

FORM 2A- RESEARCH MASTER'S PSYCHOLOGY: RESEARCH INTERNSHIP RESEARCH PROPOSAL

1. GENERAL INFORMATION

1.1 Student information

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1.2 Supervisor information

Supervisor (*eligible for the ResMas*): Tessa Blanken

Note. Eligible supervisors are staff members of the Department of Psychology with a PhD-degree and appointed as examiner by the Examinations Board of the Department of Psychology.

Specialization: Psychological Methods

1.3 Other information

Date: 23.03.2022

Number of ECs for the research internship: 24 EC

Note. 1EC = 28 hours. Minimally 18EC and maximally 24EC. The total number of EC for the Internship and Thesis should be 50EC.

Ethics Review Board (ERB) code: _____

Note. See <https://www.lab.uva.nl/lab/ethics/>

Have your research proposal signed by your supervisor (see Section 9) and submit the signed research proposal and the two peer reviews via CANVAS. Please inform by email your supervisor and the secretariat of the research master psychology (thesis-researchmaster-psy-fmg@uva.nl) that you submitted your research proposal.

9. SIGNATURES

- ☐ I hereby declare that both this proposal, and its resulting internship, will only contain original material and is free of plagiarism (cf. Teaching and Examination Regulation in the research master's course catalogue).
- ☐ I hereby declare that the results section of the internship report will consist of two subsections, one entitled "confirmatory analyses" and one entitled "exploratory analyses" (one of the two subsections may be empty):
- a) The confirmatory analysis section reports *exactly* the analyses proposed in Section 4 of this proposal
 - b) The exploratory analysis section contains not previously specified, and thus exploratory, analyses.

Location:

Student's signature:

Supervisor's signature:

Amsterdam



Research Internship Proposal

Emily Campos Sindermann

March 2022

1 Title and Summary of the Research Project – *words: 150/150*

1.1 Title

Making the Connections: Exploring the Validity and Clinical Utility of Self-reported Personalized Networks.

1.2 Summary of Proposal

While scientific advancements in the past decades have vastly contributed to increase our physical well-being, they failed to target our mental pain. Today, Major Depressive Disorder (MDD) represents a leading cause of burden worldwide. As there is accumulating evidence in favor of MDDs heterogeneous structure, it is crucial to focus on individual symptom dynamics to increase treatment efficacy. Within this project we will investigate Perceived Causal Networks (PECAN) as a method to generate personalized networks. To this end, we will investigate whether PECAN grasps the heterogeneity of MDD, whether there are PECAN characteristics relating to severity and chronicity of the disorder, how PECAN can be used to examine specific symptom pairs, taking mood-insomnia links as an example. Ultimately, establishing the methods' validity and clinical utility is key to explore its potentially major implications for personalized psychotherapy.

2 Project Description – *words: 1200/1200*

There appears to be an alarming disparity between increasing efforts to provide evidence based mental health treatment and the global prevalence of mental disorders (GBD 2019 Mental Disorders Collaborators, 2022). While medical science has shifted towards more individualized treatment, generally referred to as “precision medicine”, the field of psychology lags behind (Cuthbert & Insel, 2013). Despite an increase of people seeking treatment, there is no evidence for a decrease in the burden of mental disorders since 1990 (GBD 2019 Mental Disorders Collaborators, 2022).

With an estimated 279.6 million cases in 2019, Major Depressive Disorder (MDD) is among the most prevalent mental disorders worldwide (GBD 2019 Mental Disorders Collaborators, 2022). However, there is still a lack of understanding regarding its co-occurrence with other disorders (comorbidity) (Fried, 2015), as well as the observed heterogeneity between patients (Fried & Nesse, 2015). One potential reason for these unresolved issues can be traced back to the predominant categorical conceptualization of mental disorders (Fried, 2015). In the quest to better understand, diagnose and treat mental disorders, the field has been searching for *common causes* and categorizing certain symptom constellations respectively (Borsboom, 2017). This *common cause framework* suggests that symptoms are interchangeable and causally independent manifestations of an underlying cause (Borsboom, 2008). Individuals are thus grouped together using an unweighted sum-score of their symptoms and cut-offs, resulting in hard boundaries between disorders as well as between “healthy” and “unhealthy” individuals (Fried, 2015). This forces treatment providers to treat individuals based on group-level findings, also referred to as the *therapist’s dilemma* (Piccirillo, Beck, & Rodebaugh, 2019).

The network approach to psychopathology (Borsboom, 2008), offers an alternative way to conceptualize mental disorders. Here, the latent variable (common cause) is abandoned altogether and mental disorders are viewed as systems of mutually interacting symptoms. Hence, psychopathological phenomena are not explained by one cause per se but rather by their underlying complex symptom dynamics (Borsboom & Cramer, 2013). In theory, (degree) centrality (connectedness of a symptom) may be thought of as a main risk factor for activating further symptoms, (causal) feedback loops are thought to be associated with disorder maintenance, and network connectivity (density) may be an indicator of how prone a network is to phase transitions (transitions between “healthy” and “unhealthy” states) (see Figure 1). Furthermore, comorbidity is thought to arise via “bridge symptoms” connecting symptom clusters of different disorders (Fried et al., 2017). The network theory of mental disorders is extended by the network methodology, allowing us to estimate networks from empirical data (Fried, 2017). This combination of an innovative theoretical foundation and sophisticated statistical tools offers a new perspective to better understand the nature of mental disorders and advance precision medicine in psychopathology.

While nomothetic (group-level) networks estimated from cross-sectional data can provide clues about symptom relations across individuals, they do not allow us to examine within-person dynamics. To identify causal pathways in idiographic (personalized) networks, most studies have relied on the collection of time-series data through ecological momentary assessment (EMA) (Fisher, Reeves, Lawyer, Medaglia, & Rubel, 2017; Stone & Shiffman, 1994). Hereby, individuals are asked to report on their psychological state on

multiple occasions over time. However, there are considerable concerns about the methods’ feasibility and validity regarding missing data (Bentley, Kleiman, Elliott, Huffman, & Nock, 2019), identifying appropriate time frames to capture symptom dynamics (Fried et al., 2017), participant burden (Zimmermann et al., 2019), and failure to incorporate prior clinical knowledge (Burger et al., 2020). In fact, temporal networks from EMA data appear to differ considerably from case conceptualization, a common process in which therapist and client jointly identify present issues and adapt treatment decisions respectively (Kuyken, Padesky, & Dudley, 2008). This additionally increases clinicians’ hesitancy to employ the method in practice (Burger et al., 2020).

An alternative way to investigate causal relations between symptoms is “Perceived Causal Relationship” (PCR) scaling (Frewen, Allen, Lanius, & Neufeld, 2012). In this method, individuals first identify a set of symptoms S . In a second step, they indicate for each symptom pairing (s_i, s_j) where $s_i, s_j \in S$, the perceived reciprocal relations r_{ij}, r_{ji} , where r_{ij} is the causal relationship from s_i to s_j . Thereby, the individuals themselves build an adjacency matrix containing their perceived symptom relations, which is then translated into a network. Not only can PCR scaling be used by clinicians to include prior clinical knowledge into theory formation (Deserno et al., 2020), but it can also serve as a time-efficient tool to generate idiographic networks in psychotherapy (Borsboom & Cramer, 2013). Hence, this method could be crucial to establish a reciprocal knowledge stream in the quest to narrow the gap between research and practice. However, the methods’ validity is still understudied (Frumkin, Piccirillo, Beck, Grossman, & Rodebaugh, 2021).

Recently, Klintwall and colleagues (Klintwall, Bellander, & Cervin, 2021) have proposed Perceived Causal Networks (PECAN), a clinically adapted version of PCR including network visualizations. In their study, they investigated heterogeneity, completion times, and immediate test–retest reliability of PECAN results. Furthermore, psychotherapists rated PECAN visualizations regarding their clinical utility. Contrary to prior hesitancy towards incorporating idiographic models in practice (Zimmermann et al., 2019), 96% rated the networks as useful, and judged them to cover almost 50% of the information typically assessed by a professional. Thus, PECAN might offer a time-efficient and empirically quantifiable alternative to case conceptualization and serve as a first step in the collaboration between therapist and client.

The current project, supervised by Tessa Blanken (University of Amsterdam – *Psychological Methods*), and in collaboration with Lars Klintwall (Stockholm University – *Clinical Psychology*) and Julian Burger (University of Amsterdam – *Psychological Methods*), aims to further explore the validity and clinical utility of PECAN. We will investigate the following research questions (RQ):

1. Does PECAN account for the heterogeneity of MDD on an individual-level?
2. Are there PECAN characteristics that relate to symptom severity and symptom chronicity?
3. What are the PECAN interrelations between symptoms of MDD and insomnia?

Firstly, we will examine whether PECAN accounts for the heterogeneous structure of MDD. In line with various studies reporting heterogeneity in idiographic models of MDD (Klintwall et al., 2021; Hebbrecht et al., 2020; Fried, 2017), we expect that PECAN results will exhibit high variability regarding symptom constellation, centrality, and feedback loops. Furthermore, we will compare PECAN results with a group-level network of MDD. These are crucial insights to separate between- from within-person effects (Fried et al., 2017). Secondly, we will investigate whether there are PECAN characteristics that relate to symptom severity and symptom chronicity. Previous findings have been inconclusive as to whether network density indicates symptom severity (Pe et al., 2015; Frumkin et al., 2021), however, the number of feedback loops has been linked to symptom frequencies in PCR networks (Frewen, Schmittmann, Bringmann, & Borsboom, 2013). Lastly, we will use PECAN to “zoom” in on specific symptom connections by focussing on the links between symptoms of MDD and insomnia. MDD and insomnia symptoms often co-occur, with insomnia being a primary risk factor for the development of MDD (Baglioni et al., 2011). A previous study by Blanken and colleagues (Blanken et al., 2019), investigated cognitive-behavioral therapy for insomnia (CBTI) induced effects on symptoms on insomnia and MDD, and found that CBTI improved symptoms of MDD indirectly via insomnia symptoms. This suggests that there are causal pathways between symptoms of both disorders. We are interested to see how these dynamics are perceived by individuals.

3 Procedure – *words: 1000/1000*

3.1 Operationalization

The RQs will be operationalized as follows:

1. *Does PECAN account for the heterogeneity of MDD on an individual-level?* – Heterogeneity will be measured by the observed variability in [a-d] among PECAN results, and in (e) between an averaged PECAN and a group-level network. The more these characteristics differ, the more heterogeneity will be assigned to the sample.

- a) *What is the variability between individual symptom profiles?* – We will focus on the number of included symptoms and their constellation.
 - b) *How are symptom pairs related to each other?* – We will see whether (prominent) symptom pairs differ in their causal relationship. We will investigate whether one symptom is predominantly perceived as the cause for the other (see Figure 1) or whether there is a perceived bidirectional relationship between symptoms (see Figure 1b).
 - c) *How do feedback loops vary across individual PECAN results?* – Feedback loops will be defined as any s_1, \dots, s_n , where $n > 1$ that create a closed causal chain (see Figure 1c & 1d). We will focus on their presence and constellation.
 - d) *How does symptom centrality vary across individual PECAN results?* – As a measure of centrality we will use out-degree centrality referring to the number of connections going "out" of a symptom. The more out-going connections a symptom has, the higher its centrality (see Figure 1e).
 - e) *To what extent do PECAN results match group-level network findings?* – We will investigate this by taking the average of the PECAN results and comparing the resulting network structure with a group-level MDD network e.g., a recently published summary network of robust MDD edges (Malgaroli, Calderon, & Bonanno, 2021).
2. *Are there PECAN characteristics that relate to symptom severity and symptom chronicity?* – We will look at density and feedback loops. Density is derived from network connectivity which is constituted out of the number of present connections in the network (see Figure 1g & 1h). For both feedback loops and density we will use a binary measure (*Optional:* If there is time left, we will consider their weighted scores). Symptom severity will be operationalized by PHQ-9 scores. Symptom chronicity will be operationalized by the self-reported duration of symptomatology.
3. *What are the PECAN interrelations between symptoms of MDD and insomnia?* – We will look at the directionality of relations between MDD and insomnia specific symptoms. We are interested in examining whether symptoms of one disorder are predominantly perceived as causes of symptoms of the other disorder or whether their relationship is of a bidirectional nature (see Figure 1a & 1b).



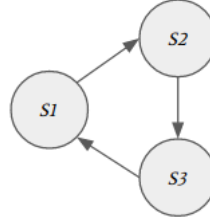
(a) There is a directed edge from S_1 to S_2 . S_1 is thought to *cause* S_2 .



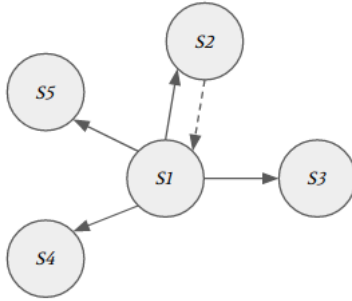
(b) The symptoms *cause* each other (*bidirectional* relationship).



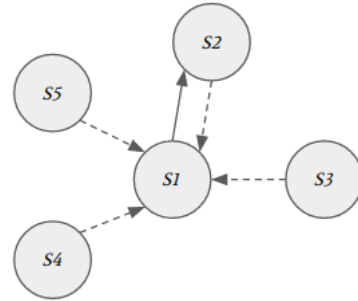
(c) Feedback loop including $n = 2$ symptoms.



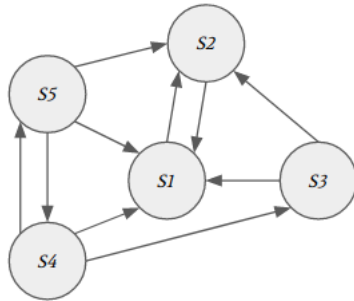
(d) Feedback loop including $n = 3$ symptoms.



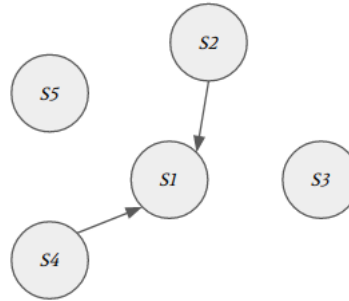
(e) S_1 is the most central symptom with a high *out-degree centrality*.



(f) S_1 is the most central symptom with a high *in-degree centrality*.



(g) Densely connected network.



(h) Sparsely connected network.

Figure 1: Directed network structures.

3.2 Dataset

We will explore an existing dataset by Lars Klintwall (Klintwall et al., 2021).

Participants. Participants had to rate item severity and causal relations twice. To ensure reliability of the subjects’ responses, we will only include respondents with an immediate test-retest reliability above 0.5 (see Figure 2). This results in the exclusion of 161 participants. The resulting dataset constitutes $N_{total} = 265$ respondents (226 female, 36 male, and 3 other), consisting of $N_{PHQ \geq 10} = 163$ and $N_{PHQ < 10} = 102$, with a mean age of 38.89 years.

Procedure. Within the online PECAN questionnaire, participants first had to give their consent. Then, respondents were asked to select between seven and 15 behavioral/emotional problem items (symptoms) they had experienced during the past week (see Table 1). The current list of symptoms was chosen due to acceptable reliability and high therapist ratings in pilot data. Afterwards participants had to rate each selected symptom for “severity” on a 0-100 scale. Before rating the perceived causal relations, participants had to undergo three training trials in which their understanding of causality was tested in three multiple choice questions. Only if answered correctly, participants were allowed to continue with the questionnaire. To rate the perceived causal relations, participants had to report for each symptom, to what degree it was caused by ≤ 3 other selected symptoms (or select “none”). If > 1 symptoms were selected as causes for a given symptom, the participant had to indicate the perceived causal strength of the causal relationship in form of percentages. Percentages could also be assigned to an option “other causes / don’t know”. The sum score of assigned percentages should be 100%, to circumvent participants’ assigning 100% to each causal relationship. The questionnaire only assessed positive relationships (if there was a causal link between s_1 and s_2 , s_1 was thought to *increase* s_2). Furthermore the questionnaire did not allow for emotion-to-emotion causality, as pilot data indicated lower therapist ratings otherwise (e.g., if one of symptoms 18-26 was selected, symptoms from 18-26 could not be selected as a possible cause). As an immediate test-retest, participants were asked to repeat the severity and causal ratings (no item re-selection). Lastly, to assess depressive severity participants completed the Patient Health Questionnaire (PHQ-9) covering the DSM-5 criteria for MDD. Furthermore, participants indicated their background information including their gender, age, education level, and experience with Cognitive Behavioural Therapy (CBT). Participants who identified as depressed additionally reported their duration of symptomatology (see Figure 3 for procedure visualization).

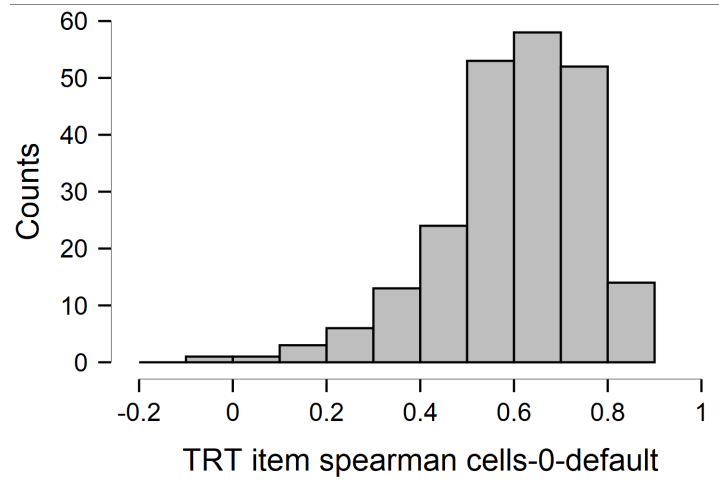


Figure 2: Test-retest reliability of PECAN.

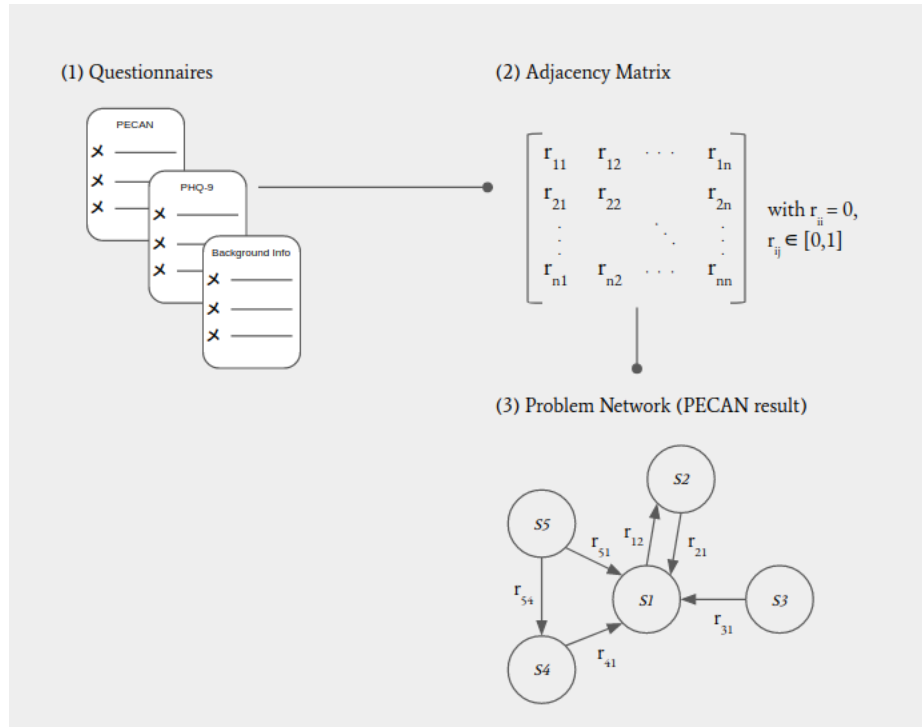


Figure 3: Procedure of PECAN.

Number	Item	Disorder
1	Eats less	Depression
2	No exercise	Depression
3	Sleep problems	Depression + Insomnia
4	Daytime resting	Depression + Insomnia
5	Conflicts	Depression
6	Hypochondric worries	Depression
7	Trouble concentrating	Depression
8	Social media use	Depression
9	Stays at home	Depression
10	Procrastinates	Depression
11	Substance use	Depression
12	Self-harm	Depression
13	Suicidal thoughts	Depression
14	Eats more	Depression
15	Compulsions (incl. avoid)	Depression
16	Ruminates (incl. avoid)	Depression
17	Worries (incl. avoid)	Depression
18*	Flashbacks (incl. avoid)	Depression
19*	Panic (incl. avoid)	Depression
20*	Pain (incl. avoid)	Depression
21*	Social anxiety (incl. avoid)	Depression
22*	Alone/sad (incl. avoid)	Depression
23*	Tired (incl. avoid)	Depression + Insomnia
24*	Stressed (incl. avoid)	Depression
25*	Bored (incl. avoid)	Depression
26*	Angry (incl. avoid)	Depression

Table 1: PECAN items. 15-26 included avoidance in their description as a cause. (*) denotes emotions.

3.3 Data Analysis

To investigate PECAN heterogeneity in a sub-sample with depressive complaints ($N_{PHQ \geq 10}$), we will use descriptive statistics (RQ1). We will identify feedback loops using the R-package **LoopAnalyst** (Dinno & Dinno, 2018). To ensure computational feasibility we will only calculate feedback loops including a maximum of four symptoms. To calculate centrality we will use the R-package **qgraph** (Epskamp, Cramer, Waldorp, Schmittmann, & Borsboom, 2012). For RQ2 we will focus on density and the number of feedback loops as predictor variables and on symptom severity (N_{total}) and symptom duration (sub-sample that identified as depressed) as outcome variables. First we will explore their separate correlations. Then, we will compute two linear models in R (one for each outcome variable). In RQ3 we will use descriptive statistics (using N_{total}). We will focus on *Alone/sad*, *Bored* and *Tired* as MDD symptoms, as these are often seen as bridge symptoms connecting both disorders. We will focus on *Sleep Problems* and *Daytime resting* as insomnia specific symptoms.

4 Intended Results – *words: 250/250*

In general, this line of research does not allow us to directly deduce information about the “true” underlying personal disorder dynamics, but only about how these are *perceived* by the individual. These insights are crucial for clinical practice to provide patient-centered care, stimulate a collaborative patient-therapist relationship, and thereby increase the efficacy of individualized treatment. If we find a high variability in PECAN results (RQ1), our findings would align with previous studies arguing for the heterogeneity of MDD, and thereby provide support for the methods’ validity. If we find less variability, this could indicate that PECAN identifies prominent symptom constellations and interrelations, but fails to grasp more fine-grained individual dynamics. While PECAN could then still be used to actively incorporate the patient in the therapeutic process, its added clinical value would be debatable. Further research should then focus on ways to optimize PECAN. If we find PECAN characteristics that predict symptom severity and/ or chronicity (RQ2), this could imply that PECAN could be used to infer treatment decisions. Further research should then focus on the effect of interventions based on PECAN, compared to other methods. If we find no significant effect, it could be that the examined characteristics are more representative of different response styles than actual underlying symptom dynamics. Future research should then focus on identifying different response styles and establish which sub-populations could benefit from PECAN. Investigating the directionality between symptoms of MDD and insomnia (RQ3) could help us to select more promising targets for prevention and intervention.

5 Work Plan – *words: 295/500*

The current research internship project is composed out of 24 EC (1 EC corresponding to 28 hours of work), and will be conducted from February 2022 to June 2022. The project includes one weekly meeting with the supervisor (Tessa Blanken) as well as collaborators (Lars Klintwall and Julian Burger), which are attended via zoom. Due to the courses ”Statistics 1” (3 EC, February 2022) and ”Structural Equation Modeling 1: Confirmatory Factor Analysis” (3 EC, March 2022), I will work half time on the project in the months of February and March (21 hours per week), and full time in the remaining months (42 hours per week). So far, we have used the months of February and March 2022 to conceptualize the research project, write the research proposal (Deadline: 24.03.20), and structure and translate the data (from Swedish to English). The period from April 2022 until mid of May 2022 is planned for data analysis and data visualization in R. We will first focus on the research plan provided in the procedure section. In case there is still time we will further

explore the parts denoted as *Optional* in the procedure section. The period from mid May 2022 until the end of June 2022 will be allocated towards the final report (Expected date of submission: 30.06.2022). The findings will be presented in the form of a poster presentation at the annual Research Master's Psychology Conference in October 2022 (see Figure 4 for an overview of the time plan). This project conforms to the storage protocol of the Research Institute of Psychology of the University of Amsterdam. The available budget of 25 EUR will be allocated towards printing costs of the final poster.

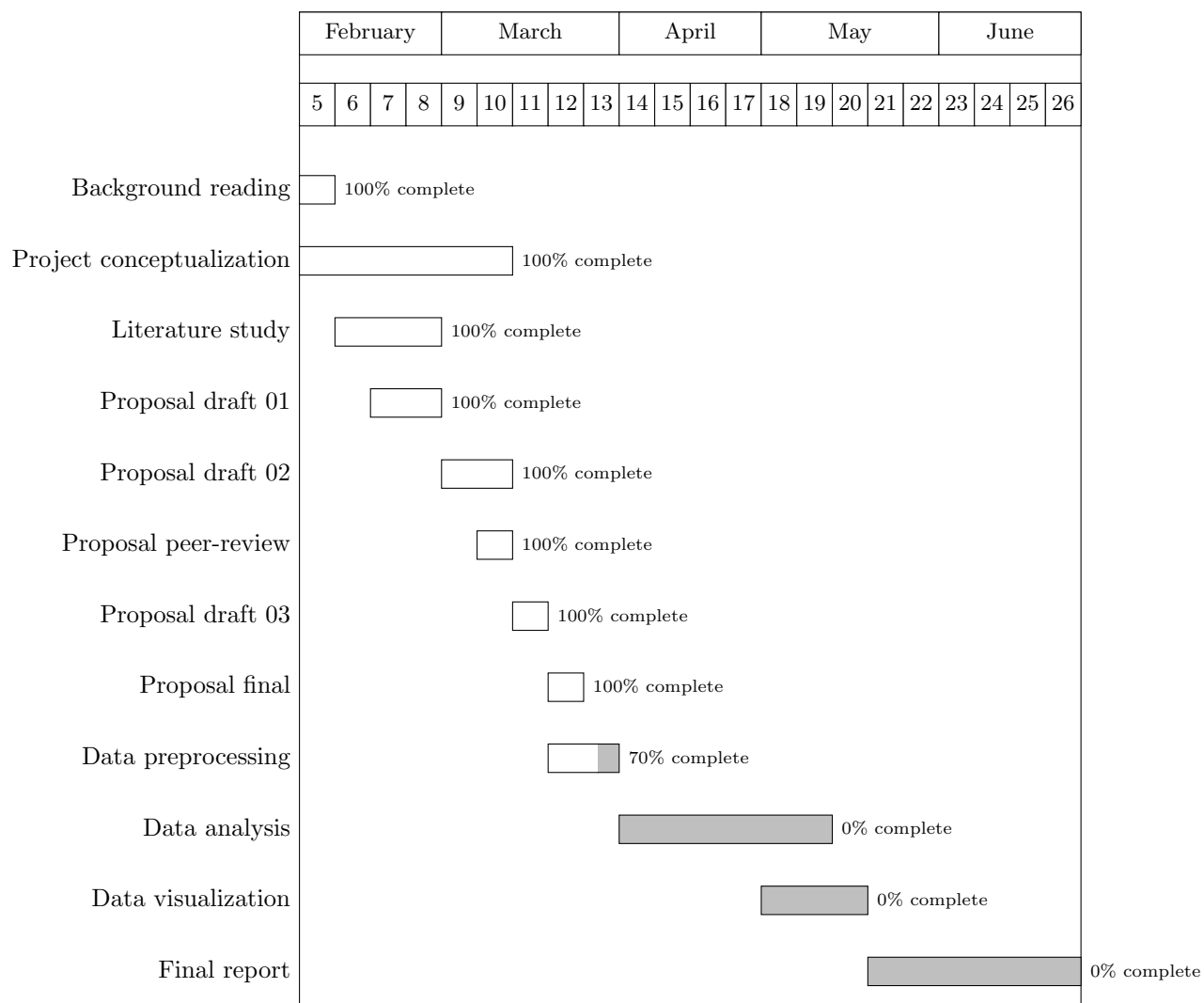


Figure 4: Overview of the time plan per calendar week.

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