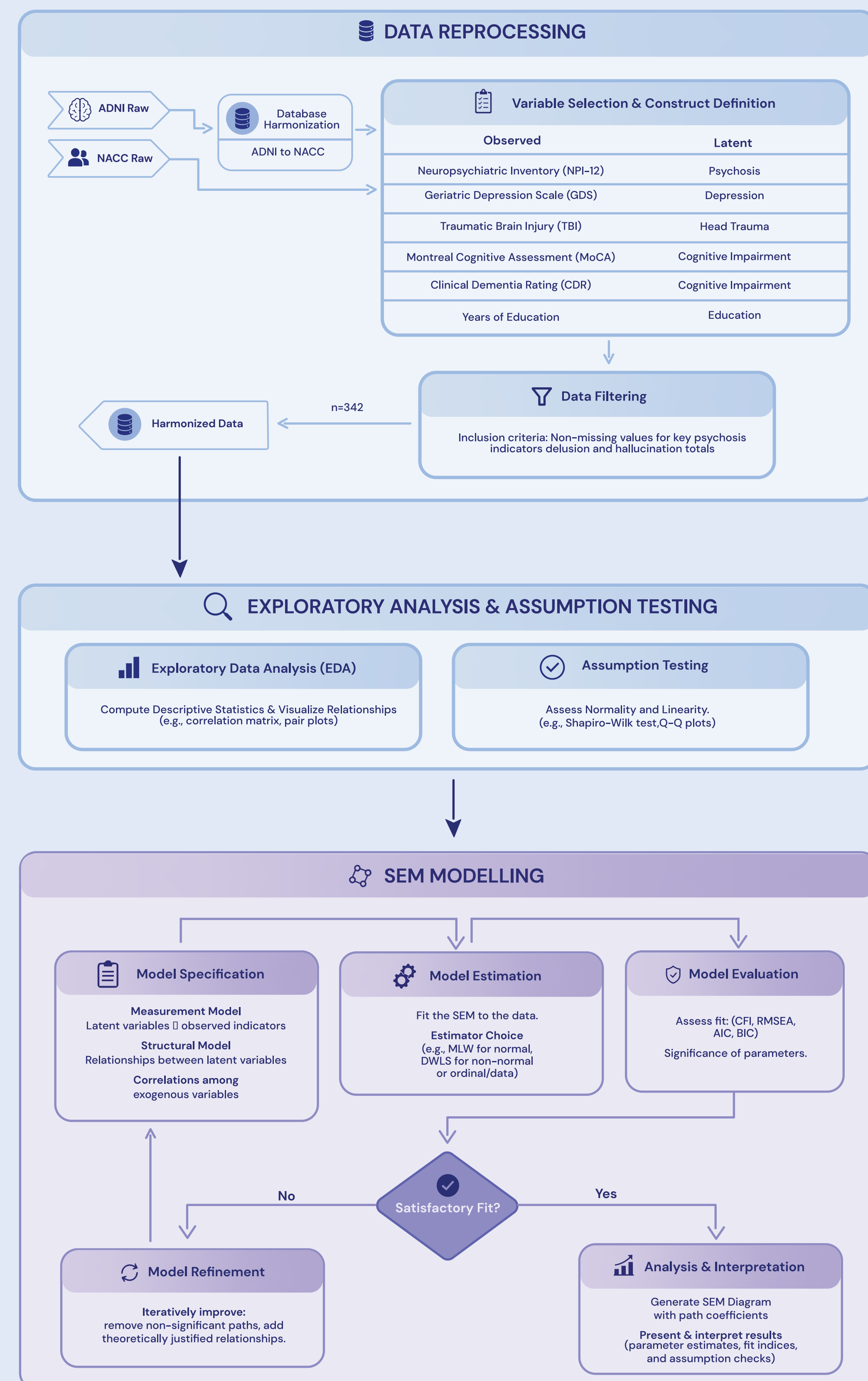




BACKGROUND

- Cognitive impairment in older adults arises from complex interactions among psychiatric symptoms, life experiences, and sociodemographic factors, yet these domains are often examined in isolation using univariate approaches.
- Structural equation modeling (SEM) has been applied in Alzheimer's disease research mostly to specific domains such as cerebrovascular disease or biomarkers¹, but rarely to model multiple clinical and sociodemographic factors within a single framework.
- This study applies SEM to examine the relative and correlated contributions of psychiatric symptoms, head trauma, and education to cognitive impairment, using data from ADNI and NACC.

METHODS



Participants and Data:

- n=342 participants drawn from clinical-based studies in ADNI and NACC.
- Inclusion criteria required non-missing values for delusion and hallucination totals; other clinical variables allowed missingness.

Constructs:

- Psychosis:** sum of NPI-12 delusion and hallucination items
- Depression:** Geriatric Depression Scale (GDS)
- Head trauma:** standardized NACC TBI indicators
- Education:** years of formal schooling
- Cognitive impairment:** CDR sum of boxes and MoCA

Analysis:

- SEM implemented in Python's Semopy, allowing parameter estimation with partially observed data without listwise deletion.

RESULTS

- Psychosis ($\beta=0.83$, $p<0.001$), depression ($\beta=1.19$, $p<0.001$), and head trauma ($\beta=0.68$, $p<0.001$) showed strong positive associations with cognitive impairment.
- Education showed a significant negative association ($\beta=-0.57$, $p<0.001$).
- Psychosis and depression were positively correlated ($r=0.54$, $p<0.01$).
- All factor loadings were significant ($p<0.01$) except the covariance between psychosis and education ($p=0.307$).

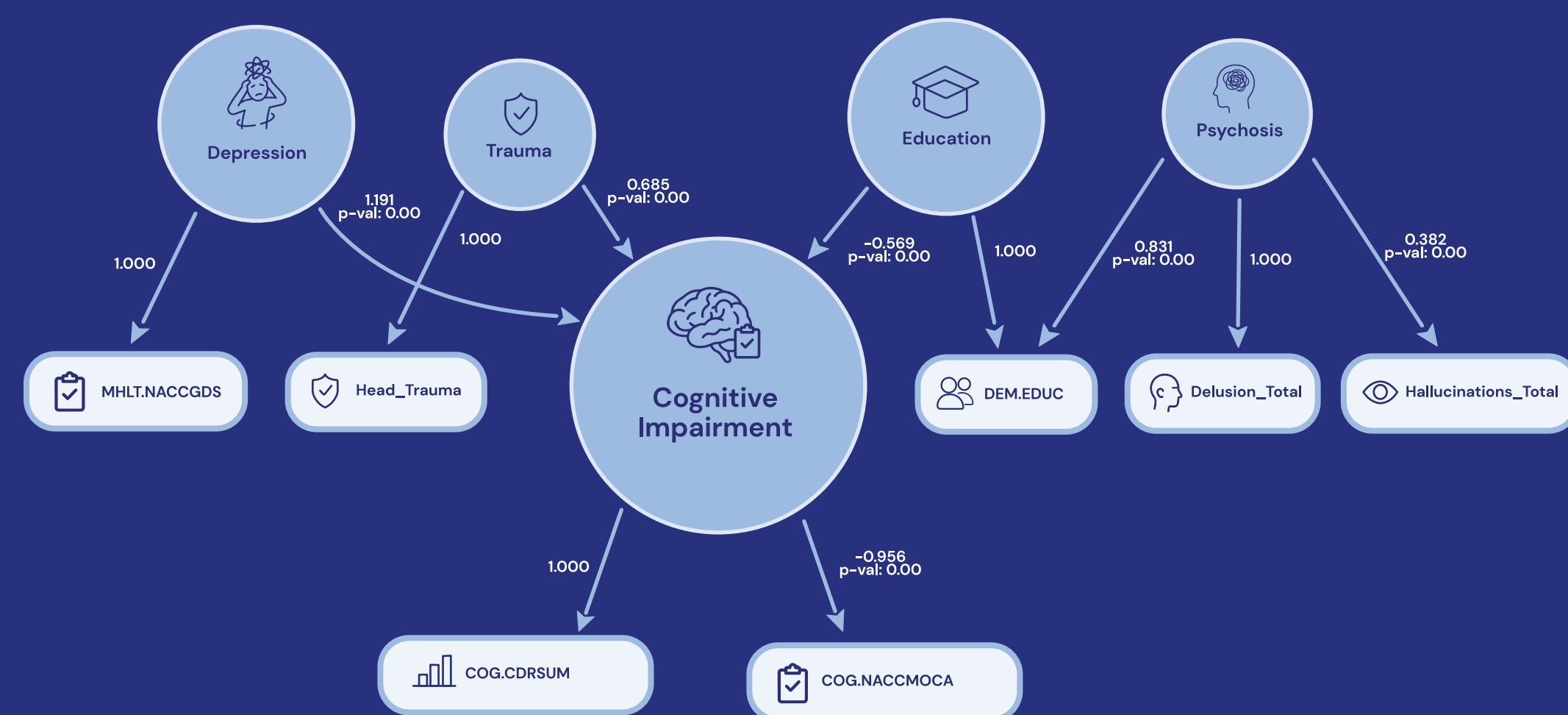


Figure 1. Structural equation model illustrating multifactorial contributors to cognitive impairment. Psychosis, depression, head trauma, and education were modeled as latent predictors of cognitive impairment using CDR sum of boxes and MoCA as indicators. Standardized coefficients and p-values are shown.



DISCUSSION

- The protective effect of education supports the cognitive reserve hypothesis. Higher educational attainment may delay the clinical onset of neurodegeneration without altering the underlying pathology.
- The association between head trauma and cognitive impairment is consistent with evidence that TBI accelerates neurodegenerative processes.
- The moderate psychosis–depression correlation likely reflects shared neurobiological mechanisms and frequent co-occurrence in older adults; a pattern that single-domain analyses tend to overlook.
- Unlike prior SEM studies in AD that focused on cerebrovascular mediators¹ or quality-of-life response shifts², this framework integrates psychiatric, traumatic, and sociodemographic domains within a single analysis.
- The non-significant psychosis–education covariance suggests these factors contribute through largely independent pathways.

CONCLUSION

Overall, this SEM analysis supports a multifactorial model of cognitive impairment in which psychosis, depression, and head trauma act as risk factors, while education shows a protective association. These findings are consistent with a multifactorial etiology of Alzheimer's disease and highlight the utility of SEM for uncovering complex pathways.



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