one reports the number of people who lacked the ability to 'use or weigh' alone in those lacking DMC, thus removing the hierarchical component, then those who lack the ability to 'use or weigh' but all other abilities are intact in those lacking DMC-R is n=15, 37%, vs in DMC-T n=47, 85%. Lacking the ability to 'understand' (and 'retain') was more common in DMC-R assessments than DMC-T.

These results complement the symptom association analysis and suggest that the impact of cognitive deficits is mediated through deficits in 'understanding' and 'retention' rather than necessarily through 'use or weigh'.

Decision and person specificity of DMC-R and DMC-T

These data strongly support the legal and conceptual premise of decision-specificity. I have found that two different decisions differ in both proportion of people having DMC and the associated symptoms. Of interest is the impact of the cognitive symptoms such as short-term memory and thought disorder (although a primary symptom of psychosis thought disorder clearly has a direct cognitive effect) and their strong impact on DMC-R but limited impact on DMC-T. One might assume that these would affect all decisions equally, however I found evidence to the contrary. While it is self-evident that some decisions may require more detailed understanding than others, the impact of symptomology on these may be different, especially if there may be prior knowledge of the subject area. Therefore, when interpreting my results, it is worth reflecting that the

impact of symptoms will not just vary by decision, but also by individual and their previous life experience and knowledge.

Limitations

Power and missing data

The study was powered to detect a large effect size between the symptom measures and DMC-R and DMC-T which I deemed to be clinically relevant. Because this is a severely unwell sample, the study is inevitably limited by missing data, particularly within the neurocognitive assessment. To compensate for this, I restricted the analysis of PANSS and neurocognitive items for cases which I had full data so that direct comparisons of symptoms associations of DMC-R and DMC-T could be made. This limits the power of the study. The results do not substantially differ from the unrestricted dataset analysis other than for those already mentioned and they enable direct comparison – which is a limitation of the unrestricted dataset.

As explained in the methods (Chapter 3 – Quantitative study analysis p.99) I selected digit span and Logical memory 1 for the main neurocognitive measures for the study given they had the most data and measuring abilities of interest (working memory – digit span, short term memory – Logical Memory 1). It is worth noting that no neurocognitive assessment is pure in the domains that they are testing and therefore there can be other hidden confounds (such as low motivation/apathy).

Selection bias

I will cover selection biases in detail in the following chapter, Chapter 6 p.123, however there are a few points worth raising here that are derived from my experience of recruitment and the study data itself, rather than the CRIS data which is the focus of the next chapter.

The primary goal was to explore the proportion of DMC-R in the inpatient population and I designed the study accordingly in order to minimise the risk of selection bias but it likely remained: The level of PANSS negative symptoms was very low in my sample (total score 12 out of a minimum and maximum range of 7-49). Given the substantial motivation required to participate in a research study comprising multiple interviews taking up over 90 minutes in total, this is unsurprising. There was a high proportion of people reporting previous participation in research in my study, and this may be representative that people who were interested and open to participation in research in general may also be likely to wish to participate in a research study. Finally, it was not possible to approach many individuals due to risk to the research team from violence or sexual disinhibition. I consider these selection biases to be of limited concern because, with consent to research, we are concerned with the population that will safely volunteer to participate in research when severely unwell in hospital; these biases would not have significantly affected recruitment from that population.

The experience of approaching people to consent to the study was such that often when people clearly in my subjective view were going to lack DMC for the present study, they also either misinterpreted a key factor of the study such that it would have been unethical to recruit them, or there was a degree of anxiety about study involvement, due to misunderstanding, and therefore they declined. An example of misunderstanding leading to non-recruitment was an individual who did not understand that the study was

a research study, rather they believed that involvement was a form of university course, and that involvement would result in a qualification.

The impact of this basic level of understanding to participate in the study may have had impact on some of its results. The appreciation that one is free to refuse to participate had the highest scores (80% scored fully, compared with 50-70% for the other 'appreciation' items. However, I probably would not have recruited people if they had disclosed to me that they considered they were not able to refuse to participate in the present study. Therefore, unlike the other selection biases that I have dismissed as they would act as persistent barriers to recruitment, there may be more subtle factors impacting on the study data.

Chapter 6. Recruitment selection bias sub-study – an analysis of non-participation and first approach

Limitations to the CRIS dataset

The data extracted from CRIS is limited to:

1. Data that are routinely coded into the EMR as part of routine clinical care.

2. Data that is embedded in the contemporaneous case notes to be processed either by manual review or automated algorithms.

Therefore, the data presented is subject to errors that derive from incorrect clinical data at the source, for example dates of ward admissions, or incorrect or non-updated diagnoses.

When interpreting the results there are several factors that need to be borne in mind:

1. Each case is an inpatient admission episode during which patients may pass between several wards. Patients may have several admissions in hospital and each admission will count as a case providing that during the inpatient admission they pass through an inpatient ward that the study was recruiting from at that time. A case is therefore an individual inpatient episode in which the patient was at risk of being approached for recruitment. Accordingly, all data is primarily analysed on the basis of these cases, however for the recruitment flow chart I present patient numbers so that this data, which is purely derived from CRIS, can

be directly compared to my own quantitative study data which used individual patients as cases.

2. The processing of the cases in the CRIS analysis differs in sequence from recruitment to my quantitative study. The CRIS sample comprises people that according to my note review alone were eligible for the study. When recruiting 'on the ground' the first assessment of eligibility was usually performed by the CSOs own note review, which will naturally differ to my own, and it was only later that there were assessed by myself for final decision on eligibility. Thus there may be patients who I considered eligible but the CSOs did not, and vice versa. This would accordingly have an effect on whether they were approached or not by the CSO. When I was recruiting I also had available to me other sources of information regarding eligibility which included information from the nursing staff (such as concerns regarding violence or patient vulnerability to distress) which was not necessarily recorded in the notes and therefore available via the CRIS note review.

3. I reviewed each case note manually to confirm study eligibility as part of the CRIS data extraction, however, I extracted the assigned diagnosis in the EMR for comparison of the sample. This assigned diagnosis will at times differ from my own assessment of eligibility, and hence diagnosis, and may result in cases deemed eligible being 'diagnosed' with ineligible illnesses in the results.

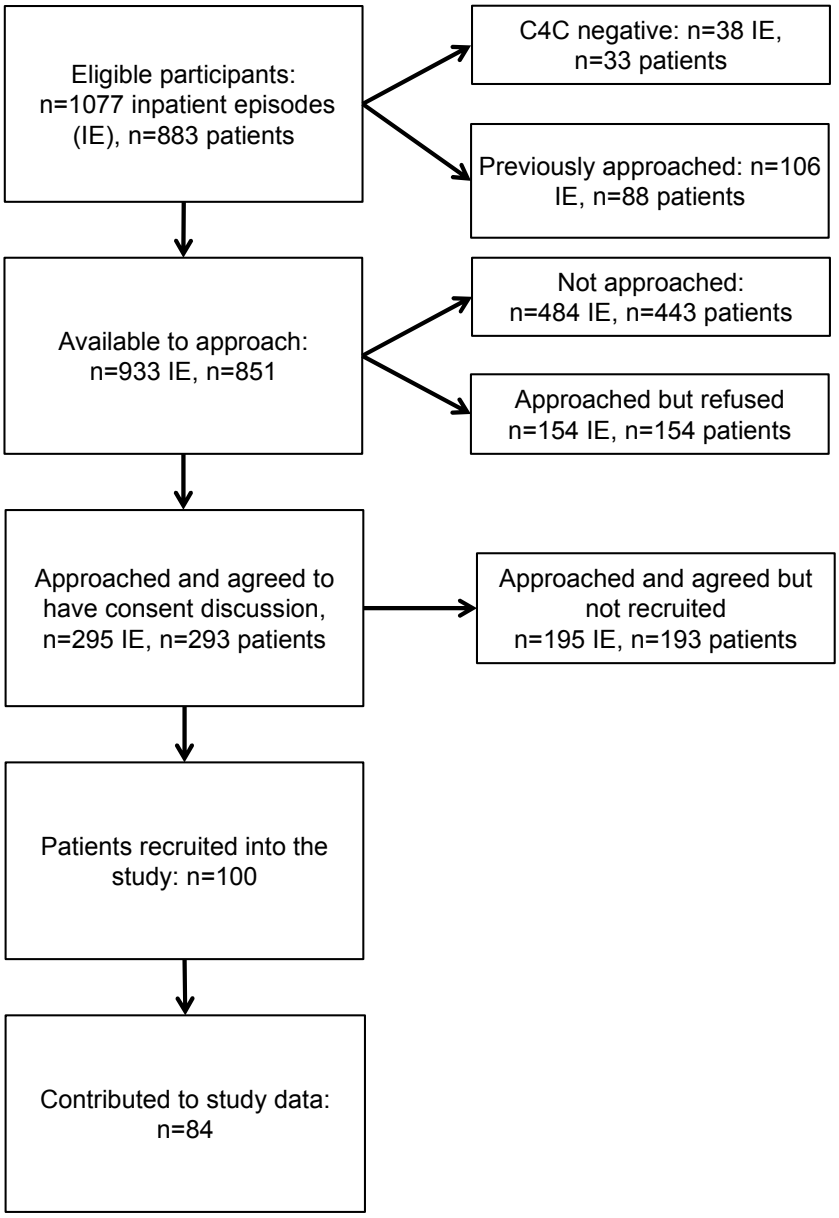
Recruitment into the quantitative arm of the study using CRIS data

From the initial CRIS search there were n=2382 inpatient episodes (IE) which were reviewed manually for eligibility (a small number of these were incorrectly divided as

separate episodes due to the limitations with CRIS so the number of unique IEs was slightly fewer). There were n=1077 IEs (n=883 patients) eligible for participation in the study during the recruitment period (see Figure 4 p.126). Of these there were n=933 IEs (n=851 patients) available to approach given no prior refusal or prior approach for involvement in research. Of these patients, just under half were not approached, and of the other half who were approached, two thirds agreed for discussion with me regarding consenting into the study. A third of the patients who met with me to discuss research consent were recruited into the study (n=100). Slightly fewer contributed to the final study data (n=84) due to ineligibility (such as violence and aggression, recovery to the point of being ready for discharge, or further information on diagnostic formulation leading to an ineligible diagnosis) or withdrawal from the study prior to key study procedures being completed. However, given that the CRIS data is provided from anonymised case records it cannot be unanonymised for cross-reference with my own recruitment logs to be more specific as to the reasons for non-contribution to the final dataset. Detailed data regarding these recruited participants who did not ultimately contribute to the dataset are provided using the study recruitment logs in the previous chapter, Chapter 5 p102.

Of the total number of unique patients admitted to hospital during the recruitment period, thus ignoring repeated admissions, I recruited 11% into the study.

Figure 4 – CRIS data on people approached/eligible by C4C and outcome of approach during study.



N.B. patient numbers do not add up as patients can have multiple outcomes.

Socio-demographical and basic clinical characteristics of non-approach vs approach and participation vs non-participation

Participants and non-participants had no significant differences on age, ethnicity, detention under the MHA, diagnosis, and illness severity when measured by HoNOS total score and individual items (see Table 9 p.128 and Table 10 p.129). However, female gender was associated with non-participation in the study, OR 2.36 95%CI 1.46-3.82, $p<0.001$.

Female gender was also associated with non-approach by CSOs or using C4C, but to a lesser extent than seen for non-participation. Younger age was also slightly associated with non-approach. Diagnosis of a psychotic illness under f23, f28, or f29 was associated with non-approach, as was diagnosis of a non-eligible psychiatric illness. Ethnicity and detention under the MHA was not associated with non-approach. Lower HoNOS scores were associated with non-approach, as were HoNOS individual items: 10 – problems with activities of daily living, 11 – problems with living conditions, 12 – problems with occupation and activities.

Symptom profiles associated with non-approach compared to non-participation

No symptoms extracted using 'TextHunting Apps' were associated with non-recruitment into the study. There were several associations with PANSS positive subscale symptoms and non-approach which included worse thought disorder and worse agitation. In contrast, worse negative symptoms were associated with being approached. There were no associations with PANSS positive total score or with the measures of affective symptoms.

Table 9 – Characteristics of participants and non-participants

	Non-Participants	Participants	Chi-Squared	d.f.	p
Total number	833	100			
Age	39.01 (11.71)	38.07 (12.27)	-0.7573a	931	0.4491
Gender (No female)	356 (43%)	24 (24%)	**12.9844**	**1**	**<0.001**
Ethnicity[b]					
White British	159 (19%)	23 (23%)			
Black African	165 (20%)	16 (16%)			
Black Caribbean	117 (14%)	11 (11%)			
Mixed	30 (4%)	5 (5%)			
Non-white other	27 (3%)	2 (2%)			
White other	60 (7%)	10 (10%)			
Other Black	210 (25%)	27 (27%)			
Other	58 (7%)	5 (5%)	4.4381	7	0.728
MHA on admission)					
Detained	571 (69%)	66 (65%)			
Not detained	262 (31%)	34 (34%)	0.2675	1	0.605
Primary diagnosis					
f20 - schizophrenia	366 (44%)	43 (43%)			
f25 - schizoaffective disorder	114 (14%)	19 (19%)			
f22 - persistent delusional disorder	10 (1%)	3 (3%)			
Other (f23, f28, f29)	130 (16%)	15 (15%)			
Other	213 (26%)	20 (20%)	4.9922	4	0.288
HoNOS[c]	14.75 (5.26)	15.65 (4.92)	1.4885[a]	736	0.1371

a, t-test, b (non-participants n=826, participants n=100), c (non-participants n=655, participants n=83).

Table 10 – Associations of research involvement

	No approach			No participation		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Age (n=933)	**0.99**	**0.98-1.00**	**0.014**	1.01	0.99-1.02	0.449
Gender (female) (n=933)	**1.62**	**1.24-2.11**	**<0.001**	**2.36**	**1.46-3.82**	**<0.001**
Ethnicity (n=925)						
White British	1					
Black African	0.89	0.59-1.34	0.565	1.49	0.76-2.93	0.245
Black Caribbean	0.82	0.52-1.29	0.400	1.54	0.72-3.28	0.265
Mixed	0.52	0.25-1.09	0.083	0.87	0.31-2.46	0.790
Non-white other	1.95	0.84-4.51	0.119	1.95	0.44-8.76	0.382
White other	0.88	0.50-1.52	0.639	0.87	0.39-1.93	0.728
Other Black	0.98	0.66-1.44	0.910	1.13	0.62-2.04	0.697
Other	1.17	0.66-2.08	0.598	1.68	0.61-4.62	0.317
Diagnosis (n=933)						
f20 - schizophrenia	1			1		
f25 - schizoaffective disorder	0.84	0.56-1.24	0.376	0.70	0.39-1.26	0.237
f22 - persistent delusional disorder	1.43	0.47-4.32	0.530	0.39	0.10-1.48	0.167
Other (f23, f28, f29)	**1.83**	**1.25-2.70**	**0.002**	1.02	0.55-1.89	0.955
Other	**2.29**	**1.65-3.20**	**<0.001**	1.25	0.72-2.18	0.430
Detained (n=933)						
Not detained	1			1		
Detained	1.14	0.86-1.50	0.356	1.12	0.72-1.74	0.605

Table 10 (continued 2/3)

	No approach			No participation		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Honos						
Total (n=738)	**0.96**	**0.93-0.98**	**0.002**	0.97	0.93-1.01	0.137
1 - Overactive, aggressive, disruptive or agitated behaviour (n=856)	0.98	0.87-1.09	0.642	0.86	0.72-1.03	0.102
2 - Non-accidental self-injury (n=855)	1.01	0.85-1.20	0.884	0.91	0.70-1.18	0.471
3 - Problem drinking or drug taking (n=828)	1.04	0.93-1.15	0.489	0.90	0.77-1.05	0.190
4 - Cognitive problems (n=850)	1.01	0.88-1.15	0.900	1.18	0.93-1.49	0.165
5 - Physical illness or disability problems (n=853)	0.91	0.79-1.04	0.169	0.94	0.76-1.16	0.537
6 - Problems associated with hallucinations and delusions (n=855)	0.89	0.78-1.01	0.064	1.06	0.86-1.30	0.596
7 - Problems associated with depressed mood (n=855)	0.99	0.87-1.13	0.885	0.99	0.80-1.23	0.945
8 - Other mental and behavioural problem (n=855)	0.90	0.79-1.03	0.138	0.91	0.73-1.13	0.390
9 - Problems with relationships (n=837)	0.92	0.81-1.04	0.179	0.90	0.74-1.09	0.284
10 - Problems with activities of daily living (n=836)	**0.82**	**0.72-0.93**	**0.003**	0.89	0.73-1.09	0.276
11 - Problems with living conditions (n=806)	**0.87**	**0.78-0.98**	**0.023**	0.95	0.79-1.13	0.550
12 - Problems with occupation and activities (n=789)	**0.82**	**0.72-0.93**	**0.003**	1.04	0.84-1.28	0.722

Table 10 (continued 3/3)

	No approach			No participation		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Variables extracted using 'TextHunting Apps'						
PANSS Surrogates						
Positive Symptoms total	1.01	0.73-1.40	0.941	1.15	0.68-1.95	0.606
Delusions	0.97	0.85-1.12	0.700	1.06	0.85-1.33	0.619
Formal thought disorder	**1.64**	**1.02-2.61**	**0.039**	1.73	0.61-4.89	0.304
Hallucinations (general)	1.16	0.91-1.47	0.228	1.36	0.85-2.19	0.199
Agitation	**1.17**	**1.03-1.33**	**0.018**	1.15	0.93-1.42	0.200
Grandiosity	0.85	0.70-1.04	0.114	0.84	0.63-1.12	0.230
Persecutory Ideation	0.95	0.82-1.11	0.530	1.07	0.83-1.37	0.602
Hostility	0.87	0.74-1.01	0.071	0.87	0.69-1.10	0.232
Negative Symptoms (general)	**0.61**	**0.39-0.95**	**0.030**	0.77	0.44-1.33	0.345
Mood						
Depressive symptoms						
Low mood	0.93	0.79-1.09	0.349	1.09	0.83-1.42	0.548
Anergia	*			*		.
Anhedonia	0.78	0.42-1.48	0.454	*		.
Manic symptoms						
Elevated mood	1.03	0.90-1.18	0.664	1.22	0.97-1.52	0.083
Pressured speech	0.99	0.86-1.13	0.841	1.05	0.84-1.30	0.682
Insomnia	0.82	0.54-1.25	0.360	1.67	0.60-4.61	0.323
Energy levels (full of energy - negative no energy)	1.09	0.70-1.72	0.694	1.57	0.56-4.44	0.393

Variables extracted using TextHunting Apps use a scale of -1 no symptoms, 0 no data or unknown, 1 symptoms present. *All episodes with symptom present were associated with non-approach/non-recruitment.

Stratification based by gender

Given that female gender was found to be strongly associated with both non-approach and non-participation in the study, a second round of analysis was performed to describe how the female full sample compared to the male sample and to break down the associations of non-approach and non-participation by gender.

There were several differences between the male and female cases (see Table 11 p.133). Females were older than males, were more likely to be detained in hospital, and were less likely to be diagnosed with schizophrenia, but more likely to be diagnosed with schizoaffective disorder. There were no differences of total symptom burden when measured by HoNOS.

There is no clear pattern of difference between associations of non-approach and non-participation with any variables stratified by gender that differs from the non-gender stratified data. This supports the hypothesis that these factors had the same effect in both females and males when present, and the difference in non-approach and non-participation in females and males is possible as a result of a difference in their baseline characteristics. However, analysis was limited by multiple testing and differences between sample size between female and male groups resulting in some differences between significant only as a result of power differences (see Appendix 5 – Table 30 p.280).

Table 11 – Demographics of females versus males – full sample

	Females	Males	Chi-Squared	d.f.	P
Total number	441	636			
Age	**41.37 (11.08)**	**37.41 (11.84)**	**-5.5379[a]**	**1075**	**<0.0001**
Ethnicity[b]					
White British	83 (19%)	129 (20%)			
Black African	96 (22%)	109 (17%)			
Black Caribbean	59 (14%)	86 (14%)			
Mixed	17 (4%)	29 (5%)			
Non-white other	19 (4%)	12 (2%)			
White other	35 (8%)	49 (8%)			
Other Black	99 (23%)	178 (28%)			
Other	28 (6%)	41 (6%)	11.9596	7	0.102
MHA (on admission)					
Detained	**314 (71%)**	**410 (64%)**			
Not detained	**127 (29%)**	**226 (36%)**	**5.3636**	**1**	**0.021**
Primary diagnosis					
f20 - schizophrenia	**155 (35%)**	**341 (54%)**			
f25 - schizoaffective disorder	**102 (23%)**	**57 (9%)**			
f22 - persistent delusional disorder	**8 (2%)**	**7 (1%)**			
Other (f23, f28, f29)	**68 (15%)**	**89 (14%)**			
Other	**108 (25%)**	**142 (22%)**	**56.5323**	**4**	**<0.001**
HoNOS[c]	14.88 (5.35)	14.77 (5.08)	-0.2847[a]	842	0.7759

a, t-test, b (women n=436, men n=633), c (women n=339, men n=505).

Discussion

Non-participation

Using the CRIS dataset all eligible inpatient episodes (n=1077 IEs, n=883 patients) 11% of the patients participated in the study and provided study data. There have been two comparable studies recruited in a similar setting that provided data on non-participants – Cairns 2005 [93] and Owen 2009 [33] (Skipworth 2013 also provided non-participant data but cannot be directly compared as it used mixed inpatient and outpatient recruitment settings [92]). Both Cairns 2005 and Owen 2009 had far higher participation than the present study: In Cairns 2005 out of n=145 people with psychosis, n=62, 43%, were recruited (however some of the people not recruited included those who would have been ineligible to participate). In Owen 2009 out of n=181 people with psychosis, n=93, 62%, were recruited.

Both of these studies recruited in inpatient wards in the same NHS Trust as the present study (albeit on different hospital sites) therefore there will be many similarities between the samples for all three studies and the difference between recruitment performance requires explanation. There are several mechanisms that could account for this difference:

1. Mechanisms associated with first approach

Scrutinising the participation data, the main drop out occurred at the approach by CSO/C4C stage (50%). Therefore, the main barrier to recruitment into the study took place at first approach. There are several reasons why people may not have been approached: those that were 'missed' by the CSO team, those for whom the clinical team

advised not to approach the patients, and those the CSOs considered were ineligible to participate.

Both the Cairns 2005 and Owen 2009 studies were able to gain direct access to patient records for recruitment in his study. Thus, there were no delays following first approach to meeting with people for research consent. These frequently occurred during the present study given that following first approach there was a delay sometimes of many days until I was able to attend the ward to discuss research consent. Secondly, as described below there are likely to be systematic differences between the evaluation of eligibility of a case in the CRIS data extraction and that used by the CSOs, and hence many 'missed' people may in fact have been people who the CSOs considered ineligible but following my assessment would have been considered eligible, again this would not have occurred in Cairns 2005 and Owen 2009. Finally, there was no mechanism in the study to record how often the clinical team advised CSOs not to approach patients. The impact of the clinical team preventing first approach is discussed further below.

2. Mechanisms associated with demographic changes between studies

The clinical mileu and nature of the inpatient population with schizophrenia may have changed over time. Cairns recruited around 12 years prior (October 2003 to February 2004), Owen 2009 around 10 years prior (February 2006 and June 2007). There is a clear difference in the number of people detained under the MHA out of the total population (not limited to those with schizophrenia) between their studies and the present one: In Cairns 2005 there were 41% of patients were detained under the MHA, and in Owen 2009 44%, whereas in the present study it was 68%. The difference in proportions of people detained in hospital between both Cairns 2005 and Owen 2009 and the present study is highly statistically significant, both $p<0.0001$. An increase in the use of detention

under the MHA over the past decade is also a phenomenon that has also been observed nationally [163].

A limitation of this comparison is that the detention data presented in both Cairns 2005 and Owen 2009 are for participants that had a range of diagnoses, and the higher proportion of people detained under the MHA in the present study could be due to higher proportion of people with schizophrenia being detained under the MHA. However, it could also be that the acuity of illness now required for admission into hospital has increased over time and thus there are now higher rates of detention under MHA. This may imply that the current inpatient population is more unwell than prior studies, and that severity of illness could be associated with non-participation. However, as the MHA is determined largely by risk, and higher use of MHA could be associated with higher risk to others in terms of aggression and violence in the sample, this increased use of the MHA could also imply increased risk to researchers and thus lead to non-approach and recruitment by the research team through this mechanism.

3. Mechanisms associated with the nature of the study procedures themselves

The study information to consent to the present study was complex. The research topic, how people make decisions about research and decisions more broadly, could have been seen as less immediate and pressing as decisions around one's own treatment in hospital, which for many participants in the study was delegated to the treating clinical team due to detention under the MHA. This may have resulted in less motivation to participate in the present study than in Cairns 2005 and Owen 2009 given that both of these were investigating DMC-T. Secondly the length of time of interviews that the patient needed to commit to in the present study was longer, and therefore this may also have been a demotivating factor.

A study specific factor within the study recruitment was simply the volume of time per participant taken to complete the research interviews. Most interviews were split over two interviews, and given the two recruitment sites and leave of the ward and ward rounds this limited the rate at which participants could be recruited and interviewed. While from my study logbook I was able to approach around 80% of those people who consented to speak to me in the study, it would be incorrect to conclude that the only rate limiting step for recruitment was necessarily approach by CSO, rather it was in my experience the time taken to perform and arrange interviews and travel between sites restricted by ward opening times was also a significant bottleneck, and if CSO approach had been greater I am not convinced recruitment rates would have substantively increased. However, this is purely a subjective assessment and without data to either confirm or refute it.

Approach vs non-approach, and participation vs non-participation

There were several socio-demographic variables that were found to be associated with either non-approach or non-recruitment into the study. Female gender was found to be associated with both non-approach and non-participation. Whilst most research finds that women are more likely than men to participate in research, in this context it is unsurprising. An exclusion criterion for risk reasons was sexual disinhibition or sexual risk, and that the overwhelming majority of first approach discussed were done with male CSOs and I am male myself. I did not apply the sexual disinhibition or sexual risk exclusion factor to eligibility for the CRIS data extraction, so this result may be a methodological artefact. However, there may be other reasons for a reduced participation and first approach in the study of females. All first approach and research consent discussions required discussion with the clinical team to ensure that there were no reasons not to approach. It is possible that female patients invoked more protective

instincts from the clinical team, or indeed female patients were more unwell than their male counterparts. However, when adjusting the results for HoNOS scores the relationship remains.

In the entire inpatient population that was eligible for recruitment, females as a group were older than males, more likely to be detained in hospital, less likely to be diagnosed with schizophrenia, and more likely to be diagnosed with schizoaffective disorder. Although a sex difference in the proportion of people diagnosed with schizophrenia of 1:1.4 between females and males has previously been reported [164], with an older age of onset [165], these are population data and does not necessarily explain the differences seen here. It may be that decisions around admission between females and males differ, with presence of affective symptoms in women (such as those leading to disinhibition and thus perceived vulnerability) may be more likely to result in admission including under the MHA. This hypothesis would also explain the bias against approach and recruitment of female inpatients.

The difference between non-approach by diagnosis irrespective of gender is likely to be due to a methodological artefact due to the detail of review of case notes prior to first approach. For the study consent I reviewed the case notes in detail to ensure eligibility as described previously, whereas the CSO may have focused more on the established diagnosis in the case notes, hence why the non-typical diagnoses, such as f23, f28, f29, and the non-eligible case note diagnoses were more likely to have not been approached. This is confirmed by the fact that the relationship is not present in the non-recruited cohort, but is present in the non-approached cohort.

The associations with the symptoms extracted using the 'TextHunting Apps' can also be understood in terms of the research recruitment environment. Agitation and thought disorder, the only positive symptoms that had an association with non-approach, are

clearly visible in an inpatient setting and can lead to advice not to approach from staff (the reasons for agitation acting as a barrier are self-evident, thought disorder could lead the clinical team to draw conclusions as to an individual who is severely unwell and due to confusion would not be able to tolerate a discussion with the CSO or may not understand the purpose of the discussion and hence needs to be protected from researchers – see Chapter 8 p.154 for more exploration of this). In contrast, greater negative symptoms are associated with higher chance of being approached. This can be understood as being due to being a 'captive audience' on the ward with greater negative symptoms leading to de-motivation, patients with these would be more likely to be on the ward or in their room when the researcher visits.

Higher HoNOS individual items associated with disability also led to a higher chance of being approached and the mechanism of this is likely to be similar as with negative symptoms. All symptoms that had an effect on approach did not impact on recruitment, and it may be the effect of the symptoms is on getting someone in a room to be able to talk to them regarding consent to participation, rather than on participation itself.

The lack of any associations with affective symptoms and approach or recruitment is interesting, as one may assume that affective symptoms such as mania may make it more likely to volunteer to talk to researchers, perhaps this effect, if present, is countered by associated irritability and distractibility that is part of the manic symptom cluster acting in the opposite direction.

Limitations

There were several limitations in the study. The aforementioned nature of the data extracted from CRIS is that it has inherent data entry and coding limitations and the

results must be interpreted with this in mind. An example here is the 'Other Black' ethnicity category, which comprised around a third of the population. Epidemiological studies performed in a similar geographical area have not used this category (see for example [166]), rather breaking down black ethnicity into black African and black Caribbean. Given that the coding of ethnicity data in the EMR included this category, and this was the sole data source used to extract ethnicity data in the present study, it was not possible to break this group down further. The impact of this in the results here is likely to be limited however, given that there were no associations with black African or black Caribbean ethnicity when the 'Other black' data were excluded'.

The selection of the date within each case's transition through the IE which was used as the reference point from which symptoms and other data were extracted is another limitation. It was not possible to use a data equivalent to the median date at which patients were first approached or consented into the study as this would inevitably be outside the scope of some of the briefest of admissions. Therefore, to reduce bias the date 'first at risk of recruitment' was used, but given that patients were approached at least 24 hours after this date by the CSOs, and that there may have been differences in the delays on different wards, this may have incorporated bias.

Finally, some patients were approached, and indeed recruited into the study even having dissented from C4C – essentially giving a priori refusal to be approached regarding research studies. It is difficult to evaluate the reasons for this; however, some patients did approach the researchers themselves when they were on the ward to discuss involvement in the study. It does, raise issues about the stability of refusal in the context of C4C and the restriction on re-approach.

Implications of CRIS data on the main quantitative study and inpatient psychosis research in general

This analysis has found several results of relevance for the interpretation of the results from the quantitative study. While the proportion recruited from the total population sample was low, 11%, only one factor I measured (gender) was statistically significantly associated with selection into the study. This matches my experience of recruitment to the study. Reassuringly no socio-demographic variable that I was able to collect data on affected either approach or recruitment into the study.

Given that the sample size of female only participants is n=21 repeating the full analysis in Chapter 5 p.102 stratified by gender is difficult due to power. However, there were no significant differences between the male and female participants on proportion with DMC-R (males 52% lacking, females 39% lacking, p=0.2567), DMC-T (males 70% lacking, females 65% lacking, p=0.6761), age (F=1.47 p=0.2295), and education (chi-squared=1.3042 p=0.253). This further supports a limited impact of any gender selection bias.

The difference between the approach and participation associations suggests that when one is in a room with someone then socio-demographic or symptom factors have little impact on whether the individual will consent to research or not, rather the most important issue is how their symptoms prevent being approached by the research team in the first place. Note that this analysis does not look at agreement to speak to the researcher at the approach stage (although it does at the recruitment) rather simply if the research nurse was able to speak to the potential participant. It would appear from these data that, at least in inpatient settings, there are many factors that can systematically affect approach by research nurses. To my knowledge this is the first study to have collected such detailed information in a systematic manner on participation of potential participants

and future studies recruiting inpatient settings should consider these selection biases to approach and design their studies accordingly: the use of female researchers and researchers interviewing in teams of two is an obvious and simple methodological recommendation.

In conclusion, non-participation in my main quantitative study was associated with female gender alone. Non-approach, a subset of non-participation, was associated worse thought disorder, agitation, and female gender whereas worse negative symptoms were associated with approach. Although the participation rate into my main quantitative study was lower than other similar studies I found no evidence from my CRIS data analysis that, other than a reduced proportion of female participants, my study sample was unrepresentative of the population. This is reassuring when interpreting the main quantitative study results. When designing future inpatient research in psychosis careful consideration needs to be given to the process of first approach.

Chapter 7. Reliability sub-study of decision-making capacity for research

Agreements and kappa

Basic demographics and clinical features of the n=50 selection of cases for the reliability study did not differ significantly from that of the main study sample (see Appendix 5 – Table 31 p. 283). The agreements of both the five-person expert panel (excluding my scores) and the six-person expert panel (including my scores) had a bimodal distribution, with the most cases being judged to have or lack DMC-R, with at most one judge dissenting (see Table 12 below and Table 13 p.144).

The five-person panel judged n=27, 54%, to have DMC-R. This is very close to the proportion with DMC-R that I found in the main quantitative study, n=43, 51%. The difference between these proportions was not statistically significant on a chi-squared test of proportions, p=0.7528.

Table 12 – Outcomes of five-person expert panel on DMC-R

	DMC-R N (%)
DMC present (majority standard)	**27 (54%)**
Five judges agree	16 (32%)
Four judges agree	8 (16%
Three judges agree	3 (6%)
DMC absent (majority standard)	**23 (46%)**
Three judges agree	4 (8%)
Four judges agree	14 (28%)
Five judges agree	5 (10%)

Table 13 – Outcomes of six-person expert panel on DMC-R

	DMC-R N (%)
DMC present (majority standard)	**25 (50%)**
Six judges agree	15 (30%)
Five judges agree	8 (16%)
Four judges agree	2 (4%)
Split panel	4 (8%)
DMC absent (majority standard)	**21 (42%)**
Four judges agree	4 (8%)
Five judges agree	12 (24%)
Six judges agree	5 (10%)

When using the continuous scores that judges gave cases (range 1-4 with 4 meaning most DMC-R), all had roughly equivalent mean DMC-R scores (2.3-2.7). The exception was the BioResource judge who had a much lower threshold to judge DMC-R present and thus had much higher average DMC-R scores and proportion rated as having DMC-R than the other four judges (see Table 14 below).

Table 14 – Expert judge mean DMC scores and percentage with DMC-R

	Expert judge				
	1 Psychiatrist one	**2 Psychiatrist two**	**3 Academic/ service user**	**4 BioResource**	**5 REC Chair**
DMC score Mean (SD)	2.68 (1.11)	2.54 (1.16)	2.56 (1.12)	3.36 (0.75)	2.30 (1.05)
Proportion DMC-R	54%	52%	50%	88%	42%
ANOVA F=2.81, p=0.0079					

Mean differences between DMC-R scores between judges are presented in Table 15 below. Consistently, the mean DMC-R score of the BioResource judge was significantly higher than all other judges, meaning a lower threshold to return DMC-R as being present. Most other mean differences between judges were non-significant.

Table 15 – Differences between mean DMC-R scores between judges

Expert judge pair	Capacity mean score difference (no signs)	Paired T-test of mean score difference	p value
Psychiatrist one - Psychiatrist two	0.14	1.4139	0.1637
Psychiatrist one - Academic/ service user	0.12	1.2876	0.2039
Psychiatrist one - BioResource	**0.68**	**5.2643**	**<0.0001**
Psychiatrist one - REC Chair	**0.38**	**3.2362**	**0.0022**
Psychiatrist two - Academic/ service user	0.02	0.2161	0.8298
Psychiatrist two - BioResource	**0.82**	**6.0251**	**<0.0001**
Psychiatrist two - REC Chair	0.24	1.8993	0.0634
Academic/ service user - BioResource	**0.80**	**6.4236**	**<0.0001**
Academic/ service user - REC Chair	**0.26**	**2.1563**	**0.0360**
BioResource - REC Chair	**1.06**	**8.2121**	**<0.0001**

Pairwise kappa statistics are presented in Table 16 p.146. Agreements between the clinicians themselves (BS, psychiatrists one and two) and the academic/service user judge were high, (k=0.68-0.88) 'substantial' to 'almost perfect' (based on the scoring scheme of Landis and Koch [167]. All agreements with the BioResource judge were 'slight' (k=0.16-0.18), and with the REC chair judge were 'fair' to 'moderate' (k=0.37-0.60). The five-and six-person panel group kappa statistics were 0.47 and 0.50 respectively, 'moderate', and between my assessments and the overall decision of the five-person panel was k=0.68, 'substantial'.

The interclass correlation coefficient, for a two-way mixed effects model (in which differences between rater DMC-R thresholds are taken into account) returned a value of 0.69, 95%CI 0.58-0.79. This is higher than the kappa for the five-person panel and demonstrates that there was a judge effect.

Table 16 – Pair wise comparisons of expert judgements

	BS	Psychiatrist one	Psychiatrist two	Academic/ service user	BioResource	REC Chair
BS	-					
Psychiatrist one	k=0.76 88%	-				
Psychiatrist two	k=0.80 90%	k=0.80 90%	-			
Academic / service user	k=0.68 84%	k=0.76 88%	k=0.88 94%	-		
BioResource	k=0.19 62%	k=0.19 62%	k=0.17 60%	k=0.16 58%	-	
REC Chair	k=0.37 68%	k=0.53 76%	k=0.56 78%	k=0.60 80%	k=0.18 54%	-
Group without BS	k=0.68 84%					

Expert panel meeting

Cases from the six-personal panel in which there was a judge split of 2:4, 3:3, or 4:2 DMC-R present:DMC-R lacking were selected for discussion. Generally, these were not cases with predominant thought disorder, but rather harder judgements in which decisions turned on the degree of understanding or the extent to which delusions impacted on the ability to 'use or weigh'. Several general themes emerged during the expert panel meeting regarding the assessment exercise:

Default presumption of DMC and the bare minimum necessary to achieve DMC-R

Many of the cases were considered to be marginal by the individual judges. In these marginal cases, commonly questions were raised about the DMC-R process itself, such as where does the default presumption of DMC impact on the assessments, and relatedly – how much does the patient need to show or demonstrate that DMC-R is present, if at all they do. Some considered a limitation of the exercise in general that it sets up an environment in which the default presumption of DMC is side-lined and that DMC-R must be evidenced by the transcript itself.

Limitations of the transcript method and need for more information

Often judges viewed that the nature of the transcript method led to difficulties in assessing DMC-R as there was other information that would have helped in decision making. There were examples of cases in which information that was known to me alone (presentation of the patient and interaction outside of the interview) would have helped the panel in decision-making, or that the written nature of the transcript missed out emotional information which would have helped in some cases (such as a case where negative symptoms and apathy featured prominently).

Whole picture

The judges frequently expressed a tension in judging a case based on the 'whole picture' and how much weight to put on isolated components. This frequently was the case in terms of the 'use or weigh' criterion in which there may have been evidence of isolated

episodes of highly distorted using or weighing, based on delusional beliefs, but the 'whole picture' of the case gave evidence of an intact using or weighing ability. In addition, when judging the case there was a primacy effect – clear statements at the end of the transcript had more impact than those at the start.

Discussion

I have found that the measurement of DMC-R, using the paradigm that I developed in this work, was highly reliable: When individual judge thresholds for DMC was taken into account, group agreement was high (ICC 0.69, 95%CI 0.58-0.79). The proportion of people found to have DMC-R by the five-person panel, 54%, was very close to my study's result and statistically indistinguishable. This, in combination with the evidence from the selection-bias sub-study provides strong evidence supporting the validity of my results and the design methodology used.

Other investigators performing reliability assessments in DMC have used expert panels in which the judges were homogenous, such as from the same professional background [140, 159]. In using a diverse range of people with differing backgrounds some interesting results have arisen, although clearly given the small numbers one cannot conclude anything with a lot of confidence. Notably, reviewing both the average DMC scores and pairwise kappa, the following pattern is evident:

1. The clinician judges (BS, psychiatrists one and two) and the academic/service user judge are all very similar.

2. The REC chair judge has a high threshold to judge DMC-R present.

3. The BioResource judge has a low threshold to judge DMC-R present.

The similarity between the clinicians and the academic/service user judge is interesting given that often people equate service users with anti-psychiatry. However, there could be an effect of similar training or research environment (the academic/service user is a member of the same research group as BS and psychiatrist one). The high threshold of

the REC chair judge could denote the context in which the REC chair operates, one of protecting patients from research involvement, and requiring a high level of DMC in order to allow participation. In converse, the BioResource judge recruits people to the study, and therefore has a low threshold to assume to allow participation. It is worth reflecting though, that on many judgements the BioResource judge reported that they would have returned and re-assessed again later prior to recruitment, and thus the low threshold on this exercise may represent an informal DMC-R screening process. However, the interview transcripts would likely contain substantially more information than the BioResource judge would have collected on screening and re-assessment.

Whatever the reasons behind the difference, there is a difference between different professional groups on the panel as to thresholds of DMC-R. No similar exercise has been done with DMC-T to my knowledge, and therefore it is difficult to know if this is specific to DMC-R, or would affect other DMC decisions.

To my knowledge Kim 2007 [168] is the only person to have used an expert panel method to assess DMC-R in schizophrenia as a categorical outcome using the 'judgement standard'. This study used the CATIE study as its 'parent study' (a naturalistic antipsychotic treatment study [169]), and included as its cases for the panel 55 people enrolled into the CATIE study, 36 participants with psychosis not enrolled into the CATIE study (which included some with affective psychoses), and 10 community controls. Research discussions were structured using the MacCAT-CR and videotaped. The videotapes were reviewed by three expert judges (and one additional judge where some were unavailable) all of whom were psychiatrists. Pairwise kappa scores ranged from 0.56-0.9, with a group kappa 0.69. The proportion of people found to have DMC-R was low, n=7 from n=55, 13%, CATIE participants; n=25 from n=101, 25%, total participants (this included community controls). This is also interesting given that this is less than my inpatient DMC-R proportion, but the difference may be due to the fact that the CATIE

study is a therapeutic research study and due to a greater impact of insight on DMC-R the proportion may be lower (see Chapter 9 p.199 for a discussion on the impact of insight on DMC-R). Comparisons between different expert panel paradigms are not only limited due to differences in the nature of the decision for which DMC is assessed and the illness studied, but also the statistical features of the kappa statistic itself. Kappa is sensitive to baseline rate, such that very high or low proportions lead to smaller kappas, whereas kappa scores are higher when outcomes are equi-probable (which they were for the clinicians and service user/academic group in my panel) [170]. Therefore, there are limitations in comparing these panel results with that of Kim's.

The expert panel raised several interesting issues in the assessment of DMC-R. Perhaps the most important is the role of the default presumption of DMC in this exercise. In setting of assessment of DMC-R where there is both restricted contextual data, and deliberate and detailed scrutiny of the data available over and above the usual process of assessment of DMC-R and research consent, does it invite the assessor to require the patient to prove their abilities in the transcript? Or in contrast does it remove important contextual information and therefore in the absence of evidence of lack of abilities in the transcript then the can only be a conclusion of no lack of DMC-R. Related to this is the question as to where the DMC-R threshold is set (as a low risk, low benefit study). It is also unknown how much a 'normal person' would need to understand or perform in order to have DMC-R, and arguable that this process (and the method of assessment of DMC-R for my study in general) sets too high a bar in order for someone to have DMC-R.

Given the limitations of the transcript approach, it could be argued that these disputed cases are all ones in which there is low data – and that the judges would want to have more information to decide – and in a low data environment professional training and biases had a strong effect. Expert panel assessments are in general limited due to the

lack of contextual information and cues. Cairns 2005 [140] found that providing a vignette along with the transcript improved reliability, mean kappa of 0.82 vs 0.60. A transcript can never be as good as a face-to-face assessment of DMC for two main reasons:

1) The interviewer is able to ask questions to the interviewee and clarify for themselves any areas of uncertainty, while the expert panel judge has to rely solely on what is transcribed,

2) The interviewer has access to a broad range of contextual information (body language, information taking place outside of the interview) etc. that the expert panel judge does not have.

Although the second point could be argued as a strength as it removes potential biases from the assessment. However, given the perspective of the panel judges themselves, they viewed the constraints of only having access to an interview transcript and vignette as a substantial weakness of the approach. Kim also found similar issues were raised in his study regarding the need to fill the gaps of the case and considering the 'big picture' [159].

In conclusion, only one fifth of cases were clearly contested, and the assessment of DMC-R by myself in the main study was found to be highly reliable. Cases were often seen as marginal by the panel members themselves, and the most frequent feature of the cases was one of where to set the threshold or the operation of presumption of DMC, or driven by limitations of the transcript method. The conclusions drawn regarding the differences between the judges are limited due to the small numbers and bias in their selection, however they show an interesting pattern that is consistent with anecdotal presumptions about professional roles with the REC Chair judge having the highest

threshold to assign DMC-R and the BioResource judge having the lowest threshold with the clinicians and academic/service user judges in the middle.

Chapter 8. Qualitative sub-study: Assessing or asserting decision-making authority

To address aim 3:

3. To investigate the suitability of interventions to enhance DMC-R and explore views on the current framework around consent for research.

Methods

Methodological considerations and analytical framework

I aimed to assess the suitability of an intervention or views on the current framework around consent to research. From the outset of the study I had a clear idea of the areas that I wanted to probe with my participants. These ideas were derived from my own perspective of research regulation as described in Chapter 2 – Research consent and p.22 and the proposed interventions for enhancing DMC-R, Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37. Therefore, a wholly inductive approach, such as 'grounded theory' [171] would not have been suitable and I needed to select a qualitative methodology that took primarily a deductive approach but also allowed for inductive reasoning.

There are strong parallels with my research area of interest and research into policy. The link between views on research governance and policy research is self-evident; the appraisal or suitability of an intervention can also be framed as testing suitability of a

proposed policy. Furthermore, research into policy starts with a clear set of objectives to explore with pre-formed ideas on the subject, therefore the considerations regarding the balance between deductive and inductive reasoning are similar.

Previous qualitative research into policy has used a 'framework approach' designed for applied policy research [172] (see also [173-176] for further background and examples). The framework approach involves a sequence of '1) interview transcription, 2) familiarisation with the interview, 3) coding, 4) developing a working analytical framework, 5) applying the analytical framework, 6) charting data into the framework matrix, 7) interpreting the data' (after Gale et al. 2013 [174]).

The framework approach is a 'matrix-based approach to data management' [176]. In essence, this means charting the data onto a framework that comprises a matrix with categories (comprising a family of codes) as the columns and individual cases as the rows. Each cell in the framework matrix is populated or charted through with a descriptive summary of the codes from the cross-section of that particular case and category. When used as a whole the framework approach facilitates analysis of the themes that occur not just by category but also across the individual cases. With policy research, there will be pre-specified topics of interest to explore (through deductive coding) and the framework matrix can be pre-specified and modified during the research as a result of the emergent codes and themes (through inductive coding).

I decided to supplement the framework approach with 'iterative categorisation', as described by Neale [177], which has previously been used with the framework approach successfully [177, 178]. Iterative categorisation is a systematic method for data handling that provides a clear audit trail of analysis, superior to that of the framework approach, and allows for the researcher to easily return to the primary data based on emergent themes. Iterative categorisation follows three stages: 1) familiarisation with the data and

coding, 2) descriptive analysis following a selection of categories, and 3) interpretative analysis. When used in conjunction with the framework approach the descriptive and interpretative stages of iterative categorisation are used at the charting and interpreting stages, stages 6 and 7, as described above.

Throughout this work, both in developing topic guides and the analysis of the data, I consulted with a consultant (TG – a service user and expert in philosophy, classics, and mental health). Qualitative analyses were performed using MAX QDA 12 (VERBI GmbH, Berlin) and MS Word for Mac 2017.

Selection of cases and topics of interest

A study of itself

From the outset, I recognised that a strength of my study was the potential for self-reflexivity. My study was a study into DMC-R but also covered areas of research governance and specifically the research recruitment and consent process. In order to study these areas, I would also have to perform the same tasks that I was studying in order to collect the data. In this way, and through my study design, I was able to collect data in such a way to facilitate self-appraisal. This is evident in the quantitative sections of the study (for example the recruitment selection bias sub-study – Chapter 6 p.123), but it is in the qualitative process that I took maximum advantage of this opportunity. My decisions around selection of cases and pre-specified topics of interest derive not just from the literature, but issues that occurred to me as I was designing the study, applying for ethical approval, and during the early stages of the research consent process itself.

I was interested in the views of people who, in my opinion, are key stakeholders in the research consent process: patients who would be participants in inpatient research, clinicians (mainly doctors and nurses who would be managing their care while in hospital), and the family/friends/carers of patients who could act as a 'research proxy' (the term I used for a person supporting decision-making around research as one of my interventions), or as a consultee/PLR (see Chapter 2 – Research when DMC-R is lacking p. 22). Naturally the research proxies were also interesting in terms of having an interest in the care of their loved one.

Therefore, I specified three categories of participants to recruit for in-depth interview:

1. Patient participants – Initially, for the qualitative sub-study, I aimed to purposively sample a selection of people deemed to have 'marginal capacity' from those who took part in my quantitative study (when I subdivided the groups into 'definitely has DMC-R', 'definitely lacks DMC-R', and those who were in the middle, see Chapter 4 – DMC-R p.83). My reasoning was that it would be the 'marginal capacity' group of people who would form the main target of an intervention to enhance DMC-R, and that it was those with 'marginal capacity' for whom lacking DMC-R and risk of consultee decision-making may be more salient. As the study progressed very few people fell into this category and therefore I expanded my recruitment to include people outside of the 'marginal capacity' group. This was not problematic as it was a finding of interest in itself with relevance to the application of any intervention and as the study progressed other areas of interest developed.

2. Research proxy participants – I aimed to purposively sample consultees who had already performed a consultee role in the study, and people who had been selected by a patient participant as being a prospective candidate for supported decision-making. However, the numbers of people who I judged lacked DMC-R to consent to participation in my own study, and thus requiring contact to family/friends/carers for consultee approval were very low; when I attempted to contact relatives to perform the consultee role it was difficult to get a response, and often they declined to participate. Therefore, I later expanded the recruitment strategy to include family/friends/carers of people who had DMC-R to participate in my study. As above this was not problematic as it was a finding of interest in itself with relevance to the application of any intervention.

3. Clinical participants – I aimed to purposively sample clinical participants including doctors and nurses from those who were intimately involved in my recruitment of patient participants to the quantitative study, or who raised issues around participation in research during this process.

Research proxy participants were recruited through direct contact following permission from the patient participant. Clinical participants were recruited through direct contact on the wards in which participants are being recruited. The same inclusion and exclusion criteria for the quantitative study applied to the recruitment of patient participants to the qualitative sub-study, however research proxy and clinical participants were only required to be adults aged over 18 with fluency in English to a level able to undergo a semi-structured interview. The same informed consent procedures that applied to the participants in the quantitative study also applied to the research proxy and clinical participants, however I did not recruit people who lacked DMC-R to consent to the qualitative sub-study itself. A further £10 compensation was given to patients who

participated in the qualitative sub-study. Research proxy participants were also offered £10 as compensation for their time.

All participants underwent a 60-minute interview with each interview tailored according to the participant group and structured using a topic guide. The interviews were audio-recorded and transcribed.

The purposive recruitment aimed for thematic saturation [179] and I anticipated recruiting six participants from each group, given time constraints and the relatively homogeneous nature of the groups and topics (see also [180] for a discussion on decisions regarding the number of subjects required for qualitative research). I made decisions about recruitment in consultation with TG and my supervisors in an ongoing manner as part of the iterative analysis.

Topics of interest

I structured the interviews using topic guides, adapted during the study as an iterative process as the data was analysed and themes emerged aiming for theoretical saturation. Half way through recruitment to the qualitative sub-study a preliminary round of analysis of a set of selected interviews was performed, including developing a draft framework as described in the analysis section later in this chapter (First phase of analysis p.162). The results of this preliminary analysis were used to guide the further refinement of the interview guide based on areas that warranted further exploration as themes emerged.

I initiated the study with a set of pre-specified topics of interest, derived from my study objectives and insights from the self-reflective nature of my study (as described above),

which I used to develop the first iteration of semi-structured interviews (see Appendix 7 – Initial topic guides p.284 for the first set of topic guides):

- **The current process of consent to research participation** (attitudes and beliefs about the research interview and consent process, barriers to involvement in research).

- **The involvement of consultees in those who lack DMC-R** (the role the consultee performs, the differences in selection of consultee between CTIMP and Non-CTIMP studies, and if applicable – how they would choose a consultee/the process of selection, concerns about this role and its selection/concerns and views about their own selection for this role).

- **Involvement in biomedical research projects while in hospital** (motivation to participate, concerns and barriers to involvement in research, and if applicable – the patient participant's involvement in biomedical research, do they support it, what are their fears and concerns, what are their priorities regarding the patient participant).

- **Supported decision-making for biomedical research** (views and concerns regarding involvement of carers/relatives/friends, concerns/expectations about this, do they support it and the barriers to involvement in research discussions, and if applicable – who they would chose and why, involvement of themselves for supported decision-making, are they contactable).

- **Use of neurocognitive tools to support decision-making in hospital** (acceptability of use of multimedia and pictorial methods to explain research).

- **The attitudes and beliefs of the clinical team members regarding their role in first approach to recruit participants for biomedical research** (when are they 'too unwell' to approach or consent and when are they 'well enough'). This was a topic of interest that developed as I designed the study and developed recruitment strategies based around first approach (first approach for participation in research is performed by individuals other than the research team, and that the researchers cannot have access to confidential medical information see Chapter 4 – First approach and recruitment strategy p.78). I found during the design phase that first approach seemed like it could act as a potential barrier to recruitment and accordingly decided to explore it further in the qualitative sub-study.

Results

Participants

I recruited eight clinicians, three carers, and seven patients to the qualitative sub-study. Recruitment of clinicians was relatively straightforward following direct approach, given that I worked and met with them on a daily basis during the recruitment to the quantitative study. Of the clinicians, four were doctors, two female and two male, and four were nurses, all female.

Around half of the patients who took part in the study gave me permission to contact their relatives n=46, 55%. In attempting to contact relatives for either consultee or involvement in research, I approached eighteen people, six refused or disengaged, six I could not contact, five consented, and one I was not able to contact due to advice from the clinical team. As a result, the number of research proxies I was able to recruit into the study

was small. All research proxies recruited were carers (and first-degree relatives) and accordingly for this analysis I have renamed them accordingly as carers.

As a group, the carers were interesting as each had strong motivations for participating in research, either seeing it as: part of their carer role (Carer Q3), to do anything to potentially help their loved one (Carer Q1), and to assert their views regarding being central and involved in decision-making regarding their loved one (Carer Q2). There was an interesting disconnect between the general disengagement/difficulty recruiting carers and the strong motivations/agenda of those who were recruited. Two of the carers were female and one was male.

Progression of analysis and development of the framework matrix

First phase of analysis

After I had recruited three to four participants from both the clinicians and patient groups I performed an initial analysis of several interviews. I coded the initial interviews using principally deductive codes derived from my pre-specified topics of interest, however during this process I also allowed for inductive codes emerging from the interviews themselves. I summarised them into a draft framework matrix also based on the broad categories of enquiry in my pre-specified topics of interest (without using the process of iterative categorisation which I adopted later in the study) with each individual case forming a separate row on the matrix. TG also coded several interviews so that coding could be compared.

Following discussion of this initial analysis I refined the topic guide in order to allow more detailed exploration of both the pre-specified topics of interest and those emerging from

the inductive coding that were related to my research aims and thus needed further exploration.

The new topic guides were structured accordingly (see Appendix 7 – Revised topic guides p.300 for the revised set of topic guides) and covered the following domains:

A) Facilitators and barriers to involvement in research

Motivations to participate in research, procedure, environment, should different research be treated differently.

B) Research Governance and procedure

Rules and regulations, clinical responsibility, worth of involvement in research, process of consent, role and interaction with the MHA, who should do research and their agendas, purpose of information sheet.

C) Decision-Making not by participant

Who decides, and using which model of decision-making, reasons for their decision making, supported decision-making and consultee approval, neurocognitive support tools.

D) Research Consent Capability

'Voluntariness', insight, what do people think about 'wishes and feelings' and decision-making of the person without DMC.

Based on the similarities between responses between members of the same participant groups (clinician, carer, and patient) I decided that rather than treat each participant as a separate case and thus with a separate row on the framework matrix I would group all participants of the same type together for the future framework matrix. As a result of the

analysis the first version of the framework matrix was developed and is presented in Table 17 p.166.

During this early stage, I started to explore a conceptual model which could be an alternative to the MCA model of DMC-R based around what I called 'voluntariness'. This model was based on a 'bare minimum' model of DMC-R requiring only 1) understanding that the project is research, 2) one is free to decline to participate, 3) motivation to take part is not-disordered. This section was later dropped following the second phase of analysis as the concept was difficult to explore (see the following section), and during the work I realised its limitations as a model and latterly developed a different conceptual model (see Chapter 9 p.199).

Second phase of analysis

After I had completed all of the remaining interviews all interviews were entirely re-coded afresh using again a combination of deductive and inductive coding. The deductive codes I had used in the first phase were refined. During the coding, I met with TG and several decisions were made as to which areas to keep in the framework matrix with a view to meeting the aims and objectives of the analysis and given the nature and scope of the data obtained. Table 18 p.167 shows the refined second version of the framework matrix.

Several decisions made regarding the exclusion of topics from the framework matrix were due to limited responses when they were explored with participants. These included topics covering advance directives in research, the definition of DMC-R, 'voluntariness', and the role of part IV of the MHA when considering therapeutic research in hospital (to do with the regulation of medical treatment for mental disorder). My

experience probing these areas during the research interviews was that most of the interview was invested in explaining a complex and nuanced area of mental health and mental capacity law. The coverage of these topics in the research interviews did not aid my understanding of the area, and this was clearly evident at the coding stage where most responses by participants were of passive concordance with what I was saying or asking. Understandably they were not topics that most participants felt ready or able to answer on and in retrospect it is clear that my selection of participants to answer these questions should have been a different group (such as people with intimate experience of research governance).

Third and final phase of analysis

I charted the data onto the framework matrix using the process of iterative categorisation as described above. Once I had completed the descriptive analysis stage and prior to moving onto the interpretative analysis I further refined the framework matrix. I dropped the categories 'relationships' and 'status of participant' as both the coded sections and the beginnings of the emergent themes I could see in these were covered within other categories in the framework matrix. In addition, and related to the above, I noticed that these categories were acting as themes across the framework matrix and thus were best handled as themes in the analysis rather than discrete categories within the framework matrix. I proceeded to the interpretative analysis and this was reviewed in a research meeting with TG. The final version of the framework matrix is shown in Table 19 p.168.

Table 17 – Framework version 1

	Categories														
	Facilitators / barriers		Decision-making			People					Governance				
Cases	Motivation for research, facilitators of research, overcoming barriers to research	Benefits and disadvantages of participating in research	Support Vs consultee approval	Use of neurocognitive supported decision making	Helping people make decisions about research	Who decides	Who is responsible	Who should research	Relationships	Status of patient (issues and concerns)	Advance directives, loss of DMC, Part IV of the MHA	1st approach	Different regulations for different research/insight/DMC-R definitions	Best interests	'Voluntariness'
Clinicians															
Carers															
Patients															

Table 18 – Framework version 2

	Categories								
	Participant decision-making			Decision-makers					
	What helps people make a decision (DMC-R)		Motivations, barriers, facilitators (wishes and feelings)	Consultee vs supported decision making	Relationships	Insight	Who decides and why		
Cases	Neurocognition	Helping people make a decision					1st approach	Status of participant	Patient as decision maker vs other models
Clinicians									
Carers									
Patients									

Table 19 – Framework version 3 (final version)

	Categories						
	Participant decision-making				Decision-makers		
	What helps people make a decision (DMC-R)					Who decides and why	
Cases	Neurocognition	Helping people make a decision	Motivations, barriers, facilitators (wishes and feelings)	Insight	Consultee vs supported decision making	1st approach	Patient as decision maker vs other models
Clinicians							
Carers							
Patients							

Interpretative analysis of final framework matrix

From the outset, I aimed to explore research regulation and evaluation of the acceptability of proposed interventions for enhancing DMC-R. For clarity, I will address each separately and in turn starting with the proposed interventions including other direct interventions emerging from the analysis.

Acceptability of proposed interventions

Neurocognition

When exploring the views of participants regarding the utility of neurocognitive interventions many of the themes raised here also occurred when I explored how to facilitate research participation generally (in terms of helping people understand better what the purpose of the research or reason they should get involved). All participant groups thought that an intervention to help understanding would be useful, and there was a particular focus on using multi-media (videos, iPads) and other non-written means of putting across information:

> **Clinician Q2:** I do think that we are now a generation of video watchers, and you just have to go on Facebook and see… if you scroll up on Facebook and see how many videos people upload, or there are on the internet, or on Twitter, or whatever. Um… people are used to watching videos about stuff all the time, and you know, our iPhones are kind of… I'm just saying I think it would be quite a helpful. people would find it… would adopt that quite well, I think.

All participant groups suggested simplification. This included condensing the key information to be understood to fit on one sheet of A4 paper, and to use bullet point and checklists. However, both clinicians and patients warned that over-simplification could be patronising or insulting, and that any intervention of this nature would need to be

tailored to the individual. This theme was present when exploring more broadly how best to help people make a decision: clinicians and patients both considered that the information provided during the research consent process need not just to be as simple as possible, but also that the information was sufficient to make the decision.

> **[Discussing how to help people make decisions about research]**
>
> **Clinician Q4:** And not necessarily dumb it down, but put it into a lot less jargon, and a lot simpler as to what's going on, and what is expected to happen during this research project, and what is completely expected of you. […] Um… just more… more information, but concise.
>
> **BS:** Um… what do you think would be the best way to help people make decisions about research?
>
> **Patient Q4:** Just give them all the information they need.
>
> **BS:** Yeah.
>
> **Patient Q4:** Um… make it easy on them as well.

Clinicians focussed on the attractiveness of how information was presented, ensuring that the potential participant could understand it, while carers focused on ensuring that the potential participant could tolerate the interview seeking to avoid them getting fed up, tired, or overwhelmed.

In summary, neurocognitive interventions were uncontroversial and considered acceptable by all participant groups. I found consensus that the information provided for research consent needs to be simple, but not too simple, and tailored to the individual to ensure it is not patronising and meets their individual needs.

Clinicians and carers considered that people present to support people make decisions could be useful, although the patient's views were mixed as for the most part they felt it was not necessary. There were two prominent themes regarding the relationship of the chosen individual to support with both the participant and the research team, including their independence from both, and issues of trust.

Clinicians viewed the process as particularly useful if the person doing the supporting was someone whom they knew and trusted, and at times this trust was linked to independence from the research team.

> **BS:** … that the person trusts, or an independent person, to take part in the research discussions with that person… do you think that could be useful? I mean, thinking of your experience on the ward and the patients you've looked after. Do you think that third party present would be useful?
> **Clinician Q5:** Yes... yeah… yeah. I think our patients have very different conversations with people they trust than they do with us….so, have different conversations with people that they perceive as being independent.
>
> […]
>
> **BS:** And you're saying one of the big issues is about trust… is there any other thing that you think would be important in selecting that third person to take part in those discussions?
> **Clinician Q5:** Um… it's a very difficult one, because again it's very much dependent on the individual, I think. I think trust is probably the most important one, that the patient trusts them… um… And I suppose, you know, it would have to be somebody who doesn't stand to gain either way.

Patients also considered that the main factor involved in the supporting was trust in that individual:

[Discussing patient's daughter's involvement in supported decision-making]

BS: Would she, erm, so let's say you were really unwell.

Patient Q3: Yeah.

BS: Um, and you were really paranoid,

Patient Q3: Yeah.

BS: didn't want to talk,

Patient Q3: Yeah.

BS: and if a researcher you didn't know,

Patient Q3: Yeah.

BS: not me, but somebody completely separate

Patient Q3: Yeah.

BS: came and spoke to you, if it was, let's say, you know, if [daughter's name] was there,

Patient Q3: Yeah.

BS: would that help you?

Patient Q3: YES, yes, yes, yes, yes, that would that would

BS: How would that…

Patient Q3: because I'm trusting her, everything, (incomprehensible) inside my head, despite of me, and I'll always should trust my daughter.

BS: Yeah?

Patient Q3: Yeah, I'll always trust her.

BS: So you, you personally would find that quite, would find that useful?

Patient Q3: Yeah.

Clinicians considered that a close relative/family member or independent advocate could help them feel secure, and that the process of supported decision-making would act as a further safeguard in the research process. However, they were mindful that there could be disagreement between the supporter and the patient themselves and that the process of acting as supporter it could impact on their relationship in a negative way. Family/friends/carers might also not be willing to take on the role or have it high on their priorities.

Clinicians considered independence from the research team more important than the relationship with the patient; some clinicians ruled themselves out from performing the supporting role as despite considering their relationship with the patient as possibly

helpful, the risk of role confusion for the patient or that they would not be seen as or actually be independent overshadowed it. Similar challenges arose with independent advocates and their own personal agendas: can they ever support decision-making about research participation while being independent from the research team and also trusted?

> **Clinician Q8:** Ok, I think a separate group of advocates would be ok, and I think… erm… that might help people to decide whether or not to take part, because they would have an outside, independent view of it.
>
> **BS:** Sure.
>
> **Clinician Q8:** Erm… I don't know how relevant they would find the people. It depends on what they… you know, they might just think, "well, who's this person; I don't know them; they're nothing… they're independent of the doctors; they're independent of the researchers; what's it got to do with them?" kind of thing.
>
> **BS:** Sure.
>
> **Clinician Q8:** I suppose it would be hard to say, "I'm independent, but this is what the research is"… I think. There seems to be some sort of motive towards it… to it… doesn't there?
>
> **BS:** No, I see what you mean. So they're in the same position as the researchers…
>
> **Clinician Q8:** Yes, exactly, basically.
>
> **BS:** … it's a person that you don't know…
>
> **Clinician Q8:** No, exactly.
>
> **BS:** … except they're not…
>
> **Clinician Q8:** It's not… yeah, not biased one way or the other.
>
> **BS:** Yeah.
>
> **Clinician Q8:** Um… the mental health advocates that we have on the ward now, I think, it's probably too much of a crossover of the role. I think the trust needs to be gained with those people… um… and they're there to support people and help them, and I think sort of promoting… well I suppose it's not promoting research, is it?... but informing them about research might… well, it's not really in their remit, and I don't think it necessarily should be.

Patients also scrutinised possible supported decision-makers based on knowledge and trust of the individual and accordingly the limitations of independent advocates also

occurred with the patients, one saw them as not beneficial due to their independence limited their knowledge of the individual:

> **[Speaking about supported decision-making]**
>
> **BS:** How do you feel, about, err, an independent advocate doing that?
>
> **Patient Q7:** I would feel alright if I knew the advocate.
>
> **BS:** Yeah, what if you didn't know them at all, what if, erm, it was provided by the hospital.
>
> **Patient Q7:** Oh right, I would see that as a, as a problem […] because you would not know unless you talk to them exactly who they were and […] whether you got on with them or not.
>
> **BS:** Ok, so they wouldn't have, I mean would there be any disadvantages or advantages in terms of their knowledge about you or, urm?
>
> **Patient Q7:** Well for me personally […] Umm, I would need to know them, but for some people it might work because they, they might have similar interests, they might get on with each other. But for me personally it wouldn't work for me because I prefer people to know […] my social background, and what my interests are and how that would affect.
>
> **BS:** How about the fact that they were entirely independent and so quite removed from, you know removed from your social background, would, is that?
>
> **Patient Q7:** I would say some people might find that helpful but you would get a number of people that wouldn't find that helpful.

However, the patients did not echo the concerns that clinicians had about clinicians themselves fulfilling the supported decision-making role; clinicians were viewed as potentially useful due to their expert knowledge but limited by time. Patients considered family useful due to more detailed personal knowledge of the person and were able to re-assure and give confidence. For the patients, the fact that the supporter was trusted was key to their utility in this role:

> **BS:** Ok, erm, do you think, erm, a..aside from that situation do you think it would be useful to have someone you trust with you when you are thinking about taking part in research?
>
> **Patient Q7:** Yes,
>
> **BS:** So let's say you're part of an …
>
> **Patient Q7:** I do think that.
>
> **BS:** Can you tell me a bit more, ugh, about that?

Patient Q7: I think that if they can trust their decision, that they are more likely to accept the process of interviewing,

BS: Right, um.

Patient Q7: Because they've got someone else to second that and they've got someone else to listen.

Carers considered support from the family as helping give people confidence/for moral support, and that the family were *there for the journey* in that they had an ongoing relationship with the patient and would continue to be involved after the research was complete.

All carers interviewed were happy to be involved and saw few disadvantages from being present although one raised concerns about independent advocates fulfilling this role and in acting on behalf of the patient being antagonistic to family and carers:

Carer Q3: It depends on the relationship with the advocate. Sometimes, advoca…, I've seen advocates that, erm, sometimes even I have problems with, they'll blame me, like: "oh why have you called the police" I'll say, "I don't call the police, they, you know my loved one don't want to take medication, doesn't want to go to the ward, so obviously, when they come to try to take her in they have to…" [laughing] but they, they blame me. So you can get advocates who are, you known, overprotective for the patient, or maybe they're not, they don't want to be there, and they disagree anyway. They might not always have to pay interest. It's different, it really goes down to the person.

When exploring the related and overlapping area of consultee approval for participation in research when lacking DMC-R, generally speaking the consultee/PLR model for research consent was viewed as acceptable. Similar difficulties to supported decision-making were raised such as when clinicians take on the consultee role due to conflict and crucially the unavailability of relatives (due to their own personal pressures and time constraints). The latter point is of great significance for supported decision-making: As described, in my own study half of the patients declined to let me approach their relatives. Of those I had permission to contact I was unable to recruit

many due to refusal, disengagement, or inability to contact them. As detailed in Chapter 2 – Research when DMC-R is lacking p.22, when the consultee approval process has been systematically studied inability to contact relatives and when contacted they declined acted as a substantial barrier [43, 44]. In schizophrenia, refusal of potential participants to contact relatives would seem to act as a barrier as well. This does bring into question though the viability of the intervention when relying on the involvement of relatives, as I have already demonstrated *in vivo*, and the aforementioned limitations of using independent advocates or clinicians.

In summary, supported decision-making interventions were considered acceptable by all participant groups. I found consensus that it is key that the supporter is trusted, and that the nature of their relationship is very important. Independent advocates were deemed particularly limited in this regard due to not having a pre-existing or trusted relationship and their motives were viewed with suspicion, whereas close family were viewed as the ideal but there may be substantial barriers in terms of availability in them performing this role.

Other direct interventions

Clinicians raised several barriers to participation: the person's mental state (such as paranoia, agitation, etc.), non-mental state related psychological barriers (that their priorities may lie elsewhere at the time approached on the ward where their priority may be leaving hospital), and barriers due to NHS systems issues (e.g. staff availability, training, and interests). The patients similarly considered barriers in terms of mental state (e.g. hearing voices, low mood, paranoia) and non-mental state (e.g. low motivation, apathy).

Consequently, along with the carers they all saw the facilitators to research partly in terms of helping providing information better and making the research easier (as above) but mainly through creating a 'culture of research' on the ward such as through the establishment of research clinics and integrating research into routine clinical care. All groups thought other people were also important here: patients wanted the support and involvement of other people, especially kind, friendly, trusted people, making research a pleasant and enjoyable experience and providing other rewards for participation such as food; clinicians thought staff and family attitudes and involvement such as promoting hope and support were important; and carers also recommended group discussions with a facilitator.

In summary, in terms of other direct interventions, there is support for developing a 'culture of research'. This would also involve embedding research into usual clinical routine through the use of research clinics and other settings to facilitate patients to routinely hear about opportunities for research as part of their usual clinical care.

Research governance

Here I present a summary and discussion of the three main emergent themes from the overall analysis of the framework, that of: '*right' and 'wrong' reasons for research*, *capacity as validity of the person*, and of *respect for the views of the person versus duty of care*. All three themes are incorporated within the overall model of *assessing or asserting decision-making authority*. I cover individual categories from the framework within each theme when they relate to it and when the descriptive analysis has research policy implications.

When considering reasons and motivations for participating, there were stark differences between those raised by the clinicians and the patients. As I will explore here, clinicians focused on benefit to others and altruism, whereas patients focussed on personal benefit such as receiving financial gain and getting better.

Financial gain as a reason was raised by all participants, however, clinicians commonly further appraised financial gain as to whether it was a 'right' or 'wrong' reason for research. This concept of 'right' or 'wrong' (or 'good' and 'bad') reasons for research had emerged in early interviews, and following the first phase of analysis was set as a particular topic to explore in the topic guides. While many clinicians considered 'right' or 'wrong' reasons, there was lack of clarity over exactly what a 'right' or 'wrong' reason was.

> **[Discussing vulnerability of patients]**
>
> **Clinician Q8:** Yeah… erm… I suppose they are vulnerable. They're vulnerable in very many ways, and erm… I guess, if there's a financial to… you know, to taking part in the research, then… is that very ethical in terms of like, you know… are they doing it for the right reasons? Is the research… is the person the right person, or is it someone to put on there? But I hope that the research that takes place is obviously all safeguarded properly and… participants are… appropriate. Um…
>
> […]
>
> **BS:** Erm… you mentioned… um… doing research for the right reasons, so… doing it purely for money wouldn't be a right reason?
>
> **Clinician Q8:** Yeah.
>
> **BS:** Would you mind explaining to me what are the right reasons for doing research?
>
> **Clinician Q8:** Well, to help… help with the treatment of mental illness, or whatever the research project is. Erm… and to, you know, I… yeah… that's it really. And I mean, obviously the two are not adverse to each other, you can get both at the same time. [laughing]

[Returning to the topic again later in the interview]

Clinician Q8: Er… vulnerable to… I don't know what… I don't really know how to describe it. Um… so, vulnerable to taking part because… through coercion, I suppose.

BS: Ok.

Clinician Q8: Yeah. Or for the wrong reasons. I'm not sure what the wrong reasons are… but, you know…

BS: And you mentioned earlier that for you the wrong reasons would be, because the aim of it is not to help others…

Clinician Q8: Yeah.

BS: So…it's because you think it's going to help yourself, because [incomprehensible]

Clinician Q8: Yeah, so I suppose there's that side of it, but more to do with coercion, I think.

BS: Coercion?

Clinician Q8: Yeah, yeah.

Suggestions included that misguided or misunderstood reasons could be 'wrong' reasons, or being under the influence of explicit or implicit coercion. Participation for financial gain was viewed as potentially a wrong reason if it was coercive (explicit coercion) along with wanting to please one's doctor or feeling one must take part due to the power of the clinical team (implicit coercion). Reasons that were 'right' reasons focussed on altruism such as helping others, and for the good of the research or academic endeavour:

Clinician Q6: I think maybe there's an ideal that… that would be the… sort of… you know, there would be one cohort of patients who would be like that, but I don't think it has to be that way. I think there are other groups of patients who can be recruited into studies, who may be doing it for other reasons. Maybe they want not so much to help others, but to help themselves, within their own condition, they want to help… um… develop a treatment that will benefit them in ten years' time, twenty years' time, or… which is more, you know, less altruistic. Or maybe that they need the money and they're doing it just purely because they're being paid to do so. I don't think those are wrong reasons, but they're perhaps… different reasons.

As mentioned, patients differed in their reasons, such as focussing on personal benefit from both receiving financial gain and getting better. In contrast to the clinicians they did not view any reasons as 'wrong', but also saw a mixture of reasons as 'good' such as helping oneself, helping others, and one saw financial gain as a 'good' reason due to it motivating people to participate. Similarly, carers focused on reasons concerned primarily with patient benefit.

Similar themes emerged when exploring the role or need for insight into one's illness when making a decision about participating in research into that illness. Many clinicians believed that it was possible to have DMC-R and lack insight, but the *motivation* to participate despite lacking insight was viewed as a concern. The worry was that agreement to participate in this context could suggest that the patient was taking part for the 'wrong' reasons or raise concerns around coercion.

> **Clinician Q8:** [N]o, I don't think they do need to have insight. I think people have valid… erm… opinions and thoughts about their treatment and about what's happened to them, even if they don't believe that they have any sort of illness… um… which is quite common, certainly in the people that I nurse. Erm… no, I don't think there does need to be insight. I think the only sort of risk is that someone becomes irritable because, you know, you're implying by doing this research that they do have an illness, and they might… I suppose that's the danger, isn't it of them taking part for the wrong reasons, i.e. the financial benefit? If they don't believe they've got an illness then why are they doing it?
>
> **[Discussing agreeing to participate in low-risk research when lacking insight]**
>
> **Clinician Q4:** But then it would also question why the bloody hell are you going to do it, just because you're a good person? That doesn't… that would then not be… that would then not really be enough…
>
> **BS:** You don't think that counts then?
>
> **Clinician Q4:** You'd need to have a little bit more of a valid reason as to why you were … why you were wishing to get involved in it.
>
> **BS:** "I'm bored."?
>
> **Clinician Q4:** I'm bored. Anything else?
>
> **BS:** I don't know. I mean, would that be a valid reason? I mean, how about low risk/low benefit research?

> **Clinician Q4:** I mean, you get… you do a lot… I do a lot of stupid things because I'm bored. So I don't think that's…
>
> **BS:** No? What do you think are the right reasons for people to take part in research?
>
> **Clinician Q4:** Intrigue and curiosity which would… […] … which would fill in with that, and fill in the boredom. […] and intention to help others. […] Um… and intention to help yourself. Um….and… and yeah, the ability to learn.

Clinicians considered that the patient would need to have valid views around the nature of the research procedures that would take place should they participate when lacking insight. They also reflected that, if insight was required to participate in research, it would act as a huge barrier to participation in research. However, when developing policy to increase participation in research, either way one approached it there were concerns around 'parity of esteem': either through insight being required and thus excluding swathes of acutely unwell mental health patients from research or having different consent standards for research on psychiatric patients from physical health patients and thus treating the two groups differently.

In contrast, carers did not think that lack of insight should be a block to participation and that it should be down to individual choice. From the patient's perspective, they also thought that insight should not be a block and it should be down to patient choice, although there was one dissenting voice seeing insight as necessary.

The disconnect between the main reasons presented by clinicians and patients and the concern by clinicians that some reasons may be the 'wrong' reasons is noteworthy. It suggests that there is a gap between what people who are involved in consenting and performing research consider should be the factors taken into account and those that people actually do when making research decisions, with clinicians following a moralising ethical model versus patients following an experiential model. Do clinicians expect a higher normative standard than actually takes place? If so, could a possible reason be that the culture and process of REC ethical approval expects that participants are

motivated by altruism; that research with human participants is ethical providing participants are engaged for altruistic rather than selfish motives.

Primary motivation for personal benefits is central to TM (see Chapter 2 – MacCAT-CR 'appreciation' and the 'therapeutic misconception' p.28), in that a participant's misconception as research as being primarily for their personal benefit rather than the benefit of research must derive from the fact that personal benefit is a central motivation for that patient. Kim has previously reported that desire for personal benefit was a main driving force for participation in research when exploring participant's motivations behind research participation [52, 54]. Is some of the furore in the academic literature regarding TM due in part to this disconnect between patients and clinicians, that clinicians do not expect patients to be primarily motivated by personal benefits when it comes to research, and thus when it arises is must be due to a 'misconception'?

Ultimately the tension between the moralising and experiential models of participation raises serious issues for both research governance and models of DMC-R: For DMC-R the evidence for a plurality of different reasons to participate in research and perceived benefits that are considered by the participant need to be taken into account in any model of DMC-R. It further supports my evidence for the limitations of the MacCAT-CR model of DMC-R which is narrowly circumscribed to TM, ignoring other benefits of participation such as alleviation of boredom and financial inducements. I consider further the plurality of reasons expressed for participation in research when exploring the concept of DMC-R in Chapter 9 – Delving deeper into 'use and weigh' under the MCA p.225.

For RECs the implications are more subtle. There is a need to consider that, when designing participant information sheets and considering research consent discussions, the normative frame with which these need to be written may differ from that of the researchers or REC panel: For many people making decisions regarding participation

in research, the benefits to society and academic endeavour may be secondary issues compared to immediate and direct benefits to themselves. Thus, the direct benefits to themselves may be the areas on which they want the most detail, not the academic worth of the research which often for them, may be an irrelevance.

Capacity as validity of the person

The second main emergent theme was that of judgements as to the validity of the information gained from a participant. When discussing the process of first approach, and the factors that the clinicians used to decide whether it was appropriate to approach someone about participation in research, they considered several factors including mental state, risk, DMC-R, and being able to take part in the research procedures and back out if they wanted to. Often being 'too unwell' for research was considered and this had several meanings including aggression, inability to communicate, and what was termed 'capacity'.

Lack of 'capacity' here did not mean lack of DMC-R, rather it appeared to be understood by clinicians as catch all statement to describe disability. Other phrases or statements at times were also used with same meaning. Lack of 'capacity' lead to negative views about suitability for research in terms of the potential value or veracity of data gained by the study if the person participated in it. If the person lacked 'capacity' then how could their research participation be useful and may it be risky to them?

> **Clinician Q8**: Ok so, I think I mean obviously the purpose of the study is to research with people who are unwell so it doesn't exclude people just because they happen to be unwell at the moment, it shouldn't exclude them from the study. However, there are some people who don't even know their own name and are very confused and disorientated, and have varying symptoms from, you know, psychotic symptoms, and I don't think it's worthwhile adding to their distress by asking lots of questions that they are not necessarily capacitous

to answer, you know, in a meaningful way, and may cause them more distress by giving them more to think about, that they are not sure about.

BS: [Y]ou were saying about [incomprehensible] my different tests for capacity for research. Do you ever consider yourself whether they may have capacity for research? or, or not?

Clinician Q3: Erm, [long pause] because first of all, the question, like I mean introducing you to the patient, the process could be a start, this is a researcher, they might not understand what a researcher is, not because of anything, but just they don't understand, so when you explain to them but they still don't understand, that means they seem to not have a certain degree of understanding of what you are going to do, so then I don't know how that would be benefitting to your research.

Similar concerns about the validity of research participant's answers were raised by a patient in the context of lacking insight:

Patient Q1: erm well, because they'll say, they'll say things and believe things about their state of mind that may not be accurate so yes they are filling in a questionnaire, yes they are helping with the research, but because their frame of mind is not what it should be, maybe their answers are not as accurate as perhaps they would be, myself included as well, some of us are in a better position than others in mental health, some of us are a bit further off than others, some of us are really not well at all, and some of us are just not somewhere.

Some carers also considered that when unwell the research data or expressed views of the patient were invalid or of little use to research and they needed to be compared or cross-referenced to the patient's views when well.

[Discussing her son's participation in the quantitative study]

Carer Q2: Um… ideally I would have like to have been… have been consented before he took part, because I wasn't quite sure, at the time, if he was able to make… to make any sort of valuable input on anything, because he seemed very confused when he was admitted into hospital. But obviously, it went ahead and took part without me knowing. That's the only thing that I wasn't quite agreeable on, but it happened already. But I think, in future, if the carer… care-giver, or the nearest relative… should be informed if the person is not capable mentally of taking in a research. Because I just think it wouldn't

benefit the person anyway, and the information would be… probably not as correct as it could have been, had he been a little bit more capacitated.

[…]

Carer Q2: Obviously he's over 21, but again, because of the circumstances and his mental health at the time, I don't know if the information that you got would have been valid, because he was so confused, or whether that was the aim, to take the interview with him while he was confused. That's what I'm saying.

[…]

Carer Q2: I think there should be a before and after process, like interviewing while he's mentally ill and confused, and then interviewing with the same set of questions after, when he's getting better, and compare the difference of how he thought at the time, and how he presently is feeling.

BS: Mmmm. And are your main concerns over the… um… the sort of quality of the answers that the researcher's getting… er… from, you know, from interviewing somebody who's like that? Or is it something else that you're concerned about that's happening? Or what are your concerns?

Carer Q2: No. The concerns is that I'm not sure if the information that is taken from him at the time would be valid for a research, because of his confused state of mind.

In some ways, the use of 'capacity' by clinicians to describe overall disability or invalidity of responses is entirely understandable: in medical settings, the presence or absence of DMC is used to differentiate between 'wishes and feelings' that have decision-making and legal authority and those that are overruled where necessary by surrogate decision-making through the process of 'best interest' decision-making. Although this may involve going against the expressed wishes of the patient, these 'wishes and feelings' should be held in high regard when making 'best interest' decisions (see for example the MHA code of practice describing a central role of 'wishes and feelings' in treatment decisions [181] and Chapter 2 – What is decision-making capacity? p.17). It is easy to see how one may consider the 'wishes and feelings' as invalid, if one is going to act against them on behalf of the person's 'best interests'.

However, it is concerning here that there is a lack of decision-specificity being applied to the concept of 'capacity' by the clinicians: Lack of 'capacity' is used to equate with overall disability or in this context the invalidity of the person for participation in research and to produce meaningful responses. This is in contrast to the decision-specificity that the clinicians should be applying when making assessments of DMC. We now know that lack of DMC-T is more common than DMC-R in inpatient settings, an attitude that lack of DMC equate to disability and invalidity of responses may lead to systematic exclusion of participants at the point of first approach if they happen to lack DMC-T (but not DMC-R). My recruitment selection bias sub-study showed that around half of all potential participants were not approached in my study. Although I have no data to explore the reasons as to why people were excluded at first approach when it happened, future work into first approach should explore views surrounding the validity of any data collected from the potential participant. These findings also suggest a need to dispel assumptions about the meaning and validity of patient responses when unwell, not just for the clinicians, but also for the carers and possibly even the patients themselves.

Respect for the views of the person vs duty of care

This theme focusses on the views of clinicians and carers, with the contrast between their views and those of the patients discussed in the following section *(assessing or asserting decision-making authority*).

Clinicians throughout the work negotiated a tension between wanting to respect the views of their patients and their duty of care to protect them (including from themselves and others). This played out in several ways: when considering the position of patients' expressed wishes, the default was one of respect for them, subject to several caveats

where the clinicians could override and have executive decision-making (risk, lack of DMC, and institutional powers gained by virtue of being a clinician). When this was applied to research the outcomes were complex as the clinicians struggled with pulls on them to respect patient views, protect them from researchers, protect the research, and protect the patients from decisions made without DMC-R.

In considering consultee approval for participation in research when DMC-R is lacking, clinicians generally thought consultee approval was positive and appropriate. They were supportive that doctors not only could but should be the decision-makers (specifically in terms of their role as PLR for therapeutic studies), and that in effect since they would be the ultimate prescriber they were the executive decision-maker anyway or that they were best placed due to medical knowledge or appraising best interests in this context.

> **Clinician Q6:** Right, ok… yeah. I probably would agree with that as it stands, to be honest. I think if it's a therapeutic trial, then it's more relevant to go to the clinician about it, because the clinician presumably has the knowledge of the pros and cons of that particular treatment approach in that particular patient. […] It would still be useful for that clinician to discuss matters with the… obviously with the patient, but also with the family as well… er… with the family as well. But I still think the overall… you know, what's in the best interest of the patient when they lack capacity, probably does fall to the clinician in charge of their care, with regards to therapeutic treatments.
>
> **BS:** Mmmm. So you see it, in some ways, as a best interest decision as well… with regards to therapeutic interventions?
>
> **Clinician Q6:** Yes. But with non-therapeutic interventions, I might think it's… it would be… it makes sense for it to sit… not in… for it to sit with the consultee, you know, from the family… I'd say, yeah.

Some agreed that the role of consultee for non-therapeutic research sat best with non-medical professionals, however, one participant felt indignant that they were blocked from making these decisions and wondered why patients needed protecting from clinicians given their primary duty of care.

Clinician Q5: I think it's er… it's quite interesting, isn't it? It's sort of… blocking a doctor or a nurse from being a consultee, I'm not entirely sure what the… what the motivation would be there. […] Um… because it's strange… because part of me is going with if it's sort of a medical intervention, of course you need to be talking to a nurse or a doctor, that's my first instinct.

BS: Then.

Clinician Q5: But then it's also like, well no, not necessarily just because you might understand a little bit more about the process doesn't necessarily mean you understand more about what's best for…

BS: For the person?

Clinician Q5: … for the patient, yeah… yeah… so… but then for a normal medical intervention to block a doctor or a nurse… why is that? Is there a reason given for that?

[…]

Clinician Q5: Yeah. I find it interesting because… because I have a very strong sense of… my sense of duty and protection towards my patients has come up in this interview a couple of times, so to find myself blocked from that… it's a kind of, 'Oh, why would they do that?'

There were mixed views about overriding a decision by a patient to participate when lacking DMC-R and acting as a consultee. The position of the 'wishes and feelings' of the patient were given strong weight but the process was again seen as a 'best interest' decision, and accordingly the weight given to these varied but both the view that the research can always return later (and so the need to participate in research then is not so immediate) and the counter view that as the decision is about participation in research there are no strong reasons to override a decision to participate. In 'best interest' decision-making remember it is of course others and not the patient who decide what is in their 'best interests'.

[Discussing helping consultees perform their consultee role]

Clinician Q3: It's like it's like when we do capacity assessments, well we always do things if they don't lack capacity, if they lack it, we do it in their best interests and I hope that will be the basis of the decision, the best interests of the patient.

> **BS:** How would you, erm, who would you, how would you think about what the best interests of the patient might be in that situation, when it's a research study, what sort of things might you think about?
>
> **Clinician Q3:** So, in terms of the family and relative and friends, erm, hopefully they [incomprehensible] [long pause] erm what affect it might have on the patient, so what's the study about, is it something that's going to have think about the past or their diagnosis, and they'll just weigh that up and see how the patient is, and they can always seek advice from the doctors and see if it's suitable, and likewise with the medical profession, professional, best interests of the patient, is it going to be beneficial to the patient in terms of physical, mental health, [incomprehensible] even their social situation, and once again they can always seek advice from the family or the nearest relative as well.

Carers also saw the process of consultee approval positively; however, they were concerned that their relative was not listened to in general and wanted the family to be involved and have control of these decisions, especially when their loved one was unwell or lacking DMC-R (although it was mainly one carer participant strongly pushing this last point):

> **Carer Q2:** Um… because, I think that you… I'm not sure if it's you, but when I say that I mean, you know, if somebody's going to go into hospital and take part in… patients are going to take part in a research, especially when patients are confused and mentally ill like my son was, I think the person who is caring for him, or the nearest relative, or next of kin, whomever it comes… whomever that might be… should be told that, "Look, we want to take part, we want your son to take part in a research, how would you feel about that?" and then ask me first, rather than just going in.
>
> *(see also the quote from this participant on p.184)*

It was in discussing first approach and their core role as gatekeeper to research participation that the tensions of a duty of care to their patient (which included a protective element), but also respect for the individual and their choice strongly arose. Only clinicians were coded in the topic of first approach, and they saw process as one that helps education of the patient around research, planting the seed, but also allowing for the ability to back out and not be coerced into participating. They also saw the process of first approach to protect patients from researchers (either by taking advantage of them

or worsening their mental state) and themselves. This came with its own consequences in that several expressed being torn between wanting to protect the patients but also respecting their views and wanting to help with the research process.

BS: When you were saying you felt the process was a bit paternalistic…?

Clinician Q2: Yeah, I think it felt… like I was….it felt…it's a funny experience… I felt like I was going to help… it was good to feel like I was helping you, or helping some sort of research project going ahead. I was aware that I'm now in my third year of psychiatric training, and I've hardly… I haven't really seen much in the way of… um… clinical research, on the wards. […] That was… I think that was probably one of the first times that something like that… I was experiencing something like that. Um… so… I felt like… I felt like I wanted to get involved, and to help out, and to see how I could… you could get a live, in vitro… no in vivo… study going on, on the ward. Um… but I also felt like I wanted to protect my patient, and make sure that they weren't going into something that they would find uncomfortable, or feel coerced into.

[Discussing overriding patient decisions in general through consultee decision-making and clinicians' involvement in the process]

Clinician Q5: Mmmm. You see, I feel a little torn on this. Because part of me is that actually I feel the patient's decision… um… gosh, I don't know, I'm finding this really hard ethically, actually. Because I do… part of me feels like the patient's decision should be final, but then also I know that I… I go against my patient's decisions all the time… Like, not all the time, but I have people that make a decision that they don't want to take medication, and we do a capacity assessment, and we go, "We'd give you medication in your best interest"… and I'm… as a newly qualified nurse, I find that ethically very difficult. As a … you know, four years in… I don't particularly find it… it's not that… I'm not blasé about it in any way, but it's not something that I'm struggling with anymore. […] So…

BS: Do you think it's in people's best interests to take part in research?

Clinician Q5: I think it can be. I don't think it's… I can't really imagine a situation where it's the opposite of somebody's best interest.

BS: Yeah.

Clinician Q5: You know, that it's in somebody's worst interest to take part in research… I can't imagine, you know, that sort of situation.

BS: Mmmm. What if there's a conflict? What if there's conflicts between different actors, conflict between the patient and the relatives… the relatives say no and the patient says yes…? Can you think of ways… what do you think about that? I mean, just in general, do you think.?

> **Clinician Q5:** Oh again that's… erm… I mean, if there's conflict between them I think I would probably tend to plump for the status quo, which is not taking part in research just because… we know that that's not an issue.

For the clinicians, their role in first approach achieved three functions: 1) Priming people and allowing people to change their mind (respect for the person's views); 2) A risk assessment to prevent harm to patients from researchers or researchers from patients (duty of care); 3) An evaluation from the clinicians as who they think would be useful to take part in research or could *usefully* take part in research (*Capacity as validity* – discussed above).

As with the category of first approach, when exploring the category of 'patient as decision-maker' (who should have decision-making authority) the dichotomy or tension developed between wanting to put the patient's wishes first and having a duty of care to protect the patient, including from the clinicians themselves. This played out in complex ways – as there were several constraints which clinicians applied to the patient's decision-making (concerns around risk, DMC, institutional powers providing a veto/effectively making the clinician the final decision-maker). MDT decision making was suggested as the ideal decision-maker but perhaps this was a way or sharing the responsibility for removing decision-making authority from the patient. The effect of the institution itself was recognised (people being put in an environment where they do not feel they have a choice), and several clinicians reflected on how patients needed protecting from their own paternalism.

> **Clinician Q5:** Um… and it gets frustrating… and if you're stuck in a room with somebody you don't know, it's not a particularly… you know… and we do… we do… we say to patients all the time, "If you don't like it, you can leave at any point and just let me know if you're feeling uncomfortable with it", and they won't necessarily do that because it's an institution… it's an institutionalised setting, and there is, you know, "We obey"… sort of thing. "Or, if we don't obey that's rebelling". It's very sort of labelled things, you know? […] Yeah… yeah, exactly, so… in a place like this, particularly, because a lot of our patients are under section, they don't really have the freedom to act. So that you need to

> be very careful about putting them into yet another situation where they feel like they don't have a choice in it.

I have found here that clinicians struggle with an invidious balance between protection and respect for patients' views. If we are to help support patients in making decisions around research we need to be clear where the responsibility for decision-making lies, as regardless of DMC-R there are many methods by which parties other than the patient can gain decision-making authority over research decisions. While the process of consultee approval and supported decision-making is supported by all participant groups, clearly there are challenges when there is conflict with the views of the patient.

In addition, as clinicians have explained, the protection afforded by clinicians performing the role of PLR in therapeutic research is superfluous given that as they reported, if they do not prescribe the intervention the research is de facto blocked. Similar executive decision-making powers exist with non-therapeutic research, given that clinicians can block the research project at any stage. In research participation, while it is held sacrosanct that the decision of a person to refuse participation is always respected, clinicians hold executive decision-making to refuse their participation before they have even been asked. This brings me onto my central and final theme arising from this work, *assessing or asserting decision-making authority*.

Assessing or asserting decision-making authority

In contrast to the position of clinicians and carers, patients throughout the work simply wanted executive decision-making powers without constraint. They clearly and overwhelmingly wanted to the be the central decision maker and saw participation or not in research as a personal choice and one that should be respected (although a certain

times a couple conceded that it may be useful to have support from family members or someone to protect them from bad decisions such as around risky research).

BS: Do you think it would useful to have somebody you trust with you when you are making a decision about taking part in research? So like your friend?
Patient Q1: Erm, no I think I'm alright because I'm already clear and stable in my mind relatively, I think I'll be alright to make decisions at least by myself.

BS: What are your thoughts on that sort of research, people doing that sort of research?
Patient Q2: I'm open minded about it.
BS: Yeah, how about people taking part in it when they're in hospital?
Patient Q2: What the patients?
BS: Yeah.
Patient Q2: It's up to them, it up to them at the end of the day, each to their own, innit?

BS: So in that case, I mean, if you weren't in the best frame of mind, but you still wanted to take part, would you want the researchers to check with somebody, or would you want them to just go ahead anyway?
Patient Q4: Probably just go ahead.
BS: Yeah?
Patient Q4: Mmmm.
BS: Are there any situations where that might be a problem, with the researchers doing that?
Patient Q4: No.
BS: No.
[Someone opens the door and interrupts]
BS: Are there any disadvantages of the researchers checking with somebody like your mum?
Patient Q4: No.

When considering the role of consultees deciding on their behalf when lacking DMC-R their position was one of maximal autonomy where possible: Some saw it useful for people external from the situation to give an independent view or perspective, or to stand up for people when unwell. Some did not want people deciding on their behalf as a principle, but saw it as probably right if they were too unwell to make a decision on their

behalf for their own wellbeing, or that they would not volunteer in the first place if they could not make a decision.

> **BS:** Mmmm. Let's look, you know, at somebody who isn't in the right frame of mind. So they're really unwell, they can't really make decisions for themselves. Um… you know, the law has it that in those situations people can make decisions on their behalf… What do you think about that? Do you think that makes sense? Would you agree with it?
> **Patient Q5:** Like I said, in some circumstances I do agree with that. […] But in most I don't. I think as a general rule, that people should be allowed to make up their own…
> **BS:** Ok.
> **Patient Q5:** As a general rule.
>
> **Patient Q1:** If I weren't in a clear frame of mind then I wouldn't volunteer in the first place, obviously I'm not in the clearest frame of mind, but, within reason or limitations I am in a clear frame of mind.

When discussing the situation where they lacked insight this position did not change. However, as with clinicians and carers, they also saw that the doctor as being best placed to make a decision for them around participation in therapeutic research when unwell due to the doctor's specialist knowledge.

Herein lies the central theme emerging from the qualitative sub-study: a tension between the clinicians who want to respect patients' views but framed within their duty of care they must assess or decide when decision-making authority regarding participation in research can lie with the patient, whereas the patients who simply want to have unfettered decision-making authority. The answer as to where decision-making authority lies, is that it of course lies with the clinicians given that they are the arbiters as to when the patients can assert their decision-making and that the clinicians can block research taking place with their patients or on their ward. One cannot be said to have the freedom to choose if options are withheld in the first place.

However, clinicians' desire to avoid coercion recurs as a theme throughout all categories explored. This is also present in guidance for RECs, in that financial inducement may lead to coercion [9]. Most of the clinician participants worked in inpatient settings where coercion is used regularly as part of routine clinical care when people are lacking DMC-T or being treated under the MHA. Was the expression of coercion as a concern something that they were sensitive to, given the environment that they work in, or the recognition that they have the executive decision-making powers?

We have careful and complex legal frameworks to regulate the surrogate decision-making powers with regards to treatment decisions that have been explored and refined in the courts. While it is established in law that no patient can demand treatment which a doctor does not deem it to be clinically appropriate, there is a duty of care to provide care and treatment that is appropriate [see R (Burke) v GMC [182, 183] both the High Court and Court of Appeal cases for a discussion on the position of patients' requests for treatment). When I raised in Chapter 1 – The 'moral imperative' p.12 I explained that equal access to participation in research is a statutory right. Clinicians' restrictions around opportunities to research participation through first approach or more generally blocks to research participation through consultee dissent to my knowledge have never been probed by the courts. This is in contrast to consent to treatment which has been extensively covered. We need a debate as to where decision-making authority for participation should lie and the constraints that others can impose, and if these are appropriate given the position of patients themselves. I would argue that decisions made around the protection of others from harm or from themselves, especially when DMC-R is intact, is not sufficient to justify removing decision-making authority from the patient. Outside of the hospital setting this would not be the case, and we should not apply higher normative standards around participation in research when DMC-R is present merely because someone is unwell in hospital with a mental illness.

Summary - developing interventions to enhance DMC-R and acceptability of current research governance

In terms of the suitability and development of a direct intervention there were several clear conclusions:

- The information provided for research consent needs to be simple, but not too simple, and tailored to the individual to ensure it is not patronising and meets their individual needs.

- People present to support decision-making could be useful, but there may be challenges in achieving it and taking into account individual concerns. Knowledge of the patient and a trusting relationship are key here.

- We should embed research into usual clinical routine through the use of research clinics and other setting to facilitate patients to routinely hear about opportunities for research as part of their usual clinical care.

More complex interventions suggested by this work would be to ensure DMC is not conflated with disability and reinforce the importance and meaning of people's 'wishes and feelings' and to ensure we do not hold a higher normative and DMC standard for decision-making around participation in research for unwell patients than we expect for people making decisions about research in other settings. We need to explore further decision-making authority and where it lies in research decisions.

Reflexivity, limitations, and implications for interventions

It is interesting that the main themes emerging surrounding how best to help people make a decision derived from supporting and making things simpler may be in part associated with the fact that these were two key topics of my interview framework given that the study was investigating both as possible interventions. The reasons given for participating in research may also have resulted from my position as a psychiatrist and a researcher, and the nature of the study: My selection of clinicians to interview was based on people who were particularly engaged in the research process when I was recruiting to the quantitative study. Given that I am a psychiatrist and a researcher they may have been primed to give answers that they either thought I wanted to hear or were motivations for them to facilitate research on the ward (regarding motivation for research being for the greater good of society). Concerns regarding coercion were also a theme throughout the clinician interviews, and again there is a possibility this was an issue that the interviewees felt they needed to raise with me as a fellow clinician. Again, it is unclear how my position as a psychiatrist and a researcher impacted on the answers given by the patients. One option would be to use service user interviewer to see if this resulted in different emerging themes, however, my experience of the research interviews was very different to the doctor-patient relationship in usual clinical practice due to the different power dynamics (they had decision-making authority throughout and were kindly helping me out) and therefore I believe the impact of my role was limited here.

The patients' strong responses into financial inducement being a motivation may have also been influenced that their participation into both the quantitative and qualitative studies were in part influenced by financial compensation for their time, and thus this may have had a priming effect. In contrast, within the research interviews for the quantitative study helping other people and society was a common reason given for wanting to participate in the BioResource study. It may have been, however, that there

are few other reasons one may want to participate in BioResource research and the MacCAT-CR is designed to primarily probe this area as a reason.

As mentioned earlier, it was clear within the interviews with the carers that they each had strong motivations for participation in the qualitative sub-study and this was picked up during the interviews. This limitation is particularly prominent when asking on the subject of being involved in supporting decisions around research or being involved in the process as by virtue of being recruited into my study they would have a particular view on its acceptability. It is difficult to appraise how their views may differ from other carers given the difficulty in recruiting from this group, and further reinforces the difficulties in engaging patient's families for a possible intervention to enhance DMC-R.

The set topics for the interview framework had some limitations given some of the complexity of the legal issues I wished to explore. In order to cover these in more depth future work should select participants from a research governance background, but be mindful of the normative position they may also hold as discussed above.

Chapter 9. Conceptualising decision-making capacity for research: the 'salience model'

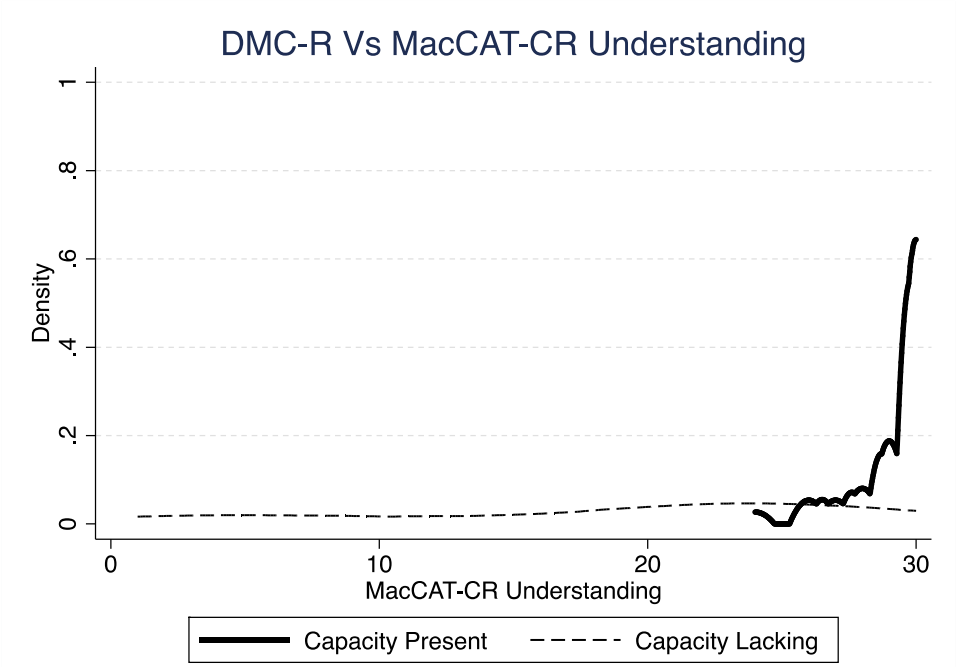
Categorical and dimensional effects of variables on DMC

The quantitative study found several associations with symptoms and DMC. Variables associated with cognition had the strongest effect on DMC-R while lack of insight had the strongest effect on DMC-T. In this section I will explore the precise relationships of cognition, insight, and other core symptoms of schizophrenia with DMC. In doing so I will perform a comparison of the 'judgement' and 'cut off' standards of DMC in order to help us to understand better the interplay between these individual symptoms and DMC.

Applying cut-offs to MacCAT scores and the 'trump error'

Figure 5 p.200 shows a series of Kernel-Density plots of individual MacCAT subscale scores ('understanding', 'appreciation', and 'reasoning') with plots for both having and lacking DMC for DMC-R and DMC-T (both using my 'judgement standard'). Often it was not possible to fully complete MacCAT scores due to concordance with the interview or severe cognitive deficits in the participant. These plots use raw un-imputed data given that the intra-participant missingness of data is so high at times that standard mean methods of imputation would lead to bias. The results must therefore be interpreted accordingly.

Figure 5 – Kernel density plots of MacCAT sub-scale scores and outcome of DMC assessments



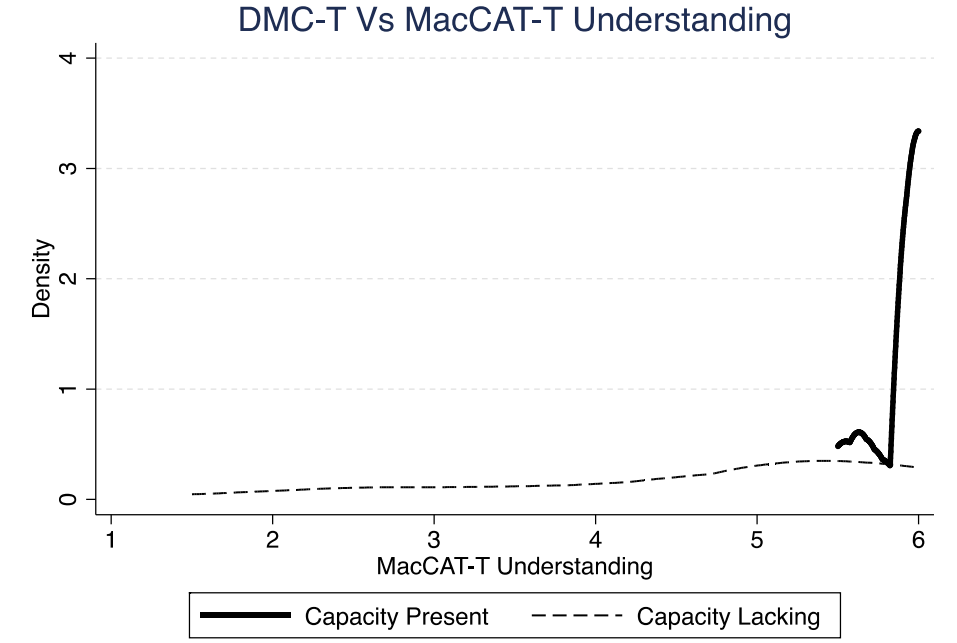
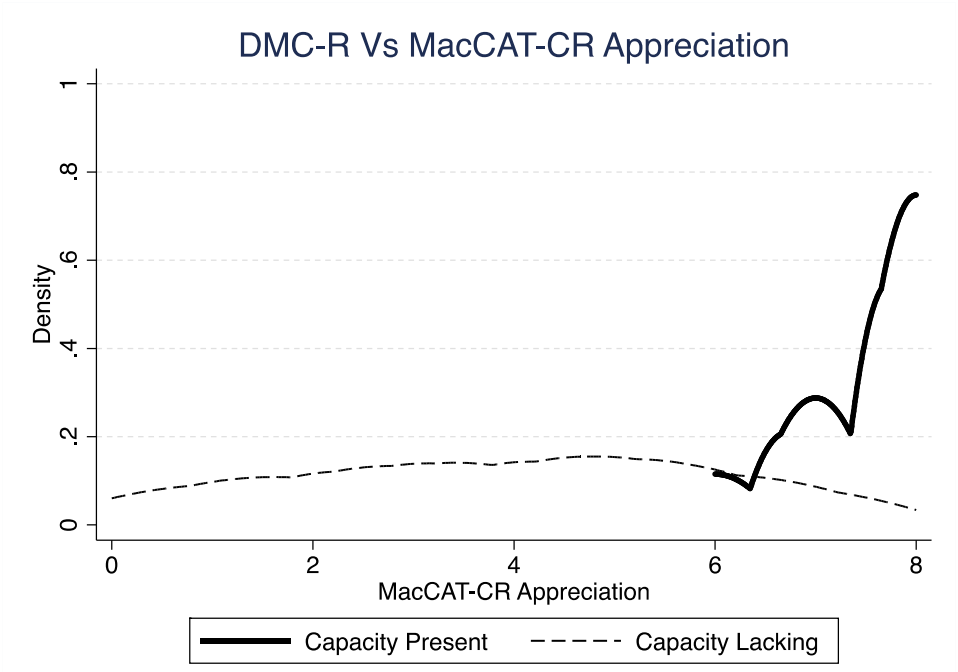


Figure 5 (continued 2/3)



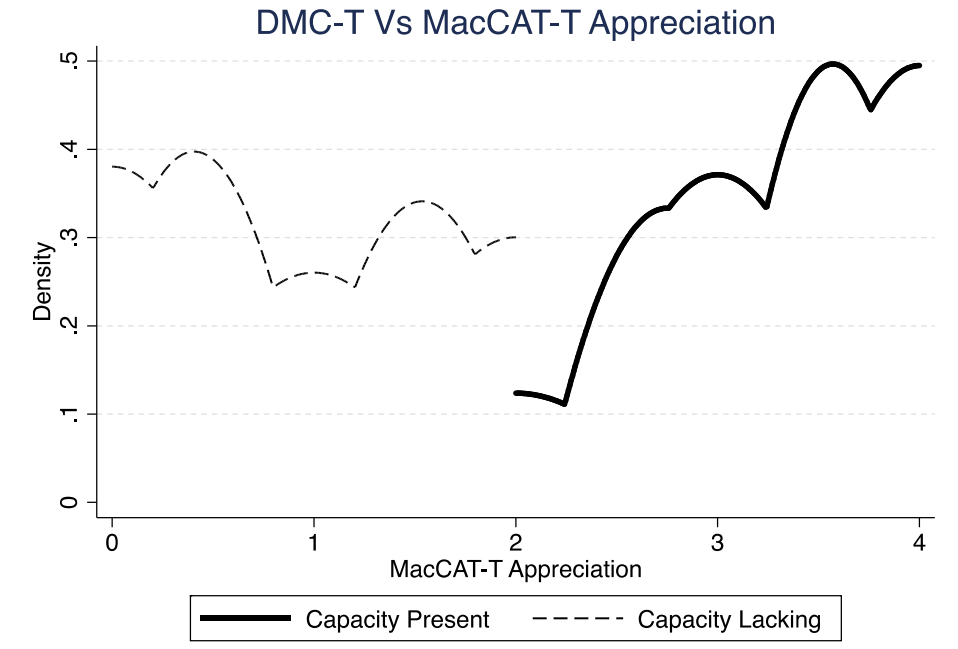
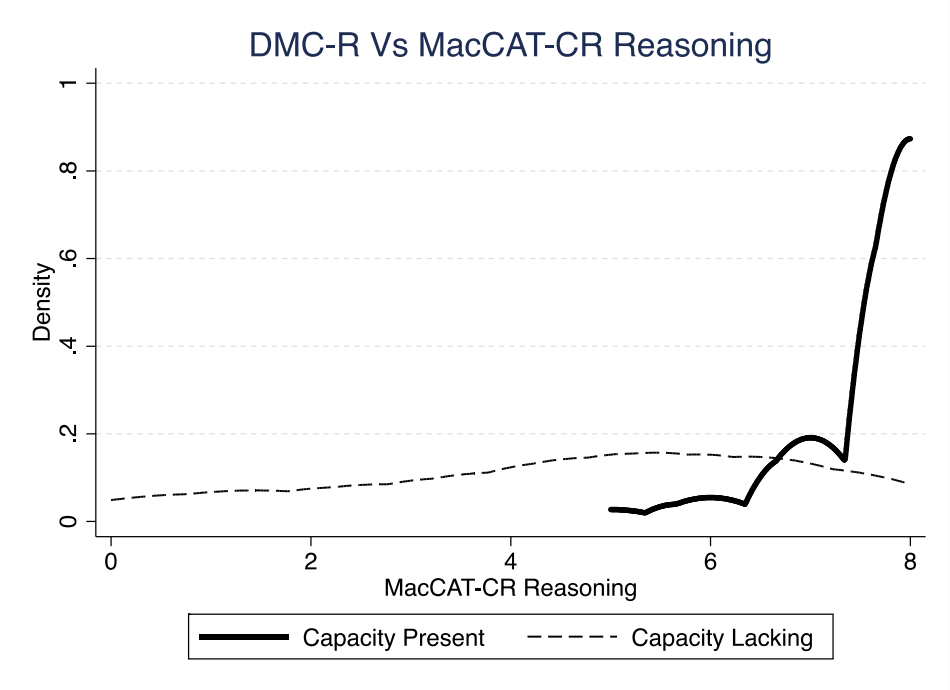
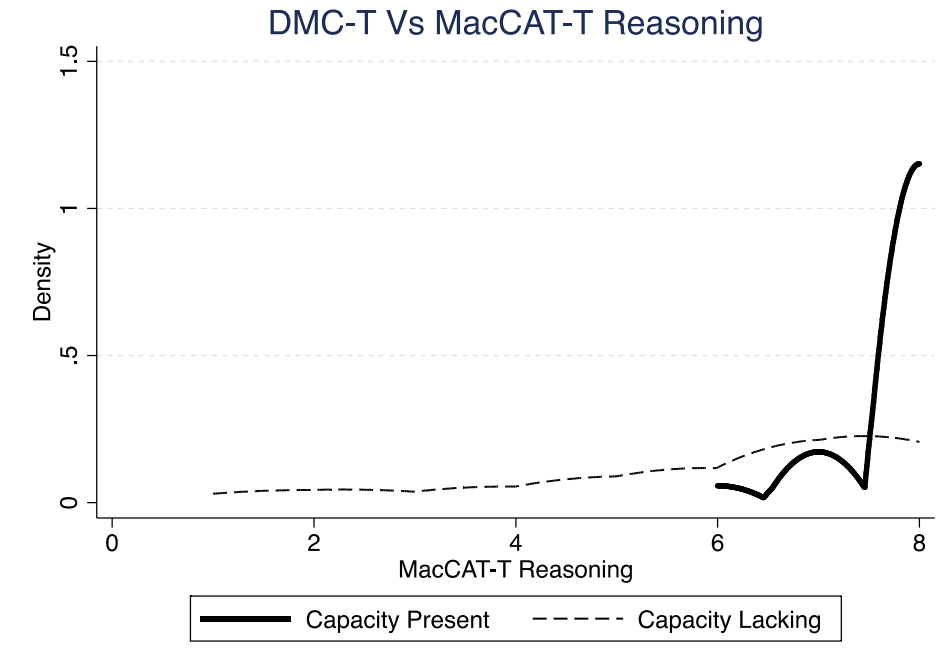


Figure 5 (continued 3/3)





What is striking is that MacCAT-T appreciation splits DMC-T at the mid-point which is unique and not the pattern for the MacCAT-CR and DMC-R. All other plots look like the MacCAT domains have high sensitivity for lacking DMC but low specificity. On all plots there are clear threshold effects for all MacCAT subscales, each having a score below which none of the participants are found to have DMC, or put another way, a minimum threshold of 'understanding', 'appreciation', and 'reasoning' in order to be able to have DMC assessed through the 'judgment standard' (see Table 20 below).

Table 20 – Minimum MacCAT scores where DMC was present

	Minimum scores in those with DMC-R		Minimum scores in those with DMC-R
MacCAT-CR U (0-30)	22.5	MacCAT-T U (0-6)	5.4
MacCAT-CR A (0-8)	6	MacCAT-T A (0-4)	2
MacCAT-CR R (0-8)	5	MacCAT-T R (0-8)	6

These minimum cut-offs can be combined and used as a cut off model of DMC (similar to the work of [94, 95]), with the cut-off model for DMC-R U≥22.5, A≥6, R≥5, and for DMC-T U≥5.4, A≥2, R≥6.

These cut-offs when applied naturally by design have perfect sensitivity for detecting lack of DMC (see Table 21 p.204 and Table 22 p.204) but also have specificities of 0.84 and 0.88 for lacking DMC-R and DMC-T respectively.

Table 21 – Sensitivity and specificity of DMC-R cut offs

	DMC-R Present	DMC-R Lacking	Total
Pass Cut Off	42	6	48
Fail Cut Off	0	32	32
Total	42	38	80

Sensitivity = 1, Specificity = 0.84

Table 22 – Sensitivity and specificity of DMC-T cut offs

	DMC-T Present	DMC-T Lacking	Total
Pass Cut Off	24	6	30
Fail Cut Off	0	43	43
Total	24	49	73

Sensitivity = 1, Specificity = 0.88

Using the cut-offs, for both DMC-R and DMC-T six cases are misclassified as having DMC when the 'judgement standard' ruled it lacking. In order to elucidate what the 'judgement standard' is detecting that the 'cut-off' standard is not (and thus domains that the MacCAT-T and my modified MacCAT-CR may be insensitive to that the clinical 'judgement standard' of DMC is assessing), we can review the cases and notes around their assessment of DMC.

Table 23 p.205 and Table 24 p.206 show the individual cases, including my rating as to whether DMC-R was marginal or not, their MacCAT scores, severity of key symptoms associated with DMC found from the quantitative study, and a narrative summary of my documented reasons for a finding of lack of DMC.

Table 23 – Characteristics of exception cases to the DMC-R cut-off

Study ID	Marginal	MacCAT-CR U	MacCAT-CR A	MacCAT-CR R	Delusions	Lack of insight	LM1	Thought disorder
P02	No	27	6	6	Severe	Moderate severe	-2	Mild
Reasons	Delusional interpretation of study information *(belief that participation would lead to developing cancer)*							
P04	No	27	6	6	Severe	Moderate severe	-1.7	Mild
Reasons	Delusional interpretation of study information *(belief that participation would lead to her curing the world through her genes)*							
P14	Yes	27	6	5	Extreme	Severe	(missing)	Moderate
Reasons	Delusional interpretation of study information							
P84	Yes	27	6	6	Moderate	Mild	-1	Mild
Reasons	Emotionally detached and apathetic due to negative symptoms (*does not care about risk to her or benefits*)							
P91	No	26	8	7	Severe	Moderate severe	(missing)	Moderate
Reasons	Delusional belief regarding study *(does not believe genes exist/biological model of illness)*							
P97	Yes	30	6	8	Moderate Severe	Mild	0	Minimal
Reasons	Delusional belief regarding study (*believes that research data will used against the individual by the conspirators*)							

Table 24 – Characteristics of exception cases to the DMC-T cut-off

Study ID	MacCAT-T U	MacCAT-T A	MacCAT-T R	Delusions	Lack of insight
P7	5.5	2	8	Moderate severe	Moderate severe
Reasons	Lack of insight – scores 1 on both 'appreciation disorder' and 'appreciation treatment'				
P15	5.5	2	8	Severe	Moderate severe
Reasons	Lack of insight – scores 1 on both 'appreciation disorder' and 'appreciation treatment'				
P29	5.8	2	8	Severe	Moderate
Reasons	Lack of insight – scores 1 on both 'appreciation disorder and 'appreciation treatment'				
P64	6	2	8	Moderate severe	Moderate
Reasons	Lack of insight – scores 1 on both 'appreciation disorder and 'appreciation treatment'				
P80	6	2	8	Absent	Moderate
Reasons	Lack of insight – scores 1 on both 'appreciation disorder and 'appreciation treatment'				
P111	6	2	8	Severe	Moderate severe
Reasons	Lack of insight – scores 1 on both 'appreciation disorder and 'appreciation treatment'				

With regards to DMC-R, with the exception of P84, all cases featured delusional beliefs that impacted on their appraisal of the risks and benefits of participation. Case P84 differed in that the reasons given were emotional detachment from the study and apathy towards the decision as a consequence of negative symptoms of schizophrenia.

In contrast, in DMC-T all misclassified cases scored middle on both 'appreciation disorder' and 'appreciation treatment' and were deemed to lack DMC-T due to lack of insight. The MacCAT-T separates 'appreciation' into 'appreciation disorder' defined as 'to determine whether patients believe that the information just provided to them actually applies to them, that is, whether they agree or disagree that they have the disorder and symptoms that have just been described' and 'appreciation treatment', defined as 'to determine whether patients believe that there might be any potential benefit from the treatment that has been described [25]. In all these cases, the participants considered

treatment as potentially beneficial but this was not entirely directed in terms of current mental health treatment for schizophrenia (such as seeing inpatient treatment in hospital beneficial for reducing stress or dealing with social consequences of illness) while they may have acknowledged past but not present mental illness.

Returning to DMC-R it suggests that the MacCAT-CR is relatively insensitive to detecting the impact on DMC of certain types of delusions, which I would argue is a direct result of the limitations of the MacCAT-CR 'appreciation' as discussed in Chapter 2 – MacCAT-CR 'appreciation' and the 'therapeutic misconception' p.28. These limitations remain despite my modifications to the tool. The nature of these delusions in all cases is that their content pertains to something that fundamentally impacts the process of 'using or weighing' the benefits versus risks of taking part. For example, believing that one's own direct participation will lead to the development of cancer, curing the world, that genes do not exist, or that the data will be available to conspirators plotting against them (all delusional beliefs I found in my study).

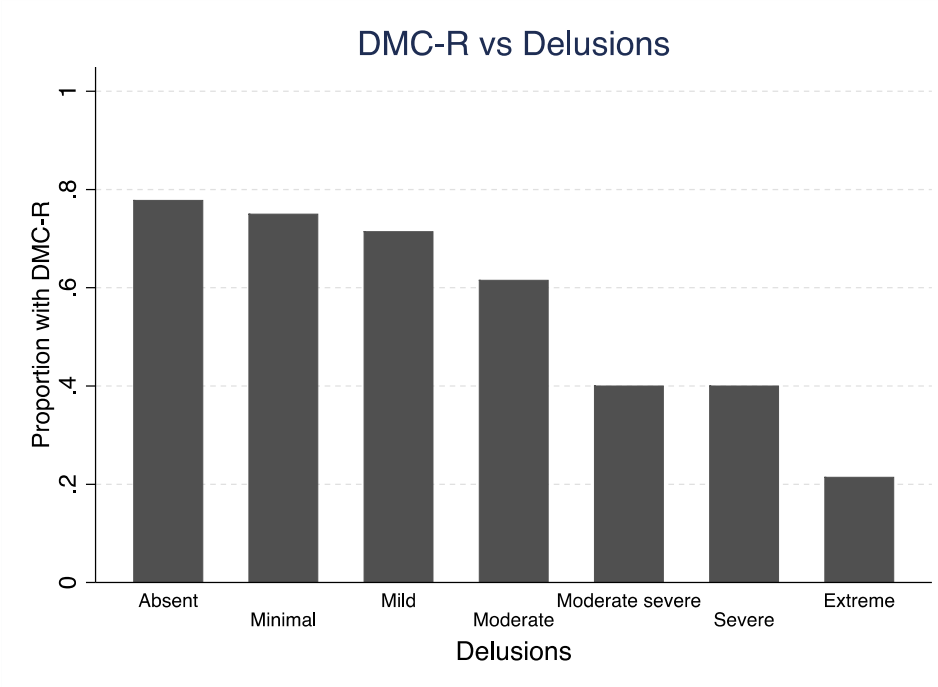
A strength of the MacCAT is the ability to provide results on continua regarding psychometric abilities known to be associated with DMC. Given that a delusion is by definition a 'belief that is firmly held on inadequate grounds' (see Chapter 1 – Schizophrenia and decision-making capacity for research p.11 for full definition) severity of delusional symptoms is often described in terms of the number and extent of a patient's delusional system. For example, the PANSS definition of the moderate and extreme delusions respectively are 'Presence of either a kaleidoscopic array of poorly formed, unstable delusions or a few well-formed delusions that occasionally interfere with thinking, social relations or behaviour' and 'Presence of a stable set of delusions which are either highly systematised or very numerous, and which dominate major facets of the patient's life. This frequently results in inappropriate and irresponsible action, which may even jeopardise the safety of the patient or others'. However, the effect of

delusions on DMC-R does not derive from their form, delusions being present or not and their extent, but rather their content. The impact depends on whether the content of the delusion affects the ability to 'use or weigh'. Thus, each delusion acts as a categorical variable with a possible binary effect on DMC-R. I have named this a trump error, in that it trumps other considerations if it forms a key part in that person's 'using and weighing' a decision to participate. A simple example may be an isolated delusional belief that there are people conspiring against oneself may not impact decisions about research participation, but a delusional belief that the researcher is conspiring against oneself may have huge impact, even though the number and intensity of the delusions are the same.

Comparison of individual clinical variables with DMC-R and DMC-T

The relationships between key predictor variables (delusions, thought disorder, hallucinations, insight, digit span, and LM1) and proportions with DMC are presented in Figure 6 p.209). Given the special interest of this work into the role of insight in DMC-R its relationship with DMC-R and DMC-T is covered in the next section.

Figure 6 – Bar charts of proportions of DMC vs individual symptoms



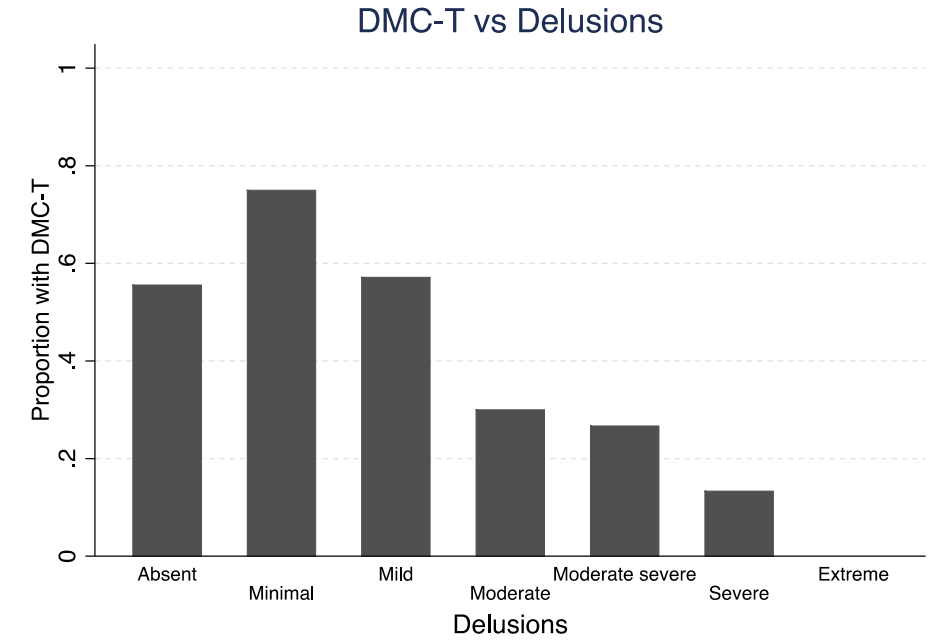
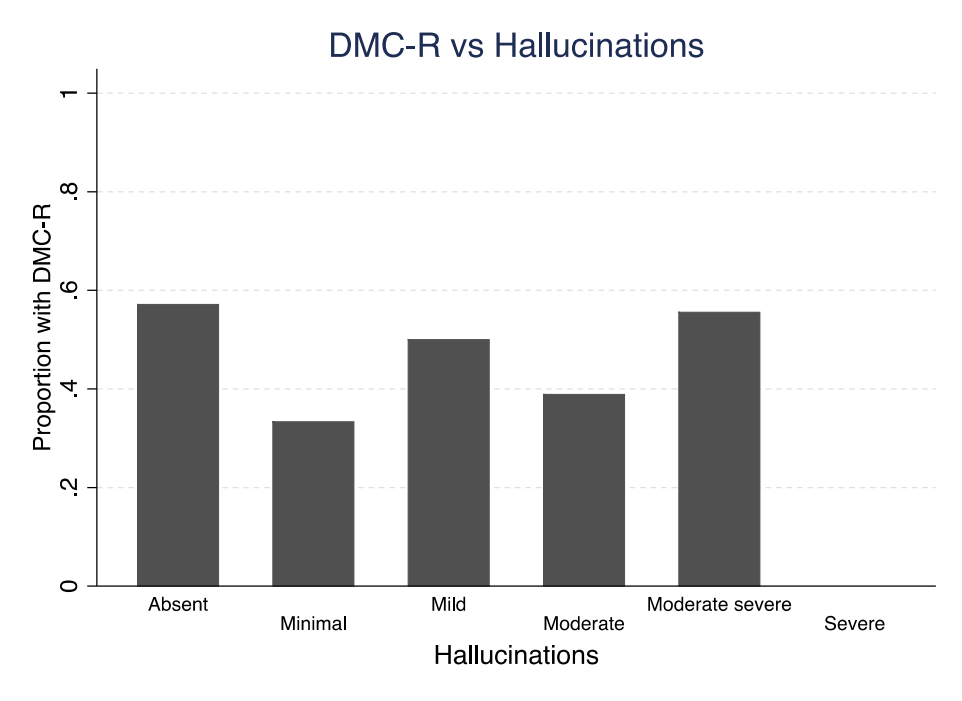


Figure 6 (continued 2/6)



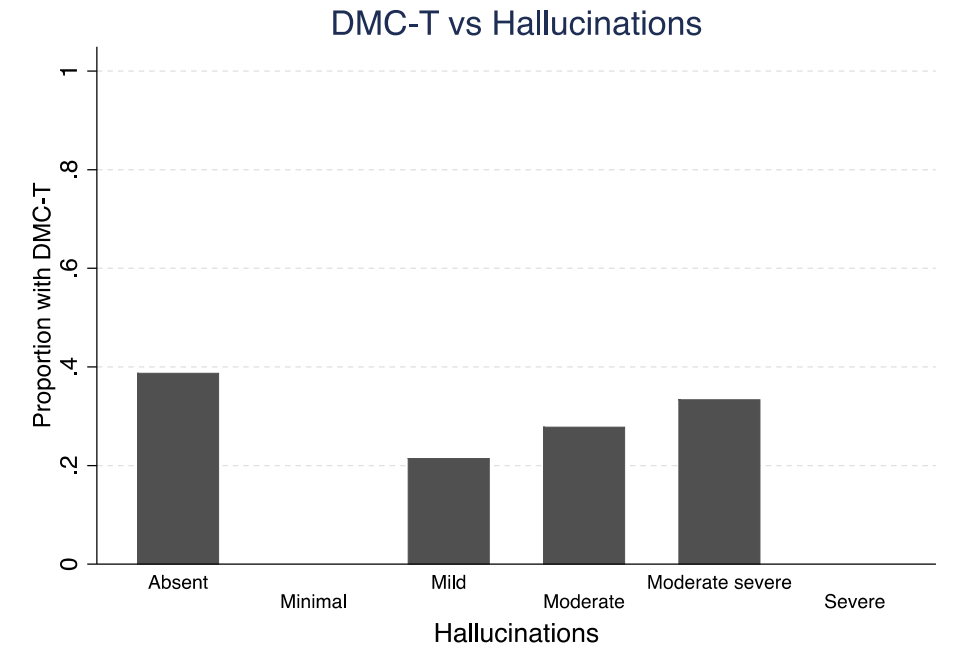
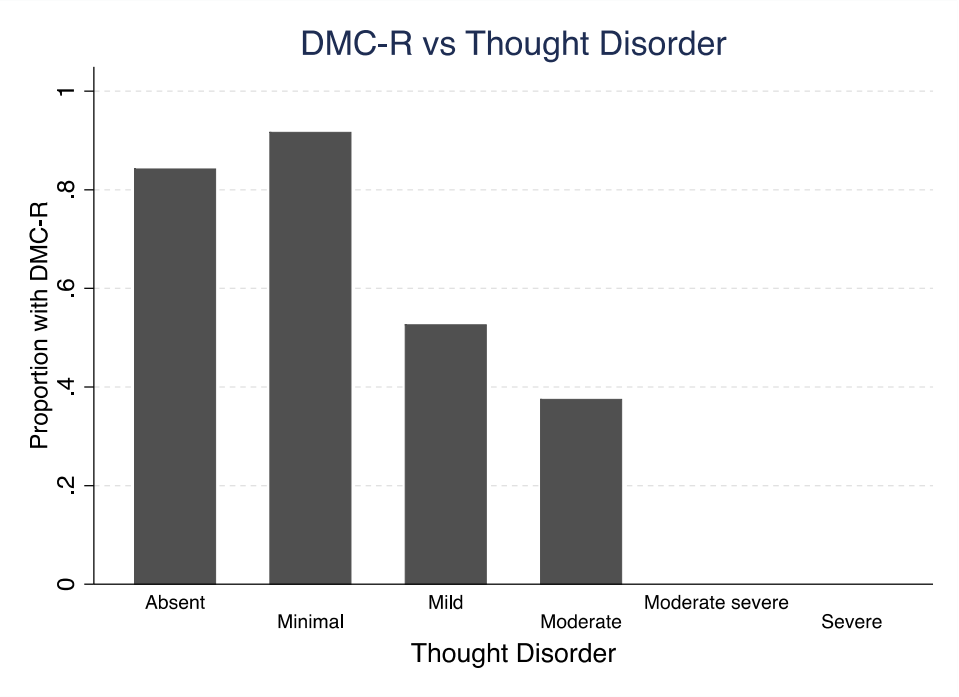


Figure 6 (continued 3/6)



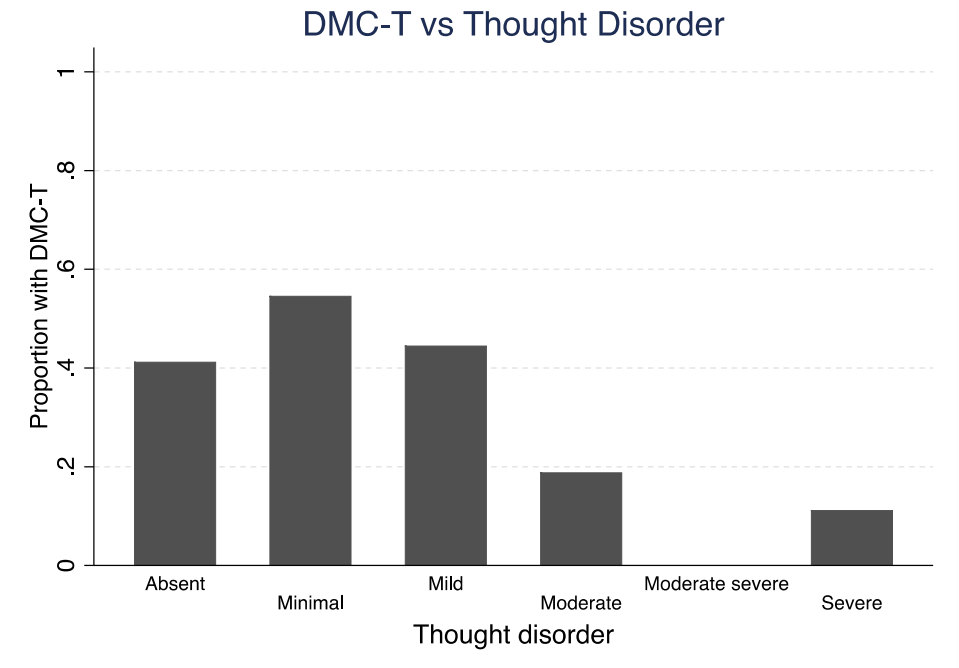
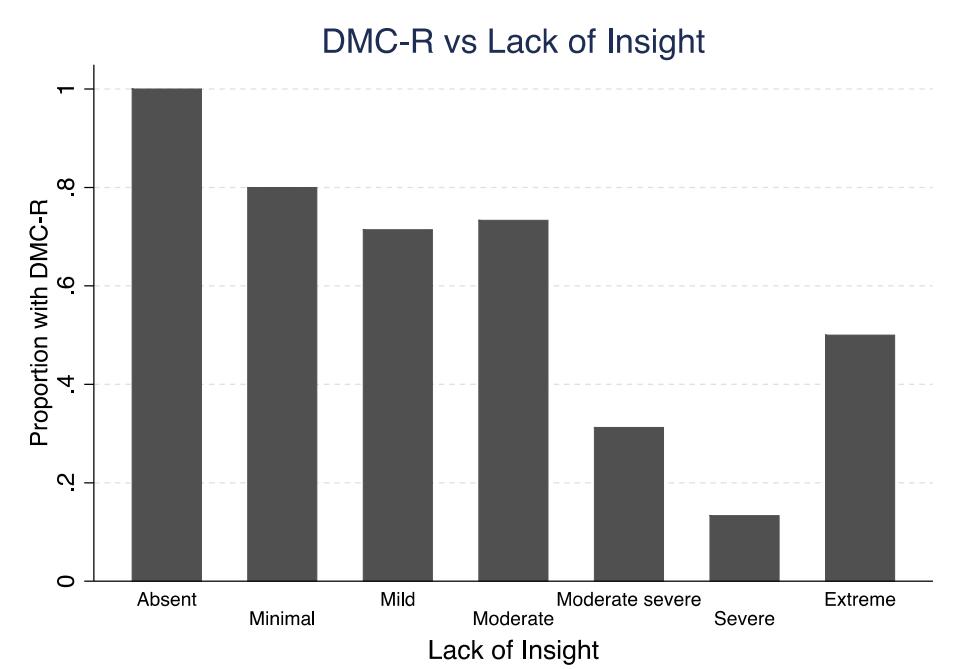


Figure 6 (continued 4/6)



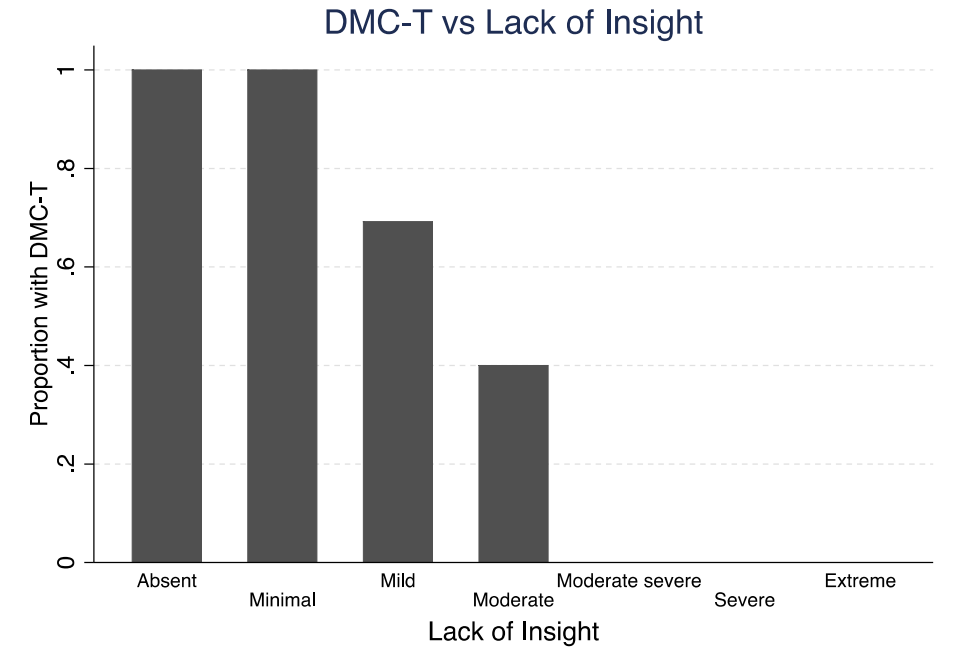
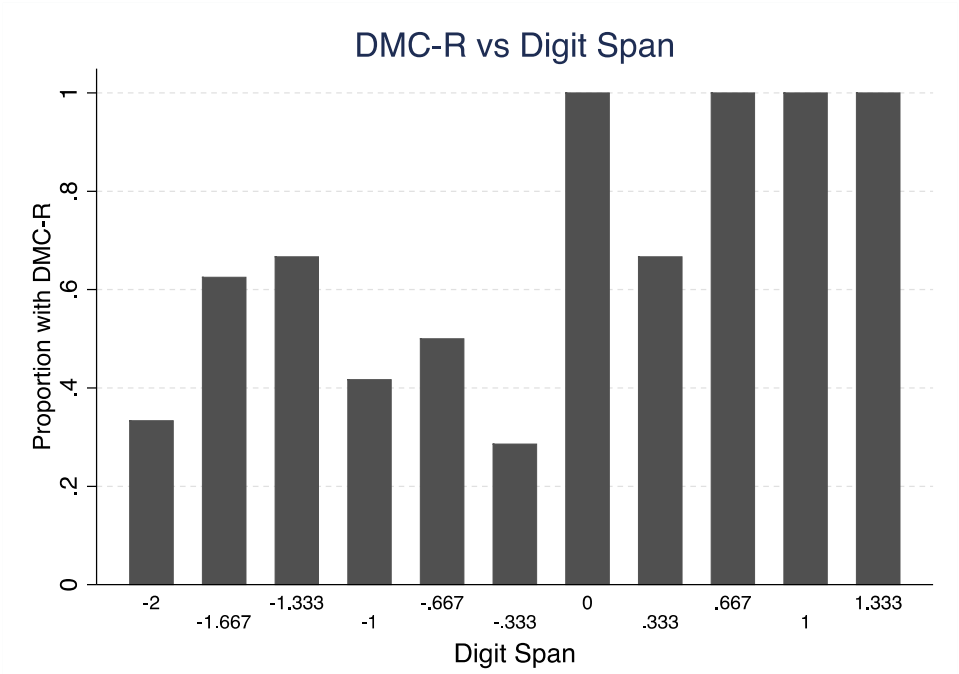


Figure 6 (continued 5/6)



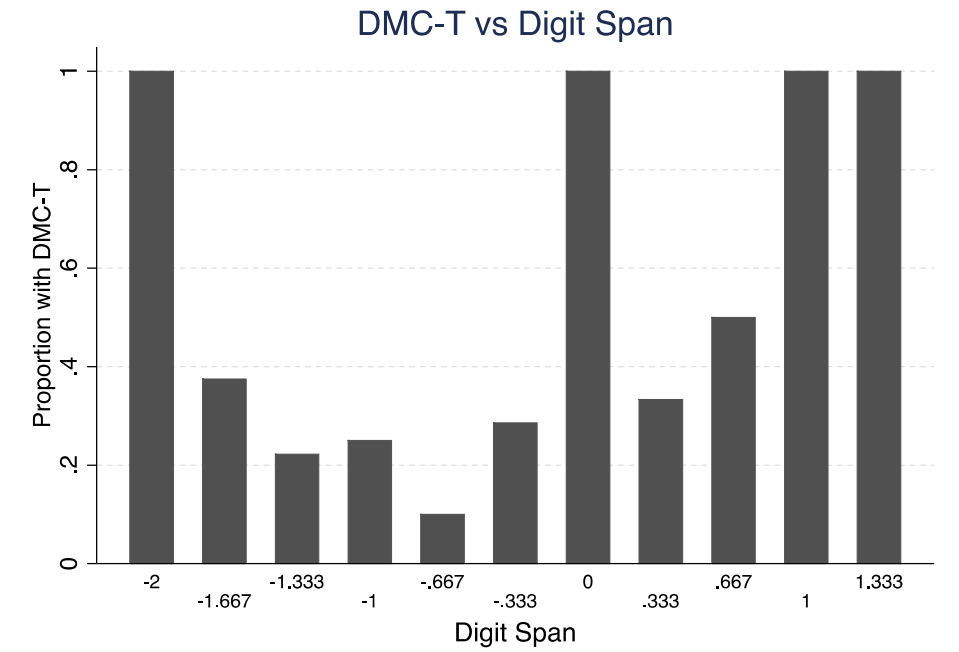
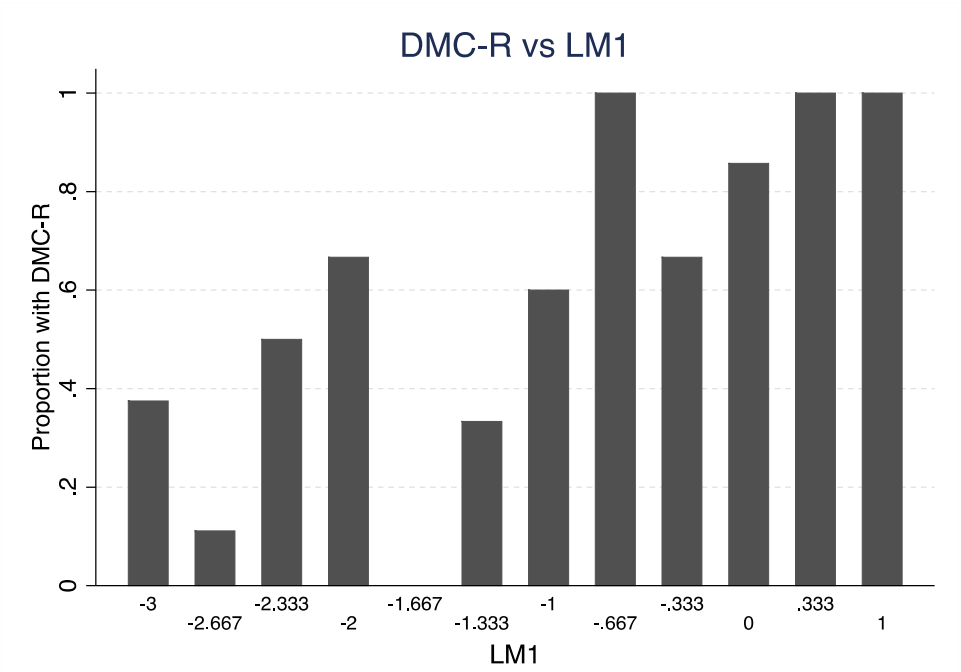
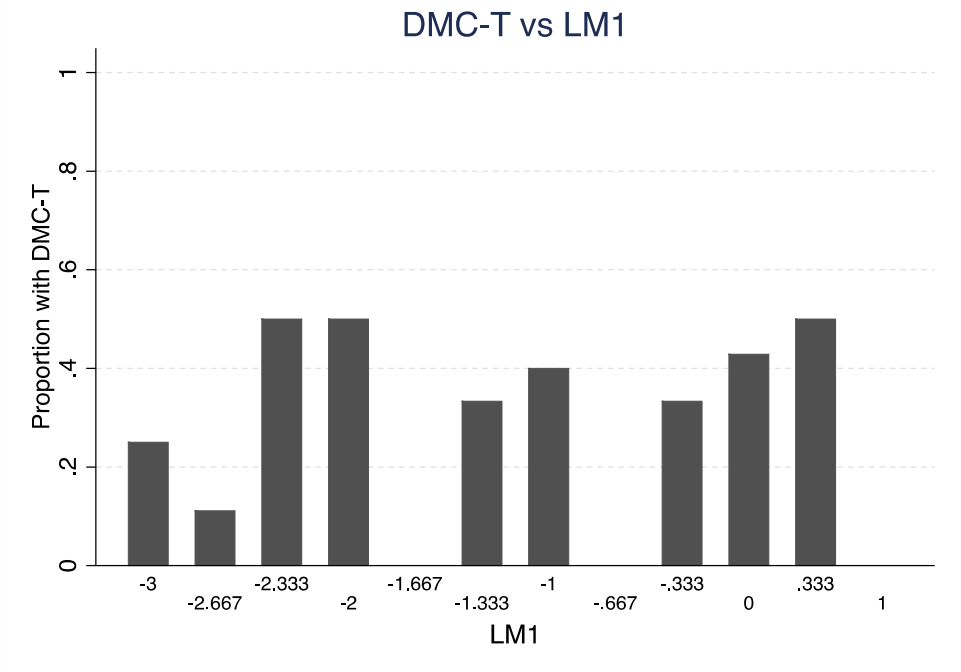


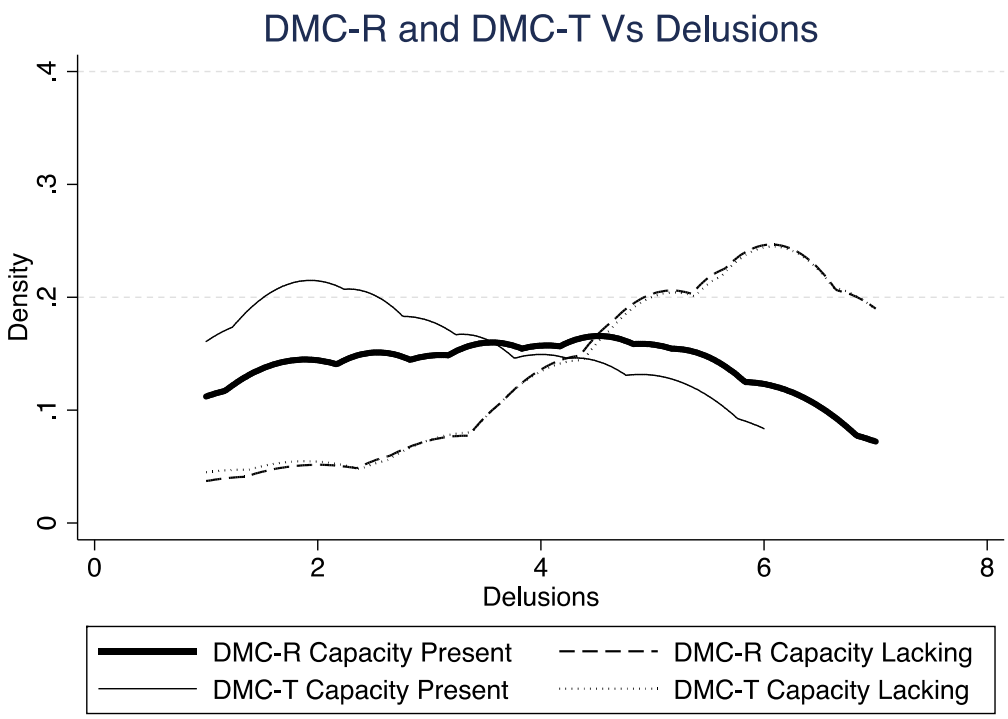
Figure 6 (continued 6/6)





For both DMC-R and DMC-T the effect of delusions looks broadly linear, with worse score on the PANSS measure of delusions leading to lower proportion of those with DMC-R. This is also evident on a kernel density plot comparing the effect of delusions on DMC-R and DMC-T (see Figure 7 below). However, it is important to note that having a high severity score of delusions remains compatible with having both DMC-R and DMC-T, and the limitation that when analysed in this fashion here and later in this section the numbers in each symptom severity band will be small. I have already discussed how the impact of delusions can at times have a categorical or binary effect, and so this linear relationship needs to be explained.

Figure 7 – Kernel density plots of PANSS delusion scores and outcome of DMC-R and DMC-T

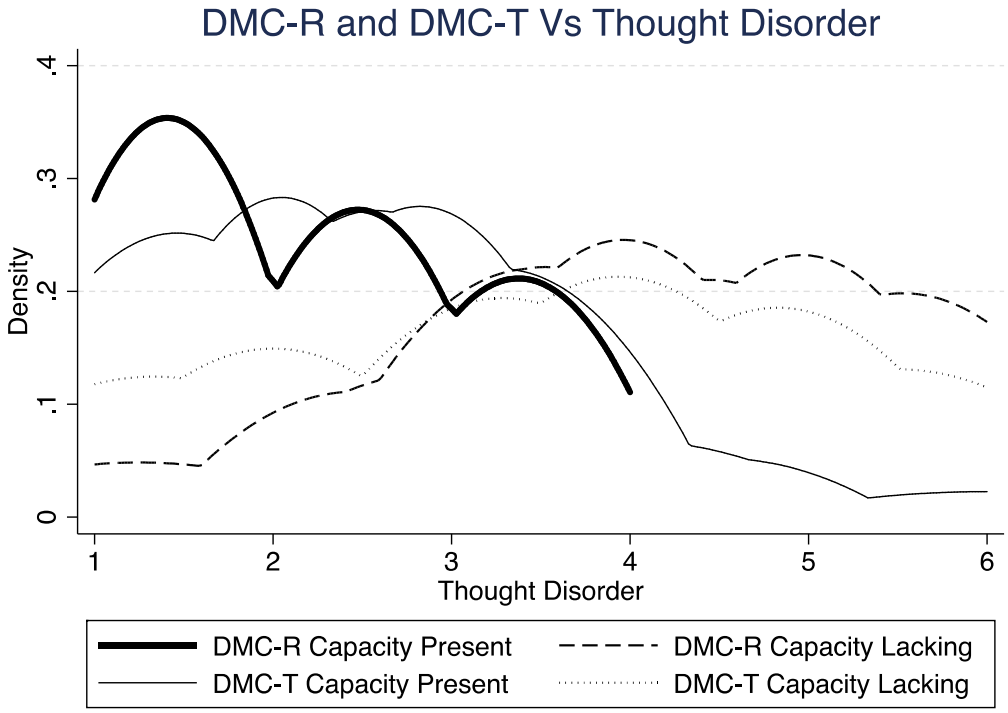


As I have already reported, the PANSS scores severity on delusions through number and intensity. If my conclusion is correct, that each isolated delusion will have binary effect, being a 'trump error' or not, then as the number of these delusions held by the individual increases so the potential for 'trump error' and this will give the PANSS delusions and DMC-R a relationship that may be quasi-linear. However, given that the tool used to measure delusions also seems to be also measuring overall illness severity

as well, an alternative explanation could be that the relationship is due to the confound of illness severity. It is not meaningful to run the regression analysis again using a measure of overall illness severity, as, of course, the overall illness severity will be related to the overall impact of delusions (the CGI z-score which is the best global measure of illness severity used in the study correlates with delusions z-score with a Pearson's r of 0.4863, $p<0.001$ – therefore these variables will be co-linear in a regression). Therefore, it remains unclear if the explanation for this relationship is also down to delusions being a proxy marker of overall illness severity.

For DMC-R the effect of thought disorder is linear but with the suggestion of a threshold effect with low thought disorder associated with high proportions of DMC-R, but greater than moderate severity (4) thought disorder was not compatible with having DMC-R. This suggestion of a threshold effect is not seen in the relationship with DMC-T and both can be demonstrated on a kernel density plot (see Figure 8 below).

Figure 8 – Kernel density plots of PANSS thought disorder scores and outcome of DMC-R and DMC-T



There is no clear relationship between hallucinations and either DMC-R and DMC-T. For both digit-span and LM1 there is evidence of a linear relationship with better performance and more DMC-R, however there is no clear relationship with these variables and DMC-T.

The relationship of thought disorder with DMC-R is as one would expect, in that if we expect the main impact of thought disorder to be on the process of 'understanding', and to a lesser extent 'using or weighing' through its impact on attention, then there would be a linear relationship with worse thought disorder leading to worse DMC-R (depending on the complexity of the task and individual factors allowing them to compensate for its effects on their thinking) with a threshold effect at which thought disorder is so severe that it is not possible to compensate for it in a given task. One would expect the same with the neurocognitive tests, but it is also possible that they were not sensitive enough to detect extreme deficits or that there were other confounds in poor performance on these tests such as participant motivation or exhaustion. The amount of missing data in the neurocognitive assessments may also have had impact here.

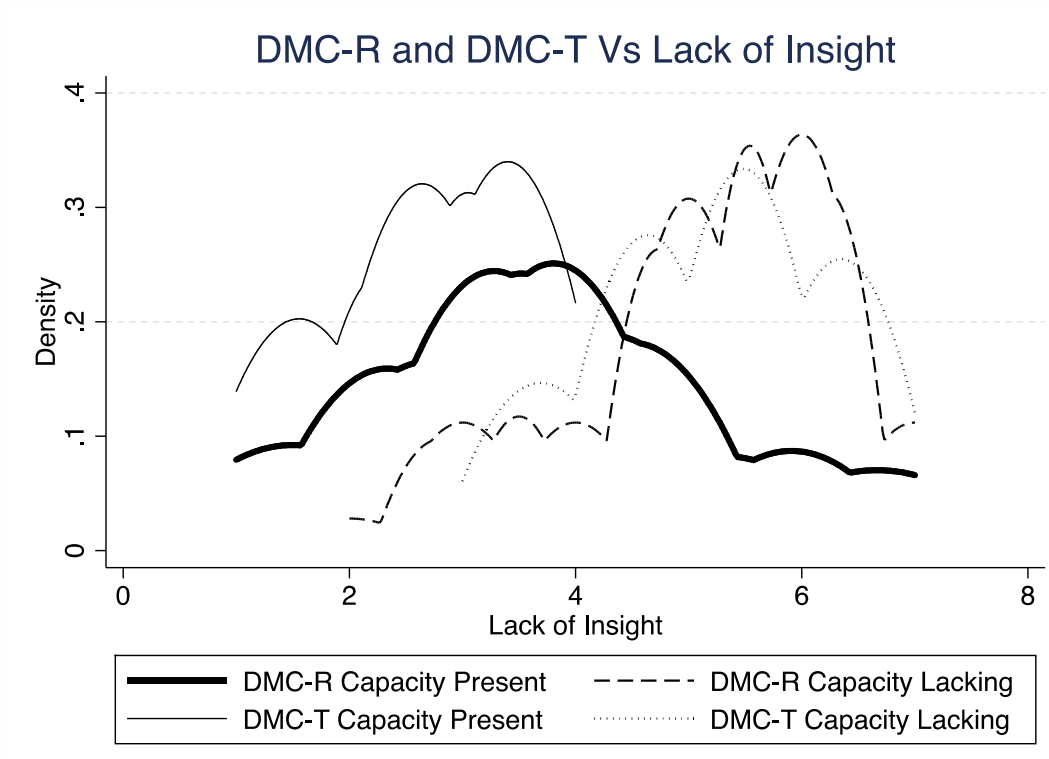
Therefore, there is evidence that the *nature* of the effect of psychopathology on DMC-R varied according to the type of symptom: some having a categorical effect (delusions), some having a dimensional effect (LM1) and some having a dimensional effect up until a threshold (thought disorder). The variables with the categorical effect were associated with the *content* of decision-making, while those with a dimensional effect with the *process* of decision-making. I shall develop this further in my exploration of the final variable of interest, insight.

Is having insight necessary to be able to validly consent to research (the role of insight in DMC-R)

Insight in DMC-T

My results confirm previous work that demonstrates the central role of insight in DMC-T. Revisiting Figure 6 p.209 focussing on insight and DMC-T, its binary relationship is very clear. This is also clearly demonstrated the kernel density plot Figure 9 below. In every participant whose lack of insight was rated as absent or minimal (1-2), DMC-T was found to be present, whereas in every participant whose lack of insight was rated as moderate severe or higher (≥5) was found to lack DMC-T. Those with mild to moderate insight (3-4) split between having and lacking DMC-T.

Figure 9 – Kernel density plots of Lack of insight and outcome of DMC-R and DMC-T



Insight in DMC-R

In contrast with DMC-T, the evidence regarding the role of insight in DMC-R from this study is complex and nuanced. In order to understand the relationship, I present here an exploration of the role of insight in DMC-R from several different modalities, the quantitative data, qualitative exploration of key cases, the qualitative sub-study, and a conceptual exploration.

Evidence from the quantitative analysis

From the quantitative full dataset, the effect of lack of insight on lack of DMC-R was an OR of 2.76, 95%CI 1.55-4.90, p=0.001. This effect remained when adjusting for other individual symptoms (see Table 25 p.219) although the effect was substantially stronger when controlling for negative symptoms, OR 4.21, 95%CI 2.01-8.81, p<0.001.

Table 25 - Insight in DMC-R adjusted for other variables

	OR	**95%CI**	**p**
Unadjusted insight z score	2.76	1.55-4.90	0.001
Adjusted for:			
CGI	2.05	1.04-4.04	0.038
HoNOS	2.75	1.45-5.25	0.002
PANSS Total	3.07	1.32-7.18	0.010
PANSS Positive	1.82	0.92-3.60	0.087
PANSS Negative (T)	4.21	2.01-8.81	<0.001
PANSS General	2.46	1.27-4.76	0.008
Delusions	2.16	1.15-4.07	0.017
Thought Disorder	3.10	1.42-6.79	0.005
Hallucinations (T)	3.03	1.64-5.61	<0.001
LM1	2.01	1.01-3.97	0.046

Reviewing Figure 6 p.209 and the associated kernel density plot, Figure 9 p.218 the binary relationship between insight and DMC, seen in DMC-T is not present. Rather for DMC-R there gives the appearance of a linear relationship with worse insight leading to lower proportions with DMC-R. However, at the most extreme end of the range the linear relationship breaks down and 50% with 'extreme' lack of insight (7) still had DMC-R.

Evidence from qualitative exploration of the cases

Cases in which lack of insight was graded at 7 ('extreme' lack of insight) are presented in Table 26 p.221, along with the performance on the MCA 'functional test', and the main reason for lack of DMC-R according to my study notes, and the expressed motivation for participation in research in those where DMC-R was present. Notably, in none of the cases in which DMC-R was lacking was lack of insight cited as a reason, rather it was predominantly issues with lack of understanding. Motivation for participation in research that was expressed ranged from alleviating boredom, helping people, and learning.

I present here a short synopsis of each case in turn in which DMC-R was present and lack of insight was rated at 7.

Table 26 – Characteristics of cases with lack of insight level 7

	DMC-R	MCA criteria				Main reason for lack of DMC-R	Motivation for participation if lacking DMC-R
		Understanding	Reasoning	Using or Weighing	Communicating a decision		
P25	+	+	+	+	+		Alleviate boredom
P52	-	-	-	-	-	Lack of understanding	
P68	+	+	+	+	+		Help people for the future
P70	-	-	-	-	+	Lack of understanding	
P76	-	+	-	-	+	Marginal understanding, delusional interpretation of disclosed information.	
P103	-	-	-	-	+	Lack of understanding	
P110	+	+	+	+	+		Helping out and learning
P112	+	+	+	+	+		Helps understanding of illnesses in general (other than psychosis) that could possibly help self in the future

P25

This case is a 22-year-old man with a diagnosis of schizophrenia, detained under section 3 of the MHA. He believed that the admission in hospital was due to a conspiracy against him, one which the doctors were involved in. He viewed his admission beneficial purely in terms that he had cut down on smoking while in hospital. He saw that his recruitment and participation in the study would be in order to provide a wider spectrum of the population (and not on the basis of his disorder at all, which he vehemently denied). His reasoning around taking part was that he is 'terribly bored in here' and that if he had met me on the street he would have refused, but it is 'something to do' while in hospital. He had a full and complete understanding of the study.

Here, although insight was compromised, within his process of 'using or weighing', factors relating to either the presence of his mental illness or its treatment did not directly feature. Rather other factors were important for him, the alleviation of boredom and the need of the research to recruit a broad spectrum of society (irrespective of illness state).

P68

This case is a 28-year-old man with a diagnosis of schizophrenia, detained under section 2 of the MHA. He believed that his admission into hospital was a component of the conspiracy against him, and disavowed the possibility of any mental illness.

When considering the research options, he considered several issues: 1) that this was an opportunity for the research to explore his medical notes and DNA and therefore prove that his is not ill, 2) that he would leave his mark/contribute to medical research, and 3) that the research will happen anyway if agencies want it to with or without his

consent, so he may as well consent to it. Otherwise he had full and complete understanding of the research and the connected issues.

Here, insight did impact in that motivation for participation was clearly linked to disproving his diagnosis. In my assessment, I ultimately considered that he had DMC-R as I believed his main motivation for participation was to help others and altruism and it was these factors that he was 'using or weighing'.

P110

This case is a 48-year-old woman with a diagnosis of schizophrenia, detained under section 3 of the MHA. She disavowed having mental illness and saw the laws of the county to try to persecute her.

She had full understanding of all issues in the research project, and considered the risks and benefits of the research, including discomfort and concerns around blood testing. She was motivated to take part to 'be nosy wanting to know … science how they look at things and how other people look at things'. She explained that she was looking forward to learning about the results of the project and googling them in the future. In terms of her own participation she explained 'it's 'good to be part of something' even if there was no direct benefit to herself, but also recognised a selection criterion that she met was her being in hospital.

P112

This case is 43-year-old man with a diagnosis of schizophrenia, detained under section 2 of the MHA. He disavowed having any mental disorder: 'you seem to have the impression that I am psychotic, I am far from that… how I ended up here is a mystery'.

He had a full and complete understanding of all issues within the BioResource study, and was appropriately concerned about issues around confidentiality and ability to get work/possible discrimination. Regarding selection and participation he saw this as being down to his presence within the hospital rather than due to illness, 'because I am in a psychiatric environment where I am deemed to be psychotic despite my belief to the contrary'. He hoped that following the research 'my treatment and the analysis can be better, can be improved' but that the research would be able to 'focus is on illness diagnosed in other ways', possibly this was related to a belief it would ultimately disprove his diagnosis. His reasons for participating were that he was contributing to something positive and promoting medical care. He considered that although it would be unlikely that his involvement would have direct benefit, but any study of his genetic and any disorders therein would possibly help him if he suffered from them in the future (any study of his genome could only benefit him if they discover and learn more about his genes and related illnesses).

There are also several cases where insight, when present, was clearly linked to the motivation to participate as case P85 demonstrates:

P85

This case is a 27-year-old woman with a diagnosis of schizophrenia, detained under section 2 of the MHA. Her lack of insight was graded as '3' (mild). She understood all details of the research clearly and comprehensively. Her decision to participate in the research was a recognition of her illness and a desire to participate in research into that illness to prevent other people having the illness, including her son, in the future.

In all of these cases, the unifying theme is that there are a variety of primary reasons or motivations presented for participating in research (again summarised in Table 26 p.221 along with main reasons for lacking DMC-R and the individual abilities on the MCA 'functional test'). Where do these fit with the model of DMC-R under the MCA?

As I stated in Chapter 2 p.17 the assessment of 'use or weigh' involves considering the information necessary to be understood *'relevant to the decision'* with '*the reasonably foreseeable consequences of the decision'*. It may include the risks or benefits to society (I shall call these indirect risks and benefits), and non-medical direct benefits (such as alleviation of boredom or financial reward). This leaves a large scope for the decision-maker in terms of framing their decision to participate or not, according to what is *relevant* to their decision. For some people, a desire to help others and one's family will be an important factor to 'use or weigh' (e.g. P85), whereas for some people a desire to alleviate boredom will be an important factor (e.g. P25). The legal test for DMC must be tailored by the situation, and the importance of considering each of these factors within the process of 'using or weighing' will vary by individual as will the personal impact of these factors (obviously someone without children would not 'use or weigh' the impact of their decision on their offspring). Previous authors have assumed that the risk/benefit appraisal within DMC-R is homogeneous between individuals [168]. In contrast, I submit that the decision-specificity of DMC is by nature not just limited to the *individual decision* but also the *individual decision-maker*, based on the consequences (risks/benefits) of the decision that are meaningful or relevant to them.

What is the relationship of motivation with these consequences? I submit that here one can consider motivation as the weight or **salience** of a perceived benefit to an action as part of the decision-making process. For example, a motivation to help others through

participation in research is linked to considering that helping others is an important benefit to 'weigh' against other benefits and risks. It may be that for a particular decision an individual considers that only the alleviation of boredom is an important benefit to consider, and it leads logically to a question as to are there different risks or benefits that *must* be used or weighed in the decision-making process in order to have DMC?

In many of my assessments of DMC-T people were happy to remain in hospital for reasons separate to their assessment or treatment for mental disorder (such as to give up smoking), whilst disavowing the current existence of disorder. Of interest, all of the cases misclassified by the 'cut-off' standard reported above were of this nature: In these assessments of DMC-T I judged that there was a requirement to 'use or weigh' the direct medical risks and benefits of the treatment and failure to do so resulted in a judgement of lack of DMC-T. On this basis, I would submit that there are some risks/benefits that must be 'used or weighed' for a particular decision, for medical treatment it would include the direct medical risks and benefits of that treatment.

In this regard, the construct of DMC-T is simpler than DMC-R. DMC-T is two-dimensional in that an evaluation of risks and benefits of treatment is generally limited to direct medical and social benefits to oneself of treatment (although there could be other direct non-medical benefits such as reducing other people's anxieties and thereby having an easier life). Whereas decisions around DMC-R have many planes or dimensions regarding decision-making both indirect and non-medical direct risks and benefits (see Table 27 p.228). It is difficult to see where how under most circumstances motivations such the alleviation of boredom having substantial impact on decisions around medical treatment, and thus form part of the 'use or weighing' process; a decision to consent to medical treatment based primarily on alleviation of boredom would raise concerns about DMC-T. However, in decisions about research I have found that these are not just common considerations but can be decisive in their decision-making process. Thus, the

construct of DMC-R under the MCA, contrary to some claims, is not a less personal construct than that of DMC-T.

Therefore, the low insight cases show us that there can be different sets of 'using and weighing' processes, which are often very personal or fact sensitive and relevant to DMC-R depending on the differential importance, or salience, of a foreseeable risk or benefit to that individual. These can outbalance the effect low insight has on the 'using and weighing' process. In DMC-R the process of 'using or weighing' is in fact more personalised or fact sensitive than is often presumed in the literature. I shall name this paradigm of DMC-R (and DMC in general) the 'salience model'.

Table 27 – Direct and indirect risks and benefits for DMC-T and DMC-R

	Direct medical benefits	**Direct medical risks**	**Direct non-medical benefits**	**Direct non-medical risks**	**Indirect benefits**	**Indirect risks**
DMC-T	Treatment of disorder	Side-effects of treatment	Social consequences of recovery (anxiety reduction in family)	Social consequences of treatment plan (social stigma)	None	None
DMC-R (non-therapeutic research)	*Incidental findings (very low probability)*	*Discomfort from blood taking (very low impact)*	Financial incentive Alleviation of boredom	Data breaches Social consequences of involvement (time)	Helping others	None
DMC-R (therapeutic research)	Treatment of disorder	Side-effects of treatment	Social consequences of recovery (anxiety reduction in family) Financial incentive Alleviation of boredom	Data breaches Social consequences of treatment plan (social stigma)	Helping others	None

So far, I have considered the role of insight in decisions for non-therapeutic research and compared it to decisions regarding treatment, but can my theory regarding the varied impact of insight on the ability to 'use or weigh' also apply to therapeutic research and what circumstances may alter this?

A key feature of therapeutic research is that there is a therapy which the person may receive, and thus there is the possibility of direct medical risks and benefits. I have already discussed above that in my assessment of DMC-T there was a requirement to 'use or weigh' the direct medical risks and benefits of treatment, thus given the therapeutic research has direct medical risks and benefits, I would submit that it would have this requirement as well. Therefore, let us consider two studies shown in Table 28 p.229, one therapeutic and one non-therapeutic following the schematic of risk/benefits in Table 27 above:

Table 28 – Comparison or risk benefit analysis of therapeutic versus non-therapeutic research

Study	1- low risk/no direct benefit to patient *(such as a study interviewing people in hospital about their use of cannabis prior to admission. Compensated financially for participating.)*	2 - high risk/potential high direct benefit to patient *(such as a trial using an experimental medication for treatment of psychosis. Not compensated financially for participating.)*
Insight	Denies illness (low insight).	Denies illness (low insight).
A - Medical direct risk/benefits	Acknowledges personal benefits (none) of participation. Acknowledges personal risks (low) of participation.	Cannot acknowledge personal benefits (high) of participation. Can/cannot acknowledge personal risk (high) of participation.
B - Non-medical direct risk/benefits	Acknowledges personal gain – financial incentive – (medium) of participation. Acknowledges personal risk – data risk – (low) of participation.	Acknowledges personal gain – financial incentive – (none) of participation. Acknowledges personal risk – data risk – (low) of participation.
C - Indirect risk/benefits	Acknowledges societal benefits (high) of participation.	Acknowledges societal benefits (high) of participation.

We can see that in study 2, the drug trial, the important factors to 'use or weigh' in the risk benefit analysis are the medical direct risks and benefits and the indirect benefits (to society). As the medical direct benefits require insight to be able to 'use or weigh' then insight is required for decisions regarding therapeutic research (the medical direct risks of a drug such as a side-effect may be acknowledged even when lacking insight).

In study 1, the cannabis survey, the only factors that are medium-high effect are those of the non-medical direct risk and benefits and the indirect risk and benefits. Thus, insight is not always necessary in order to be able to adequately 'use or weigh' in this model, but to labour the point, if people wanted to participate to help prevent others from developing schizophrenia by better understanding their own history of cannabis use and

how it led to them developing the illness, then insight might be instrumental in 'using or weighing' the indirect benefits to society.

The model is clearly an oversimplification as all of the risks and benefits presented could involve considerations relating to recognition of illness. For example, in considering the indirect societal benefits of research, is there a requirement to appreciate that one has the disorder being studied? Are the societal benefits of research viewed as disorder specific or not? Take case P85, the appreciation of benefit to others directly resulted from her knowledge of illness in terms of how her participation can help society and her children through better understanding of her disorder. During my consent discussions, there were many people who refused participation as in their view they were not suffering from a psychotic illness, and thus while they wanted to help society, in their opinion their participation would be of no benefit as they did not have the disorder being studied. This lends further support to my 'salience model' theory as it allows for the variable impact of insight on the ability to 'use or weigh' – understanding that for each individual their interpretation and prioritisation of the main issues of the study will vary based on their personal motivations.

Finally, as discussed in Chapter 2 – MacCAT-CR 'appreciation' and the 'therapeutic misconception' p.28, many researchers have used TM (an incorrect belief or strong expectation that, when participating in research study, the procedures of the study will work towards their individual therapeutic benefit rather than for the benefit of the research study itself) as the central model to define 'appreciation' within non-MCA models or tools to measure DMC-R. I submit that limiting 'appreciation' to TM is an overly constrained and incorrect view of DMC-R. I have found a plurality of pathologies surrounding abnormal beliefs in research (as discussed earlier) that have their effect on 'appreciation' and certainly not limited to *misconceptions* about direct medical benefit. The 'salience model' is nevertheless able to handle situations in which there is a strong TM given that

this would result in incorrect judgements regarding the medical direct benefits of participation, and if this was an important consideration in the individual's 'using or weighing' then it could lead to DMC-R being judged as lacking. However, for TM alone to lead to a lack of DMC-R using the MCA legal framework it would need to be 'due to' the relevant psychopathology (the 'diagnostic threshold' as described in Chapter 2 – What is decision-making capacity? p.17), a *misconception* alone would not suffice.

'Salience model' and contested assessments

An implication of the 'salience model' of DMC-R is that there will be some difficult judgements when squaring, in the same individual, pathological or distorted 'use or weigh' processes with other 'use or weigh' processes that are not necessary pathological or distorted. Many of the difficult cases within the reliability sub-study were of this nature. Cases that posed particular difficulty to the panel often resulted around a delusional interpretation of the study design or a particular benefit to that individual, and how this was balanced with other considerations of participation (such as indirect benefits (benefit to society) and non-medical direct risks of participation). These were often reported as challenging due to where to set the threshold – how much weight being placed on a particular perceived benefit or risk is too much for 'using or weighing' to be intact.

Case P91 is the clearest exemplar I have found for this difficulty (although was not considered in the reliability study as it did not form one of the 50 consecutive cases) and it demonstrates the need for the 'salience model' in the formulation of these difficult cases: This case concerned an individual who did not believe that genes existed or biological explanations for illness due to a series of delusional beliefs surrounding this, but recognised that participation in research would be helpful to society and recognised the low medical and non-medical direct consequences to him of participation. On this

basis, he decided that he wanted to participate. I would submit that this case poses a particular difficulty in terms of considering how he 'uses and weighs' the information regarding the indirect benefits of participation. Can he 'use or weigh' the information regarding the benefits to society of research participation if due to a delusional belief does not believe the fundamental design of the research project is valid? Or is his recognition that all research has broad benefit to society sufficient to be able to 'use or weigh' these benefits? The answer to this will decide whether one thinks he can or cannot use this information, and thus whether he can 'use or weigh'. If instead, despite having this delusional belief, he cared little for the indirect benefits of research participation, and based his decision around the non-medical direct benefits to himself (financial incentive) and limited non-medical direct risk of participation, and his process of 'using or weighed' was based on this, then one may judge him as having DMC-R.

Summary - the 'salience model' and impact of psychopathology on DMC-R and implications for future research

Kim 2006 asserted that research into DMC-R in schizophrenia was straightforward as, broadly speaking, the same benefits and disadvantages are to be considered by all and thus unlike DMC-T there was a degree of homogeneity [168]. With regards to the role of insight and other pathologies such as delusions in DMC-R, my data do not support this assertion. There is evidence from this work that the relationships between delusions and insight with DMC-R is complex:

1) The quantitative data do not show a straightforward linear association or otherwise.

2) The complex cases demonstrate cases in which insight can be very important in the 'using and weighing' of the benefits and disadvantages of participation in research, but

that this varies on a case by case basis. This is also true of individual delusions that the individual may have, whether they are 'trump errors' or not.

I have devised a model named the 'salience model' that explains my findings. It allows for individual differences in motivation for participation as a result of the varied and multi-dimensionality of research decisions when appraising both direct and indirect risks and benefits compared to treatment decisions, the differential salience of each of these to the individual in making their decision.

It is ironic that I chose the 'parent study' for this research as non-therapeutic research as I wanted to minimise the effect of insight. In Chapter 3 p.40 I criticised other work for choosing 'parent studies' in which the role of insight on DMC-R was heterogeneous by individual (such as studies using cognitive enhancing drugs). I considered that it was the possibility of viewing the therapeutic agent as related or not to one's present disorder as driving this heterogeneous impact on DMC-R. My findings and conceptual exploration of DMC-R show that I was wrong, and that both insight and delusions can have heterogeneous effects on DMC-R that vary by individual even in non-therapeutic research paradigms. I would submit that any pathology in which the content may impact on the ability to 'use or weigh' (insight and delusions) will lead to heterogeneous effects. This heterogeneity with insight is not so strongly seen in DMC-T, but this is because consideration of medical direct risks and benefits is always necessary to 'use or weigh' to have DMC-T. Given this, my clinical epidemiological approach has contributed to understanding DMC-R, however, a detailed qualitative approach would be a fitting next step to explore the phenomenon further. I have shown that the decision-specificity of DMC-R also includes person-specificity.

Limitations in comparing DMC-R to DMC-T

The contexts in which DMC-T and DMC-R are assessed in practice are very different, as are possibly the pressures and factors for which the assessment takes into account. The stakes involved in a DMC-T assessment usually are high, surrounding the risk of harm to an individual through non-treatment of disorder if found to have DMC-T when refusing (the context of refusal of treatment is the usual one for DMC-T assessments [184]). To the individual there is little harm from non-participation in research, and therefore do different thresholds for DMC-R and DMC-T exist, and could these explain some of the differences (the argument being that in fact the formulation of DMC-R and DMC-T is the same, but the thresholds applied to them are different)? Kim has demonstrated how clinicians use a risk sensitive model when judging DMC-R [160], could the increased impact of cognitive symptoms on DMC-R result not from a difference in the nature of the two decisions, but rather could it result instead from the assessors requiring a higher standard of 'understanding' for them to allow participation (through use of labelling someone as having DMC-R or not). This can only be further explored through further research comparing two studies similar in all respects other than risk of harm through participation.

Chapter 10. Meeting key aims and hypotheses, interventions to enhance decision-making capacity for research, final conclusions and policy recommendations

Revisiting central aims and hypotheses

Aim 1. To describe the proportion of people with DMC-R in adults admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

I have shown that half of participants I recruited had DMC-R (51%, 95%CI 40-62%) and a third had DMC-T (31%, 95%CI 21-43%), this difference was statistically significant, $p<0.01$. My sample was biased in that women more likely to be recruited than men into the study (OR, 2.36, CI 1.46-3.82, $p<0.001$) but there was no impact from other socio-demographic or clinical factors. The method I used to assess DMC-R in the study, my clinician 'judgement standard', was highly reliable when compared to the group decision of a panel of experts reviewing the assessment transcripts (kappa=0.68 'substantial'). There are no other data in the literature found by my systematic review with which I can directly compare my main results.

Although I have found no evidence that my recruited sample was substantially different than the rest of the eligible population, despite the gender differences, there are features of the non-approached patients which may have impacted on decisions to approach them to discuss research participation. I found support for this in the qualitative

sub-study, Chapter 8 p.154, where I found that decisions made around first approach included clinicians' views on their ability to 'meaningfully' answer questions. Therefore, I cannot conclude definitively that those who were not recruited were different in ways that might impact their DMC-R. This needs to be studied further.

Aim 2. To determine how the symptoms of psychosis impact on DMC-R compared to DMC-T in this population.

I found that thought disorder was most associated with lacking DMC-R (OR 5.72, 95%CI 2.01-16.31, p=0.001) whereas lack of insight was most associated with lacking DMC-T (OR 26.34, 95%CI 3.60-192.66, p=0.001). This is consistent with the published data from previous studies (if one considers the impact of thought disorder to be within the same domain as neurocognitive deficits).

Hypothesis 1. DMC-R does not share the same proportion or symptom associations as DMC-T in adults who are admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses.

My data strongly support the rejection of the related null hypothesis, that 'DMC-R does share the same proportion or symptom associations as DMC-T in adults who are admitted to psychiatric hospitals for the assessment and/or treatment of schizophrenia and related non-affective psychoses'.

Aim 3. To investigate the suitability of interventions to enhance DMC-R and explore views on the current framework around consent for research; Hypothesis

2. It may be possible to improve a person's DMC-R if we support their cognitive function or trust.

The proportion of people who had DMC-R in those I was able to recruit was high, half of the sample, whereas the proportion of people whose DMC-R was judged as 'marginal' was very low.

The results from the quantitative study demonstrate that any intervention to enhance DMC-R, chosen on the basis of effect size of symptoms on lacking DMC-R alone, should target cognitive deficits, aimed at supporting short-term memory or ameliorating the effects of thought disorder. Given the lack of associations with the 'trust score' there is little evidence from my results that would support my hypothesis that supporting 'trust' or reducing paranoia should be a target for an intervention to enhance DMC-R.

The qualitative sub-study supports the acceptability by clinicians, carers, and patients alike of an intervention to enhance DMC-R based around supporting cognition. This would need to be flexible and tailored to the individual to avoid the risks of over simplicity or patronising the participant. Equally, the qualitative sub-study also supports the use of other trusted people being present in research discussions to help explain information and reduce anxiety, both of which will support cognition, although again there are barriers with family/friends/carers performing this role: My study, as with previous studies, struggled to gain their involvement. This is entirely understandable given that when their loved ones are unwell they have a lot of other more pressing priorities. It is unclear whether independent advocates would be useful here given their mixed acceptability.

Although these interventions appear acceptable and relatively easy to implement, they are likely to have modest impact on both enhancing DMC-R and increasing recruitment to research of those who have DMC-R given my findings above. Rather the main barrier

or block seems to occur at first approach to discuss research participation due to beliefs and assumptions about the individual's ability to consent or meaningfully participate in research, or structural factors preventing routine involvement in research.

On this basis, my overall findings suggest a rather different approach:

1. There is an argument for a structural/systems intervention to support recruitment into research: that of research clinics and making discussions regarding participation in research part of routine clinical practice and available to all patients. My findings suggest that the rate of DMC-R is high and motivation to participate is strong even what lacking DMC-R, we just need to talk to people.

2. Participation of those lacking DMC-R into research may be being undermined by the legislation around consultee approval given that I, like others, found substantial barriers to their involvement. How can we give due respect to a person's 'wishes and feelings' when lacking DMC-R? Is the process of consultee approval, and the barriers it creates, truly a proportionate response to safeguard the risk of research participation to these patients? This needs to be further explored.

3. There is evidence that we need to explain and educate key stakeholders regarding the decision-specificity of DMC. I found that DMC-R substantively differs from DMC-T in both proportion of people having it and the symptoms that impact on it. It is not possible to draw inferences regarding the presence or absence of DMC-R based solely on their DMC-T. Even generalisations regarding the impact of specific symptoms or overall illness severity on DMC-R are difficult to make as the decision-specificity of DMC-R includes a person specific element (although thought disorder is an exception beyond a certain threshold of severity).

In general, conclusions regarding a patient's DMC-R cannot be made without an assessment of DMC-R.

4. We need to consider the normative standards that we expect when people are making decisions regarding participation in research and ensure we are not applying higher standards for people whose DMC-R we are assessing than the rest of the population. I found that people can have a variety of reasons to participate in research and these can be deeply personal. In contrast, there is evidence that people involved in research consent (such as clinicians) may expect decisions to be based around altruism or helping research endeavour with concerns about their DMC-R being raised if other reasons are presented.

For future research – the design and testing of an intervention to enhance DMC-R

There is evidence from observational studies that cognitive deficits are ubiquitous in people with schizophrenia (see for example [185]). There has been previous work aimed at enhancing cognitive function globally rather than aimed at a specific task, such as DMC-R. Some work has focussed on an intervention, Cognitive Remediation Therapy (CRT), defined as 'a behavioral training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalization' [186]. A meta-analysis of the effect of CRT on people with schizophrenia demonstrated a small to moderate effect on improvement of cognition following CRT and also general functioning [186], however there are some studies with negative results or effect on cognition that do not translate to functional benefits [187]. Other work has looked at the effect of cognitive enhancing drugs, such as the use of modafinil [187], however the results have been mixed [188].

As discussed in Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37 previous work on specifically enhancing 'understanding' in DMC-R has focussed on educational interventions, which include use of repetition, simpler information, and multimedia. While these are not strictly interventions aimed at targeting neurocognition in a clinical sense, rather supporting one of the functional abilities of the 'four factor model' ('understanding'), it can be assumed that their mechanism of action is through supporting neurocognitive processes involved in 'understanding'. Furthermore, as discussed in my systematic review (Chapter 3 p.40) there is extensive evidence that in DMC-R neurocognitive deficits are associated with worse 'understanding'.

I proposed in Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37 that an intervention to enhance cognitive function (working and verbal memory) could involve presenting information to participants in 'chunks' (categorizing and grouping information to reduce the sets of information that needs to be attended to) and to present information through different perceptual pathways such as in simple diagrams or icons rather than written or spoken words. My findings, and published work on enhancing neurocognition in schizophrenia both globally and in order to support DMC-R, support my proposition that an intervention should be designed to support working and verbal memory.

In order to test a more specific intervention to enhance cognitive functioning, and its resultant impact on DMC-R, an RCT is required. Again, as mentioned in Chapter 2 – Can DMC-R in schizophrenia be enhanced? p.37, this intervention could take the form of a manual to guide the presentation of information to people with psychosis and design of participant materials in those with neurocognitive deficits and could be tested against 'consent as usual'.

Final conclusions

I have already covered the main outcomes and aims of the work in the previous chapters, including limitations and recommendations for future research. In the final conclusions of my thesis I want to re-visit the central ethical and conceptual drivers behind the work, the 'moral imperative' and the 'research paradox'.

The results from my study strengthen the case for the importance of the 'moral imperative' (to both adequately protect people from the consequences of a decision made when DMC is lacking but also to ensure autonomy is respected and DMC maximised): I demonstrated that many people when unwell were commonly able to make decisions about participation in research and wanted to. We need to ensure that this group is not systematically excluded from research due to assumptions otherwise. We can try to achieve this by supporting decision-making, making it easier to participate in research through a 'culture of research', and informing key stakeholders about decision-specificity of DMC and the prevalence of people having DMC-R when unwell. Only then may we have a chance of overcoming the 'research paradox'.

The MCA is still relatively new, and to my knowledge there has been no work exploring the meaning of what DMC-R is in the context of the MCA. My 'salience model' is a step forward in understanding the requirements for DMC-R and should serve to help researchers in their research discussions.

Regardless, I met many people during the recruitment to my study, people who wanted to participate in research and people who wanted to facilitate it on their wards. My study itself is a proof of principle, I could do it, so can others.

Summary of policy recommendations

1. Beliefs and assumptions regarding an inability of people with schizophrenia to make decisions regarding participation in non-therapeutic research need to be challenged and key stakeholders (RECs, leading academics in the field, etc.) need to lead on promoting recruitment to research in this group (in order to tackle the 'research paradox'). Deliberate non-recruitment of this population without clear justification may be viewed as discriminatory (and counter to the 'moral imperative' of this work).

2. It may be possible to support people to make decisions when unwell using neurocognitive interventions aimed at short-term memory and attention, especially for people with thought disorder. Although formally testing this in a study has substantial methodological challenges, ultimately providing clear, straightforward information can also be viewed as enhancing the consent process and should be followed regardless. However, there is suggestion from my findings that the impact may be limited.

3. A 'culture of research' should be encouraged in inpatient settings. This would include supporting and developing close working relationships between researchers and clinicians, with regular research clinics and integration of research into the routine of the ward as much as possible.

4. We need to have a re-think about the research governance and normative standards we apply with regards to decision making about participating in research. We need to ensure that our desire to protect vulnerable people does not lead to an inequality about the standards we expect them to achieve in relation to values within decision making and life choices, or extra protections

such as consultee approval do not, in turn, act as barriers in themselves to research participation.

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Appendices

Appendix 1. List of publications arising from this work to date

Published:

Spencer BWJ, Shields G, Gergel T, Hotopf M, Owen G. Diversity or disarray? A systematic review of decision-making capacity for treatment and research in schizophrenia and other non-affective psychoses. Psychological medicine. 2017 Aug; 47(11):1906-1922. doi: 10.1017/S0033291717000502.

In submission:

Spencer BWJ, Gergel T, Hotopf M, Owen G. Unwell in hospital but not incapable: dissociation of decision-making capacity for treatment and research in inpatients with schizophrenia. A cross sectional study.

Appendix 2. Systematic review supplemental data

Table 29 – Systematic review full characteristics of all studies included

Title	Setting	Study N	n with DMC	Proportion (95% CIs)	Measure correlated against	Lack of Insight	PANSS (Total (T), General (G), Positive (+VE). Negative (-VE)				BPRS	Affective symptoms	Neurocognitive performance (unless stated z score)	Socio-Demographics	Education (y)
DMC-R or T	Tool Used		Nature of decision				T	G	+VE	-VE					
Specific Issues and other results															
Weinstock 1984	N/A	N=2	n=2	1 (0.34-1)											
DMC-T	C		Unrelated medical treatment		P	-	-	-	-	-	-	-	-	-	-
Specific features: Medically unwell in a physical health hospital referred for determination of DMC-T for medical treatment															
Veliz 1987	Inpatients	N=35	n=4	0.11 (0.05-0.26)											
DMC-T	C		Related psychiatric treatment		P	-	-	-	-	-	-	-	-	-	-
Specific features: Referred to the Court for determination of lack of competency to refuse or consent to treatment forensic population															
Bean 1994	Inpatients	N=32	n=19	0.59 (0.42-0.75)											
DMC-T	C		Related psychiatric treatment		P	-	-	-	-	-	-	-	-	-	-
Specific features: Inpatients requiring ECT															

Wong 2000 DMC-T	Mixed C	N=21	n=19 Blood test - unclear degree related	0.90 (0.71-0.97)	P	-	-	-	-	-	-	-	-	-	-
Bellhouse 2003 DMC-T	Inpatients C	N=9	n=6 Related psychiatric treatment	0.67 (0.35-0.88)	P	-	-	-	-	-	-	-	-	-	-
Moye 2008 DMC-T Specific features: ≥ 60 years old. Other results: U 'rate of impairment' 35%, A 'rate of impairment' 55%, R rate of 'impairment' 45%, C 'rate of impairment' 40%	Outpatients 'ACCT' interview assessing four factor model with cut off	N=20	n=4 Unrelated medical treatment	0.2 (0.08-0.42)	P	-	-	-	-	-	-	-	-	-	-
					U	-	-	-	-	-	-	-	-	-	-
					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-
Skipwork 2013 DMC-T Specific features: Mixed inpatients and outpatients under forensic services	Mixed C, M-T	N=97	n=63 Related psychiatric treatment	0.65 (0.55-0.74)	P	-	-	-	-	-	-	-	-	-	-
					U	-	-	-	-	-	-	-	-	-	-
					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-

Vollmann 2003	Inpatients	N=43	n=35	0.81 (0.67-0.90)	P	-	-	-	-	-	-	-	-	**0 age*, 0 gender***	**0***
DMC-T	C, M-T		Related psychiatric treatment		U	-	-	-	-	-	-	-	-	-	-
Specific features: No detained patients. Other results: 'Impairment standard' requiring understanding D and T>4; reasoning >3; AD and AT >0. If not then meet 'impairment standard'. In this sample n=23 had impairment using this standard. *against 'impairment standard'					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-
Cairns 2005	Inpatients	N=62	n=30	0.48 (0.36-0.61)	P	-	-	-	-	-	-	-	-	-	-
DMC-T	C, M-T		Related psychiatric treatment		U	-	-	-	-	-	-	-	-	-	-
					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-
Owen 2009/11	Inpatients	N=93	n=24	0.26 (0.18-0.36)	P	**-L SAI**	-	-	-	-	**-M**	-	-	-	-
DMC-T	C, M-T		Related psychiatric treatment		U	-	-	-	-	-	-	-	-	-	-
					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-

Di 2013	Inpatients	N=192	n=138	0.72 (0.65-0.78)	P	-	-	-	-	-	*	-	-	**0 age, 0 gender**	**+L 7 - 9 years, +L 10-12, +M >12 (reference < 7 years)**
DMC-T	'SSICA' interview assessing four factor model with cut off		Related psychiatric treatment		U	-	-	-	-	-	-	-	-	-	-
Specific features: Guardian also needed to agree in order to participate in study. * Data reported uninterpretable.					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-
Grisso 1995/95	Inpatients	N=75	n/a	n/a	U	-	-	-	-	-	**-M***	-	**+M VCF***	**+M SES***	**
DMC-T	M-T precursors		Related psychiatric treatment		A	-	-	-	-	-	**0***	-	**0 VCF***	**0 SES***	**
Specific features: Clinicians requested severely unwell people to not be recruited Other results: 48.1% demonstrated adequate performance across measures of U, A, and R (C not included) judged by an arbitrary cut-off but the authors clearly state they do not consider this to equate to a lack of DMC-T. BPRS factor 3 (thought disorganisation) - M for U. *Several individual tools were used to measure each domain of U, A, R, and C. The authors interpreted presence of at least one statistically significant association with a tool within a domain as sufficient to demonstrate association, strongest associations reported here. **Included in SES					R	-	-	-	-	-	**0***	-	**+M VCF***	**+S SES***	**
					C	-	-	-	-	-	-	-	-	-	-
Grisso 1997	Inpatients	N=40	n/a	n/a	U	-	-	-	-	-	**0**	-	-	**0 age, 0 gender, 0 race**	**0**
DMC-T	M-T		Related psychiatric treatment		A	-	-	-	-	-	**0**	-	-	**0 age, 0 gender, 0 race**	**0**
					R	-	-	-	-	-	**0**	-	-	**0 age, 0 gender, 0 race**	**0**
					C	-	-	-	-	-	**0**	-	-	**0 age, 0 gender, 0 race**	**0**

Palmer 2004	Outpatients	N=59	n/a	n/a	U	-	-	-	**0**	**0**	**0**	-	**+M DRS**	**0 age, 0 gender, 0 race**	**0**
DMC-T	M-T		Related psychiatric treatment		A	-	-	-	**0**	**0**	**0**	-	**0 DRS**	**0 age, 0 gender, 0 race**	**0**
Specific features: Outpatients, although most living at community assisted living facilities, age ≥ 40.					R	-	-	-	**0**	**0**	**0**	-	**+M DRS**	**0 age, 0 gender, 0 race**	**0**
					C	-	-	-	**0**	**0**	**0**	-	**+M DRS**	**0 age, 0 gender, 0 race**	**0**
Koren 2005	Inpatients	N=21	n/a	n/a	U	-	-	-	-	-	-	-	-	-	-
DMC-T	M-T		Related psychiatric treatment		A	-	-	-	-	-	-	-	-	-	-
Specific features: Within two weeks of admission when clinician has determined them able to cooperate. (data only presented as individual cognitive sub-scale scores)					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-
Wong 2005	Inpatients	N=81	n/a	n/a	U	**-M G12 PANSS**	**-L**	**-**	**-M**	**-M**	-	**0 MADRS**	-	**0 age**	**+L**
DMC-T	M-T		Related psychiatric treatment		A	**-M G12 PANSS**	**-M**	**-**	**0**	**0**	-	**0 MADRS**	-	**0 age**	**0**
Specific features: Before discharge from hospital Other results: 0 on side effect measures and U,A,R; with U drug attitude 0; with drug attitude inventory 0; with R drug attitude inventory +S (greater score on drug attitude = more complaint with medication)					R	**-M G12 PANSS**	**-M**	**-**	**0**	**0**	-	**0 MADRS**	-	**0 age**	**+S**
					C	-	-	-	-	-	-	-	-	-	-
Capdevielle 2009	Outpatients	N=60	n/a	n/a	U	**0 SUMD***	**-M**	**0**	**0**	**-M**	-	**0 BDI**	-	**0 age**	**+M**
	DMC-T	M-T	Related psychiatric treatment		A	**-L SUMD***	**0**	**0**	**0**	**0**	-	**0 BDI**	-	**0 age**	**0**
Specific features: Treatment not changed for past month. Other results: All 0 for anxiety scores (state and trait) and U,A,R,C. *Summary SUMD score was not provided, rather a breakdown of the five components of the SUMD and their correlations. The authors interpreted presence of at least one statistically significant association as sufficient to demonstrate association (for A and R there were associations with all 5 components, with C only 2).					R	**-L SUMD***	**0**	**0**	**0**	**0**	-	**0 BDI**	-	**0 age**	**0**
					C	**-M SUMD***	**0**	**0**	**0**	**0**	-	**0 BDI**	-	**0 age**	**0**

Raffard 2013 DMC-T Specific features: Treatment not changed for past month Other results: All 0 for anxiety scores (state and trait) and U,A,R,C; BCIS 'self reflectiveness) + M with R, all other BCIS and U,A,R,C correlations 0	Outpatients M-T	N=60	n/a Related psychiatric treatment	n/a	U	-	**-L**	**-L**	**0**	**-L**	-	**0 BDI**	-	**0 age**	**+M**
					A	-	**0**	**0**	**0**	**0**	-	**0 BDI**	-	**0 age**	**0**
					R	-	**0**	**0**	**0**	**0**	-	**0 BDI**	-	**0 age**	**0**
					C	-	**0**	**0**	**0**	**0**	-	**0 BDI**	-	**0 age**	**0**
Norko 1990 DMC-T Specific features: No detained patients Other results: Proportion meeting standards: minimum, 80%, Broad 75%, Legal 45%, Combined 63%	Inpatients Tool assessing 4 factor model	N=22	n/a Related psychiatric treatment	n/a	Minimum	-	-	-	-	-	-	-	-	-	-
					Broad	-	-	-	-	-	-	-	-	-	-
					Legal	-	-	-	-	-	-	-	-	-	-
					Combined	-	-	-	-	-	-	-	-	-	-
Chiu 2014 DMC-T Specific features: People having ECT without consent Other results: n=13 0.76 (0.53-0.90) of those having ECT without consent lacked DMC-T	Inpatients C	N=17	n/a Related psychiatric treatment	n/a	Not relevant.										

Jeste 2009	Outpatients	N=66		0.47 (only a sub-portion had the clinical scores)	P	-	-	-	-	-	-	-	-	-	-
DMC-R	M-CR, C assessment involving review of M-CR records*		Hypothetical decision about an unclearly related RCT (cognition enhancing drug)		U	-	**0**	**0**	**0**	**0**		**0 HAM-D**	**+L RBANS**	**0 age, 0 gender**	-
					A	-	-	-	-	-	-	-	-	-	-
Specific features: Outpatients aged >40 *The UBACC (University of California San Diego Brief Assessment for Capacity to Consent) tool was also used but data not extracted to prevent repetition of data presented from the same sample.					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-
Carpenter 2000	Mixed	N=30	n/a	n/a	U	-	-	-	-	-	**0**	-	**+L RBANS**	-	-
DMC-R	M-CR		Hypothetical RCT of antipsychotic medication related to disorder		A	-	-	-	-	-	**0**	-	**0 RBANS**	-	-
Other results: with U and BPRS Factor 1 'psychosis factor' –M; with A and BPRS Factor 1 –M; with R and BPRS Factor 1 –L; with C and BPRS Factor 1 0					R	-	-	-	-	-	**-M**	-	**+L RBANS**	-	-
					C	-	-	-	-	-	**0**	-	**0 RBANS**	-	-
Moser 2002	Mixed	N=25	n/a	n/a	U	-	-	-	-	-	*	-	**+L RBANS**	-	-
DMC-R	M-CR, ESC		Hypothetical decision about an unclearly related RCT (cognition enhancing drug)		A	-	-	-	-	-	*	-	**+L RBANS**	-	-
Specific features: Mixed outpatients and inpatients, some recruited from a mental health research centre. Other results: With U SANS/SAPS –VE -L, disorganized -M, psychotic 0; With A SANS/SAPS –VE 0, disorganized -L, psychotic 0; with R SANS/SAPS –VE -L, disorganized -M, psychotic 0; * reported in regression analysis but not as individual bivariate correlations					R	-	-	-	-	-	*	-	**0 RBANS**	-	-
					C	-	-	-	-	-	-	-	-	-	-

Kovnick 2003 DMC-R	Inpatients M-CR	N=27	n/a Hypothetical RCT of antipsychotic medication related to disorder	n/a	U	-	-	-	-	-	**-L**	-	**+L VCF**	-	-
					A	-	-	-	-	-	**-L**	-	**+L VCF**	-	-
					R	-	-	-	-	-	**0**	-	**0 VCF**	-	-
Specific features: Long stay patients on a research ward with schizophrenia Other results: With U BPRS Subscales Psychoticism -M, withdrawal -L; depression and hostility 0; With A BPRS Subscales Depression -M, withdrawal -L; hostility and psychoticism 0; With R BPRS Subscales, psychoticism , depression, withdrawal, hostility all 0					C	-	-	-	-	-	-	-	-	-	-
Cohen 2004 DMC-R	Inpatients M-CR	N=6	n/a Hypothetical decision about involvement in research, one study treatment related to disorder, the other is an imaging study using ketamine	n/a	U	-	-	-	-	-	-	-	-	-	-
					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
Specific features: Results of the study dichotmised by willingness to participate. Only presented proportion data on MacCAT-CR scores for willing and unwilling people by study Other results: Scores on the MacCAT-CR were not associated with a willingness to participate.					C	-	-	-	-	-	-	-	-	-	-
Palmer 2005 DMC-R	Outpatients M-CR*	N=35	n/a Hypothetical decision about an unclearly related RCT (cognition enhancing drug)	n/a	U	-	-	-	**0**	**0**	-	-	**+M MMSE**	**0 age**	**0**
					A	-	-	-	**0**	**0**	-	-	**0 MMSE**	**0 age**	**+L**
					R	-	-	-	**0**	**0**	-	-	**0 MMSE**	**0 age**	**0**
Specific features: All clinically stable outpatients recruited through clinical research programmes at the university. Aged ≥60 * The three item questionnaire tool was also used but data not extracted to prevent repetition of data presented from the same sample.					C	-	-	-	**0**	**0**	-	-	**0 MMSE**	**0 age**	**0**

Stroup 2005	Mixed	N=1447	n/a	n/a	U	-	-	**-S**	**0**	**-S**	-	-	**+S**	**0 age, 0 gender, 0 'non-white'**	**+S**
DMC-R	M-CR		Real decision about involvement in a naturalistic treatment trial related to their disorder.		A	-	-	**-S**	**0**	**-S**	-	-	**+S**	**0 age, 0 gender, -S 'non-white'**	**+S**
Specific features: Mixed inpatients and outpatients already recruited to the CATIE study (having suboptimal antipsychotic treatment) and passing a MacCAT-CR based DMC-R threshold (U ≥ 16).					R	-	-	**0**	**0**	**-S**	-	-	**+S**	**-S age, 0 gender, -S 'non-white'**	**+S**
					C	-	-	-	-	-	-	-	-	-	-
Candilis 2006/08	Mixed	N=52	n/a	n/a	U	-	**-M**	**-L**	**0**	**-L**	-	-	**+L MMSE**	**0 age, 0 gender, 0 race**	**+M**
DMC-R	M-CR		Hypothetical decision about an RCT using antibiotics for sore throats, unrelated to their disorder.		A	-	**0**	**-L**	**-M**	**-L**	-	-	**+L MMSE**	**0 age, 0 gender, 0 race**	**+M**
Other results: With U SF36 physical functioning +M; With A SF36 physical functioning +L; With R SF36 physical functioning +M; with C SF36 physical functioning 0					R	-	**0**	**-L**	**-M**	**0**	-	-	**+L MMSE**	**0 age, 0 gender, 0 race**	**+S**
					C	-	**0**	**-M**	**0**	**0**	-	-	**0 MMSE**	**0 age, 0 gender, 0 race**	**0**
Palmer 2006	Mixed	N=70	n/a	n/a	U	**0 BIQ**	-	**-S**	**0**	**-M**	-	**0 HAM-D**	**+M**	**0 age**	**0**
DMC-R	M-CR		Real decision about observational study of side effects related to their treatment with antipsychotics related to their disorder		A	**0 BIQ**	-	**0**	**0**	**0**	-	**0 HAM-D**	**+M**	**0 age**	**0**
Specific features: Mixed inpatients and outpatients, some in board and care homes. Aged ≥40					R	**0 BIQ**	-	**0**	**0**	**0**	-	**0 HAM-D**	**0**	**0 age**	**0**
					C	**0 BIQ**	-	**-S**	**0**	**0**	-	**0 HAM-D**	**0**	**0 age**	**0**

Dunn 2007 DMC-R	Mixed M-CR	N=91	n/a Hypothetical RCT of antipsychotic medication related to disorder	n/a	1	**-M BIQ**	-	**0**	**0**	**-S**	-	**0 HAM-D**	**0, 0 DRS**	**0 age**	**0**
					2	**-S BIQ**	-	**-M**	**0**	**-M**	-	**0 HAM-D**	**+M, +M DRS**	**0 age**	**+S**
Specific features: Mixed outpatient and inpatients, including board and care homes, aged ≥50. Data analysed by standards of thresholds on sub-scale scores. Other results: Standard 1:Least U>15, proportion=0.923; Standard 2:Intermediate U≥20, proportion =0.813; Standard 3:Most U≥18, A≥5, R≥6, proportion=0.429					3	**-M BIQ**	-	**0**	**0**	**0**	-	**0 HAM-D**	**+M, 0 DRS**	**0 age**	**0**
Eyler 2007 DMC-R	Outpatients M-CR	N=14	n/a Real decision about recruitment into an fMRI observational study that is not clear if relevant to that disorder.	n/a	U	-	-	**0**	**0**	**0**	-	-	-	**0 age**	**0**
					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
Specific features: Outpatient study recruiting from board and care homes					C	-	-	-	-	-	-	-	-	-	-
Linder 2012 DMC-R	Inpatients C, M-CR	N=21	Not reported Hypothetical 'clinical trial' no further information.		P	-	-	-	-	-	-	-	**+M FAB, 0 ACE**	-	-
					U	-	-	-	-	-	-	-	-	-	-
Specific features: Voluntary inpatients admitted for > 6 months Other results: MacCAT-CR total and FAB +L; MacCAT-CR total and ACE +L					A	-	-	-	-	-	-	-	-	-	-
					R	-	-	-	-	-	-	-	-	-	-
					C	-	-	-	-	-	-	-	-	-	-

Lan 2013	Inpatients	N=139	n/a	n/a	U	**-S G12 PANSS**	**-M**	**-M**	**-S**	**-S**	-	-	**+M MMSE**	-	-
DMC-R	C*, M-CR			Hypothetical decision about an unclearly related RCT (cognition enhancing drug)	A	**-S G12 PANSS**	**-M**	**-M**	**-S**	**-M**	-	-	**+M MMSE**	-	-
Specific features: Members of a hospital based therapeutic community. Stable patients.					R	**-S G12 PANSS**	**-S**	**-S**	**0**	**-M**	-	-	**+S MMSE**	-	-
Other results: With U CGI 0; With A CGI –S; With R CGI – S; With C CGI 0. *'Brief judgement score' of clinicians assessment of audio-interviews also used but no absolute scores reported or tested for correlations of variables of interest.					C	**0 G12 PANSS**	**0**	**0**	**0**	**-S**	-	-	**0 MMSE**	-	-
Fischer 2013	Outpatients	N=59	n/a	n/a	mESC	-	-	-	-	-	**0**	-	**0**	-	-
DMC-R	mESC			Real decision about involvement in an RCT related to their disorder											
Specific features: Already recruited to the parent study, all data is for baseline Other results: BPRS negative 0, BPRS psychosis 0 (both at baseline testing); compared research experience group with non-research experience and no significant difference between scores															
Eyler 2005	Outpatients	N=44	n/a	n/a	Only presents % score data and correlations with interventions										
DMC-R	M-CR			Decision about involvement in an fMRI study on DMC-R in Schizophrenia (related)											
Specific features: Outpatient study recruiting from board and care homes															
Moser 2005	Outpatients	N=10	n/a	n/a	Only data on correlations is effect of interventions (medication free period)										
DMC-R	M-CR			Hypothetical decision about an unclearly related RCT (cognition enhancing drug)											
Specific features: People admitted for monitoring during the course of a medication free period during a study.															

Moser 2006	Outpatients	N=30	n/a	n/a	Only data on correlations is effect of interventions (educational)
DMC-R	M-CR			Hypothetical decision about an unclearly related RCT (cognition enhancing drug)	
Specific features: Mixed inpatients and outpatients involved in research programmes					

Key

Tool Used:		**Other:**	
ACCT	Assessment of Capacity to Consent to Treatment Interview (Factor scores)	ACE	Addenbrooke's Cognitive Exam
C	Clinical Assessment (Judgement standard)	AD	Appreciation Disorder
ESC	Evaluation to Sign Consent (Cut off standard)	AT	Appreciation Treatment
M-CR	MacCAT-CR (Factor scores)	BDI	Beck Depression Inventory
M-T	MacCAT-T (Factor scores)	BIQ	Birchwood Insight Questionnaire
		BPRS	Brief Psychiatric Rating Scale
Measure of DMC:		CGI	Clinical Global Impression
P	Proportion with DMC	DRS	Mattis Dementia Rating Scale
U	Understanding	FAB	Frontal Assessment Battery
A	Appreciation	HAM-D	Hamilton Depression Rating Scale
R	Reasoning	MADRS	Montgomery-Åsberg Depression Rating Scale
C	Expressing a Choice	MMSE	Mini-Mental State Exam,
		PANSS	Positive and Negative Syndrome Scale
Measures of association		RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
		SAI	Schedule for the Assessment of Insight
S	Small effect size	SES	Socio-Economic Status
M	Medium effect size	SUMD	Scale to assess Unawareness of Mental Disorder
L	Large effect size	VCF	Verbal Cognitive Functioning
0	No association found/not significant		
-	Not measured		

Appendix 3. The MacCAT-CR modified for BioResource Research

(Disclosed text in bold)

U-1 Disclosure – Nature of Project

a – What is the study and its aim?

I want to talk to you about taking part in a study called the 'BioResource study'. The aim of the study is build a BioResource.

A BioResource is a giant library of information about people. This includes information about their individual biological makeup, such as their genes, and the illnesses they suffer from.

Researchers want to use the BioResource to understand better the illnesses people suffer from and the links to their individual biological makeup. From this they hope that they will be able to develop better treatments.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
a – Purpose of project (make a BioResource) [If subject fails to mention spontaneously, ask: 'What is the purpose of the research project I described to you?'		

b – Who is taking part and why have I been approached?

One of the reasons I'm asking you today is because you are in hospital in South London and Maudsley with psychosis. But, we're asking as many people as possible to take part with different types of illnesses, including healthy people. We are hoping to have 50,000 volunteers take part by 2017.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
b – Population studies/who invited (Procedural element No.2) [If the subject fails to mention spontaneously, ask: 'Why have you		

been approached today/Who is taking part in the study?']		

c – What will happen?

The research involves giving a sample of saliva or blood. This will be analysed in a lab to look at your genes, but also other things individual to you like your antibodies. The information in the sample would be linked to your medical records (the one here in South London and Maudsley and your GP's).

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
c – Biological Sample and data linkage (Procedural element No. 3) [If subject fails to mention spontaneously, ask: 'What sorts of things will be done with people who agree to be in the study?/What will be done with the sample?/Are researchers requesting the medical record – what for?']		

d – What will the researchers do?

The information that you provide would be anonymised and mixed with thousands and thousands of others. That way researchers could look at it all together to see patterns they couldn't see by looking at one person alone. Researchers will use the library for lots of different research projects in the future. I can't tell you exactly what these might be as there are lots of different projects that people might think about using the library for in the future.

If further explanation needed:

It's a bit like, you can't learn about waves and the ocean by looking at individual drops of water, you need to look at it all together.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
d – Broad consent for future research (Procedural element No. 4)		

[If the subject fails to mention spontaneously, ask: 'How will researchers use the BioResource in the future?']		

e – Is there any other way I could be affected?

Researchers might find something of interest to their research in your medical record or in your sample like your genes. They might need more information from you, or ask you to do something for their research project which they couldn't do just by using the library alone.

If that did happen they would contact you to talk about taking part in other studies. If they did contact you, you would be under no obligation to take part in these just because you had agreed to taking part in the BioResource study.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
e – Re-contact based on pheno/genotype (Procedural element No. 5) [If the subject fails to mention spontaneously, ask: 'How else are the researchers planning to use the BioResource/are they contacting people for other research?']		

Summary score

	Understanding Nature of Project – Summary	

U-2 Disclosure – Primary Purpose is Research, not individualised care

Will this affect my care?

It is important for you to understand that the project that you have been asked to participate in is a research project. That means its main purpose is to help the researchers understand why different illnesses happen and develop different treatments for them in the future. The research won't help you or change your care today, that's not its purpose, the purpose is to help our understanding of illness.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
1 – [If subject fails to mention spontaneously, ask: 'What is the main purpose of what the doctors are trying to do in this study?']		
	Understanding Primary Purpose is Research – Summary	

U-3 Disclosure – Effect of research methods on individualised care

What will I have to do?

Because this is a research project, the researchers will be doing things that they would not do in ordinary hospitals/clinics.

Depending on what you would prefer, we would take a sample of either your blood or saliva and then this would be analysed in a lab. This would be linked with information from your medical records to make the library.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
1 – Provide biological sample [If subject fails to mention spontaneously, ask: 'What will you have to do if you take part in the study?']		

The tests that the lab would do on the sample are very complex, such as analysing your genes. You would not normally get any information back from the lab following their analysis, unlike other blood tests you may have had. But, if when the researchers are processing the sample something jumps out at them. Something that you need to know about urgently for your health, then they would let your GP/doctors know to talk to you about it. This is very unlikely to happen. Normally you would never hear anything about the sample you give.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
2 – Incidental findings with modifiable clinical impact will be returned, but not other information returned normally.		

[If the subject fails to mention spontaneously, ask: 'Would the lab give you any results back about the sample?']		

Researchers might contact you in the future to ask if you would like to take part in other research projects. This might happen if they found something interesting to them in your sample or your medical record, or purely because they want to understand more about people who suffer from psychosis.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

3 – Possibility of future re-contact [If a subject fails to mention spontaneously, ask: 'Might anyone contact you in the future?']		

Summary Score

	Understanding Effect of research methods on individualised care – Summary	

U - 4a Disclosure - Benefits of participation

Are there any benefits for me?

There are several benefits that could result if people agree to be in this project:

The researchers will be able to find out how people's individual biological makeup such as their genes can influence the illnesses they develop. This will help us develop better diagnosis and treatments for everyone who has the illness in the future. This won't help anyone now though, but hopefully will help many people in the future.

There would be no benefit to you personally right now other than knowing you are helping out with this process.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
1 – Societal Benefit [If a subject fails to mention spontaneously, ask: 'What might researchers learn and who might it		

help if people decide to be in this research project?']		
2 – Personal Benefit [If subject fails to mention spontaneously, ask: 'How could you be personally better off by taking part in this research project?']		
	Understanding Benefits – Summary	

U - 4b Disclosure – Risks/Discomforts of participation

Are there any risks to me?

There are also some issues people who take part in the study need to consider.

You need to give a sample of blood or saliva that you may find uncomfortable.

You will have no control over the research that would be done with the BioResource. A committee in charge of the BioResource will decide what research it is used for. You have to trust that the committee will use the BioResource appropriately and not be misused by researchers or for inappropriate or unethical research studies.

There is always a risk in any research with the safety and security of your personal information. There are procedures in place to keep your information confidential and anonymous. The people who process the sample in the lab won't know that it's from you. Only the lead researchers will be able to link the information in the BioResource to you personally.

'Do you have any questions about what I just said?'

'Can you tell me your understanding of what I just said?'

Disclosure	Patient Response	Rating
1 - Risk 1 biological sample [If subject fails to mention spontaneously, ask: 'Is there anything uncomfortable you may have to do?']		
2 – Risk 2 data governance [If subject fails to mention spontaneously, ask: 'Who decides how the BioResource is used, and are there any issues around this?']		

3 – Risk 3 confidentiality [If subject fails to mention spontaneously, ask: 'Are there any concerns or risks to your personal information?']		
	Understanding Risks/Discomforts of participation – Summary	

U-5 Disclosure – Ability to Withdraw/Receive Ordinary Care

Do I have to take part?

No one has to be in this study. If you decide not to take part it would not affect your care in any way.

People who agree to be in this research project can change their minds at any time. This includes after you have taken part and given a sample. If you later decided to stop you could contact the research team and your data and sample would be destroyed. Again this would not affect your care in any way.

'Do you have any questions about what I have just said'

'Can you tell me your understanding of what I just told you?'

Disclosure	Patient Response	Rating
1 – [If subject fails to mention spontaneously, ask: 'What will happen if a person refuses to be in the research project, or decides to stop once it begins?']		
	Understanding Ability to Withdraw/receive ordinary care – Summary	

Appreciation

A-1 Subject believes that they will not benefit or suffer from being involved in the research (his or her personal benefits are not the primary objective of the study)

'Do you believe that you have been asked to be in this study primarily for your personal benefit?'

☐ Agrees ☐ Disagrees ☐ Ambivalent

'What makes you believe that this (was/wasn't) the reason you were asked?'

Explanation	Appreciation – Personal Benefit	Rating

Anchor statements

2 - Subject acknowledges that he or she is being recruited for a valid reason unrelated to potential personal benefit from being in the study (e.g being an inpatient in SLaM, has a condition of relevance to the study)

1 - subject acknowledges being recruited for reasons both related and unrelated to personal benefit.

OR

Subject maintains he or she is being recruited for a reason related only to potential personal benefit, but has a plausible explanation for why this is the case.

0 - Subject maintains he or she is being recruited for a reason related only to potential personal benefit but does not have a plausible explanation for why this is the case.

OR

Subject offers response that is unrelated to the question or unintelligible.

A-2 Subject believes that the BioResource will be used for a range of research projects that the subject themselves does not decide on

'How do you believe the BioResource will be used?'

	Have no control		Has control		Ambivalent

‘What makes you believe that this (could/couldn’t) happen in your case?’

'Would you have any influence on the research that is done?'

Explanation	Appreciation – broad consent	Rating

Anchor Statements

2 - Subject acknowledges that decisions about what personal research data will be used for will be made by the research team for different projects in the future over which they have no control.

1 - Subject acknowledges that researchers will use research data for other studies but believes retains an element of influence over this - such as being re-contacted for further consent or informed/updated about it, but without executive control.

0 - Subject does not appreciate that researchers may use data for other studies in the future (such as the current study is to answer one current question only), or retains executive control.

OR

Subject offers response that is unrelated to the question or unintelligible, or provides a clearly distorted or delusional interpretation of the research.

A-3 Subject believes that they may be contacted in the future if eligible for other studies based on genotype/phenotype.

‘Might researchers contact you in the future to take part in other studies?’

'What would be the reasons for them contacting you?'

	Agrees		Disagrees		Ambivalent

‘What makes you believe that this (could/couldn’t) happen in your case?’

Explanation	Appreciation – re-contact	Rating

Anchor Statements

2 - Subject acknowledges that might or might not be re-contacted by researchers for other studies on basis of biological sample or clinical characteristics, and gives a plausible reason for this either way which could include being admitted to hospital for psychosis, but equally other information in their medical record.

1 - Subject considers it certain that they will or will not be contacted by researchers and gives a plausible reason for this

OR

Subject acknowledges that might or might not be re-contacted by researchers for other studies but gives an implausible reason for this.

Subject does not acknowledge that they might be contracted by researchers, or considers it certain that they will be contacted and gives a plausible reason for this, such as unique characteristics in medical record.

0 - Subject considers it certain that they will or will not be contacted by researchers and gives a bizarre or implausible reason for this.

OR

Subject offers response that is unrelated to the question or unintelligible, or provides a clearly distorted or delusional interpretation of the research.

A-4 Subject believes that involvement in research is entirely voluntary (regardless of legal status, a decision to withdraw will be respected).

'What do you believe would happen if you were to decide not to be in this study?'

'What makes you believe that this would happen?'

Explanation	Appreciation – ability to withdraw	Rating

Anchor statements

2 - Subject acknowledges that failure to participate or later withdrawal will not adversely affect him or her (in particular, in the context of treatment setting, that subject can continue to receive ordinary care, assuming that this is the case). Subject believe that participation is a free and voluntary choice irrespective of their legal status on the ward, and that refusal to participate will not adversely affect them.

1 - Subject is uncertain whether failure to participate or later withdrawal will adversely affect him or her.

OR

Subject believes failure to participate or later withdrawal will adversely affect him or her and has a plausible explanation for why this is the case.

OR

Feels indirectly coerced to participate, or that ability to withdraw is curtailed, such as through being detained on the ward, or to ensure the doctors are kept happy.

0 - Subject believes failure to participate or later withdrawal will adversely affect him or her and does not have a plausible explanation for why this is the case.

OR

Subject offers response that is unrelated to the question or unintelligible.

OR

Subject considers self entirely compelled or coerced into taking part through legal status on the ward or delusional interpretations of the research study.

Expressing a Choice and Reasoning

First choice

'As you know, you have been invited to participate in a research project to make a BioResource. Do you think you are more likely to want to participate or not want to participate?'

Choice: _____

R-1/R-2 Consequential and comparative reasoning

'You think that you are more likely to want [patient's choice] in the study. Tell me what it is that option better than the other.'

Discuss explanation to explore reasoning process.

Explanation	Rating	
	Consequential	
	Comparative	

R-3 Generate Consequences

'I told you about some of the possible benefits and risks or discomforts of participating in the research project.

The benefits are to find the links between genes and illnesses, and to allow people to research this to hopefully develop better diagnosis and treatments in the future.

The risks are the discomfort of providing a sample, trusting the research group with how they will use the BioResource for research, and maintaining your confidentiality. You may also be contacted in the future to see if you wanted to take part in other research.

What are some ways that these could affect (could have affected) you if you take part in the research project?'

[If the subject fails to mention a consequence of either the benefits or the risks/discomforts, ask: 'how might (restate benefit or risk) affect you everyday life?']

Consequences	Rating

Generate Consequences Summary

Final Choice

'A few minutes ago you told me that you favoured participating/not participating in the research project. What do you think now that we have discussed everything? What do you want to do?'

Choice	Express Choice

R-4 Logical Consistency of choice

[Interviewer records and explains presence or absence of logical consistency in subject's choice.]

Examiner's Explanation	Logical Consistency

A-5 Overall Appreciation.

Now that we've finished talking about the BioResource study, would you tell me what it means for you and taking part or not?

Probe questions – how might being in the study affect you, what is your motivation for taking part, could you help me to understand why you've decided to not take part?

Explanation	Overall Appreciation	Rating

Anchor statements:

2 - Full appreciation of research study and how it affects them individually, motivation and interpretation of research is sound and voluntary.

1 - Appreciate key components of research study, but slightly misinterprets or puts excessive emphasis on certain components, motivation or interpretation of the research study is slightly aberrant but not frankly disordered. (Marginal DMC)

0 - Does not appreciate key component of research study, (such as that is research, no benefit to self etc), or motivation/interpretation of research is for delusional or bizarre reasons (such as believes is compelled to take part in research, research is for a bizarre purpose).

OR

Subject offers response that is unrelated to the question or unintelligible, or provides a clearly distorted or delusional interpretation of the research.

Appendix 4. The Modified SAI-E

Summary of compliance with BioResource recruitment

1. Rejects discussing BioResource.
2. Agrees to discuss BioResource and would reject.
3. Agrees to discuss BioResource, ambivalent and would not discuss again.
4. Agrees to discuss BioResource, ambivalent and would discuss again.
5. Agrees to discuss BioResource and agrees with conditions that may disqualify.
6. Agrees to discuss BioResource and agrees with conditions that would not disqualify.
7. Agrees to discuss BioResource and agrees with no conditions.

Explanatory comments if appropriate.

Appendix 5. Associations of research involvement in women versus men

Table 30 – Associations of research involvement in women versus men

	No approach								No participation							
	Female				Male				Female				Male			
	n	OR	95%CI	p	n	OR	95%CI	p	n	OR	95%CI	p	n	OR	95%CI	p
Age	380	0.98	0.96-1.00	0.065	553	**0.98**	**0.97-1.00**	**0.011**	380	1	0.97-1.04	0.836	553	1	0.98-1.02	0.966
Ethnicity	375				550				344				550			
White British		1				1				1				1		
Black African		0.74	0.39-1.40	0.353		0.94	0.54-1.63	0.816		1.41	0.41-4.83	0.583		1.44	0.64-3.26	0.377
Black Caribbean		**0.39**	**0.19-0.82**	**0.013**		1.33	0.74-2.39	0.333		0.79	0.23-2.76	0.717		2.24	0.84-5.98	0.107
Mixed		0.46	0.14-1.53	0.206		0.56	0.21-1.49	0.246		*				0.64	0.21-1.95	0.429
Non-white other		1.90	0.57-6.35	0.300		1.44	0.42-5.02	0.563		*				0.84	0.17-4.24	0.833
White other		0.58	0.24-1.42	0.237		1.15	0.57-2.33	0.700		0.71	0.16-3.05	0.641		0.96	0.37-2.51	0.935
Other Black		0.83	0.43-1.59	0.574		1.14	0.70-1.87	0.592		1.70	0.46-6.27	0.427		1.08	0.55-2.13	0.824
Other		1.29	0.50-3.34	0.605		1.08	0.51-2.29	0.847		2.29	0.26-19.99	0.452		1.49	0.47-4.77	0.498
Diagnosis	380				553				380				553			
f20 - schizophrenia		1				1				1				1		
f25 - schizoaffective disorder		0.76	0.44-1.31	0.323		0.68	0.35-1.33	0.263		0.51	0.18-1.43	0.202		0.51	0.23-1.12	0.095
f22 - persistent delusional disorder		2.38	0.45-12.75	0.310		0.68	0.12-3.80	0.665		**0.15**	**0.02-0.89**	**0.037**		0.73	0.08-6.44	0.778
Other (f23 , f28, f29)		**2.00**	**1.06-3.78**	**0.032**		1.62	0.99-2.65	0.054		1.75	0.35-8.68	0.493		0.79	0.40-1.57	0.497
Other		**3.03**	**1.69-5.43**	**0.000**		**1.87**	**1.23-2.82**	**0.003**		1.34	0.38-4.72	0.647		1.11	0.59-2.07	0.752
Detained	380				553				380				553			
Not detained		1				1				1				1		
Detained		1.17	0.74-1.84	0.500		1.06	0.75-1.51	0.747		0.87	0.33-2.24	0.766		1.12	0.68-1.86	0.649

* All episodes with symptom or socio-demographic variable present were associated with non-approach/non-recruitment.

Table 30 (continued 2/3)

	No approach								No participation							
	Female				Male				Female				Male			
	n	OR	95%CI	p	n	OR	95%CI	p	n	OR	95%CI	p	n	OR	95%CI	p
Honos																
Total	297	0.97	0.92-1.01	0.113	441	**0.95**	**0.91-0.99**	**0.007**	297	0.94	0.87-1.02	0.166	441	0.98	0.93-1.03	0.353
1 - Overactive, aggressive, disruptive or agitated behaviour	354	0.91	0.75-1.09	0.306	502	1.03	0.89-1.19	0.689	354	0.90	0.63-1.30	0.588	502	0.86	0.70-1.06	0.159
2 - Non-accidental self-injury	353	0.79	0.61-1.04	0.091	502	1.19	0.95-1.50	0.127	353	**0.63**	**0.42-0.94**	**0.022**	502	1.10	0.77-1.57	0.591
3 - Problem drinking or drug taking	344	1.06	0.87-1.28	0.554	484	1.11	0.97-1.27	0.118	344	0.84	0.61-1.17	0.312	484	0.99	0.82-1.19	0.904
4 - Cognitive problems	351	1.17	0.95-1.44	0.145	499	0.89	0.74-1.06	0.190	351	1.67	0.96-2.91	0.068	499	1.04	0.80-1.36	0.752
5 - Physical illness or disability problems	353	1.00	0.81-1.22	0.964	500	**0.79**	**0.65-0.96**	**0.019**	353	1.07	0.70-1.62	0.763	500	0.84	0.66-1.08	0.174
6 - Problems associated with hallucinations & delusions	354	0.86	0.70-1.05	0.134	501	0.89	0.75-1.06	0.182	354	1.02	0.69-1.51	0.908	501	1.06	0.83-1.35	0.664
7 - Problems associated with depressed mood	353	0.97	0.79-1.18	0.735	502	0.97	0.81-1.15	0.697	353	0.83	0.56-1.23	0.347	502	1.01	0.78-1.31	0.917
8 - Other mental and behavioural problem	354	0.93	0.75-1.16	0.544	501	**0.83**	**0.70-0.99**	**0.042**	354	0.93	0.60-1.44	0.742	501	0.84	0.64-1.09	0.193
9 - Problems with relationships	345	0.85	0.71-1.03	0.100	492	0.96	0.81-1.13	0.602	345	1.03	0.70-1.50	0.888	492	0.83	0.66-1.06	0.131
10 - Problems with activities of daily living	345	0.87	0.71-1.06	0.165	491	**0.80**	**0.67-0.95**	**0.011**	345	0.74	0.50-1.10	0.133	491	0.98	0.76-1.25	0.847
11 - Problems with living conditions	323	0.94	0.78-1.14	0.521	483	**0.83**	**0.72-0.97**	**0.018**	323	0.88	0.61-1.26	0.485	483	0.97	0.79-1.20	0.793
12 - Problems with occupation & activities	319	0.87	0.71-1.06	0.160	470	**0.79**	**0.66-0.94**	**0.008**	319	0.79	0.53-1.17	0.237	470	1.16	0.91-1.49	0.232

Table 30 (continued 3/3)

	No approach								No participation							
	Female				Male				Female				Male			
	n	OR	95%CI	p	n	OR	95%CI	p	n	OR	95%CI	p	n	OR	95%CI	p
PANSS Surrogates																
Positive Symptoms total	380	0.84	0.50-1.41	0.521	553	1.15	0.76-1.75	0.511	380	0.93	0.33-2.61	0.883	553	1.26	0.68-2.33	0.470
Delusions	380	0.95	0.76-1.18	0.647	553	0.98	0.82-1.18	0.867	380	0.97	0.62-1.50	0.887	553	1.09	0.84-1.42	0.531
Formal thought disorder	380	1.43	0.73-2.81	0.299	553	1.79	0.94-3.43	0.079	368	*			553	1.39	0.48-4.07	0.545
Hallucinations (general)	380	0.97	0.67-1.41	0.890	553	1.30	0.95-1.77	0.096	380	1.51	0.53-4.27	0.442	553	1.33	0.78-2.27	0.299
Agitation	380	1.08	0.88-1.32	0.479	553	1.24	1.04-1.46	0.014	380	0.97	0.64-1.48	0.902	553	1.22	0.95-1.56	0.121
Grandiosity	380	0.85	0.61-1.20	0.358	553	0.88	0.69-1.12	0.302	380	0.86	0.46-1.63	0.653	553	0.87	0.63-1.20	0.390
Persecutory Ideation	380	0.87	0.69-1.10	0.242	553	1.01	0.83-1.23	0.903	380	1.01	0.63-1.63	0.963	553	1.09	0.81-1.45	0.573
Hostility	380	0.89	0.70-1.14	0.352	553	0.86	0.70-1.04	0.126	380	0.83	0.52-1.32	0.426	553	0.88	0.67-1.16	0.381
Negative Symptoms (general)	380	0.72	0.34-1.53	0.391	553	0.58	0.33-1.02	0.060	380	0.63	0.21-1.85	0.398	553	0.86	0.45-1.62	0.636
Mood																
Depressive symptoms																
Low mood	380	0.96	0.75-1.24	0.777	553	0.88	0.71-1.09	0.238	380	0.87	0.54-1.41	0.575	553	1.16	0.84-1.61	0.371
Anergia	377	*			552	*			377	*			552	*		
Anhedonia	380	1.45	0.47-4.52	0.521	553	0.47	0.16-1.38	0.171	376	*			547	*		
Manic symptoms																
Elevated mood	378	1.12	0.91-1.38	0.283	550	0.94	0.79-1.12	0.511	378	0.97	0.63-1.47	0.870	550	1.29	0.99-1.68	0.063
Pressured speech	380	1.11	0.90-1.38	0.321	553	0.91	0.76-1.08	0.274	380	1.06	0.69-1.64	0.783	553	1.04	0.81-1.34	0.766
Insomnia	380	1.19	0.62-2.30	0.603	553	0.57	0.30-1.10	0.095	369	*			553	1.39	0.50-3.89	0.529
Energy levels (full of energy - negative no energy)	380	1.54	0.80-2.97	0.193	553	0.48	0.18-1.28	0.144	367	*			553	1.02	0.33-3.12	0.972

* All episodes with symptom or socio-demographic variable present were associated with non-approach/non-recruitment.

Appendix 6. Demographics and clinical features of the reliability study participants

Table 31 – Characteristics of 50 participants for the expert panel

Age (n=50)		39.04 (12.04)
Gender (n=50)	Number female	12 (24%)
Ethnicity (n=46)		
	White British	11 (23%)
	Black African	11 (23%)
	Black Caribbean	11 (23%)
	Mixed	6 (13%)
	Non-white other	5 (11%)
	White other	3 (6%)
Education (n=)		
	GCSE or below	21 (42%)
	A-Level or above	29 (58%)
Current employment (n=)		
	Employed	5 (10%)
	Unemployed	45 (90%)
Previous involvement in research (n=)		
	Other research - prior involvement	20 (40%)
	No prior research discussions	30 (60%)
Days from admission to recruitment (n=)		16.5 (21)*
Primary diagnosis (n=)		
	f20 - schizophrenia	38 (76%)
	f25 - schizoaffective disorder	7 (14%)
	f22 - persistent delusional disorder	2 (4%)
	Other (f23, f28, f29)	3 (6%)
MHA status at time of Interview (n=50)		
	Informal	10 (20%)
	Section 2	21 (42%)
	Section 3	19 (38%)

Results are presented as means and standard deviations unless specified. * Median and interquartile range.

Appendix 7. Qualitative Topic Guides

Initial topic guides

Patient Participants

Text in italics are prompts if needed.

Opening

Thanks for agreeing to take part in this interview. As I mentioned I'm interested in finding out what people think about taking part in research.

Can I confirm that you consent to take part in this face-to-face interview as part of this study and that you consent to the interview being audio recorded?

Do you have any questions about this?

Warm up

How have you found the process of taking part in research so far?

Why did you agree to take part in research while in hospital?

Do you think there were any benefits to you in taking part?

Do you think there are any disadvantages to you in taking part?

How about in general? We talked earlier about taking part in a medical research study in hospital, what are your thoughts on research like this?

Why did you think people agree to take part in research while in hospital?

Do you think there are any benefits to people taking part while in hospital?

Do you think there are any disadvantages to people taking part while in hospital?

Barriers and facilitators of research participation, research consent

What do you think might stop people from taking part in research when they are in hospital?

Could you tell me more about the barrier/difficulty?

Are there any ways in which it could be changed?

What do you think helps people take part in research while in hospital?

Could you tell me more about what helps?

Are there any ways in which it could help more/have more effect?

What do you think about the consent process? This is the process where we go through the information about the study, and then go through a form writing down what parts you agree to do.

How do you find the information presented to you?

Was it straightforward?

Was there anything you might change about how people go through it?

What did you think about the consent form?

Was it straightforward?

Was there anything you might change about how people go through it?

Consultee approval in those lacking DMC

Usually, to be able to sign up to taking part in research people have to be able to understand the research project and how it may affect them.

Sometimes when people are unwell, they are not in a clear or best frame of mind to make a proper decision about taking part in research, but still really want to help.

Thinking about a situation in which someone was not in a totally clear frame of mind, but still wanted to help, the law has special rules that allows them to still take part if they want to.

Here the researchers have to ask a relative or friend of the person who wants to take part in research. The relative or friend can't decide for them, or force them to take part. But if the relative or friend has concerns they can block them from taking part, even if the person wants to.

Would you like me to explain this again?

What do you think about this?

While for most studies it has to be a relative, friend, carer, or advocate who the researchers have to ask, for drug trials (research that tests if medication works) only, it can be the doctor who makes the decision.

If you weren't in the best frame of mind to make a decision for yourself, but wanted to help, who would you want the researchers to contact to help out?

Why have you chosen them?

Is there anyone else you would want them to talk to?

What are the advantages of the researchers checking with this person?

What are the disadvantages of the researchers checking with this person?

What about the situation where this is your doctor?

Do you think that someone should decide on your behalf?

Are there any difficulties/barriers they may have to face?

Are there any benefits to them?

Is there anything that may help them decide?

Is there anything else you think about this?

Role of consultees in shared decision-making

Do you think it would be useful to have someone you trust with you when you are thinking about taking part in research? Like, let's say your partner or a friend?

How could they help?

If you were to ask someone to do it for you, who would it be?

Would there be any disadvantages with them being there?

Do you think they would be able to help you make a decision?

How would you feel about an independent advocate doing it?

What about your doctor?

Use of neurocognitive support tools

Another way we can help people make decisions is by going through the facts about the research project together differently. We could go through the facts several times and learn them together. This could also use things like pictures and videos.

Do you think this could help?

Would there be any problems with doing this?

Other strategies

Are the any other things you could think of to help you make a decision about taking part in research?

What would be the advantages/disadvantages of …?

Overall what do you think would be the best way of helping people make decisions?

Overall reflection

Thinking about taking part in research in general are there any things you think should be changed?

(if yes)

how would you change it?

what would be the benefit of changing it?

what would be the disadvantages of changing it?

What do you think would be the best way to help people make decisions about research?

Closing

I appreciate the time you took for this interview. Is there anything else you think would be useful for me to know?

Thanks again.

Text in italics are prompts if needed.

Opening

Thanks for agreeing to take part in this interview. As I mentioned I'm interested in finding out what people think about taking part in research.

Can I confirm that you consent to take part in this face-to-face interview as part of this study and that you consent to the interview being audio recorded?

Do you have any questions about this?

Warm up

As you know, you (friend/relative/partner) has taken part in a research project while in hospital. What are you thoughts about this?

Do you support them taking part in research?
Do you have any fears or concerns about them taking part in research?
What are your priorities with regards to your (friend/relative/partner)?
Do you think there were any benefits to them in taking part?
Do you think there are any disadvantages to them in taking part?

How about research in general? One area I am interested in is medical research while people are hospital. This type of research looks at things in people's blood and genes in order to make a library of information to better understand illnesses and how to treat them. What are your thoughts on research like this?

Why did you think people agree to take part in research while in hospital?

Do you think there are any benefits to people taking part while in hospital?

Do you think there are any disadvantages to people taking part while in hospital?

Do you have any specific concerns for you (relative/friend/partner) for this type of research?

Barriers and facilitators of research participation

What do you think might stop people from taking part in research when they are in hospital?

Could you tell me more about the barrier/difficulty?

Are there any ways in which it could be changed?

What do you think helps people take part in research while in hospital?

Could you tell me more about what helps?

Are there any ways in which it could help more/have more effect?

Consultee approval in those lacking DMC

Usually, to be able to sign up to taking part in research people have to be able to understand the research project and how it may affect them.

Sometimes when people are unwell, they are not in a clear or best frame of mind to make a proper decision about taking part in research, but still really want to help.

Thinking about a situation in which someone was not in a totally clear frame of mind, but still wanted to help, the law has special rules that allows them to still take part if they want to.

Here the researchers have to ask a relative or friend of the person who wants to take part in research. The relative or friend can't decide for them, or force them to take part. But if the relative or friend has concerns they can block them from taking part, even if the person wants to.

Would you like me to explain this again?

What do you think about this?

While for most studies it has to be a relative, friend, carer, or advocate who the researchers have to ask, for drug trials (research that tests if medication works) only, it can be the doctor who makes the decision.

Would you/Did you have any concerns about performing this role?
Are there any difficulties/barriers that you may/had to face?
Are there any advantages or benefits about you doing this role?
What if you disagreed with your (friend/relative/partner) taking part?
Is there anything else you think about this?

D*o you think the doctor could or should do this?*
What are the advantages of it being the doctor?
What are the disadvantages of it being the doctor?
Do you think you or the doctor would be best in doing this role?
Are there any difficulties/barriers they may have to face?
Are there any benefits to them?
Is there anything that may help them decide?

Is there anything else you think about this?

Role of consultees in shared decision-making

One way of helping people make decisions about research is for them to make the decision with you. So you would be there to discuss taking part in research with your (friend/relative/partner) when they were being consented for the project?

Do you think you could help?
Would there be any disadvantages with you being there?
Would there be any benefits with you being there?
Do you think you would be able to help them make a decision?
Do you have any fears or concerns about being there?
Would you be willing to do it?

Use of neurocognitive support tools

Another way we can help people make decisions is by going through the facts about the research project together differently. We could go through the facts several times and learn them together with your (friend/relative/partner). This could also use things like pictures and videos.

Do you think this could help?
Would there be any problems with doing this?

Other strategies

Are the any other things you could think of to help people make a decision about taking part in research?

What would be the advantages/disadvantages of …?

Overall what do you think would be the best way of helping people make decisions?

Overall reflection

Thinking about taking part in research in general are there any things you think should be changed?

(if yes)

how would you change it?

what would be the benefit of changing it?

what would be the disadvantages of changing it?

What do you think would be the best way to help people make decisions about research?

Closing

I appreciate the time you took for this interview. Is there anything else you think would be useful for me to know?

Thanks again.

Text in italics are prompts if needed.

Opening

Thanks for agreeing to take part in this interview. As I mentioned I'm interested in finding out what people think about taking part in research. One area I want to look into is doctors' and nurses' involvement in the research consent process.

Can I confirm that you consent to take part in this face-to-face interview as part of this study and that you consent to the interview being audio recorded?

Do you have any questions about this?

Warm up

How have you found the process of talking to patients and introducing them to researchers so far?

Why did you think people agree to take part in research while in hospital?
Do you think there are any benefits to people taking part while in hospital?
Do you think there are any disadvantages to people taking part while in hospital?

Barriers and facilitators of research participation, research consent

Do you support patients taking part in research while unwell in hospital?

can you tell me more?

What do you think about the first approach process? This is where doctors and nurses check with patients first, before they introduce them to researchers, rather than letting researchers approach them directly.

What do you think it is for?

Are there problems with researchers having direct access to patients to recruit?

Are there any disadvantages of the first approach process?

What are your priorities regarding the patient?

Before you select a patient as suitable for 'first approach' what do you consider?

How you think people make decisions about someone being 'too unwell' to take part?

Can you tell me more/how would you define this/what symptoms would lead you to thinking this?

Do you consider whether they may be vulnerable?

Can you tell me more/how would you define this/what symptoms would lead you to thinking this?

What things do you think they may be vulnerable to?

Do you consider whether they may not have Decision-Making Capacity to consent to research?

how would you define this?

how would you test this?

What do you think might stop people from taking part in research when they are in hospital?

Could you tell me more about the barrier/difficulty?

Are there any ways in which it could be changed?

What do you think helps people take part in research while in hospital?

Could you tell me more about what helps?

Are there any ways in which it could help more/have more effect?

What do you think about the consent process?

do you think it is a useful way to protect participants?

if yes – how do you think it protects?

if no – what do you think needs to be done to make it better?

Consultee approval in those lacking DMC

Usually, to be able to sign up to taking part in research people have to be able to understand the research project and how it may affect them.

Sometimes when people are unwell, they are not in a clear or best frame of mind to make a proper decision about taking part in research, but still really want to help. They lack Decision-Making Capacity for research, but still want to take part.

Thinking about a situation in which someone lacked Decision-Making Capacity for research, but still wanted to help, the law has special rules that allows them to still take part if they want to.

Here the researchers have to ask a relative or friend of the person who wants to take part in research. The relative or friend can't decide for them, or force them to take part. But if the relative or friend has concerns they can block them from taking part, even if the person wants to.

Would you like me to explain this again?

What do you think about this?

While for most studies it has to be a relative, friend, carer, or advocate who the researchers have to ask, for drug trials (research that tests if medication works) only, it can be the doctor who makes the decision.

If the patient wasn't able to make a decision for themselves, but wanted to help, who would you want the researchers to contact to help out?
Why have you chosen them?
Is there anyone else you would want them to talk to?
What are the advantages of the researchers checking with this person?
What are the disadvantages of the researchers checking with this person?
What about the situation where this is the patient's doctor?
Do you think that someone should decide on your patient's behalf?
Are there any difficulties/barriers they may have to face?
Are there any benefits to them?
Is there anything that may help them decide?
Is there anything else you think about this?

Role of consultees in shared decision-making

Do you think it would be useful to have someone that the patient trusts with them when they are thinking about taking part in research? Like, let's say their partner or a friend?

How could they help?

Would there be any problems with them being there?

Do you think they would be able to help your patient to make a decision?

If you were to ask someone to do it for your patient, who would it be?

How would you feel about an independent advocate doing it?

What about their doctor?

Use of neurocognitive support tools

Another way we can help people make decisions is by going through the facts about the research project together differently. We could go through the facts several times and learn them together. This could also use things like pictures and videos.

Do you think this could help?

Would there be any problems with doing this?

Other strategies

Are the any other things you could think of to help people make a decision about taking part in research?

What would be the advantages/disadvantages of …?

Overall what do you think would be the best way of helping people make decisions?

Overall reflection

Thinking about taking part in research in general are there any things you think should be changed?

(if yes)

how would you change it?

what would be the benefit of changing it?

what would be the disadvantages of changing it?

What do you think would be the best way to help people make decisions about research?

Closing

I appreciate the time you took for this interview. Is there anything else you think would be useful for me to know?

Thanks again.

Revised topic guides

Opening

Thanks for agreeing to take part in this interview. As I mentioned I'm interested in finding out what people think about taking part in research.

Can I confirm that you consent to take part in this face-to-face interview as part of this study and that you consent to the interview being audio recorded?

Do you have any questions about this?

Warm up

How have you found the process of taking part in research so far?

Why did you agree to take part in research?

Facilitators and barriers to involvement in research

Why do you think people take part in research?

What do you think about these reasons?

Money?

Boredness?

Helping others?

Helping self?

To please someone else?

Any other reason?

How far do you think the researchers can say what the research will achieve? Might it be seen as coercive?

Do you think different types of research should be treated differently?

How about therapeutic research?

How about non-therapeutic research?

How about risky research?

How about non-risky research?

What do you think might stop people taking part in research while in hospital?

What do you think helps people taking part in research while in hospital?

Could you tell me more about the barrier/facilitator?

Are there any ways in which it could be changed?

Could you tell me more about what helps?

Are there any ways in which it could help more/have more effect?

Research governance and procedure

What things do you think are important in regulating how research in conducted?

What do you think about the consent process?

Is there anything you would change?

How do you find the information presented to you?

Was it straightforward?

What did you think about the consent form?

Some people think the consent process protects people – would you agree? If so why?

Who should be responsible for when research goes wrong? The researchers, the care team, the patient, the family?

First approach process

Power of vito from first approach?

Things to consider from first approach?

Who is the right person to be doing research? (doctors, researchers, advocates, service users) Why?

Agendas of people doing research?

What about people under section – does this change things? Why?

Therapeutic research subject to part IV of the mental health act?

Decision-making without participant

Who should decide about taking part in research?

Is it appropriate for other people?

Who and why? Doctors, friends, family, carers, advocates? Advantages and disadvantages of each?

How should they decide? For them, on behalf of them, overrule them, with them? Or any other way?

What about the person's involvement in that process?

What if they disagree?

What if they lack DMC?

What about disordered motivation?

What about conflict?

Does type of research make a difference?

How about the first approach process?

How can we help people decide?

How about involvement of someone to support or help them make a decision?

Who and why? Doctors, friends, family, carers, advocates? Advantages and disadvantages of each?

What about conflict?

Does type of research make a difference?

Consultee approval when lacking DMC

Who and why? Doctors, friends, family, carers, advocates? Advantages and disadvantages of each?

Acceptability of proxy decision making?

What about conflicts?

Agendas?

Does type of research make a difference?

How can help consultee?

Would you be willing to do it? Disadvantages to consultee?

What about neurocognitive support tools?

Any other strategies?

Research consent capability

Voluntariness standard (Understand that it is research – not treatment as usual – and bare minimum essential information; Not coerced either way (motivated to take part or not take part due to significant advantage or disadvantage to themselves outside of that from one would reasonably expect from involvement in the study); Understand they are free to refuse)

Lose ability for DMC during study

Advance directives for research

Insight in research

High risk/high benefit research?

High risk/low benefit research?

Low risk/high benefit research?

Low risk/low benefit research?

Different standards for different types of research?

Should people who lack DMC take part in research? Validity of results?

Overall reflection

Thinking about taking part in research in general are there any things you think should be changed?

What do you think would be the best way to help people make decisions about research?

Closing

I appreciate the time you took for this interview. Is there anything else you think would be useful for me to know?

Appendix 8. Study information sheets and consent forms

Understanding the ability of people with psychosis to make decisions around taking part in research.

The DECIDE Study

Study Number: 15/LO/0427

The DECIDE Study.

We would like you to consider taking part in our study but before you do so it is important you understand what it is about, and the possible benefits and disadvantages. You are under no pressure to take part, and we are grateful for your time in reading this information sheet. Please ask questions and discuss with others if you want to. There is a researcher available to talk to if anything is not clear. Thanks again for your time.

What is the research about?

Psychosis is a common illness that can affect people in different ways. In general people with psychosis often experience unusual thoughts or experiences.

There is still a lot that we don't know about these illnesses, such as how to prevent them and how best to treat them. We need people with psychotic illnesses to take part in research to answer these questions.

People who take part in research need to be able to understand the purpose of the research, and be able to make a decision around participating in the research. However, psychosis is an illness that can affect people's ability to make decisions when unwell. If they are unable to make this decision for themselves but still want to participate, then their relatives/friends/carers also have to agree.

We don't know how many people in hospital can actually make these decisions. People may be keen to participate, but excluded because they are assumed to be unable to make an informed decision about participation.

We want to recruit people with psychosis in hospital to find out what number of people might actually be able to make a decision about participating in research. To help us understand psychosis clearly we will focus on psychotic illnesses where problems with mood are not seen to be the cause of the illness, this includes but is not limited to illnesses such as schizophrenia, schizoaffective disorder, and acute and transient psychosis.

We want to understand more about making a decision about participating in research. We also want to find out your views on research and the rules around it, and those of your

relatives/friends/carers. We want to explore possible ways of supporting people to make decisions.

We hope to use this information to design a way to support people with psychosis in making decisions about participating in research and develop guidance on research in people with psychosis. This will help make research more inclusive and relevant to people with psychosis, and ensure it is safe to recruit people for research who are admitted to hospital.

Why have I been invited?

We are approaching people with psychosis who are in hospital in South London and Maudsley NHS Trust, whom we think we can learn from.

Do I have to take part?

No. Taking part in this study is entirely voluntary, and at any time you can withdraw from the study for any reason. If you do decide to withdraw the researcher may ask you some questions to make sure it is not because you have found the study upsetting, or any other similar reasons for no longer wanting to take part.

What will happen to me if I take part and what will I have to do?

If you agree to take part in the study we would ask you to take part in two interviews lasting around 45 minutes each.

In the first interview we would describe a research project to you. This would be a research project that would involve genetic testing. **You would not be asked to take part in that project**, rather explain how you might make decisions about it. We would also talk to you about your current admission and treatment in hospital, and how you would make decisions around this.

In the second interview we would ask you questions around your current symptoms, and perform some simple tests of your memory and concentration. We would also collect information from your medical notes.

You would be able to take breaks at any time during and between the interviews for as long as you wanted.

We may ask if there was someone you would let us talk to further about their views on research and your involvement in it. We would not contact them without your permission.

We may also invite you to another more detailed discussion about research in general, again this is optional, and you would be under no obligation to take part. This could take around an hour and would be done while you are in hospital.

You will be offered £10 compensation for your time for the first two interviews, and also for the optional third interview.

What will happen to me if I do not want to take part?

You will be thanked for your time in hearing about the study. It will not affect you or your future care in any way.

Are there any possible benefits to me if I take part?

You may find it helpful to talk to someone about your current admission and treatment, and how you make decisions around this and participating in research. We cannot promise the study will help you but the information we get from this study will help improve the care of people with psychosis.

What are the possible disadvantages and risks to me if I do take part?

We think these are not serious but you may have worries about confidentiality or talking about matters sensitive for you.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time, and can withdraw any stored data that can be identified as yours up to three months after being recruited to the study.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised. Only if we detect a very serious harm to self or others may we need to discuss with other professionals.

Interviews will be audio-recorded. A trained secretary will transcribe the tapes of the the interviews and the transcriptions (the typed record of the interview) will be anonymised.

What will happen to the results of the study?

After the study is finished we will keep the raw information we have collected in case we need it again to help design the next work we do, but after 7 years we will delete the information. We will also offer to give you a summary of our findings.

We aim to publish the results in research journals. The publications will include some quotations from the interviews that illustrate important issues. The quotations will not have your name or anything else identifiable on them. If you would like a copy of the publications arising from the research please contact Dr Spencer.

Who is organising and funding the study?

Dr Benjamin Spencer is funded by a National Institute for Health Research Doctoral Research Fellowship. This study is funded by the National Institute for Health Research.

What if something goes wrong?

It is unlikely that something will go wrong given the nature of the study, however as we will be covering some areas that may be upsetting perhaps some of the discussions you may find difficult. If you have any concerns you can contact the Principle investigators, or to contact SLAM's Patient Advice and Liaison Service (PALS) call **0800 731 2864,** or email **pals@slam.nhs.uk**.

Who has reviewed the study?

All research in the NHS is approved by a local NHS ethics committee. This particular study has been approved by the Camberwell and St Giles Research Ethics Committee.

Further information and contact details.

For any further information regarding the study please contact:

Dr Benjamin Spencer
Department of Psychological Medicine,
Institute of Psychiatry, Psychology and Neuroscience,
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Weston Education Centre,
10 Cutcombe Road,
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Benjamin.spencer@kcl.ac.uk
0207 848 5512

THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION SHEET

NHS
National Institute for Health Research

Understanding the ability of people with psychosis to make decisions around taking part in research.

The DECIDE Study

Study Number: 15/LO/0427

The DECIDE Study.

We would like you to consider taking part in our study but before you do so it is important you understand what it is about, and the possible benefits and disadvantages. You are under no pressure to take part, and we are grateful for your time in reading this information sheet. Please ask questions and discuss with others if you want to. There is a researcher available to talk to if anything is not clear. Thanks again for your time.

What is the research about?

Psychosis is a common illness that can affect people in different ways. In general people with psychosis often experience unusual thoughts or experiences.

There is still a lot that we don't know about these illnesses, such as how to prevent them and how best to treat them. We need people with psychotic illnesses to take part in research to answer these questions.

People who take part in research need to be able to understand the purpose of the research, and be able to make a decision around participating in the research. However, psychosis is an illness that can affect people's ability to make decisions when unwell. If they are unable to make this decision for themselves but still want to participate, then their relatives/friends/carers also have to agree.

We don't know how many people in hospital can actually make these decisions. People may be keen to participate, but excluded because they are assumed to be unable to make an informed decision about participation.

We want to recruit people with psychosis in hospital to find out what number of people might actually be able to make a decision about participating in research. We want to understand more about making a decision about participating in research, and your role in first contact for patients involved in research. We want to find out your views on research and the rules around it. We want to explore possible ways of supporting people to make decisions. To help us understand psychosis clearly we will focus on psychotic illnesses where problems

with mood are not seen to be the cause of the illness, this includes but is not limited to illnesses such as schizophrenia, schizoaffective disorder, and acute and transient psychosis.

We hope to use this information to design a way to support people with schizophrenia in making decisions about participating in research and develop guidance on research in people with psychosis. This will help make research more inclusive and relevant to people with psychosis, and ensure it is safe to recruit people for research who are admitted to hospital.

Why have I been invited?

We are approaching doctors and nurses working on inpatient wards in South London and Maudsley NHS Trust, whom we think we can learn from.

Do I have to take part?

No. Taking part in this study is entirely voluntary, and at any time you can withdraw from the study for any reason. If you do decide to withdraw the researcher may ask you some questions to make sure it is not because you have found the study upsetting, or any other similar reasons for no longer wanting to take part.

What will happen to me if I take part and what will I have to do?

If you agree to take part in the study we would ask you to take part in one interview lasting around 60 minutes. It will cover your views on research regulation, views on research in people with psychosis, and on 'first contact' for researchers.

You would be able to take breaks at any time during the interview for as long as you wanted.

What will happen to me if I do not want to take part?

You will be thanked for your time in hearing about the study. It will not affect you or your employment in any way.

Are there any possible benefits to me if I take part?

You may find it interesting to talk to someone about research in psychosis. The information we get from this study will help improve the care of people with psychosis.

What are the possible disadvantages and risks to me if I do take part?

We think these are not serious but you may have worries about confidentiality or talking about matters sensitive for you.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time, and can withdraw any stored data that can be identified as yours up to three months after being recruited to the study.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised. Only if we detect a very serious harm to self or other may we need to discuss with other professionals.

Interviews will be audio-recorded. A trained secretary will transcribe the tapes of the the interviews and the transcriptions (the typed record of the interview) will be anonymised.

What will happen to the results of the study?

After the study is finished we will keep the raw information we have collected in case we need it again to help design the next work we do, but after 7 years we will delete the information. We will also offer to give you a summary of our findings.

We aim to publish the results in research journals. The publications will include some quotations from the interviews that illustrate important issues. The quotations will not have your name or anything else identifiable on them. You will not be published/presented as a case-report unless you have given separate consent for this. If you would like a copy of the publications arising from the research please contact Dr Spencer.

Who is organising and funding the study?

Dr Benjamin Spencer is funded by a National Institute for Health Research Doctoral Research Fellowship. This study is funded by the National Institute for Health Research.

What if something goes wrong?

It is unlikely that something will go wrong given the nature of the study, however as we will be covering some areas that may be upsetting perhaps some of the discussions you may find difficult. If you have any concerns you can contact the Principle investigators, or to contact SLAM's Patient Advice and Liaison Service (PALS) call **0800 731 2864,** or email **pals@slam.nhs.uk**.

Who has reviewed the study?

All research in the NHS is approved by a local NHS ethics committee. This particular study has been approved by the Camberwell and St Giles Research Ethics Committee.

Further information and contact details.

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Institute of Psychiatry, Psychology and Neuroscience,
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Weston Education Centre,
10 Cutcombe Road,
London,
SE5 9RJ

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THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION SHEET

NHS
National Institute for Health Research

Understanding the ability of people with psychosis to make decisions around taking part in research.

The DECIDE Study

Study Number: 15/LO/0427

The DECIDE Study.

We would like you to consider taking part in our study but before you do so it is important you understand what it is about, and the possible benefits and disadvantages. You are under no pressure to take part, and we are grateful for your time in reading this information sheet. Please ask questions and discuss with others if you want to. There is a researcher available to talk to if anything is not clear. Thanks again for your time.

What is the research about?

Psychosis is a common illness that can affect people in different ways. In general people with psychosis often experience unusual thoughts or experiences.

There is still a lot that we don't know about these illnesses, such as how to prevent them and how best to treat them. We need people with psychotic illnesses to take part in research to answer these questions.

People who take part in research need to be able to understand the purpose of the research, and be able to make a decision around participating in the research. However, psychosis is an illness that can affect people's ability to make decisions when unwell. If they are unable to make this decision for themselves but still want to participate, then their relatives/friends/carers also have to agree.

We don't know how many people in hospital can actually make these decisions. People may be keen to participate, but excluded because they are assumed to be unable to make an informed decision about participation.

We want to recruit people with psychosis in hospital to find out what number of people might actually be able to make a decision about participating in research. To help us understand psychosis clearly we will focus on psychotic illnesses where problems with mood are not seen to be the cause of the illness, this includes but is not limited to illnesses such as schizophrenia, schizoaffective disorder, and acute and transient psychosis.

We want to understand more about making a decision about participating in research. We also want to find out your views on research and the rules around it, and those of your relative/friend/person you care for. We want to explore possible ways of supporting people to make decisions. We are exploring the possibility that people like you could act as a 'research proxy': someone who helps support people to make decisions about involvement in research, or make decisions on their behalf.

We hope to use this information to design a way to support people with schizophrenia in making decisions about participating in research and develop guidance on research in people with psychosis. This will help make research more inclusive and relevant to people with psychosis, and ensure it is safe to recruit people for research who are admitted to hospital.

Why have I been invited?

We are approaching people with psychosis who are in hospital in South London and Maudsley NHS Trust, and their relatives/friends/carers, whom we think we can learn from. We are interested in finding out your personal views about people with psychosis taking part in research while in hospital and research in general. We hope to learn from your experience as the relative/friend/or carer of someone who has a psychotic illness, and as someone who might be asked to make decisions about them taking part in research if they did not have the ability to make the decision for themselves. We have recruited your relative/friend/person you care for to this study and they have suggested you and agreed for us to contact you.

Do I have to take part?

No. Taking part in this study is entirely voluntary, and at any time you can withdraw from the study for any reason. If you do decide to withdraw the researcher may ask you some questions to make sure it is not because you have found the study upsetting, or any other similar reasons for no longer wanting to take part.

What will happen to me if I take part and what will I have to do?

If you agree to take part in the study we would ask you to take part in one interview lasting around 60 minutes. It will cover your views on research regulations and involvement in discussions around research, and your views on supporting your relative/friend/person you care in making decisions around research.

You would be able to take breaks at any time during the interview for as long as you wanted.

You will be offered £10 compensation for your time.

What will happen to me if I do not want to take part?

You will be thanked for your time in hearing about the study. It will not affect you or your relative/friend/person you care's future care in any way.

Are there any possible benefits to me if I take part?

You may find it helpful to talk to someone about your relative/friend/person you care for's care and how to support him or her in making decisions. We cannot promise the study will help them but the information we get from this study will help improve the care of people with psychosis.

What are the possible disadvantages and risks to me if I do take part?

We think these are not serious but you may have worries about confidentiality or talking about matters sensitive for you.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time, and can withdraw any stored data that can be identified as yours up to three months after being recruited to the study.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised. Only if we detect a very serious harm to self or other may we need to discuss with other professionals.

Interviews will be audio-recorded. A trained secretary will transcribe the tapes of the the interviews and the transcriptions (the typed record of the interview) will be anonymised.

What will happen to the results of the study?

After the study is finished we will keep the raw information we have collected in case we need it again to help design the next work we do, but after 7 years we will delete the information. We will also offer to give you a summary of our findings.

We aim to publish the results in research journals. The publications will include some quotations from the interviews that illustrate important issues. The quotations will not have your name or anything else identifiable on them. If you would like a copy of the publications arising from the research please contact Dr Spencer.

Who is organising and funding the study?

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NHS
National Institute for Health Research

Understanding the ability of people with psychosis to make decisions around taking part in research.

The DECIDE Study

Study Number: 15/LO/0427

The DECIDE Study.

Introduction

We are inviting your relative, friend, or person you care for to participate in a research study. Because there are concerns that she may not understand enough about the study to give informed consent. We are asking you to advise on participation as a consultee. This is standard practice in research.

She has expressed a willingness to participate but we would like to know whether you feel she would have agreed if she understood more. We ask you to consider what you know of her prior wishes and feelings, and to consider her interests. Please let us know of any advance decisions she may have made about participating in research. These should take precedence. If you are unsure about taking the role of consultee you may seek advice. We will understand if you do not want to take on the role of consultee.

Before you advise it is important for you to understand why the project is being done and what it will involve. Please take time to read the following information. It is the same as would have been provided to your relative/friend/person you care for. Please ask questions and discuss with others if you want to. There is a researcher available to talk to if anything is not clear. Thanks again for your time.

What is the research about?

Psychosis is a common illness that can affect people in different ways. In general people with psychosis often experience unusual thoughts or experiences.

There is still a lot that we don't know about these illnesses, such as how to prevent them and how best to treat them. We need people with psychotic illnesses to take part in research to answer these questions.

People who take part in research need to be able to understand the purpose of the research, and be able to make a decision around participating in the research. However, psychosis is an illness that can affect people's ability to make decisions when unwell. If they are unable to make this decision for themselves but still want to participate, then their relatives/friends/carers also have to agree.

We don't know how many people in hospital can actually make these decisions. People may be keen to participate, but excluded because they are assumed to be unable to make an informed decision about participation.

We want to recruit people with psychosis in hospital to find out what number of people might actually be able to make a decision about participating in research. To help us understand psychosis clearly we will focus on psychotic illnesses where problems with mood are not seen to be the cause of the illness, this includes but is not limited to illnesses such as schizophrenia, schizoaffective disorder, and acute and transient psychosis.

We want to understand more about making a decision about participating in research. We also want to find out the views of your relative/friend/person you care for on the current regulations around research, and your own views. We want to explore possible ways of supporting people to make decisions.

We hope to use this information to design a way to support people with schizophrenia in making decisions about participating in research and develop guidance on research in people with psychosis. This will help make research more inclusive and relevant to people with psychosis, and ensure it is safe to recruit people for research who are admitted to hospital.

Why has my partner/friend/relative been invited?

We are approaching people with psychosis who are in hospital in South London and Maudsley NHS Trust, whom we think we can learn from.

Does she have to take part?

No. Taking part in this study is entirely voluntary, and will only go ahead if both you and your partner/friend/relative agree. At any time she can withdraw from the study for any reason, or you can withdraw them. If you do decide to withdraw the researcher may ask you some questions to make sure it is not because you have found the study upsetting, or any other similar reasons for no longer wanting to take part.

What will happen to her if she takes part and what will she have to do?

If you and your relative/friend/person you care for agree to take part in the study we would ask her to take part in two interviews lasting around 45 minutes each.

In the first interview we would describe a research project to her. This would be a research project that would involve genetic testing. **She would not be asked to take part in that project**, rather explain how she might make decisions about it. We would also talk to her about her current admission and treatment in hospital, and how she would make decisions around this.

In the second interview we would ask her questions around her current symptoms, and perform some simple tests of her memory and concentration. We would also collect information from her medical notes.

She would be able to take breaks at any time during and between the interviews for as long as she wanted.

We may ask if there was someone she would let us talk to further about their views on research and he involvement in it. We would not contact them without her permission.

We may also invite her to another more detailed discussion about research in general, again this is optional, and she would be under no obligation to take part. This could take around an hour and would be done while she is in hospital.

Your relative/friend/person you care for will be offered £10 compensation for their time for the first two interviews, and also for the optional third interview.

What will happen to her if I do not want her to take part?

You will both be thanked for your time in hearing about the study. It will not affect her or your future care in any way.

Are there any possible benefits to her if she takes part?

Your relative/friend/person you care for may find it helpful to talk to someone about her current admission and treatment, and how they make decisions around this and participating in research. We cannot promise the study will help them but the information we get from this study will help improve the care of people with psychosis.

What are the possible disadvantages and risks to her if she takes part?

We think these are not serious but you may have worries about her confidentiality or talking about matters sensitive for her.

What will happen if she doesn't want to carry on with the study?

She can withdraw from the study at any time and any stored data that can be identified as theirs will be destroyed if they wish.

Will her taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information that is collected about her during the course of the research will be kept strictly confidential. Any information about her that leaves the hospital will have her name and address removed so that she cannot be recognised. Only if we detect a very serious harm to self or others may we need to discuss with other professionals.

Interviews will be audio-recorded. A trained secretary will transcribe the tapes of the the interviews and the transcriptions (the typed record of the interview) will be anonymised.

What will happen to the results of the study?

After the study is finished we will keep the raw information we have collected in case we need it again to help design the next work we do, but after 7 years we will delete the information. We will also offer to give you and your relative/friend/person you care for a summary of our findings.

We aim to publish the results in research journals. The publications will include some quotations from the interviews that illustrate important issues. The quotations will not have her name or anything else identifiable on them. If you would like a copy of the publications arising from the research please contact Dr Spencer.

Who is organising and funding the study?

Dr Benjamin Spencer is funded by a National Institute for Health Research Doctoral Research Fellowship. This study is funded by the National Institute for Health Research.

What if something goes wrong?

It is unlikely that something will go wrong given the nature of the study, however as we will be covering some areas that may be upsetting perhaps some of the discussions you may find difficult. If you have any concerns you can contact the Principle investigators, or to contact SLAM's Patient Advice and Liaison Service (PALS) call **0800 731 2864,** or email **pals@slam.nhs.uk**.

Who has reviewed the study?

All research in the NHS is approved by a local NHS ethics committee. This particular study has been approved by the Camberwell and St Giles Research Ethics Committee.

Further information and contact details.

For any further information regarding the study please contact:

Dr Benjamin Spencer
Department of Psychological Medicine,
Institute of Psychiatry, Psychology and Neuroscience,
Kings College London,
Weston Education Centre,
10 Cutcombe Road,
London,
SE5 9RJ

Benjamin.spencer@kcl.ac.uk
0207 848 5512

THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION SHEET

Understanding the ability of people with psychosis to make decisions around taking part in research.

The DECIDE Study

Study Number: 15/LO/0427

The DECIDE Study.

Introduction

We are inviting your relative, friend, or person you care for to participate in a research study. Because there are concerns that he may not understand enough about the study to give informed consent. We are asking you to advise on participation as a consultee. This is standard practice in research.

He has expressed a willingness to participate but we would like to know whether you feel he would have agreed if he understood more. We ask you to consider what you know of his prior wishes and feelings, and to consider his interests. Please let us know of any advance decisions he may have made about participating in research. These should take precedence. If you are unsure about taking the role of consultee you may seek advice. We will understand if you do not want to take on the role of consultee.

Before you advise it is important for you to understand why the project is being done and what it will involve. Please take time to read the following information. It is the same as would have been provided to your relative/friend/person you care for. Please ask questions and discuss with others if you want to. There is a researcher available to talk to if anything is not clear. Thanks again for your time.

What is the research about?

Psychosis is a common illness that can affect people in different ways. In general people with psychosis often experience unusual thoughts or experiences.

There is still a lot that we don't know about these illnesses, such as how to prevent them and how best to treat them. We need people with psychotic illnesses to take part in research to answer these questions.

People who take part in research need to be able to understand the purpose of the research, and be able to make a decision around participating in the research. However, psychosis is

an illness that can affect people's ability to make decisions when unwell. If they are unable to make this decision for themselves but still want to participate, then their relatives/friends/carers also have to agree.

We don't know how many people in hospital can actually make these decisions. People may be keen to participate, but excluded because they are assumed to be unable to make an informed decision about participation.

We want to recruit people with psychosis in hospital to find out what number of people might actually be able to make a decision about participating in research. To help us understand psychosis clearly we will focus on psychotic illnesses where problems with mood are not seen to be the cause of the illness, this includes but is not limited to illnesses such as schizophrenia, schizoaffective disorder, and acute and transient psychosis.

We want to understand more about making a decision about participating in research. We also want to find out the views of your relative/friend/person you care for on the current regulations around research, and your own views. We want to explore possible ways of supporting people to make decisions.

We hope to use this information to design a way to support people with schizophrenia in making decisions about participating in research and develop guidance on research in people with psychosis. This will help make research more inclusive and relevant to people with psychosis, and ensure it is safe to recruit people for research who are admitted to hospital.

Why has my relative/friend/person I care for been invited?

We are approaching people with psychosis who are in hospital in South London and Maudsley NHS Trust, whom we think we can learn from.

Does he have to take part?

No. Taking part in this study is entirely voluntary, and will only go ahead if both you and your relative/friend/person you care for agree. At any time he can withdraw from the study for any reason, or you can withdraw them. If you do decide to withdraw the researcher may ask you some questions to make sure it is not because you have found the study upsetting, or any other similar reasons for no longer wanting to take part.

What will happen to his if he takes part and what will he have to do?

If you and your relative/friend/person you care for agree to take part in the study we would ask him to take part in two interviews lasting around 45 minutes each.

In the first interview we would describe a research project to him. This would be a research project that would involve genetic testing. **He would not be asked to take part in that project**, rather explain how he might make decisions about it. We would also talk to him about his current admission and treatment in hospital, and how he would make decisions around this.

In the second interview we would ask him questions around his current symptoms, and perform some simple tests of his memory and concentration. We would also collect information from his medical notes.

He would be able to take breaks at any time during and between the interviews for as long as she wanted.

We may ask if there was someone he would let us talk to further about their views on research and his involvement in it. We would not contact them without his permission.

We may also invite him to another more detailed discussion about research in general, again this is optional, and he would be under no obligation to take part. This could take around an hour and would be done while he is in hospital.

Your relative/friend/person you care for will be offered £10 compensation for their time for the first two interviews, and also for the optional third interview.

What will happen to his if I do not want his to take part?

You will both be thanked for your time in hearing about the study. It will not affect his or your future care in any way.

Are there any possible benefits to him if he takes part?

Your relative/friend/person you care for may find it helpful to talk to someone about his current admission and treatment, and how they make decisions around this and participating in research. We cannot promise the study will help them but the information we get from this study will help improve the care of people with psychosis.

What are the possible disadvantages and risks to him if he takes part?

We think these are not serious but you may have worries about his confidentiality or talking about matters sensitive for her.

What will happen if he doesn't want to carry on with the study?

He can withdraw from the study at any time, and can withdraw any stored data that can be identified as his up to three months after being recruited to the study.

Will his taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information that is collected about his during the course of the research will be kept strictly confidential. Any information about his that leaves the hospital will have his name and address removed so that he cannot be recognised. Only if we detect a very serious harm to self or others may we need to discuss with other professionals.

Interviews will be audio-recorded. A trained secretary will transcribe the tapes of the the interviews and the transcriptions (the typed record of the interview) will be anonymised.

What will happen to the results of the study?

After the study is finished we will keep the raw information we have collected in case we need it again to help design the next work we do, but after 7 years we will delete the information. We will also offer to give you and your relative/friend/person you care for a summary of our findings.

We aim to publish the results in research journals. The publications will include some quotations from the interviews that illustrate important issues. The quotations will not have his name or anything else identifiable on them. If you would like a copy of the publications arising from the research please contact Dr Spencer.

Who is organising and funding the study?

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What if something goes wrong?

It is unlikely that something will go wrong given the nature of the study, however as we will be covering some areas that may be upsetting perhaps some of the discussions you may find difficult. If you have any concerns you can contact the Principle investigators, or to contact SLAM's Patient Advice and Liaison Service (PALS) call **0800 731 2864,** or email **pals@slam.nhs.uk**.

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Further information and contact details.

For any further information regarding the study please contact:

Dr Benjamin Spencer
Department of Psychological Medicine,
Institute of Psychiatry, Psychology and Neuroscience,
Kings College London,
Weston Education Centre,
10 Cutcombe Road,
London,
SE5 9RJ

Benjamin.spencer@kcl.ac.uk
0207 848 5512

THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION SHEET

Institute of Psychiatry at The Maudsley

South London and Maudsley NHS
NHS Foundation Trust

KING'S College LONDON

DECIDE Consent Form Patient Participant - PPCF

Study Number: 15/LO/0427

Participant Identification Number for this study:

CONSENT FORM

Title of Project: **Understanding the ability of people with psychosis to make decisions around taking part in research.**

(The DECIDE Study - Decision-Making Capacity in Deciding to Enrol in Research in Psychosis Study)

Name of Researcher: **Dr Benjamin Spencer**

Please initial box

1. I confirm that I have read and understand the information sheet dated **04/04/2016** (**PPIS3 version 3**) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I give permission to the researchers to access to my confidential medical notes. ☐

4. I consent to my interview being audio recorded. ☐

5. I understand that direct quotes may be published in papers arising from this research. I understand confidentiality and anonymity will be maintained and it will not be possible to identify me in any publications. ☐

6. I understand that a small number of participants may be asked to take part in a face-to-face interview with the researcher to discuss views on research in more detail. I consent to take part in this interview process. ☐

7. I give permission for the researcher to contact a friend, relative, or carer, chosen by myself to invite them to take part in the study. ☐

8. I wish to receive a copy of the final published report (and will provide contact details for receipt of this report). ☐

9. I agree to take part in the above study. ☐

Name of Participant	Date	Signature
Name of Person taking consent.	Date	Signature

DECIDE Consent Form Clinician Participant - ClinPCF

Study Number: 15/LO/0427

Participant Identification Number for this study:

CONSENT FORM

Title of Project: **Understanding the ability of people with psychosis to make decisions around taking part in research.**

(The DECIDE Study - Decision-Making Capacity in Deciding to Enrol in Research in Psychosis Study)

Name of Researcher: **Dr Benjamin Spencer**

Please initial box

1. I confirm that I have read and understand the information sheet dated **04/04/2016** (**ClinPIS3 version 3**) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I consent to my interview being audio recorded. ☐

4. I understand that direct quotes may be published in papers arising from this research. I understand confidentiality and anonymity will be maintained and it will not be possible to identify me in any publications. ☐

5. I wish to receive a copy of the final published report (and will provide contact details for receipt of this report). ☐

6. I agree to take part in the above study. ☐

Name of Participant	Date	Signature
Name of Person taking consent.	Date	Signature

Study Number: 15/LO/0427

Participant Identification Number for this study:

CONSULTEE DECLARATION FORM

Title of Project: **Understanding the ability of people with psychosis to make decisions around taking part in research.**

(The DECIDE Study - Decision-Making Capacity in Deciding to Enrol in Research in Psychosis Study)

Name of Researcher: **Dr Benjamin Spencer**

Please initial box

1. I _____ have been consulted about _____'s participation in the DECIDE Study. I have had the opportunity to ask questions about the study and understand what is involved. ☐

2. I confirm that I have read and understand the information sheet dated **04/04/2016** (**CMPIS3/CFPIS3 version 3**) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

3. In my opinion he/she would have no objection to taking part in the above study. ☐

4. I understand that I can request he/she is withdrawn from the study at any time, without giving any reason and without his/her care or legal rights being affected. ☐

5. I agree to their interview being audio recorded ☐

6. I understand that direct quotes may be published in papers arising from this research. I understand confidentiality and anonymity will be maintained and it will not be possible to identify my friend/relative/partner in any publications. ☐

7. I understand that a small number of participants may be asked to take part in a face-to-face interview with one of the researchers to discuss views on research in more detail. I agree for my friend/relative/partner to take part in this interview process. ☐

8. I wish to receive a copy of the final published report (and will provide contact details for receipt of this report). ☐

Name of Consultee	Date	Signature

Relationship to participant:

Person undertaking consultation (if different from researcher):

Name	Date	Signature

Researcher	Date	Signature

DECIDE Consent Form Research Proxy Participant - RPPCF

Study Number: 15/LO/0427

Participant Identification Number for this study:

CONSENT FORM

Title of Project: **Understanding the ability of people with psychosis to make decisions around taking part in research.**

(The DECIDE Study - Decision-Making Capacity in Deciding to Enrol in Research in Psychosis Study)

Name of Researcher: **Dr Benjamin Spencer**

Please initial box

1. I confirm that I have read and understand the information sheet dated **04/04/2016** (**RPPIS3 version 3**) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I consent to my interview being audio recorded. ☐

4. I understand that direct quotes may be published in papers arising from this research. I understand confidentiality and anonymity will be maintained and it will not be possible to identify me in any publications. ☐

5. I wish to receive a copy of the final published report (and will provide contact details for receipt of this report). ☐

6. I agree to take part in the above study. ☐

Name of Participant	Date	Signature
Name of Person taking consent.	Date	Signature