not be sensitive to the initial signs of amyloid deposition. Cut-points are also highly dependent on many analytical issues including: region of interest (ROI), reference region, partial volume correction, and the statistical criteria for choosing the cut-point. In the absence of CT scanning, quantifying amyloid load with combined PET/MR scanners requires novel techniques for attenuation correction. We examined these aspects in a large UK sample of individuals born in the same week in 1946, all scanned on the same PET/MR scanner. **Methods:** PET and MR data were acquired on 250 participants enrolled in Insight 1946, a sub-study of the MRC National Survey of Health and Development (NSHD). Scanning was performed on a Siemens Biograph PET-MR scanner using 18F-florbetapir. PET images were reconstructed from 50 to 60 minutes post-injection using two different attenuation correction techniques: an ultrashort echo time (UTE) and a pseudo CT (pCT) method. Volumetric T1 MR data were parcellated into ROIs and co-registered to PET to compute standard uptake value ratios (SUVR) against four commonly used reference regions, with and without partial volume correction. Cut-points for amyloid positivity were created by fitting Gaussian mixture models (with 1 to 3 clusters) and using the 99th percentile of the Gaussian representing the amyloid negative population. **Results:** 240 participants with suitable T1 and amyloid PET data were included in the analysis. The mixture modelling for cortical ROIs typically resulted in 2 clusters, confirming the expected bimodal distribution of amyloid deposition. Across the different reference regions, the rate of amyloid positive individuals was consistently 15 – 18% without PVC correction and 19-23% with PVC correction (Table). Precuneus and posterior cingulate SUVRs classified slightly more participants as amyloid positive, while those based on occipital lobe were much lower (Figure). Subcortical ROIs provided inconsistent evidence of bimodal distributions. **Conclusions:** Quantification of SUVR based measures of amyloid load using data acquired on PET/MR produces consistent rates of amyloid positivity across a variety of analysis options.

IC-P-005 CONCORDANCE BETWEEN CEREBROSPINAL FLUID AMYLOID-β AND [^{18}F]FLORBETABEN PET IN AN UNSELECTED COHORT OF MEMORY CLINIC PATIENTS

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Background: A decreased amyloid-ß 1-42 (Aß$_{42}$) in cerebrospinal fluid (CSF) and increased Aß tracer uptake in the brain, as measured using positron emission tomography (PET), could support a clinical diagnosis of Alzheimer's disease (AD). The purpose of this study was to investigate the concordance between CSF biomarkers and [^{18}F]Florbetaben (FBB) PET in an unselected sample of memory clinic patients. **Methods:** From March 2015 to November 2016, [^{18}F]FBB PET was offered to all patients visiting our memory clinic. A total of 104 AD patients, 43 non-AD patients, 61 patients with mild cognitive impairment (MCI) and 99 normal controls (NC) with available CSF and [^{18}F]FBB PET were included. CSF biomarkers were considered abnormal when either Aß$_{42}$ was $<$640 nl/L or the ration of Aß$_{42}$ and tau (tau/Aß$_{42}$ CSF ratio) was $>$ 0.52. [^{18}F]FBB scans were visually rated as normal or abnormal. Concordance between CSF Aß$_{42}$ and [^{18}F]FBB PET was determined across diagnostic groups. For concordant and discordant cases with abnormal [^{18}F]FBB PET, total tau and ptau were compared within diagnostic groups. **Results:** Overall concordance between CSF Aß$_{42}$ and [^{18}F]FBB PET was 81%, and between CSF ratio and [18F]FBB PET it was 88%. When discordant, PET was abnormal in 86% of the cases. Within groups, concordance of CSF Aß$_{42}$ and [^{18}F]FBB PET was highest for NC (86%), followed by AD (81%), non-AD (81%) and MCI (72%). Concordance between CSF ratio and [^{18}F]FBB PET was higher (AD:91%, MCI:90%, NC:90%, non-AD:81%). There was no difference in CSF total tau and ptau levels between concordant and discordant MCI and AD patients with abnormal [^{18}F]FBB PET (Table 1). **Conclusions:** In this unselected cohort of memory clinic patients we found a high concordance between CSF Aß$_{42}$ and [^{18}F]FBB PET. The combination of CSF Aß$_{42}$ and total tau provided better concordance than Aß$_{42}$ alone. Discordant MCI and AD patients, based on [^{18}F]FBB PET positivity alone, showed increased CSF total tau and ptau values and Aß$_{42}$ values near the cut-off, suggesting that

Table 1
Comparison of concordant and discordant cases within diagnostic groups with abnormal [^{18}F]FBB

	NC concordant	NC discordant	MCI concordant	MCI discordant	AD concordant	AD discordant
n	9	12	13	16	64	18
Age (±SD)	65 ± 6	64 ± 7	62 ± 7	68 ± 6	65 ± 7	63 ± 7
Gender (% male)	4 (44%)	7 (58%)	8 (62%)	8 (50%)	33 (51%)	7 (39%)
MMSE (±SD)	29 ± 4	27 ± 4	27 ± 2	27 ± 2	22 ± 4	22 ± 3
APOE, E4 carrier (%)	5 (56%)	5 (42%)	11 (85%)	11 (69%)	64 (70%)	11 (61%)
CSF* Aß$_{42}$ (IQR)	594 (73)	733 (460)	488 (177)	732 (197)	537 (124)	722 (95)
CSF* total tau (IQR)	630 (764)	394 (477)	619 (217)	640 (492)	642 (486)	680 (546)
CSF* ptau (IQR)	85 (62)	60 (57)	73 (27)	85 (44)	81 (41)	82 (56)

NC, normal controls; MCI, mild cognitive impairment; AD, Alzheimer's disease; SD, standard deviation; IQR, interquartile range.
* median.

borderline CSF Aß$_{42}$ can already be indicative of underlying AD pathology. Future research should focus on discordant cases to clarify the underlying possibly neuropathological causality.

IC-P-006 EARLY AMYLOID ACCUMULATION AND ITS COGNITIVE CONSEQUENCES IN HEALTHY ADULTS

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Background: The recent failures of anti-amyloid clinical trials has led to a shift towards trials aimed at earlier intervention, underscoring the need for information about the earliest stages of amyloid accumulation and its impact on cognition. Autopsy and amyloid PET imaging data have converged to suggest that the orbitofrontal cortex (OFC) may be one of the earliest sites of amyloid accumulation, whereas posteromedial regions exhibit accumulation later and are potentially more closely linked to dementia onset. In the present study, we examined whether the OFC and penumbral regions may provide a window into the earliest stages of amyloid accumulation by measuring change in amyloid over 4 years, particularly in middle-aged adults and those who were initially amyloid-negative. Additionally, we assessed whether this early accumulation was associated with subtle cognitive deficits. In comparison, we also examined whether posteromedial amyloid accumulation appears later and is associated with AD-related cognitive deficits. **Methods:** 83 participants (age 30-89) were included from the Dallas Lifespan Brain Study who completed florbetapir PET and a cognitive battery at baseline and 4-year follow-up. Regional amyloid accumulation was measured (Time 2-Time 1 SUVR) in the following Freesurfer-derived ROIs: OFC ROIs (medial OFC, lateral OFC, pars orbitalis); Posteromedial ROIs (precuneus, posterior cingulate, isthmus cingulate). **Results:** Consistent with the lateral OFC and pars orbitalis as early sites of amyloid accumulation, accumulation was detected in both middle-aged adults and adults who were amyloid negative at baseline (Figure 1a). The rate of accumulation in lateral OFC and pars orbitalis was associated with deficits in follow-up reasoning performance (but not episodic memory or processing speed), even after restricting to those who were amyloid negative at baseline (Figure 2). In comparison, high precuneus amyloid accumulation was predominately restricted to older, amyloid positive adults (Figure 1b) and was associated with AD-typical deficits in episodic memory. **Conclusions:** These findings support the use of the OFC and penumbral regions as markers of the earliest stages of amyloid accumulation, and provide evidence that even at this early stage, negative consequences of amyloid accumulation may already be apparent.

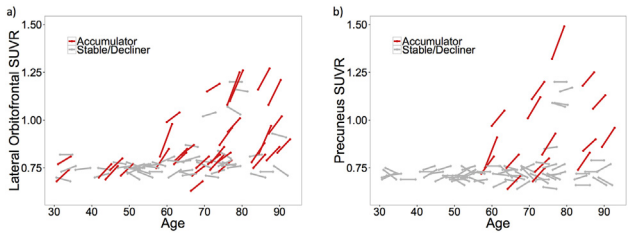

Figure 1. Regional Amyloid Accumulation over 4 Years across the Lifespan. Lines represent change in SUVR as a function of age for (a) lateral orbitofrontal cortex and (b) precuneus. Within each region, individuals were grouped into accumulators (red) and stable/decliners (gray) based on a cluster analysis. Consistent with the OFC as an earlier site of accumulation, chi-square tests revealed a higher proportion of accumulators in the lateral orbitofrontal cortex than the precuneus across the full sample, in middle-aged adults alone and in those who were amyloid negative at baseline.

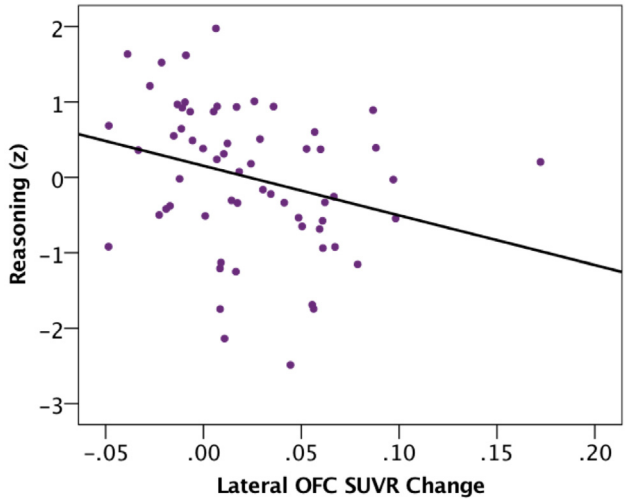

Figure 2. Cognitive Consequences of Early Amyloid Accumulation in OFC. In those who were amyloid negative at baseline, increasing regional amyloid accumulation in the lateral orbitofrontal was related to lower follow-up reasoning performance, suggesting accumulation in the OFC may have negative consequences for reasoning even at this early stage of disease progression.

IC-P-007 HOW AMYLOID PET CHANGES COGNITIVE CARE: A BROADER VIEW

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Background: Amyloid PET imaging is a reliable biomarker of Alzheimer's disease pathology and could prove valuable in clinical care. A standard formulation is that diagnostic testing should be performed only if it modifies drug or surgical treatment. There are, however, many additional reasons for knowing the cause of the cognitive impairment with greater certainty. Although some recommendations are relevant irrespective of diagnosis, others depend upon the specific cause of cognitive impairment identified. Provider confidence in the diagnosis also affects the willingness to discuss difficult, lifechanging recommendations. **Methods:** We identified 8 independent, non-drug care recommendations that would be altered depending upon the cause of cognitive impairment and used them as outcomes in a study of the clinical use of amyloid PET. Amyloid PET with 18F-flutemetamol was performed in 15 patients (9 men, 6 women, mean age 64.6, age range 51-85) whose diagnosis was uncertain after an otherwise complete dementia specialist evaluation. Scans were read visually, aided by quantitative analysis using Cortex ID software and classified as either positive indicating significant pathology or negative. We evaluated changes in physician diagnosis, diagnostic confidence and recommended care practices before and after amyloid PET imaging. **Results:** Significant binding in the cerebral cortex was present in 13 (87%) of the scans. In 14 patients (82%) recommended care practices changed after amyloid PET. These recommendations involved planning for likely stable or progressive disease course (33% change), monitoring for disease complications (13%), disease specific