

WP 3

Trials readiness				
Start date: 1 July 2014			Completion date: 30 June 2020	
<p>Overall work package objectives: The dementia readiness cohort, involving the re-phenotyping (including brain imaging) of 10,000 UK Biobank participants at two years, supports the third DPUK strategic objective of re-purposing cohorts for trials readiness.</p> <ol style="list-style-type: none"> 1. To establish a liaison structure with UK Biobank (UKB) to develop the readiness cohort protocol 2. The liaison group will consider all dependencies between UKB and DPUK, focusing on the imaging cohort of 100,000 and the nested readiness cohort of 10,000 participants 3. Potential dependencies with EPAD and DFP to be explored 4. To recruit 10,000 participants with two year re-assessment for trials readiness. 				
Deliverables	Milestones	Milestone deadline	Work package dependencies	Person(s) responsible
Objective 1:				
D1.1 Regular meetings with UKB	M1.1.1 Establish a regular agenda item on DPUK at the UKB Steering Group meetings	M1.1.1 Complete	None	JG
	M1.1.2 Meet with UKB Steering Group annually	M1.1.2 Complete		
Objective 2:				
D2.1 Re-imaging protocol agreed with UKB	M2.1.1 Imaging protocol working group established	M2.1.1 Complete	None	AB
	M2.1.2 Re-imaging proposals submitted to UKB	M2.1.2 Complete		
D2.2 A biosampling protocol agreed with UKB	M2.2.1 Biosampling working group established	M2.2.1 Complete	Samples will be assayed as a component of WP6	SL
	M2.2.2 Biosample protocols agreed with UKB	M2.2.2 Complete		
D2.3 Cognitive assessment and questionnaire protocol	M2.3.1 CA working group established	M2.3.1 Complete	Dependent on WP10	JG
	M2.3.2 CA protocols submitted to UKB	M2.3.2 Complete		
D2.4 Brain banking protocol	M2.4.1 BB protocols	M2.4.1 Complete	Dependent on WP13	PF
	M2.4.2 BB protocols submitted to UKB	M2.4.2 Mar 2019		CS
	M2.4.3 BB pilot study	M2.4.3 Mar 2019	Dependent on UKB cohort-partner policy As for M2.4.2 As for M2.4.2	JG
	M2.4.4 BB implemented in UKB	M2.4.4 Jun 2019		JG
D2.5 Re-contact protocol	M2.5.1 Initiate discussions with UKB	M2.5.1 Complete	None	JG
	M2.5.2 Re-contact protocol agreed with UKB	M2.5.2 Complete	Dependent on UKB recontact policy	

D2.6 Participant selection algorithm	M2.6.1 Meet analysts to explore and test algorithms	M2.6.1 Complete	None	JG
	M2.6.2 Algorithm agreed with UKB	M2.6.2 Complete		
D2.7 Finalise readiness cohort protocol	M2.7.1 Identify optimum repeat assessment period	M2.7.1 Complete		JG
	M2.7.2 Agree intercalation of programme between baseline and repeat imaging	M2.7.2 Complete		
Objective 3:				
D3.1 Establish recruitment pathway for EPAD / DFP	M3.1.1 Submit EPAD and DFP data access requests to UKB	M3.1.1 Complete	None Dependent on UKB data access agreement None Dependent on UKB recontact policy	JG ST, JS (DFP), DG (EPAD)
	M3.1.2 Acquire UKB data instance on portal	M3.1.2 Complete		
	M3.1.3 Install 'Prepad' on data portal	M3.1.3 Complete		
	M3.1.4 Begin EPAD / DFP recruitment	M3.1.4 Complete		
Objective 4:				
D4.1 Finalise readiness cohort protocol	M4.1.1 Integrate the various components for the protocol from Objective 2 and agree with UKB a final protocol	M4.1.1 Complete	None	JG, AB
D4.2 Conduct pilot study	M4.2.1 Begin re-assessment of 500 participants	M4.2.1 Complete		JG
	M4.2.2 Review data and adjust protocol	M4.2.2 Complete		
D4.3 Conduct re-assessment on all participants	M4.3.1 Begin re-assessments	M4.3.1 Complete		JG
	M4.3.2 Complete re-assessments	M4.3.2 Feb 2023		JG
Updates on delivery against milestones since last report				
<ul style="list-style-type: none"> • M2.4.2 BB protocols submitted to UKB (Mar 19) See summary below • M2.4.3 BB pilot study (Mar 19) See summary below • M2.4.4 BB implemented in UKB (Jun 19) See summary below • M3.1.4 Begin EPAD / DFP recruitment (Feb 19) See summary below • M4.2.2 Review data and adjust protocol (Jun 19) Complete • M4.3.1 Begin re-assessments (Jul 19) Complete 				
Team members funded (full or part-time) by DPUK		Dependencies to and from other work packages, networks and themes		
None		No dependencies from other WPs.		
Team members involved with the project but not funded by DPUK		WP16 (DFP) is dependent on this WP.		
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Summary of plan to deliver on outstanding work (with dates)				
<p>Brain Banking: A small expert group comprising David Bennett (Chicago), John Hardy (UCL), Jonathan Mill (Exeter) and Colin Smith (Edinburgh), chaired by John Gallacher has been formed to prepare a brain donation pilot study proposal for submission to the UKB Enhancements Committee. This group has been selected to represent a range of scientific and practical interests. It will hold its first meeting in December. The challenge is to identify strategies for enable brains to be selected for scientific informativeness prospectively, focussing on the UKB imaging and re-imaging cohorts.</p>				

<p>EPAD / DFP recruitment: DFP is being used as the Proof of Concept for recruiting from UK Biobank. UKB has recently received ethical approval of their required amendment and their dedicated website is due to go online by the second week of November 2019, initially recruiting to the Oxford and Exeter sites. The process will be reviewed by UKB before any decision is taken to recruit to EPAD.</p>	
<p>Risks</p> <ol style="list-style-type: none"> 1) Low response rate to repeat imaging invitation 2) Reputational risk to UKB by recruiting to clinical studies 3) The brain donation protocol is not accepted by the UKB Enhancements Committee 	<p>Mitigation</p> <ol style="list-style-type: none"> 1) Response running at around 60% so no mitigation required 2) UKB are undertaking a recruitment pilot (using the DFP study) in which they have full control of the invitation process 3) Liaison between DPUK and the UKB Enhancements Committee will be undertaken to identify and mitigate risk of rejection
<p>Outcomes</p> <ul style="list-style-type: none"> • Repeat imaging protocol • Brain donation consent protocol • DPUK Data Portal Analysis Environment • DPUK Data Portal website and tools – https://portal.dementiasplatform.uk • DPUK Data Portal: Data Resource Profile – https://www.biorxiv.org/content/10.1101/582155v1 	
<p>Project narrative</p> <p>The aligning of procedures between DPUK and UKB has proven challenging in terms of scientific priorities and logistics. However, both parties have worked hard to establish synergy.</p> <p>For imaging repeat, the work has begun. DPUK funding of repeat brain imaging in 10,000 ‘biobankers’ has led to further funding being acquired for a full (brain and body) repeat imaging assessment. In turn, this has paved the way for seeking further funding to increase substantially the overall size of the repeat imaging cohort. This funding exercise is ongoing.</p> <p>For recruitment to trials, in-part in response to DPUK’s interest in developing experimental medicine recruitment, UKB have designed, and will shortly launch, a trials recruitment web-site to be piloted using the DFP study.</p> <p>For brain banking, DPUK is now in a position to prepare a proposal for brain donation to be submitted to the UKB Enhancements Committee.</p>	