

## Cohort platform – 5-year work plan

The implementation of the National Cohort Integration Platform (NCIP) will comprise five work packages that will galvanize the unique availability of large, longitudinal cohorts, broad expertise in deep phenotyping, multimodal data analysis, preclinical modeling as well as the governance of large-scale multisite research programs into an accessible, transparent and interoperable infrastructure to support the translational chain within CHILDhealth and across DZKJ partner institutions. These work packages are: I) cohort integration, IT infrastructure and governance, II) development and roll-out of phenotyping SOPs and IT analysis framework, III) multimodal precision biomarkers of somatic and mental health risk, IV) Preclinical integration and developmental, and V) scientific communication and public relation.

*The cohort integration, IT infrastructure and governance work package* will implement a cohort communication platform within DZKJ and other German Health Centers and extend this to other national and international partners. It will include harmonization of clinical, laboratory, neuroimaging, ambulatory and omics measures available across the CHILDhealth cohorts with specific focus on the integration of birth, childhood and adolescent data, interoperability of longitudinal measures, as well as harmonization of environmental risk exposure data, and will develop an accessible and transparent IT framework that records data availability, manages consent requirements, and provides the basis for direct data integration, as well as distributed statistical and machine learning analysis. *The platform phenotyping SOPs and IT analysis work package* will establish a service unit and support center and roll-out SOP pipelines that facilitates DZKJ and other partners access to data, assistance with harmonized patient recruitment, patient consent management, and biomarker validation. *The precision biomarker discovery work package* will identify multimodal risk signatures for mental and somatic health, across clinical studies for patient stratification, and for transdiagnostic subgroups and neurobehavioral domains (RDoC), and address comorbidity. *The preclinical integration and developmental inference work package* will identify risk periods for onset of illness-relevant developmental trajectories, prioritize, and cross-validate findings in international NCIP cohorts. *The scientific communication and public relation work package* will focus on publication pipelines like for rationale, method and recommendation papers as well as papers on risk signatures and developmental time window-specific topics.

GANTT chart DZKJ National Cohort Integration Platform (NCIP)		Year 1	Year 2	Year 3	Year 4	Year 5
P1	Cohort registration, IT infrastructure and governance					
	MS1.1	Implementation of a cohort communication platform with DZKJ sites and other DZs (↔ ZIHUB)	█	█	█	█
	MS1.2	Extension of cohort communication platform to other national and international partners	█	█	█	█
	MS1.3	Consensus and implementation of scalable interoperable IT framework for cohort variable queries, designs, consents, accessibility	█	█	█	█
	MS1.4	Development of scalable governance infrastructure for data access	█	█	█	█
P2	Development and roll-out of phenotyping SOPs and IT analysis framework					
	MS2.1	Implementation of a NCIP support center for participating partners	█	█	█	█
	MS2.2	Consensus and roll-out of phenotyping SOPs with/to DZKJ sites and other DZs (↔ ZIHUB)	█	█	█	█
	MS2.3	Consensus and roll-out of IT analysis framework with/to DZKJ sites and other DZs (↔ ZIHUB)	█	█	█	█
	MS2.4	Consensus and roll-out of phenotyping SOPs with/to other national and international partners	█	█	█	█
	MS2.5	Consensus and roll-out of IT analysis framework with/to other national and international partners	█	█	█	█
P3	Multimodal precision biomarkers of somatic and mental health risk					
	MS3.1	Consensus and roll-out of distributed machine learning code with/to DZKJ sites, national and international partners	█	█	█	█
	MS3.2	Identification of multimodal signatures for mental and somatic health risk	█	█	█	█
	MS3.3	Identification and validation of transdiagnostic subgroups in mental and somatic illness	█	█	█	█
	MS3.4	Joint machine learning of mental and somatic illness for identification of comorbidity signatures	█	█	█	█
	MS3.5	Provisioning of risk-signatures across clinical studies for patient stratification	█	█	█	█
	MS3.6	Identification of multimodal signatures for transdiagnostic, neurobehavioral domains (RDoC)	█	█	█	█
P4	Preclinical integration and developmental inference (↔ Platforms 2-4)					
	MS4.1	Consensus and roll-out of distributed, multimodal normative modeling code with/to DZKJ sites, national and international partners	█	█	█	█
	MS4.2	Determination of normative models associated with multimodal signatures for mental and somatic illness	█	█	█	█
	MS4.3	Identification of individual-level, developmental trajectories associated with multimodal signatures	█	█	█	█
	MS4.4	Identification of risk periods for onset of illness-relevant developmental trajectories	█	█	█	█
	MS4.5	Prioritization of patients for mechanistic, cellular analysis through preclinical modeling	█	█	█	█
	MS4.6	Iterative optimization of multimodal, individual-level signatures based on mechanistic insight	█	█	█	█
P5	Scientific communication and public relation					
	MS5.1	Publication of NCIP rationale, methods and recommendations white paper	█	█	█	█
	MS5.2	Joint publication of time window-specific and overarching developmental signatures	█	█	█	█
	MS5.3	Joint publication of shared and specific signatures for somatic and mental health risk and protection	█	█	█	█
	MS5.4	Preparation of recommendations for prevention and treatment guideline development (↔ Platforms 3 and 4)	█	█	█	█
P5	MS5.5	Preparation of recommendations for stakeholders (↔ Platforms 3 and 4)	█	█	█	█