

The CEBA project

Chronic fatigue following acute EBV infections in adolescents

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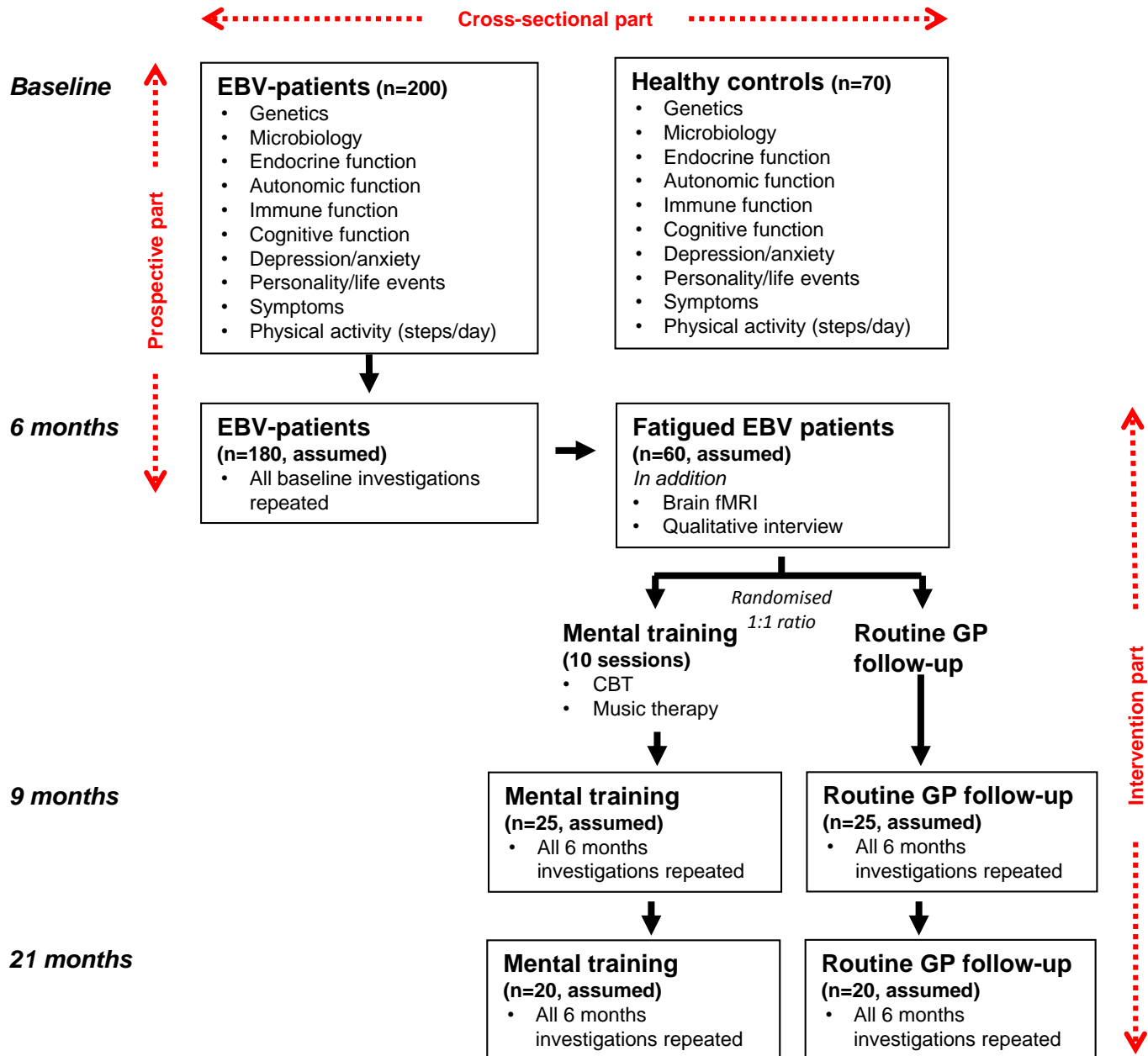
Background – the ‘sustained arousal’-model

Predisposing factors

Genetics

Personality

CEBA – design overview



Inclusion and exclusion

Inclusion criteria

Exclusion criteria

Criteria for the prospective and cross-sectional part (*applies to both patients and healthy controls)

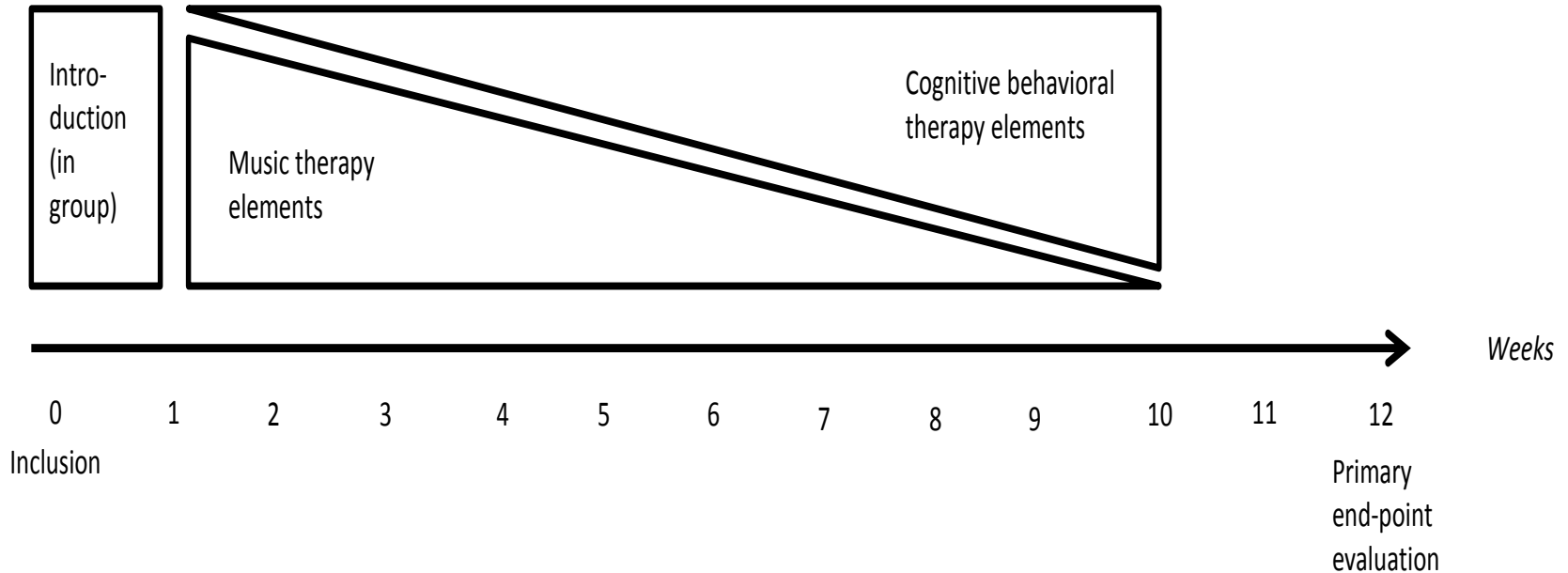
Age \geq 12 years and $<$ 20 years*

Serological confirmation of acute EBV infection

Lives in one of the following Norwegian counties: Oslo, Akershus, Buskerud, Vestfold, Østfold*

<i>EBV-VCA-IgM</i>	<i>EBV-VCA-IgG</i>	<i>EBNA-IgG</i>	<i>Interpretation</i>	<i>Conclusion</i>
Positive	Negative	Negative	Infection (debut 1-3 weeks ago)	Eligible
Positive	Positive	Negative	Infection (debut 2-8 weeks ago)	

Intervention



Differences from traditional CBT

- Tailored towards stress physiology and conditioned responses
- Music therapy included
- More focused on emotional aspects
- More focused on unconscious experiences
- Individually adjusted, parents included

Data – predisposing and precipitating factors

Genetics

- DNA from whole blood -> SNPs and epigenetics
- DNA from PBMC -> SNPs and epigenetics
- mRNA from whole blood

Personality/life events

- Child-Adolescent Perfectionism Scale
- Toronto Alexithymia Scale
- Brief Illness Perception Questionnaire
- The Penn State Worrying Questionnaire
- Life Event Checklist

Microbiology

- EBV PCR (blood and pharynx)
- EBV serology
- Co-infection serology (CMV, *Borrelia burgdorferi*)

Data – perpetuating factors

Cognitive function

- Digit span test
- Color-Word Interference Test
- Hopkins Verbal Learning Test
- IQ-test

Endocrinology

- Catecholamines: Plasma
- HPA-axis: Cortisol in plasma, urine, hair; ACTH in plasma

Autonomic cardiovascular control

Non-invasive, multivariate, real-time data acquisition of heart rate, blood pressures, stroke volume at

- Supine rest
- Fixed breathing
- Upright standing

Immunology

- Plasma cytokines (Multiplex and Elisa)
- NK cells: number and cytotoxic function
- PBMC: snap frozen for subsequent analyses

Data – symptoms and function

Symptoms

- **Chalder Fatigue Scale**
- Brief Pain Inventory
- Pain threshold (algometer)
- Autonomic Symptom Profile
- Karolinska Sleep Questionnaire
- Hospital Anxiety and Depression Scale
- CSF case definitions

Function

- **Steps/day (accelerometer)**
- Functional Disability Inventory
- Peds QL

Data – additional data in the RCT part

Brain fMRI

- Resting state -> Connectivity analyses

Semi-structured interview

- Experiences with the intervention program
- Affect consciousness

Biobank

Biobank

- Whole blood (DNA/epigenetics)
- PAXgene blood (RNA)
- PBMC
- Plasma
- Serum
- Urine (morning spot)

Progression

First patient included in prospective part:	March 2015
First patient included in RCT part:	October 2015
Prospective part completed:	Spring 2017
RCT part completed:	Autumn 2018