WP7: EVALUATION REPORT

The effects of a case management approach on the quality of life of rare disease patients in Salaj, Romania: a pilot randomised control trial of efficacy

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TABLE OF CONTENTS

1. ABSTRACT ..... - 8 -

2. QUANTITATIVE ANALYSIS ..... - 10 -

2.1 INTRODUCTION ..... - 10 -
2.1.1 Background ..... - 10 -
2.1.2 Research Questions ..... - 11 -

2.2 METHODS ..... - 12 -
2.2.1 Trial Design ..... - 12 -
2.2.2 Participants ..... - 14 -
2.2.3 Intervention ..... - 15 -
2.2.4 Outcomes ..... - 20 -
2.2.5 Sample Size ..... - 25 -
2.2.6 Randomisation ..... - 26 -
2.2.7 Implementation ..... - 32 -
2.2.8 Blinding ..... - 32 -
2.2.9 Statistical Methods ..... - 32 -

2.3 RESULTS ..... - 35 -
2.3.1 Participant flow ..... - 35 -
2.3.2 Recruitment ..... - 39 -
2.3.3 Baseline Data ..... - 39 -
2.3.4 Numbers Analysed ..... - 40 -
2.3.5 Outcomes and Estimation ..... - 40 -
2.3.6 Ancillary Analyses ..... - 85 -
2.3.7 Harms ..... - 99 -

2.4 DISCUSSION ..... - 99 -
4.2.1 Limitations ..... - 99 -
4.2.2 Generalisability ..... - 100 -
4.2.3 Interpretation ..... - 100 -

3. QUALITATIVE ANALYSIS ..... - 104 -

3.3 THE NETWORKS OF THE CASE MANAGERS: 1ST AND 2ND PHASE OF THE INNOVCARE PILOT- 104 -
3.3.5 Case manager 1 ..... - 104 -
3.1.2 Case manager 2 ..... - 106 -
3.1.3 Case manager 3 ..... - 107 -
3.1.4 Case manager 4 ..... - 109 -
3.1.5 List of institutions/contacts ..... - 110 -
3.1.6 Changes in the network and duration of contacts ..... - 114 -
3.1.7 Frequency of communication ..... - 115 -
3.1.8 Organisations missing in the network ..... - 116 -
3.1.9 Exchange of information between case managers ..... - 117 -
3.1.10 Community support network ..... - 118 -

3.2 The INNOVCare Intervention ..... - 118 -
3.2.1 Description of work as a case manager with the patients and their families in the framework of the INNOVCare project ..... - 118 -
3.2.2 Number of cases ..... - 120 -
3.2.3 Needs of patients ..... - 120 -

3.2.4 Solving the needs of the patients ..... - 121 -
3.2.5 Time dedicated to each case and determining the intensity of work ..... - 122 -
3.2.6 Determining the achievement of goals..... - 122 -
3.2.7 Well working aspects ..... - 123 -
3.2.8 Challenges and not well working aspects ..... - 123 -
3.2.9 Differences between case management service and previous tasks/offers for patients and their families - 124 -
3.2.10 Contacts with participants from the 1st cohort after the intervention..... - 125 -
3.2.11 Independent management of care by patients through support of case management ..... - 125 -
3.2.12 Was the 9 months intervention period enough? ..... - 126 -
3.2.13 Conclusions by case managers ..... - 126 -

4. NETWORK ANALYSIS: THE NETWORKS OF SERVICE PROVIDERS ..... - 127 -

4.1 Assessment of cooperation between services 2016 (before first phase of intervention) . - 128 -

4.2 Assessment of cooperation between services 2017 (first phase of intervention)..... - 129 -

4.3 Assessment of cooperation between services 2018 (second phase of intervention)..... - 130 -

5. CONCLUSIONS AND RECOMMENDATIONS ..... - 131 -

6. ANNEXES ..... - 133 -

6.1 R Markdown document ..... - 133 -

6.2 Intensity of communication between the case manager and service providers ..... - 133 -

6.3 Interview guideline: Phase 1 ..... - 134 -

6.4 Interview guideline: Phase 2 ..... - 136 -

7. OTHER INFORMATION..... - 138 -

8. REFERENCES ..... - 139 -

TABLE OF TABLES

Table 1: The TIDieR (Template for Intervention Description and Replication) Checklist (Appendix 3 of (Hoffmann, et al., 2014; 348)) ..... - 15 -
Table 2: The different versions of the patient questionnaire, their components and target groups ..... - 20 -
Table 3: Representativeness of the selected sample to the rest of the population (1st selection) ..... - 26 -
Table 4: Balancing test for the full sample (1st selection) ..... - 28 -
Table 5: Representativeness of the final INNOVCare Sample to the rest of the population ..... - 30 -
Table 6: Balancing table for the final INNOVCare sample ..... - 31 -
Table 7: Baseline demographics of the INNOVCare pilot sample ..... - 39 -
Table 8: n analysed by measurement tool for quality of life and by objectives for direct objectives of the pilot ... - 40 -
Table 9: DISABKIDS-SMILEY descriptive statistics ..... - 43 -
Table 10: anova results - disabkids – smileys ..... - 44 -
Table 11: Mauchly's Test for Sphericity - DISABKIDS - SMILEYS ..... - 44 -
Table 12: DCGM-12 descriptive statistics ..... - 44 -
Table 13: anova results dcgm-12 (short version) ..... - 46 -
Table 14: mauchly's test for sphericity - dcgm-12 (short version) ..... - 46 -
Table 15 Sphericity Corrections -"DCGM-12 (SHORT VERSION)" ..... - 46 -
Table 16: EQ-5D-Y descriptive statistics ..... - 47 -
Table 17: ANOVA RESULTS EQ-5D-Y ..... - 48 -
Table 18 MAUCHLY'S TEST FOR SPHERICITY - "EQ-5D-Y" ..... - 49 -
Table 19 SPHERICITY CORRECTIONS -"EQ-5D-Y" ..... - 49 -
Table 20: The control and intervention trial making up the INNOVCare pilot by cohort ..... - 49 -
Table 21: Knowledge of disease/condition: Between-groups ..... - 54 -
Table 22: Knowledge of disease/condition: Within-groups ..... - 55 -
Table 23: Understanding of rights as patients: Between-groups ..... - 57 -
Table 24: Understanding of rights as patients: Within-groups ..... - 58 -
Table 25: Knowledge on available health and social services: Between-groups ..... - 59 -
Table 26: Knowledge on available services: Within-groups ..... - 60 -
Table 27: Ability of self-management of care: Between-groups ..... - 61 -
Table 28: Ability to manage own care: Within-groups ..... - 63 -
Table 29: Communication skills: Between-groups ..... - 64 -
Table 30: Communication skills: Within-groups ..... - 65 -
Table 31: Number of people in contact with people in a similar situation by cohort (patient) ..... - 66 -
Table 32: Coordination among providers: Between-groups ..... - 69 -
Table 33: Coordination among providers: Within-groups ..... - 70 -
Table 34: Understanding and acceptance in the community: Between-groups ..... - 71 -
Table 35: Understanding and acceptance in the community: Within-groups ..... - 72 -
Table 36: Summary of the outcome variables from the patient dataset: between-groups ..... - 74 -
Table 37: Summary of the outcome variables from the patient dataset for the 1st cohort (n=24): within-groups - 75 -
Table 38: Summary of the outcome variables from the patient dataset for the 2nd cohort (n=26): within-groups - 76 -
Table 39: Between-groups analysis of the outcome variables at month 9 based on the family dataset ..... - 79 -
Table 40: Within-groups analysis of the outcome variables for the 1st cohort (n=55) based on the family dataset- 82 -
Table 41: Within-groups analysis of the outcome variables for the 2nd cohort (n=48) based on the family dataset- 83 -
Table 42: Number of people in contact with people in a similar situation by cohort (family) ..... - 84 -
Table 43: Linear Mixed Effects MODEL – DISABKIDS - SMILEYs ..... - 86 -
Table 44: LINEAR MIXED EFFECTS MODEL -DCGM-12 (Short Version) ..... - 87 -
Table 45 LINEAR MIXED EFFECTS MODEL - "EQ-5D-Y" ..... - 89 -
Table 46: Efficacy of the INNOVCare intervention on NoRo beneficiaries vs. external patients by cohort (patient perspective) ..... - 90 -
Table 47: Efficacy of the INNOVCare intervention on different age groups by cohort (patient perspective) ..... - 91 -

Table 48: Efficacy of the INNOVCare intervention on different genders by cohort (patient perspective)..... - 92 -
Table 49: Efficacy of the INNOVCare intervention on people living in different locations by cohort (patient perspective) ..... - 94 -
Table 50: Efficacy of the INNOVCare intervention according to levels of disability by cohort (patient perspective)- 96 -
Table 51: Subgroup analysis of family data..... - 98 -

TABLE OF FIGURES

Figure 1: The INNOVCare evaluation design - a basic two-condition repeated measures design / rotation design (adapted from (Field & Hole, 2003, p. 82)) ..... - 13 -
Figure 2: Expected changes ..... - 41 -
Figure 3: Distribution of scores of the DISABKIDS-SMILEY tool ..... - 42 -
Figure 4: Effect of the INNOVCare pilot on the quality of life of patients over time (DISABKIDS-SMILEY) ..... - 43 -
Figure 5: Distribution of scores of the DCGM-12 tool ..... - 45 -
Figure 6: Effect of the INNOVCare pilot on the quality of life of patients over time (DCGM-12) ..... - 45 -
Figure 7: Distribution of scores of the EQ-5D-Y tool ..... - 47 -
Figure 8: Effect of the INNOVCare pilot on the quality of life of patients over time (EQ-5D-Y) ..... - 48 -
Figure 9: Differences between cohorts by measurement points of the INNOVCare efficacy index ..... - 51 -
Figure 10: Efficacy of the INNOVCare pilot at the intervention and control trials by cohort ..... - 53 -
Figure 11: Differences between-cohorts in knowledge of disease/condition by measurement points ..... - 54 -
Figure 12: Differences within-cohorts in knowledge of disease/condition by measurement points ..... - 56 -
Figure 13: Differences between-cohorts in understanding of rights by measurement points ..... - 57 -
Figure 14: Differences within-cohorts in understanding of rights by measurement points ..... - 58 -
Figure 15: Differences between-cohorts in knowledge of available services by measurement points ..... - 59 -
Figure 16: Differences within-cohorts in knowledge about available services by measurement points ..... - 60 -
Figure 17: Differences between-cohorts in ability to manage own care by measurement points ..... - 62 -
Figure 18: Differences within-cohorts in ability to manage own care by measurement points ..... - 63 -
Figure 19: Differences between-cohorts in communication skills by measurement points ..... - 64 -
Figure 20: Differences within-cohorts in communication skills by measurement points ..... - 65 -
Figure 21: Dependence of participants on their peers for an accurate medical diagnosis by cohort ..... - 66 -
Figure 22: Dependence of participants on their peers for information about prescription drugs by cohort ..... - 67 -
Figure 23: Dependence of participants on their peers for recommendation for a doctor or a specialist by cohort - 67 -
Figure 24: Dependence of participants on their peers for emotional support by cohort ..... - 68 -
Figure 25: Dependence of participants on their for a quick solution for an everyday issue by cohort ..... - 68 -
Figure 26: Differences between-cohorts in coordination among providers by measurement points ..... - 70 -
Figure 27: Differences within-cohorts in coordination of care among providers by measurement points ..... - 71 -
Figure 28: Differences between-cohorts in understanding and acceptance in the community by measurement points ..... - 72 -
Figure 29: Differences within-cohorts understanding and acceptance in the community by measurement points - 73 -
Figure 30: Dependence of participants on their peers by cohort (family) ..... - 84 -
Figure 31: Distribution of scores of the DISABKIDS-SMILEY tool by gender ..... - 85 -
Figure 32: Effect of the INNOVCare pilot on the quality of life of patients over time (DISABKIDS-SMILEY) by gender - 86 -
Figure 33: Distribution of scores of the DCGM-12 tool by gender ..... - 87 -
Figure 34: Effect of the INNOVCare pilot on the quality of life of patients over time (DCGM-12) by gender ..... - 88 -
Figure 35: Distribution of scores of the EQ-5D-Y tool by gender ..... - 88 -
Figure 36: Effect of the INNOVCare pilot on the quality of life of patients over time (EQ-5D-Y) by gender ..... - 89 -
Figure 37: Efficacy of the INNOVCare intervention on NoRo beneficiaries vs. external patients by cohort (patient perspective) ..... - 90 -
Figure 38: Efficacy of the INNOVCare intervention on different age groups by cohort (patient perspective) ..... - 91 -
Figure 39: Efficacy of the INNOVCare intervention on different genders by cohort (patient perspective) ..... - 93 -
Figure 40: Efficacy of the INNOVCare intervention on people living in different locations by cohort (patient perspective) ..... - 94 -
Figure 41: Distribution of level of disability over the whole innovcare sample (n=120) ..... - 95 -
Figure 42: Distribution of level of disability in the sample considered for analysis (n=50) (family) ..... - 95 -
Figure 43: Efficacy of the INNOVCare intervention according to levels of disability by cohort (patient perspective) - 96 -
Figure 44: Case manager 1's network during the first nine months of the intervention ..... - 105 -
Figure 45: Case manager 1's network during the last nine months of the intervention ..... - 105 -

Figure 46: Case manager 2's network during the first nine months of the intervention ..... *- 106 -*
Figure 47: Case manager 2's network during the last nine months of the intervention ..... *- 107 -*
Figure 48: Case manager 3's network during the first nine months of the intervention ..... *- 108 -*
Figure 49: Case manager 3's network during the last nine months of the intervention ..... *- 108 -*
Figure 50: Case manager 4's network during the first nine months of the intervention ..... *- 109 -*
Figure 51: Case manager 4's network during the last nine months of the intervention ..... *- 110 -*
Figure 52: Network of service providers in 2017 ..... *- 128 -*
Figure 53: Network of service providers in 2017 ..... *- 129 -*
Figure 54: Network of service providers in 2018 ..... *- 130 -*

1. ABSTRACT

Trial design
The efficacy of the INNOVCare pilot was measured based on a basic two-condition repeated-measures design or rotation design which ensures that all participants receive the intervention; just at different times. These analyses were supplemented by qualitative and social network analyses.

Methods
Participants are rare and complex disease patients and their families living in the county of Salaj in Romania. All 60 beneficiaries from the NoRo Centre implementing the intervention were automatically eligible. To add an element of external validity, further 60 individuals were randomly sampled from the rare disease registry of the county using proportional stratified sampling.

All 120 participants were randomly allocated into two cohorts using a randomised block design. The first received the intervention during the first nine months and the second, during the following nine months of the pilot.

Intervention
Case management services were offered to the participants aiming at relieving their burden of care management by linking health services to employment, social and support services.

Objectives
The overarching goal of the INNOVCare pilot was to improve quality of life of the participants. Direct objectives included improvement in:

1. Self-management of care
2. Communication skills
3. Disease-related peer-to-peer learning
4. Understanding and acceptance in community
5. Coordination of care among stakeholders

and knowledge about:

6. Disease
7. Patient rights
8. Services

Quality of life was measured using generic instruments while specific objectives were measured using tailored questions. The resulting questionnaires for patients and their families were completed at three points in time.

Results
Significant improvements were realised in all the specific objectives of the intervention; but to varying degrees. Nevertheless, results show that the intervention had no significant impact on quality of life of the patients and their families per se. The highest impact was realised in terms of increasing the participants' knowledge on the services available to them, their rights and the disease. Significant strides to improve their ability of to manage their own care were also made; however to a lesser extent. There were also indications of significant improvements with regards to the objectives that rather than targeting the patients and their families directly, targeted the community. These include increasing

coordination among providers as well as raising awareness in the community hence increasing the community's understanding and acceptance with regard to rare and complex disease patients and their families and their struggles. These improvements although statistically significant, were minimal. External patients as well as those living in rural areas and patients over the age of 60 benefitted most from the intervention.

Conclusion

The intervention can be considered successful in terms of its social impact e.g. patients are more empowered, informed and have higher self-confidence. Although there were no measurable effects regarding quality of life, it should be considered that quality of life: Can only be affected indirectly, is a complex phenomenon and requires time to improve considerably and is additionally affected by external factors e.g. disease and degree of disability which could not be affected by the intervention.

2. QUANTITATIVE ANALYSIS

2.1 INTRODUCTION

2.1.1 BACKGROUND

The INNOVCare project was funded under the EaSI PROGRESS programme of the European Commission's Directorate General of Employment, Social Affairs and Inclusion. The project concept was developed as a response to a call for proposals for social policy innovations supporting reforms in social services (EaSI, 2014). The INNOVCare consortium decided to contribute to this call by 'proposing and testing an innovative care pathway for the social inclusion of a EU marginalised group of over 36 million EU citizens and households affected by rare diseases and proposing up-scaling roadmaps that can increase the model's impact to other 80 million vulnerable EU citizens (people with disabilities) and beyond (i.e. chronic diseases)' (INNOV-CARE, 2014).

The guidelines for the call for proposal out rightly encouraged the use of 'social policy experimentation as a method for testing and evaluating innovative solution with a view of scaling up' (EaSI, 2014). In response, the INNOVCare project consortium planned the implementation of social policy experimentation into the activities of the project.

The intervention was implemented in the form of an experiment and aims at 'linking health services to employment and the social and support services that a rare disease patient uses on a daily basis (school, transport, leisure services etc.), ensuring the transfer of information and expertise between service providers. The care pathway also centralises the coordination of care through a resource centre for rare diseases and regional case managers, in an effort to relieve the burden of care management for people living with a rare disease and their families' (INNOVCare, 2016) thereby improving their quality of life.
The exact intervention was designed based on available literature, the results of focus groups with rare disease patients and their families from another region in Romania, results of a EU-wide survey on the quality of life of rare disease patients carried out by the European Organisation for Rare Diseases (EURORDIS)[1] and consultations with experts working with rare disease patients in the intervention site in the county of Salaj in Romania. Further input came from the series of European events and workshops organised or co-organised by the INNOVCare project to network rare disease patients' associations, care providers and policymakers on the delivery and improvement of health and social services for this group. The intervention was defined following the 'logic model' (resources/inputs, activities, outputs, outcomes and impact) (NoRo, 2016). It was implemented following a basic two-condition repeated-measures design / rotation design which ensured that all the participants in the study received the intervention at some point during the implementation. This is important due to the

[1] EURORDIS is an organisation in France making up one of the 7 project partner organisations in the INNOVCare project. The other project partners include: The Ministry of Health, Social Services and Equality, Spain (overall project coordinators; NoRo Resource Centre, Romania; County of Salaj, Romania, Karolinska Institutet, Sweden, Inštitut za Ekonomska Raziskovanja,Slovenia and the Centre for Social Innovation (ZSI), Austria.

vulnerability of this target group as it would be considered unethical to withhold treatment from any participant.

The main question guiding the impact analysis was therefore: how does this intervention change the lives of those who benefit from it?

One of the main responsibilities of ZSI in this project was to develop the methodological framework and evaluation design for the social policy experimentation. Moreover, ZSI was responsible for the development of indicators, data collection tools, the statistical/impact analysis, the qualitative and network analysis of the intervention. The following report presents the findings of the evaluation activities carried out by ZSI in the Framework of the INNOVCare project. This quantitative section of the report is structured according to the CONSORT guidelines on reporting of trials (Elridge, et al., 2016)

2.1.2 RESEARCH QUESTIONS

The overarching goal of the social impact analysis of the INNOVCare pilot was to determine whether individual, holistic support of patients of rare and complex diseases and their families through specially trained case managers for nine months, the INNOVCare intervention (Chapter 2.2.3), increased their quality of life.

Direct objectives were to determine whether, the INNOVCare intervention (Chapter 2.2.3) was able to:

1. expand the participants'[2] knowledge of their disease or condition;
2. increase the participants' understanding of their rights as patients and rights as people with disabilities;
3. inform the participants of the health, social and educational services available to them;
4. boost the capabilities of the participants' to manage their own care even after the end of the intervention, when the case manager would no longer be available to them or not to the same intensity;
5. improve the participants' communication abilities and skills to be able to correspond with different health and social care professionals about for example their condition including symptoms, medical examinations and treatments;
6. encourage and initiate disease-related peer-to-peer learning i.e. among people suffering from the same disease or caring for someone with the same disease;
7. enhance communication and coordination among different actors involved in the participants' treatment and care;
8. raise awareness in the community for people suffering from rare and complex diseases and their families thereby increasing communal understanding and acceptance.

[2]Throughout this report, 'participants' is used to refer to both the patients with rare or complex diseases and their families selected for the trial.

2.2 METHODS

2.2.1 TRIAL DESIGN

The analysis of the INNOVCare pilot trial followed a basic two-condition repeated-measures design (Field & Hole, 2003); also known as the rotation design (Glennerster & Takavarasha, 2013). As the target group of the pilot included:

- rare and complex disease patients and their families, a rather vulnerable group;
- and also because the selected intervention, case management as an approach has been tried and tested in many other fields and can widely be considered as beneficial[3],

an important consideration while choosing the evaluation design was selecting one that did not exclude any of the selected participants from the study and at the same time, as the evaluation was aimed at measuring the efficacy of the pilot, one that was strong enough to establish causality. This evaluation design filled both these needs in that it is an experimental design, therefore bringing with it the advantages of such designs, especially their ability of showing clear relationships between the cause and effect and allowing all the participants selected for the study to receive the intervention just at different points in time.

After the partial random selection of participants into the study using 'proportionate stratified sampling' (Kumar, 2005, p. 176), they were randomly assigned into two cohorts in the ratio of 1:1 using stratified random assignment technique; also commonly referred to as a 'randomised block design' (Verma, 2016, p. 6) (Tschank & Handler, 2017). Subsequent to the allocation into the two cohorts, the

[3] Some projects that have successfully implemented a case management approach include:

1. Esther: patient-centred approach to health and social care for elderly, including case management. It was successfully piloted in a region in Sweden from which it spread out globally - http://plus.rjl.se/infopage.jsf?nodeId=31383 (Gruber & Holtgrewe, 2016, p. 7)
2. Community of matrons: Community Matrons act as a central contact point for patients with complex and multiple conditions - http://www.nuffieldtrust.org.uk/node/463 (Gruber & Holtgrewe, 2016, p. 8)
3. PRISMA: is a model successfully tested in Québec, Canada. It involved, among others, coordination between stakeholders, case management, single entry point, individualized service plan and shared information systems for older and disabled populations - http://www.cnsa.fr/parcours-de-vie/maia (Gruber & Holtgrewe, 2016, p. 14)
4. Navigators: This project makes use of experience-based knowledge of people living with rare diseases (PLWRD) or relatives of PLWRD to provide personal guidance to other PLWRD in navigating the Danish healthcare and social systems - https://innovcare.eu/wp-content/uploads/2016/09/9.INNOVCare-Workshop-Sweden_Navigators_Stephanie-Nielsen.pdf (The Romanian Prader Willi Association, 2018, p. 7)
5. ProRaris: is a pilot scheme of the Alliance for Rare Diseases Switzerland which employs the personal accompaniment of all persons living in the Valais with a recent diagnosis of a rare disease or while searching for the right diagnosis through specialists to 'make life easier' by learning about their rights, available services and reduce isolation through engagement with other people - https://www.proraris.ch/de/homepage.html (The Romanian Prader Willi Association, 2018, p. 8)
6. Parent project muscular dystrophy: implemented a case management project to ensure 'an organised, rigorous, effective and coherent multidisciplinary and interinstitutional intervention' for children living with muscular dystrophy and their families - https://www.parentproject.org.ro/ (The Romanian Prader Willi Association, 2018, p. 9)

participants were further randomly assigned to one of four case managers in the ratio of 1:15 per cohort using simple random assignment.

The first cohort received the intervention during the first nine months of the intervention while the second cohort received the intervention during the last nine months. Both cohorts were measured using the same instruments (one for patients and one for the member of their families mostly in charge of their care) at three points in time: Just before the start of the intervention (Month 1), after nine months (Month 9) and at the end of the intervention (Month 18). See Chapter 4.1 of the methodology report (Tschank, et al., 2017, pp. 8-14) for more details of the design.

The evaluation design was reviewed and approved by two ethics commissions: The ethics committee of the Romanian Prader Willi Association (Romania) and the ZSI ethics committee (Austria).

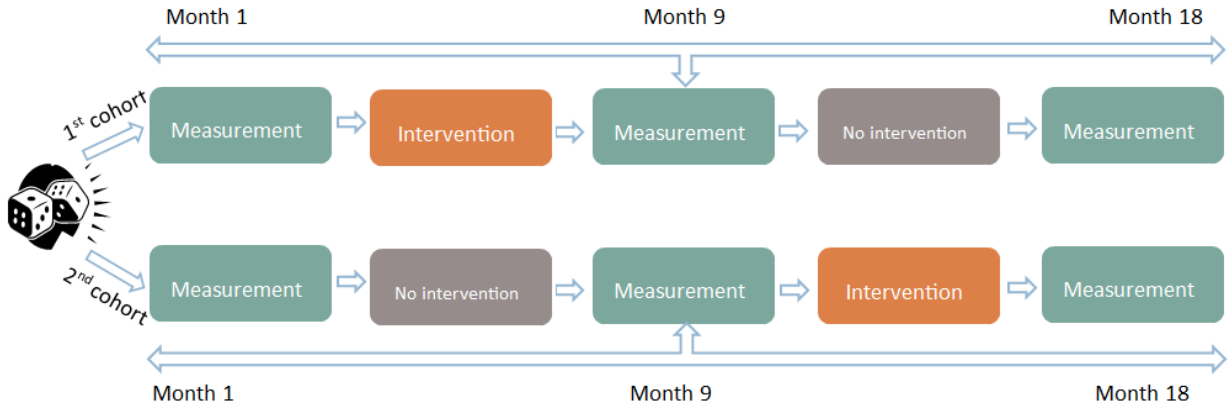

FIGURE 1: THE INNOVCARE EVALUATION DESIGN - A BASIC TWO-CONDITION REPEATED MEASURES DESIGN / ROTATION DESIGN (ADAPTED FROM (FIELD & HOLE, 2003, P. 82))

After randomly assigning 120 participants equally into two cohorts, it was ascertained that 25 of the selected participants could not or did not want to participate in the pilot for various reasons (see participant flow diagram 2.3.1.1 and the introduction of Chapter 3 in Tschank & Handler, 2017). In order to maintain statistical power to be able to detect changes caused by the intervention, but also based on ethical considerations; that it would be unethical to include 25 participants less in the study although resources to support them were available and considering that the intervention had just kicked off, the project consortium decided to select 25 new participants from the study to 'replace' the 25 non-takers.

In this process, there were a number of violations of the randomisation procedure.

- During the second selection, two participants were automatically included into the study and into the same cohorts and same case managers as two other participants who had already been randomly selected and randomly allocated to the cohorts in the first selection and randomisation procedure, because these two new persons were related to these participants, living in the same households and also suffering from a rare or complex disease.
- At the beginning of the intervention, it was determined that from the group of newly selected and randomised participants, a further relative also suffering from a rare or complex disease and living in the same household as one of the already selected participants in the second selection had to be automatically included into the study; into the same cohort and under the

care of the same case manager as his/her relative. This resulted into the two cohorts being unbalanced and having a total sample of 121 instead of 120.

- One participant who had been assigned to the second cohort had to be moved to the first cohort because s/he was planning to move from the County of Salaj in the autumn, when the second cohort was to receive the intervention.
- Two participants had to be reassigned case managers; one due to language issues (there was only one Hungarian-speaking case manager) and the other due to conflict of interest.

2.2.2 PARTICIPANTS

Participants were rare and complex disease patients and their families living in the County of Salaj in Romania. Inclusion criteria were:

1. Documentation in the rare disease registry of the County of Salaj
2. Recipient of NoRo services as a rare or complex disease patient or a patient still searching for the right diagnosis
3. Family member of a person selected for the trial, also suffering from a rare or complex disease and living in the same household as the already selected participant

As a result, the participants were recruited from two sources: From the NoRo day care centre for children with rare diseases and autism spectrum disorders which at the time of selection, March 2017, had 60 beneficiaries and from the rare disease registry of the County of Salaj which included 215 rare disease patients in the county.

After sampling the INNOVCare participants, in February and March 2017, staff from the NoRo centre contacted each of the selected participants individually, explained the intervention to them, what it involved as well as the timeline. If they agreed to participate, following Romanian law they were required to sign a contract with the NoRo centre. The informed consent form was built in to this contract. From the 120 persons sampled, 95 signed the contract thereby also signing the informed consent form. A second sampling was carried out and from the 25 participants sampled, three were non-takers, who did not consent to taking part in the study, and one was automatically added to the sample as s/he was a relative of one of the randomly selected participants, living with a rare or complex disease in the same household. As a result a total of 118 participants started the trial.

2.2.3 INTERVENTION

TABLE 1: THE TIDIER (TEMPLATE FOR INTERVENTION DESCRIPTION AND REPLICATION) CHECKLIST (APPENDIX 3 OF (HOFFMANN, ET AL., 2014; 348))

Item number	Item
	BRIEF NAME
1.	Case managers for rare and complex diseases
	WHY
2.	Case management as an approach has been tried and tested in many different fields including education, labour market integration and healthcare and has been proven as widely beneficial. Although there are a number of projects that have implemented case management for people living with rare diseases in general or for specific types of rare diseases (The Romanian Prader Willi Association, 2018, pp. 7-9), the INNOVCare intervention experimented with a number of new, innovative aspects: a. The target group: Although the INNOVCare project as a whole placed emphasis on rare diseases, the target group of the trial was not restricted to a specific rare disease. The trial was also open to people who were still officially undiagnosed, searching for the right diagnosis as well as people suffering from complex diseases. b. The carers: Unlike other projects which engage other patients in the role of a 'case manager' or a similar role or those that engage medical nurses and other medical professionals in this role, the INNOVCare pilot enlisted professionals from a wide variety of backgrounds (two social workers, a legal advisor and a special education teacher) who had a wealth of experience in dealing with the target group through their previous roles at NoRo as well as through their personal experience as all have family members affected by a rare disease. Furthermore, during the intervention, the case managers were able to co-create the training manual for case managers for rare diseases with which they were trained (The Romanian Prader Willi Association, 2018). c. The aim: The case management service offered in the framework of the INNOVCare pilot sought a holistic and

	transdisciplinary approach rather than concentrating on the medical needs of the participants. It aimed at supporting patients in a wide variety of their needs for example their medical needs but also with their psychosocial needs including matters related to employment and education. d. Evaluation: Although there are a number of projects involving the concept of case management or similar in the field of rare diseases, none have undergone such a rigorous impact and economic evaluation in an experimental setting as the INNOVCare pilot has. e. The location: In the County of Salaj in Romania there exists no similar service for rare and complex diseases.
	WHAT
3.	During the intervention periods, the cohorts were supported by case managers to navigate through the medical, social and educational systems in the County of Salaj in Romania. More detailed activities are described in the qualitative section of this report (Chapter 3)
4.	**Procedures**: The case management of patients according to the INNOVCare intervention was carried out through three distinct steps: 1. The initial evaluation stage: This stage involved a needs analysis of the patient and his/her family as well as identifying their resources and gathering all official documents from them that may be required in meeting these needs. 2. Intervention stage: Following the analysis of all the information drawn from the first stage, together with the patient and his/her family, the case manager created an action plan. 'The action plan contains the objectives, activities, deadlines and the persons responsible for carrying out the proposed activities' (The Romanian Prader Willi Association, 2018, p. 54). This is a dynamic document and is reviewed as often as necessary. After each meeting, the case manager completed a meeting report. Whenever the case manager undertook an action on behalf of the beneficiaries like making appointments, researching for information related to the case or communicates information to the client by telephone s/he completed the action report. 3. Final assessment stage: This marked the end of the intervention either as anticipated at the end of the contracted time, in this case at the end of the nine months intervention period or whenever the client decided to stop using the service before the end

of the contracted time. Here the case manager completes the case closing sheet.

During all these stages of the intervention the case manager provided counselling to the patient and his/her family, provided them with information about their condition/disease (health literacy), their rights as patients and rights as people with disabilities and available services.

As one of the main goals of the intervention was to empower the patient and his/her family to manage their own care, together, they worked on the communication skills of the patient and his/her family through the communication kit created as well as through coaching to ensure that they were able to communicate better with the people treating them and caring for them. In all these steps, the case manager encouraged the patient and their family to be more involved in decisions about his/her treatment and care by for example giving them options of different services.

Before the beginning of the intervention, NoRo mapped the services in the County of Salaj to help in the attainment of the set goals. To ensure that the case manager was able to advise the beneficiaries sufficiently, they needed to constantly network and as a result, to expand the map of services. The exchange of ideas and contacts among each other on the weekly case managers' meetings was another measure for increasing the efficiency in their work with the beneficiaries.

Each of the participants also took part in at least two group activities organised and coordinated by the case manager. These group activities depended on the needs of the patients and involved for example summer camps for the patients or the whole family, disease-specific support groups etc.

Besides these activities directly related to the patients and their families, the NoRo centre set to improve the coordination of care among professionals caring for rare and complex disease patients by creating and promoting a network dubbed the 'community

	support network'. This network comprised of community nurses and representatives from local services in Cehu - Silvaniei, Jibou, Simleul- Silvaniei and Zalau and met together with the patients, a number of times during the lifetime of the INNOVCare pilot.
	WHO PROVIDED
5.	Four case managers, two with a social work background, one with a background as a special education teacher and the other as a legal advisor. Three of the case managers had already been working at NoRo before the start of the pilot and were therefore already experienced in working with patients with rare and complex diseases and their families. All four case managers also have a personal connection to rare diseases in that they have a relative suffering from a rare disease and as such could be expected to have a special empathy and understanding to the target group as well as motivation for the job. The case managers co-created the training manual for case managers for rare diseases (The Romanian Prader Willi Association, 2018) which was the main training basis for carrying out this role.
	HOW
6.	▪ At least five individual face-to-face meetings between the patient, his/her family and the case manager at the home of the beneficiaries ▪ At least two group activities for the patient and his/her family. The meetings organised in this framework, were organised together with the community support network. The patients were invited to the group at the meeting. Those who couldn't attend were put in contact with the organisations for their specific diseases, if needed. The format of the meetings was open discussions, where each participant presented themselves, their needs and the service providers were asked how they can answer to specific needs of patients in the region. The aim of the groups was to facilitate the contact between the patients/ families and the service providers in the region. ▪ Counselling and relaying of information over the phone, unrestricted, whenever need arose ▪ Research of different services and procedures over the internet, telephone, email and through networking ▪ Weekly meetings between the four case managers to discuss complex cases, share contacts and advise and provision of psychological and emotional support to each other

	WHERE
7.	The intervention took part in the County of Salaj in Romania. Approximately 70% of the participants lived in the urban areas of the county, mostly in Zalau, the seat of the county. The rest of the participants lived in the rural areas of the county, which especially in winter, proved to be quite a challenge for the case managers to reach because of the distance from Zalau as well as the poor road infrastructure in parts.
	WHEN and HOW MUCH
8.	Unfortunately, although this information was documented, it was only available on paper in the Romanian language. As the provision of this information to the evaluation teams was not planned, no resources were available to extract this information. In general however, time dedicated to each case was officially one day per month (which means five meetings/calls for each case). Nevertheless, time really spent per case depended on their needs. Some of them dropped by the NoRo centre from time to time, others were squeezed into the schedule if they needed urgent support. Annex 6.2 gives a brief overview of the number of organisations and individuals contacted by the case managers in a bid to solve the participants'' needs.
	TAILORING
9.	As the support offered by the case managers depended wholly on the specific needs of each patient and their family, then in a sense each participant received a customised form of the case management service. The minimum of five individual meetings between the case manager and the participants as well as the participation in the two group activities were the only fixed factors of the intervention. In relation to the group activities, in addition to the meetings with the community support network, these too differed from participant to participant substantively depending on their needs.
	MODIFICATIONS
10.	Not applicable
	HOW WELL
11.	Intervention adherence or fidelity was not assessed per se but rather indirectly. The training manual for case managers for rare diseases was completed at the end of the intervention which is based on the actual activities of the intervention.

2.2.4 OUTCOMES

As the participant group of the INNOVCare trial was quite diverse, especially in terms of age, it was still considered highly important that the voices of the patients themselves, regardless of age, were heard. As a result, the measurement instruments for the INNOVCare pilot had two target groups: The patients and the family members most closely involved in the care of the patient.

The INNOVCare project planned both a social and economic impact evaluation of the pilot. ZSI was in charge of the social impact assessment while Karolinska Institutet, Sweden, was in charge of the economic impact evaluation. To reduce the burden to the patients and their families as well as the implementing organisation, NoRo, instead of applying two different questionnaires for measuring the social and economic impact, ZSI and Karolinska jointly developed the questionnaires, resulting in one questionnaire per target group.

Both questionnaires included four main blocks: health-related quality of life, social impact, economic impact and socio-demographic data of the patients, their family members and their household in general.

Quality of life was measured using three generic instruments: DISABKIDS-SMILEY (self-reported) DCGM-12 (self-reported) (Bullinger, et al., 2002) and EQ-5 D-Y (self-reported) (Wille & al., 2010) while the social and economic impact blocks included a mix of tailored questions and items from existing instruments.

Considering the age and cognitive abilities of the patients, three different versions of the patient questionnaire (Tschank & Handler, 2017) were developed:

TABLE 2: THE DIFFERENT VERSIONS OF THE PATIENT QUESTIONNAIRE, THEIR COMPONENTS AND TARGET GROUPS

Name of questionnaire	Components	Target group
Patient-SMILEY	DISABKIDS – SMILEY (self-reported)	▪ Patients aged 4 to 7 ▪ Patients older than 7 with serious cognitive difficulties
Patient-8+	▪ DCGM-12 (self-reported) ▪ EQ-5D-Y (self-reported) ▪ Social impact items	▪ Patients aged 8 and above
Patient-SOLO	▪ DCGM-12 (self-reported) ▪ EQ-5D-Y ▪ Social impact items ▪ Economic impact items	▪ Adult patients, living alone and managing their own care

The English versions of both patient and family questionnaire underwent cognitive pretesting (Tschank, et al., 2017, pp. 30-31) prior to the start of the intervention, while the Romanian version underwent a quality check from two people, one of which was completely uninvolved in the project.

The questionnaires were applied three times, in nine months intervals, during the course of the pilot: In March 2017 just before the start of the intervention, in November 2017, nine months into the

intervention (at the end of the intervention for the first cohort and at the beginning of the intervention for the second cohort) and in July 2018, at the end of the intervention. The patients and the family members most closely involved in the patients' care completed the questionnaires independently. However, the survey administrator (an employee at NoRo) or one of the other case managers, not the one assigned to that particular participant, was present during completion of the surveys to answer any questions related to the survey in general or specific questions of understanding and clarification (Tschank & Handler, 2017, pp. 6-13 - Chapter 1.1.3 and Chapter 1.2.1).

To measure the overarching goal of the intervention, its effect on the quality of life of the participants, the quality of life measurements mentioned oben (DISABKIDS SMILEY, DCGM12 and EQ-5D-Y) were used in their entirety. The DCGM12 instrument is normally targeted towards children and adolescents. However, as the INNOVCare sample was quite diverse regarding age, to allow compatibility, the DCGM12 instrument was completed by all patients older than eight years as long as they had the level of reading ability necessary for completion. As a result, the wording of three items was slightly altered: In one item the word 'play' was changed to 'carry on with daily activities' and in two items the words 'other children/adolescents' was changed to 'your peers'.

The following table shows how the direct objectives of the intervention listed in (Chapter 2.1.2) were assessed.

Direct objective of the INNOVCare pilot	Main item assessing the objective	Supporting item
1. Expanding knowledge on disease/condition	How informed do you currently feel about your condition/*the condition of the person you care for*[4]? ☐ Not informed at all ☐ Not well-informed ☐ Fairly well-informed ☐ Very well-informed	▪ Official diagnosis of disease ▪ Availability of treatment and medication for condition ▪ Assessment of all needs by health and social care staff[5]
2. Increasing understanding of their rights	How informed do you currently feel about your rights as a patient/*the rights of the person you care for* (e.g. right to personal assistant, services, benefits, tax	▪ Perception whether rights have been respected by health and social care staff

[4] This table offers the formulations of questions in both the patient and family questionnaires. In the patient questionnaire, the questions are always formulated in the first person e.g. 'your condition', 'your rights' while in the family questionnaire the questions always refer to the patient i.e. 'the condition/the rights of the person you care for'

[5] Original question: 'Have all your needs been assessed by your health and social care staff?' [☐ All of my needs have been assessed ☐ Most of my needs have been assessed ☐ Some of my needs have been assessed ☐ None of my needs have been assessed ☐ Don't know / can't remember] stems from (King, et al., 2013, pp. 102 - Q3.1 of the final question set)

	deductions, accessibility in public places, second medical opinion etc.)? ☐ Not informed at all ☐ Not well-informed ☐ Fairly well-informed ☐ Very well-informed	
3. Broadening their knowledge on available health and social services	How informed do you currently feel about the different health and social care services available to you/*the person you care for* as a consequence of your/*her/his* condition? ☐ Not informed at all ☐ Not well-informed ☐ Fairly well-informed ☐ Very well-informed	
4. Increasing ability of self-management of care	How fit do you currently feel about managing all aspects of your care/*the care of the person you care for*? ☐ Not fit at all ☐ Not sufficiently fit ☐ Fairly fit ☐ Very fit	▪ Number and relationships of people involved in care and level of contribution ▪ Involvement in decisions about care, support [6] and treatment. ▪ Availability of health and social care providers[7] ▪ Strain of organising care
5. Improving communication skills	How well do you currently feel that you can communicate about your condition/*the condition of the person you care for*, including	▪ Comprehension of health and social care professionals of patient's condition[8]

[6] Original questions: '**Were** you involved as much as you wanted in decisions about your care and support?' and '**Were** you involved as much as you wanted in decisions about your treatment?' [☐ Yes, definitely ☐ **Yes, to some extent** ☐ **No**] stem from (King, et al., 2013, pp. 103 - Q3.2a and Q3.2b of the final question set). The formulation of the items in the INNOVCare questionnaires was slightly altered: They were formulated in the present tense 'are' instead of 'were' and the answer options were extended to four instead of three: ☐ Yes, definitely ☐ Yes, to a large extent ☐ Yes, to a lesser extent ☐ Not at all

[7] Original question: 'If you have questions, when can you contact the people treating and caring for you?' [☐ During normal working hours ☐ During the evening ☐ During the night ☐ Weekends ☐ Don't know / not sure] stems from (King, et al., 2013, pp. 108 - Q3.12 of the final question set). 'Never' was added to the answer options.

[8] Original question: 'Do you feel **this person** understands about you and your condition' [☐ Yes, definitely ☐ **Yes, to some extent** ☐ **No**] stems from (King, et al., 2013, pp. 108 - Q3.13 of the final question set). 'This person' in the original questionnaire was expounded to 'health and social care professionals treating and caring for you'.

	symptoms, medical examinations and treatments, to all the different health and social care professionals treating and caring for you? ☐ Not at all ☐ Not well ☐ Fairly well ☐ Very well	
6. Support disease-related peer-to-peer learning	How much do you currently depend on your friends, family or acquaintances with the same condition as yourself/*caring for a person with the same condition as the person you care for* with the following activities?[9] a. An accurate medical diagnosis b. Information about prescription drugs c. A recommendation for a doctor or a specialist d. Emotional support in dealing with a health issue e. A quick solution for an everyday health issue ☐ Very much ☐ Fairly much ☐ Fairly well ☐ Not at all	▪ Presence of contact with other people suffering or caring for people with the same disease
7. Advance coordination among providers	[*Thinking about the person you care for*] Do all the different people currently treating and caring for you/*him/her* work well together to	▪ Perception of level of support from health and social care services[11] ▪ Quality of communication

Moreover, the answer options were extended to four instead of three: ☐ Yes, definitely ☐ Yes, to a large extent ☐ Yes, to a lesser extent ☐ Not at all

[9] This question was adapted from Pew Research Center's Internet & American Life Project (Fox, 2011, p. 4). The original question was: 'Who is more helpful when you need… a. An accurate medical diagnosis b. Information about prescription drugs c. A recommendation for a doctor or a specialist d. A recommendation for a hospital or other medical facility e. Emotional support in dealing with a health issue f. A quick **remedy** for an everyday health issue g. Practical advice for coping with day-to-day health situations' [☐Professional sources like doctors and nurses ☐Fellow patients, friends and family ☐Both Equally]

	give you/*him/her* the best possible care and support?[10] ☐ No, they do not work well together ☐ Some of them work well together ☐ Most of them work well together ☐ All of them work well together	among different health and social care actors e.g. knowledge of medical history, repetition of medical information [12] and getting contradictory information from health and social care professionals.[13]
8. Advocate understanding and acceptance in the community	How well do you currently feel that the people who are in contact with you/*with the person you care for* understand and accept your/*her/his* condition (e.g. at school or workplace, family, friends etc.)? ☐ Neither accept nor understand ☐ Not well ☐ Fairly well ☐ Very well	

After the first measurement and data exploration as well as feedback from the survey administrators, two of the supporting items were slightly altered to increase comprehensibility. Both the original items

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[11] Original item: 'Overall, do you feel that your carer/family has had as much support from health and social services as they needed?' [☐ Yes, they have had as much support as they needed ☐ They have had some support but not as much as they needed ☐ No, they have had little or no support ☐ They did not want/need support ☐ There are no family members or carers to support]. For the INNOVCare questionnaires, other than excluding the word 'overall', the question remained the same.

[10] This question originates from (King, et al., 2013, pp. 108-109 - Q3.14 of the final question set). The Answering scale was reversed in the INNOVCare questionnaires.

[12] Original questions: '**Were there times when** the person you were seeing did not know your most recent medical history?' and '**Were there times when you had** to repeat information that should be in your medical record?' [☐Never☐ Rarely ☐Sometimes ☐Often All the time] were derived from (Canadian Institute for Health Information, n.d., pp. 11-12 - Q.39 and Q.43). In the INNOVCare questionnaires, these two items were sub-questions of whether they had visited a new health or social care professional in the last 9 months and were reformulated as follows: 'Did she/he know your most recent medical history?' and 'Did you have to repeat information that should be in your medical record?' [☐ Not at all ☐ Only some parts ☐ Most of it ☐ Yes, completely]

[13] The question inquiring whether the participants received conflicting information from different health and social care professionals was extracted from the Commonwealth Fund International Health Policy Survey (SSRS research. defined., 2017, pp. 39 - Q.1226 A2). The item was adapted as follows for the INNOVCare questionnaires: '33. In the last 9 months, have you received contradictory information from different health and social care professionals involved in your treatment and care?' [☐ Not at all ☐ Only to a small extent ☐ Yes, to a large extent ☐ Yes, definitely]

brought uncertainties in terms of the kind of people or the number of people being referred to in the answers.

1. Item 38: 'Do you have a named health or social care professional who coordinates your care and support?' was modified to '**Other than the case manager**, do you have a named health or social care professional who coordinates your care and support?' – The answer to the original question make it impossible to know whether the answer provided, were made with the case manager in mind because the answer options were as follows:
   ☐ No, I coordinate my own care and support
   ☐ No, another member of my family coordinates my care
   ☐ Yes, she/he coordinates some of my care and support, but not as much as needed
   ☐ Yes, she/he coordinates my care and support to a large extent
   ☐ Yes, she/he completely coordinates my care and support
2. Item 65: 'Is there more than one person with a rare or complex condition in your household?' was modified to: '**Are there other persons** with a rare or complex condition in your household?' in the patient questionnaire and: '**Other than the person you care for, are there other persons** with a rare or complex condition in your household? The answer options were:
   ☐ No
   ☐ Yes, _____ persons in total
   It was difficult to interpret whether the answers to the original formulation of the question included the participant or not.

2.2.5 SAMPLE SIZE

The determination of the sample size of the INNOVCare pilot was based on two main aspects: Formal sample size calculations and the resources available in the project. According to calculations based on the programme G*Power[14] , a minimum total sample size of 44 (n=22 per cohort) is required for a two-way mixed ANOVA given the probability level of p=0.05, an anticipated medium effect size (Cohen's d=0.5) and a desired statistical power level of 0.95. The INNOVCare project had resources to provide the intervention for a maximum of 120 participants (n=60 per cohort) which is considerably higher than that required sample size to detect a medium sized effect at a statistical power level of 0.95. G*Power indicated that for a repeated measures design that aims to detect an interaction effect between the independent variables on the dependent variable, like the main intended test for the INNOVCare pilot, the two-way mixed design, a sample size of 120 (n=60 per cohort) at probability level of p=0.05 and statistical power level of 0.95 can detect an effect of d=0.29 equivalent to r=0.15. According to Cohen (1988) as referenced in (Field & Hole, 2003, p. 153) an effect size of r=0.1 represents small effects, 0.3 medium effects and 0.5 large effects. As a result, should the intervention have as minimal effects as r=0.15, there is a 95% chance of correctly rejecting the null hypothesis of no significant effects of the interaction with a total sample of 120 (n=60 per cohort).

[14] G*Power is a tool to compute statistical power analyses for many different t tests, F tests, χ2 tests, z tests and some exact tests. G*Power can also be used to compute effect sizes and to display graphically the results of power analyses: http://www.gpower.hhu.de/en.html

2.2.6 RANDOMISATION

To add to the 60 existing beneficiaries of NoRo as of February 2017 who were automatically eligible for the study (see Chapter 2.2.2), 60 rare disease patients from the rare disease registry of the County of Salaj were randomly sampled using 'proportionate stratified sampling' (Kumar, 2005, p. 176). The blocking variables used were: Age (nine levels) and gender (two levels)[15]. On the basis of the available variables (age, gender, degree of disability, disease cluster and location), the sample drawn was checked for its representativeness of the whole population.

TABLE 3: REPRESENTATIVENESS OF THE SELECTED SAMPLE TO THE REST OF THE POPULATION (1ST SELECTION)

Variable	P-value for: T-test for equality of means OR chi-square test
Age	0.940
Age group (9 levels)[16]	1.000
NoRo vs External[17]	<0.000*
Gender	0.996
Location[18]	<0.000*
Disease cluster[19]	<0.000*
Degree of disability[20]	0.289

As can be seen in Table 3 above, the selected participants and the remaining eligible population were balanced on all the available variables except from 'noro', 'location' and 'disease cluster' all of which are related to the fact that NoRo's patients were not randomly selected and therefore shows selectivity in terms of the location of the participants and their type of disease. Most of NoRo's patients (91.7%) lived in the City of Zalau and most came from NoRo's day care centre for children with rare disease and autistic spectrum disorders. 33.3% of NoRo's beneficiaries were suffering from: Autistic spectrum

[15] The full procedures for the random sampling and random allocation are detailed in the 'technical note on random sampling and random allocation of the participants of the INNOVCare pilot' (Tschank & Handler, 2017)
[16] The 9 levels of the variable 'age group' were: up to 3, 4 to7, 8 to 17, 18 to 24, 25 to 34, 35 to 44, 35 to 44, 45 to 54, 55 to 64 and 65+.
[17] 'NoRo vs External' represents whether the patients in the whole rare and complex disease patients of the region of Salaj are also beneficiaries at the NoRo centre.
[18] 'Location' describes whether the patient lives in the urban (Zalau) or rural areas of the County of Salaj
[19] The specific disease that the patients are suffering from were grouped together into 8 clusters: Autistic spectrum disorders, Congenital anomalies with intellectual disabilities, Epilepsies, Kidney disease, Metabolic diseases, Neurological diseases, Rare tumours and Skin and tissue complex disorders. Another cluster was added with the second selection; namely, Congenital anomalies without intellectual disabilities.
[20] There were six levels for degree of disability: No disability, mild functional deficiency, moderate functional deficiency severe functional deficiency (without personal assistant) and severe functional deficiency (with personal assistant).

disorders, 44.4% with Congenital anomalies with intellectual disabilities and 17.5% with epilepsies; whereas 82.1% of the external patients were suffering from neurological disorders.

As a next step, the selected participants were randomly assigned into two cohorts which determined when they would receive the intervention: The first cohort received the intervention during the first nine months of the study, while the second received it during the last nine months. Random assignment was implemented using the stratified random assignment technique; also commonly referred to as a 'randomised block design' (Verma, 2016, p. 6)[21]. The blocking variables were 'age', 'gender' 'type of patient' (NoRo beneficiary or not) and 'area' (urban or rural). Random allocation was computer generated using the SPSS software[22].

After randomisation, an ex-post analysis of the randomisation procedure was carried out on the variables collected in the baseline data: age, gender, degree of disability, disease cluster and location. Table 4 below shows the balancing tests for the full sample. T-tests as well as the Pearson's chi-squared tests through cross-tabulation were calculated. The t-test tests show differences between two means (Field, 2013, p. 364). To check whether the means of the two cohorts on continuous variables like age are significantly different, and therefore to ascertain whether or not the two cohorts are balanced the different variables, the 'independent-samples t-test', specifically, was carried out because it is usually used in two experimental conditions, which involve different participants in each condition (Field, 2013, p. 364). In the INNOVCare pilot, the two conditions were whether one of the cohorts was receiving the intervention at the time or not and the two cohorts were composed of different participants, randomly assigned to that cohort. For the purpose of the INNOVCare pilot, the Pearson's chi-square test was used to determine whether there was a difference between the two cohorts on the categorical variables.

[21] The full random allocation procedure can be found in the technical note on random sampling and random allocation of the participants of the INNOVCare pilot' (Tschank & Handler, 2017).
[22] SPSS is a statistical software (https://www.ibm.com/products/spss-statistics) not only used for the random sampling and allocation of participants, but also the subsequent statistical analyses of the pilot.

TABLE 4: BALANCING TEST FOR THE FULL SAMPLE (1ST SELECTION)

Variable	1st cohort: Mean OR Count	2nd cohort: Mean OR Count	P-value for: T-test OR Chi-square test
Age	M = 30.40	M = 32.42	0.656
Age group (3 levels)[23]			0.854
▪ Under 18	▪ n = 30	▪ n = 27	
▪ 18 to 64	▪ n = 24	▪ n = 26	
▪ 65+	▪ n = 6	▪ n = 7	
Type of patient			1.000
▪ NoRo	▪ n = 30	▪ n = 30	
▪ External	▪ n = 30	▪ n = 30	
Gender			0.855
▪ Female	▪ n = 32	▪ n = 33	
▪ Male	▪ n = 28	▪ n = 27	
Location			1.000
▪ Urban	▪ n = 42	▪ n = 42	
▪ Rural	▪ n = 18	▪ n = 18	
Disease cluster			0.830
▪ Autistic spectrum disorders	▪ n = 8	▪ n = 13	
▪ Congenital anomalies with intellectual disabilities	▪ n = 18	▪ n = 13	
▪ Epilepsies	▪ n = 5	▪ n = 5	
▪ Kidney disease	▪ n = 0	▪ n = 1	
▪ Metabolic diseases	▪ n = 2	▪ n = 1	
▪ Neurological diseases	▪ n = 23	▪ n = 24	
▪ Rare tumours	▪ n = 3	▪ n = 2	
▪ Skin and tissue complex disorders	▪ n = 1	▪ n = 1	
Degree of disability			0.520
▪ No disability	▪ n = 0	▪ n = 2	
▪ Mild functional deficiency	▪ n = 0	▪ n = 0	
▪ Moderate functional deficiency	▪ n = 1	▪ n = 2	
▪ Marked functional deficiency	▪ n = 22	▪ n = 20	
▪ Severe functional deficiency - no personal assistant	▪ n = 2	▪ n = 4	
▪ Severe functional deficiency - personal assistant	▪ n = 35	▪ n = 32	

The p-values for all the variables shown in the table above are higher than the significant threshold of 0.05 suggesting that the two cohorts did not differ from each other on the selected cohorts significantly at the beginning of the INNOVCare pilot.

[23] Unlike in the random sampling, where the selected sample was controlled against the remaining population on nine levels of age, here, due to sample size, only three levels were checked: under 18 - children, 18 to64 – adults in working age and 64+ - pensioners).

After the random allocation into the two cohorts, each participant was randomly assigned to one of the four case managers using simple random sampling so that each case manager would be in charge of 15 patients and their families in each phase making a total of 30 cases for each case manager over the study period. The patients who were found to be related in the sample were assigned to the same case manager.

After the selection, 25 participants were non-takers[24]. A second selection to draw a sample of 25 to 'replace' these non-takers and their subsequent randomisation into the two cohorts was undertaken (Tschank & Handler, 2017, pp. 32-63). From those who consented to take part in the study in the first selection, two participants requested for a family member in the same household, who was also suffering from a complex or rare disease, to be included in the study. As a 'case' in the INNOVCare pilot is considered as a complex or rare disease patient and his/her family, it was decided that family members, who had not already be sampled by chance, be included. In order to ease the work of the case managers, these two new participants had to be included to the same group and assigned the same case manager as their relatives already included in the study. As a result, in the second selection and randomisation, only 23 instead of 25 participants were essentially randomised into the first and second cohort (Tschank & Handler, 2017, p. 43) (see Figure 2.3.1.2 below).

Furthermore, in the second selection 10 participants were pre-defined in that six of them had joined NoRo in the time between the first selection and the start of the intervention, two were former beneficiaries of NoRo and the two remaining ones, were family members of participants selected in the first selection as described in the paragraph above. This means only 15 participants were randomly sampled from the remaining eligible population using a matching procedure (Tschank & Handler, 2017, p. 33). Of these participants, one participant was randomly sampled, however his spouse, also with a rare or complex disease was not. As a result, the wife of this participant was added to the new sample making a total of 121 participants.

The table below shows the representativeness of the final INNOVcare sample considering the second selection.

[24] The reasons included: Lack of motivation (n=11); declaration that 'they are too old to be helped' (n=3), relocation – i.e. no longer living in the county of Salaj (n=5); preference to concentrate to medical services (n=3), declaration that 'they can only be helped by God' (n=2) and death (n=1).

TABLE 5: REPRESENTATIVENESS OF THE FINAL INNOVCARE SAMPLE TO THE REST OF THE POPULATION

Variable	P-value for: T-test for equality of means OR chi-square test
Age	0.535
Age group (9 levels)	0.964
NoRo vs External[25]	<0.000*
Gender	0.948
Location	<0.000*
Disease cluster	<0.000*
Degree of disability	0.299

The result shown in Table 5 above are very similar to those from the first selection displayed in Table 3. The final sample of the INNOVCare study was balanced on all available variables except 'noro', 'location' and 'disease cluster' all of which are related to the fact that NoRo's current and former beneficiaries were automatically included and therefore shows selectivity.

Of the new sample of 121, only 118 of the participants were randomly assigned to the cohorts (see Figure 2.3.1.3 below). The two family members described in the sections above as well as the wife of the newly selected participant were automatically assigned to the same cohort and case manager as their family members.

Two participants, one from each of the two selections, did not comply with the random allocation in that both requested to be moved from the second cohort, to which they were randomly allocated to, to the first[26].

As the non-compliance of the first participant was already known at the time of the second selection, this change was considered in the random allocation of the newly selected participants to the cohorts and case managers (Tschank & Handler, 2017, p. 32). The reassignment of the second participant to the first cohort took place after the intervention had already started; no measure was taken to balance the number of participants between the two cohorts. The rest of the participants remained to their assigned cohorts.

Below, is the balancing table of the final INNOVCare sample considering the second selection.

[25] 'NoRo vs External' represents whether the patients in the whole rare and complex disease patients of the region of Salaj are also beneficiaries at the NoRo centre. The two former beneficiaries of NoRo were included as NoRo beneficiaries in the analysis

[26] One of the participants knew that s/he would need to relocate from the region Salaj in the autumn of 2017, when the intervention for the second group would start; therefore end up missing the whole intervention. His/her inclusion in the first cohort ensured the support of the case manager in preparing him/her for the move. The other participant signalled that he had urgent problems that needed support immediately otherwise he would be unable to take part in the study.

TABLE 6: BALANCING TABLE FOR THE FINAL INNOVCARE SAMPLE

Variable	1st cohort: Mean OR Count	2nd cohort: Mean OR Count	P-value for: T-test OR Chi-square test
Age	M = 29.61	M = 30.70	0.798
Age group (3 levels)[27]			0.760
▪ Under 18	▪ n = 30	▪ n = 27	
▪ 18 to 64	▪ n = 27	▪ n = 27	
▪ 65+	▪ n = 4	▪ n = 6	
Type of patient			0.933
▪ NoRo	▪ n = 33	▪ n = 32	
▪ External	▪ n = 28	▪ n = 28	
Gender			0.407
▪ Female	▪ n = 31	▪ n = 35	
▪ Male	▪ n = 30	▪ n = 25	
Location			0.645
▪ Urban	▪ n = 45	▪ n = 42	
▪ Rural	▪ n = 16	▪ n = 18	
Disease cluster			0.418
▪ Autistic spectrum disorders	▪ n = 9	▪ n = 12	
▪ Congenital anomalies with intellectual disabilities	▪ n = 18	▪ n = 13	
▪ Epilepsies	▪ n = 5	▪ n = 6	
▪ Kidney disease	▪ n = 0	▪ n = 1	
▪ Metabolic diseases	▪ n = 1	▪ n = 0	
▪ Neurological diseases	▪ n = 22	▪ n = 27	
▪ Rare tumours	▪ n = 2	▪ n = 1	
▪ Skin and tissue complex disorders	▪ n = 2	▪ n = 0	
▪ Congenital anomalies without intellectual disabilities	▪ n = 2	▪ n = 0	
Degree of disability			0.525[28]
▪ No disability	▪ n = 0	▪ n = 2	
▪ Mild functional deficiency	▪ n = 0	▪ n = 0	
▪ Moderate functional deficiency	▪ n = 1	▪ n = 2	
▪ Marked functional deficiency	▪ n = 18	▪ n = 21	
▪ Severe functional deficiency - no personal assistant	▪ n = 5	▪ n = 4	
▪ Severe functional deficiency - personal assistant	▪ n = 37	▪ n = 31	

[27] Unlike in the random sampling, where the selected sample was controlled against the remaining population on nine levels of age, here, due to sample size, only three levels were checked: under 18 - children, 18 to64 – adults in working age and 64+ - pensioners).

[28] Due to the sample size, when running the Chi-square tests some of the cells had a count of less than the minimum of 5. The variables affected were: Age group (65+), disease cluster (kidney diseases, metabolic diseases, rare tumors and skin and tissue complex disorders) and degree of disability (no disability, moderate and severe functional deficiency without personal assistant).

Like in the first sample (Table 4) the final composition of the two cohorts of INNOVCare study were balanced on all available variables all with a p-value greater than 0.05.

2.2.7 IMPLEMENTATION

ZSI, the consortium partner charged with the social impact analysis of the INNOVCare study, conducted the random sampling and allocation of participants into two cohorts supported by the statistical software SPSS. None of the employees of NoRo, the organisation charged with the implementation of the intervention, had access to the allocation procedure. NoRo provided the baseline data that founded the sampling of participants in an anonymised form; patient codes instead of names. Beneficiaries from NoRo were differentiated from the rest of the population by being assigned 'int' followed by a number. The rest of the population was assigned 'ext' followed by a number. After participant selection and assignment into cohorts and case managers, NoRo was provided with a list of the participant codes, cohorts and case managers for each of the selected participants by ZSI.

As the participant group was considered vulnerable owing to their conditions and the consequences thereof, the project consortium and specifically ZSI, NoRo and Karolinska Institutet who processed participant data, took a number of measures in terms of data protection. All three partners signed a confidentiality agreement. Anonymity of the participants was ensured by the use of participant codes as described above. NoRo was the only organisation that had access to the key containing the name of the participants and their assigned codes. Transfer of participant data among the three organisations was only permitted through a secure cloud folder on a server hosted by ZSI. In ZSI a password protected drive was set-up for the data storage[29].

2.2.8 BLINDING

None of the people involved in the study were blinded per se however, the participants were not told that they were participating in an 'experiment' situation.

2.2.9 STATISTICAL METHODS

To analyse the effect of the INNOVCare intervention on the outcome variables described in Chapter 2.2.4, two statistical software programmes were employed: R[30] for the quality of life measures and SPSS for the direct objectives of the pilot.

2.2.9.1 Quality of life measures

To determine whether the INNOVCare pilot impacted the quality of life of the participants, a dataset for each of the quality of life instrument was constructed in the following form:

[29] A more detailed account of all these steps can be found in the chapter on data protection on the INNOVCare guidelines on data collection (Tschank & Handler, 2017, p. 15)
[30] R is a free software environment for statistical computing and graphic (https://www.r-project.org/)

```
##   ResponseMean TimePoint   Cohort Code
## 1          NaN        M1     <NA>    1
## 2          NaN        M1 Cohort 2    2
## 3          NaN        M1     <NA>    3
## 4          NaN        M1     <NA>    4
## 5          NaN        M1     <NA>    5
## 6          NaN        M1     <NA>    6
```

The dependent variable, **'ResponseMean'** is the arithmetic mean of the responses of all the items of each instrument over the three measurement points and was calculated for each individual across both cohorts. **'Cohort'** is the variable assigning an individual to either first or the second cohorts and **'TimePoint'** is a variable that accounts for the different measurement points; these being (Month 1) M1, Month 9 (M9) and Month 18 (M18). Note that 'TimePoint' and 'Cohort' are both categorical variables, i.e. their values are factors.

In order to analyse potential effects, different statistical methods were deployed. Differences were visualised using boxplots and graphs depicting the (overlapping) standard errors bars. The significance of any potentially existing effect was tested with a **two-way repeated measure ANOVA**, whereby 'TimePoint' was a **within-subjects** factor and Cohort a **between-subjects** variable.

As a reminder, as it is widely known to those practicing statistical methods, ANOVA and linear regression are not just similar, but in fact the same thing; in this case where the independent variable(s) are categorical and the dependent variable a single and continuous variable. When considering the ANOVA for the underlying study in more detail, the categorical (independent) variables 'TimePoint' and 'Cohort', are effect coded, which means that each category's mean is compared to the grand mean. 'TimePoint' has three categories while 'Cohort' has two. In a hypothetical linear regression scenario, the same categorical variables would be coded as dummies. This means that there would be z-1 binary variables created for each categorical variable, whereby z stands for the number of categories the respective variable can take. Hence, for the factor 'Cohort', which has two categories, the second cohort would for example take the value of 1 and the first cohort 0. Note that no such dummy variable was created, since one is (logically) exhaustive - in this situation the first cohort is a so called reference group. Same holds analogously for the categorical variable TimePoint, which however has three categories. Consistently with this setting, each category's intercept is compared to the reference group's intercept. Since the intercept is defined as the value when all independent variables are equal to 0, and there are no other predictors, the three intercepts are just means.

The reason for clarifying this is because during the ANOVA test, a dependency relationship between the variables of interest needs to be defined, which is in fact nothing else than a form of linear regression. Furthermore, later on in the analysis, further methods will be considered, in order to make sure more than one method of identifying possibly significant results were exhausted, and these will assume a similar linear relationship. Furthermore, ANOVA assumes that the data are normally distributed and the variance across groups is homogeneous. These assumptions were tested on the ANOVA objects as well as on the residuals of the linear regression and produced different and rather less conclusive results. These are reported in the ancillary analyses section of the report (Chapter 2.3.6).

The relationship assumed is

$$ResponseMean \sim Cohort + TimePoint + Cohort * TimePoint$$

The more precise written out form of the model used to fit the ANOVA in R, as applied in the code[31], is `aov(ResponseMean ~ (Cohort*TimePoint) + Error(Code/(TimePoint)), data=DATA),` whereby the Error(Code/TimePoint) accounts for a so-called 'natural' variation from participant to participant for the within-subjects variable, i.e. TimePoint.

Later on, a linear mixed model as well as a general least squares model were used, which include a random effect, which is the element referred to as 'Error' in the ANOVA setting. The random effect should reflect the fact that it can be presumed, that there is a certain dimension of dependency between the answers of each individual due to individual reasons (of the within variable). In order to determine the autocorrelation in residuals, the ACF function in the nlme R package was used, as this would indicate the autocorrelation for lags in the time variable. In the gls model, the form of the autocorrelation structure was specified as an autoregressive model. In the case of the lme model, the function by default assumes equally spaced intervals and uses the innermost group level. After the model was fitted, an ANOVA function was run on the resulting objects.

LME

```
model.b = lme(ResponseMean ~ Cohort + TimePoint + Cohort*TimePoint,
              random=    ~1|Code    ,data=DATA,    na.action=na.omit)
valb<-ACF(model.b)[2,2]
library(nlme)
mod.lme=lme(ResponseMean ~ Cohort + TimePoint + Cohort*TimePoint,
            random=                                          ~1|Code,
            correlation  =  corAR1(form  =  ~  TimePoint  |  Code,
                                   value          =          valb),
            data=DATA,              na.action=na.omit,method="REML")
```

GLS

```
model.a  =  gls(ResponseMean  ~  Cohort  +  TimePoint  +  Cohort*TimePoint,
                data=DATA,                              na.action=na.omit)
vala   <-   ACF(model.a,   form=   ~   TimePoint   |   Code)[2,2]
mod.gls=gls(ResponseMean ~ Cohort + TimePoint + Cohort*TimePoint,
            correlation  =  corAR1(form  =  ~  TimePoint  |  Code,
                                   value          =          vala),
            data=DATA, na.action=na.omit,method="REML")
```

2.2.9.2 Direct objectives of the INNOVCare pilot

To measure the efficacy of the intervention as a whole package as well as to be able to use statistical models that require the use continuous data like different types of the analysis of variance (ANOVA), an index based on the seven of the eight outcome variables, was created. The one variable that was

[31] An R Markdown document containing the full code, its documentation and results is provided as a digital annex to this document (Annex 6.1).

excluded from the index was disease-related peer-to-peer learning because the main question assessing this objective was only posed to those participants who mentioned that they were in contact with other people in a similar condition; thereby reducing the sample size and statistical power significantly.

The aim of the evaluation design implemented in the INNOVCare pilot, the rotation design (Chapter 2.2.1), was to determine whether the INNOVCare intervention had an effect on the participants. Following this objective, the best fitting model to achieve this objective is the two-way mixed design ANOVA. This model is 'used to analyse the effect of two independent factors on some dependent variable in a situation where one factor is a between-subjects and the other is a within-subjects' (Verma, 2016, p. 125). The INNOVCare evaluation design offers two independent variables: the cohorts, which is the between-subjects factor because the two groups include different individuals, and the time, which is the within-subjects factor because all the participants were measured at three points in time. Time in this design represented the intervention as it represents when the cohorts received the intervention: the first during the first nine months and the second during the last nine months. The effect expected from the intervention was the dependent variable. When looking at the effects of the intervention as a whole, then it is the measure of the index for each participant over the three measurement periods. The main aim of running the two-way mixed ANOVA, in this case, was to ascertain whether a significant interaction effect between cohort and intervention existed, meaning whether the effect of one factor is dependent on the other factor. If a significant interaction effect was determined, then to determine the simple main effects of cohort, an independent-samples t-test was carried out. To determine the simple main effects of time, a one-way repeated-measures ANOVA was performed subsequent to the two-way mixed ANOVA.

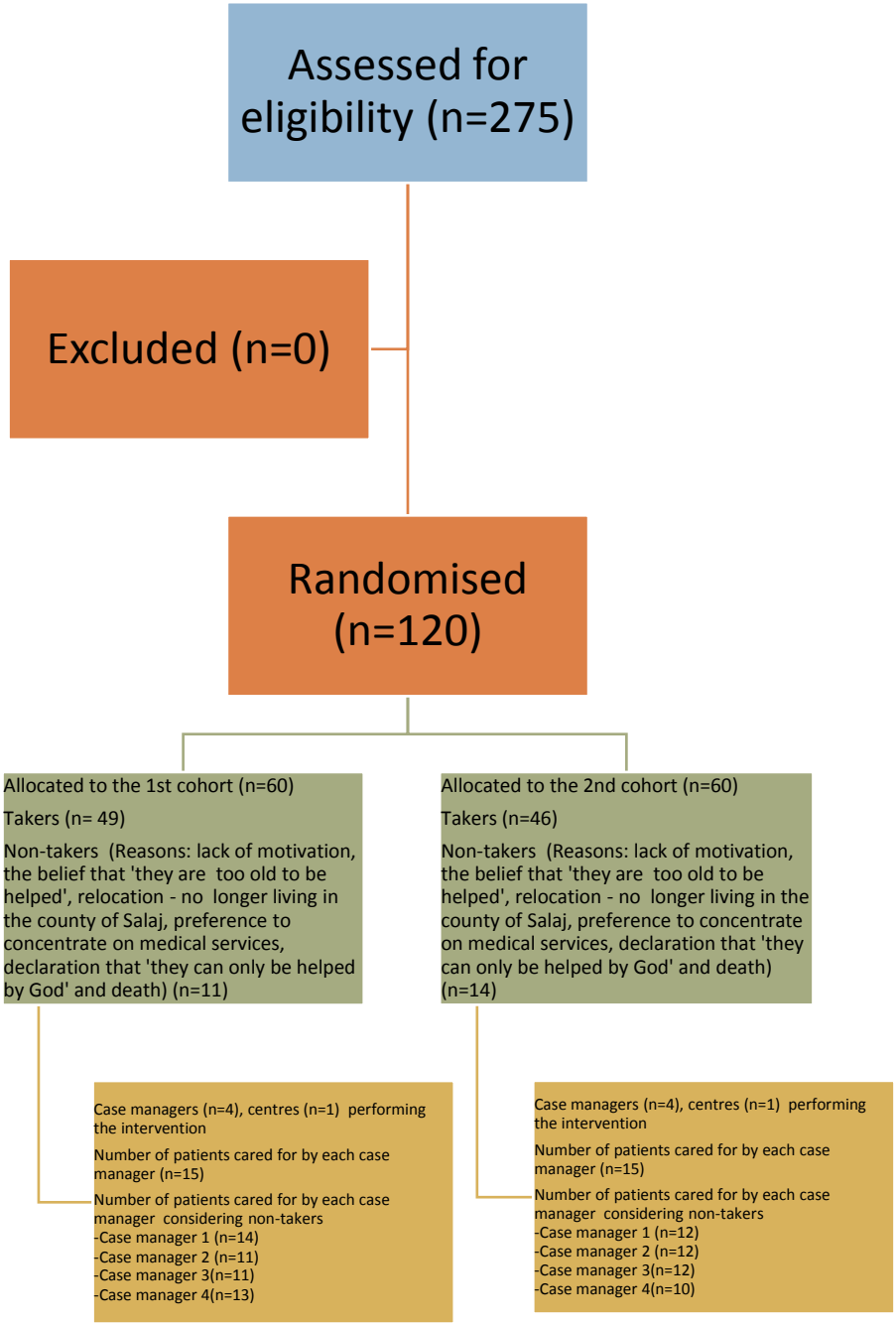
To measure the effect of the intervention on the individual outcome variables (Chapter 2.2.4), rather than applying the models described in the paragraph above, their non-parametric equivalents were applied. This is because one of the main assumptions of the ANOVA is that the dependent variable is measured at the continuous level. However, the data extracted from the individual outcome variables were all measured at a categorical level. The nonparametric equivalents of the models described above are: The Generalized Estimating Equations (GEE) for the two-way mixed ANOVA, Kruskal-Wallis test (Field, 2013, p. 877) for the one-way independent –measures ANOVA and the Friedman's ANOVA (Field, 2013, p. 875) for the one-way repeated-measures ANOVA.

The supporting items described in Chapter 2.2.4 as well as other socio-demographic data available were used in the ancillary analysis (Chapter 2.3.6) for sub-group comparisons. As the division of subgroups using the different variables such as age, gender, location of the patients etc. resulted in very unbalanced groups, the non-parametric tests listed above were used to avoid violating the assumption of the parametric tests with the index created as the dependent variable.

2.3 RESULTS

2.3.1 PARTICIPANT FLOW

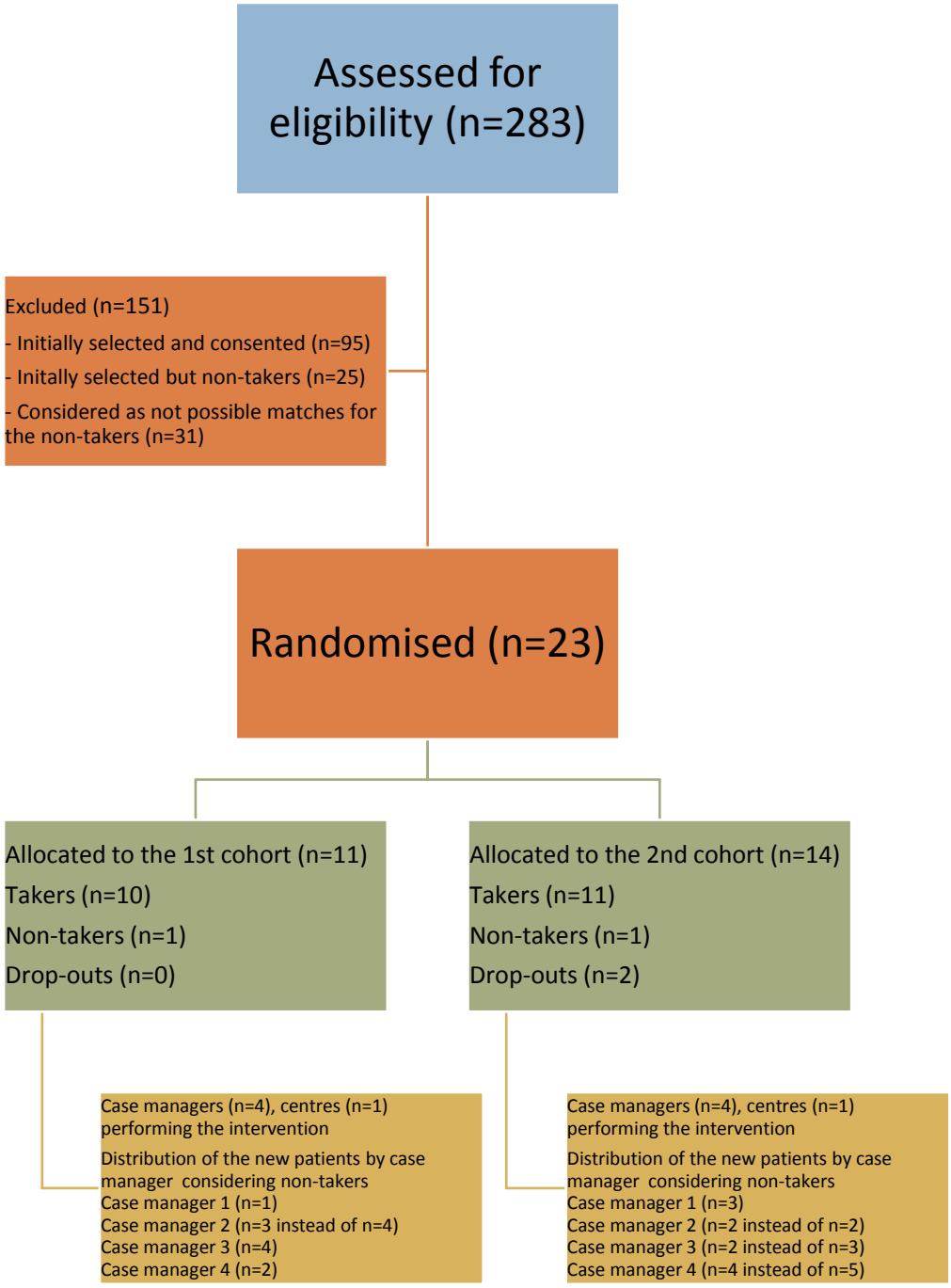
2.3.1.1 Participant flow diagramme: 1st selection



[32] 'Takers' refer to persons randomly selected to take part in the study who consented by signing the contract and thereby receiving the intervention

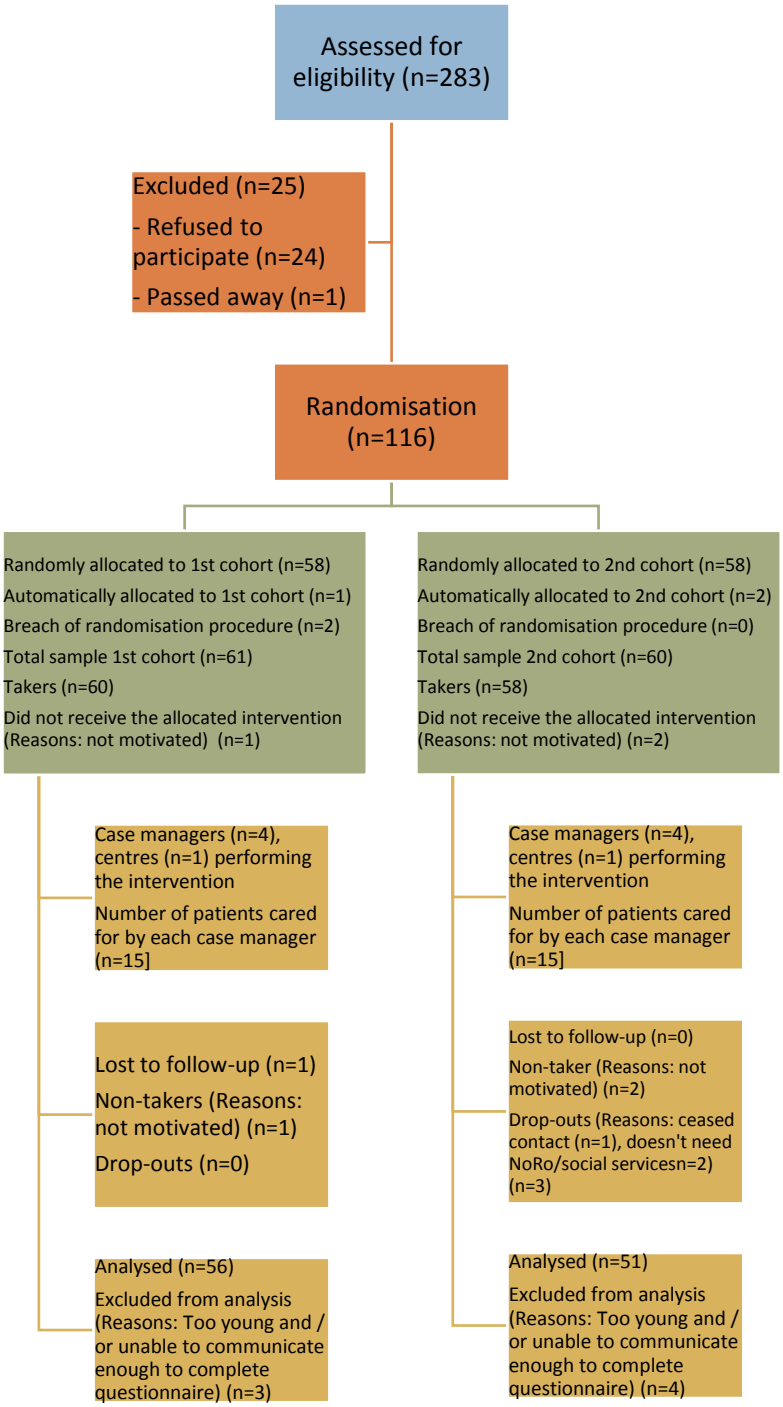
[33] 'Non-takers' refer to persons randomly selected to take part in the study but who refused to sign the contract and thereby not receiving the INNOVCare intervention.

2.3.1.2 Participant flow diagramme: 2nd Selection



[34] 'Drop-outs' refer to persons who were randomly selected to take part in the study, signed the contract and received a part of the intervention but discontinued the intervention before the end of the 9 month intervention duration.

2.3.1.3 Combined participant flow diagramme



[35] In effect, only 116 of the 121 participants were randomly assigned to the two cohorts. Three participants were included in the same cohorts as their relatives who had already been randomly assigned a cohort, while two

2.3.2 RECRUITMENT

The enrolment of the patients and their families, the participants, started in February 2017. For the participants sampled during the first selection, this process ended in March 2017 when the enrolment of the participants drawn from the second selection was made. This process was completed in April 2017.

The first cohort received the intervention from March 2017 to November 2017, while the second cohort received the intervention from November 2017 to July 2018.

2.3.3 BASELINE DATA

Table 7 below shows the baseline demographic and clinical characteristics for each cohort (only including the takers). Table 6 above shows the baseline characteristics of the whole INNOVCare pilot sample.

TABLE 7: BASELINE DEMOGRAPHICS OF THE INNOVCARE PILOT SAMPLE

Parameter	1st cohort (n=60)[38]	2nd cohort (n=58)
Females to males	30:30	33:25
Age[39]	29.35 (23.19, 35.51)	30.07 (23.98, 36.16)
NoRo to external beneficiaries	33:27	32:26
Living in urban areas to rural	44:16	40:18
Degree of disability: No disability to mild to moderate to marked to severe without personal assistant to severe with personal assistant	0:0:1:18:4:37	2:0:2:19:4:31

participants were randomly assigned to a cohort but breached the randomisation procedure by requesting to be included in the cohort that they were not assigned due to an urgent issue or relocation.

[36] Participants automatically allocated to either of the two cohorts were family members of participants who had already been randomly assigned a cohort. Because they lived in the same household with their family member, they were assigned the same cohort and case manager for practicality reasons.

[37] The final INNOVCare sample included 61 participants in the first cohort and 60 in the second. One of the participants assigned to the first cohort and two of the participants assigned to the second cohort refused to sign the informed consent form/contract therefore relinquishing their participation in the INNOVCare pilot. As a result, 60 participants in the first cohort and 58 in the second started the intervention. As can be seen in the 2.3.1.3 Combined participant flow diagramme, none of the participants from the first cohort and three participants from the second cohort dropped out of the pilot – they consented to taking part, took part in a fraction of it and then stopped.

[38] 'Lost to follow-up' refers to those participants who received the whole intervention (9 months of case management) but did not complete the final questionnaire.

[39] Mean (95% confidence interval)

2.3.4 NUMBERS ANALYSED

Table 8 below shows the number of participants included in each analysis. Unfortunately the numbers analysed for the DISABKIDS-SMILEY and DCGM instruments are relatively low. This was unfortunately due to a mix-up during the first measurement. 20 participants who were actually supposed to complete the DISABKIDS-SMILEY at all three measurements, mistakenly completed the DCGM-12 tool at the first measurement and the DISABKIDS-SMILEY at the remaining two measurements. As the methods of analysis implemented compared all three measurements, these participants were unfortunately excluded from the analysis.

TABLE 8: N ANALYSED BY MEASUREMENT TOOL FOR QUALITY OF LIFE AND BY OBJECTIVES FOR DIRECT OBJECTIVES OF THE PILOT

	Quality of life instrument	Numbers analysed in 1st cohort		Numbers analysed in 2nd cohort	
Overarching goal: Improving the quality of life of the people who benefit from it	DISABKIDS-SMILEY	17		17	
	DCGM-12	24		28	
	EQ-5D-Y	24		27	
	Objective	**Numbers analysed in 1st cohort**		**Numbers analysed in 2nd cohort**	
		Patient	Family	Patient	Family
Direct objectives of the INNOVCare pilot.	1. Information about disease or condition	24	55	26	48
	2. Understanding of rights	24	55	26	48
	3. Information on available health and social services	24	55	26	48
	4. Self-management of care	24	55	26	48
	5. Communication skills	24	55	26	48
	6. Disease-related peer-to-peer learning	Up to 10		Up to 19	
	7. Coordination among providers	24	55	26	48
	8. Understanding and acceptance in the community	24	55	26	48

2.3.5 OUTCOMES AND ESTIMATION

Looking back at the trial design, one expects the following changes:

1. Between the two cohorts:

   a. No significant differences between the two cohorts at the first (Month 1) and third measurements (Month 18)
   b. The scores for the first cohort should be significantly higher than of the second cohort at the second measurement or/and difference in the change per cohort from the first measurement at Month 1 to the second in Month 9 should be significantly higher in the first cohort than in the second
2. Within the cohorts:
   a. An improvement in the scores of the two cohort during the intervention trials:
      i. the first cohort: from the first measurement (Month 1) compared to the second measurement (Month 9)
      ii. the second cohort: from the second measurement (Month 9) compared to the third measurement (Month 18)
      iii. A significant improvement in the score of both cohorts at the third measurement (after having both received the intervention) compared to the first measurement, before any of them received the intervention
   b. No significant changes in the scores of the first cohort between the second and the third measurements (Month 9 and Month 18)
   c. No significant changes in the scores of the second cohort between the first and the second measurements (Month 1 and Month 9)

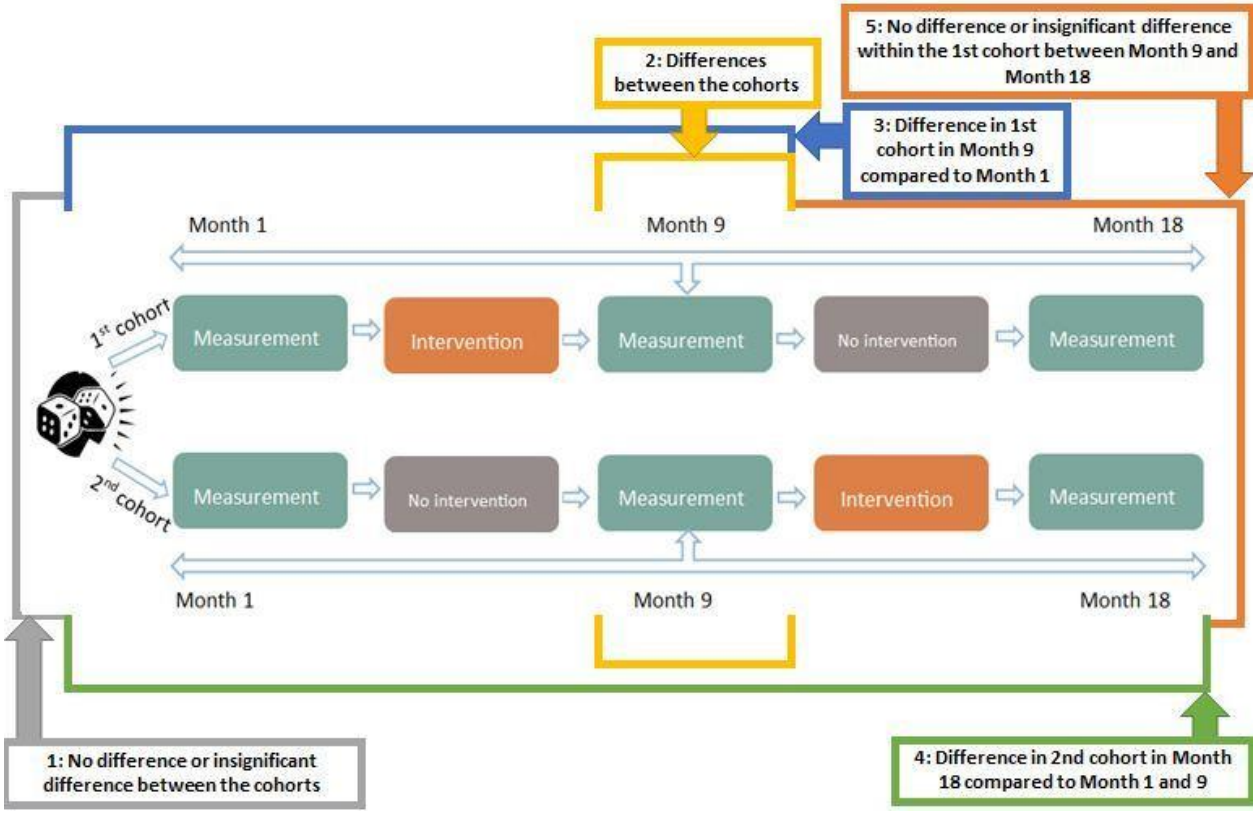


FIGURE 2: EXPECTED CHANGES

These expected changes apply to all the analyses covered in this report.

2.3.5.1 Overarching goal of the intervention: Improvement in Quality of life

The outcomes of the statistical analysis are presented separately for each quality of life measure. As is evident, no significant effects could be identified with either method. The general least squares model's results are reported in the section on Ancillary Analyses (Chapter 2.3.6.1).
Since the different quality of life measurement instruments use different scales, in R, these were automatically standardised in that they were transformed to a Likert scale with 1 as the lowest possible value and 5 the highest possible. This is however not the case in the literature, which might lead to some confusion, which is why it should be stated at this point that it is a mere technicality. In the following presentation of the results, wherever data are visualised or the results of statistical analyses are directly reported, the automatically generated Likert scale is retained. In text-form, the generalised form with 0 as its lowest score and 100 as the highest is additionally reported in parentheses. This is calculated according to a formula which transforms the number between 1 and 5 to a number lying between 0 and 100[40].

2.3.5.1.1 DISABKIDS - SMILEYS

The boxplot suggests that the **median** of the second cohort and thus 50% of the individuals assigned to it had more positive responses with regard to their well-being. Since this was already the case at M1, the latter confirmation could be a persistence of that effect.

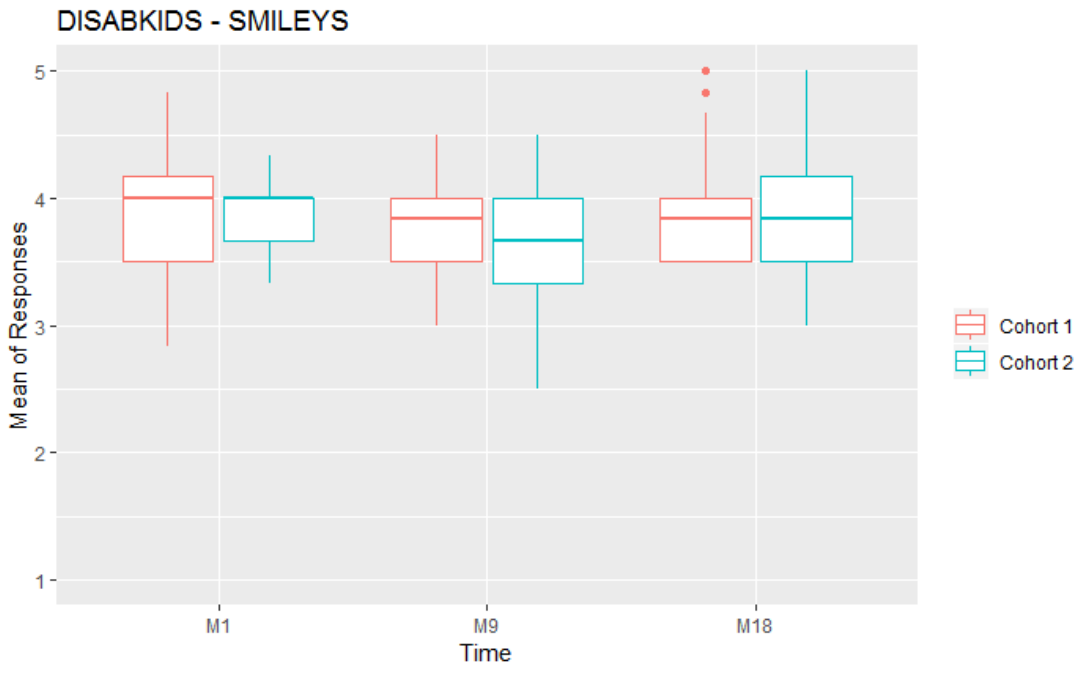


FIGURE 3: DISTRIBUTION OF SCORES OF THE DISABKIDS-SMILEY TOOL

[40] $score_{0-100} = (score_{1-5} - 1)\frac{100}{4}$

TABLE 9: DISABKIDS-SMILEY DESCRIPTIVE STATISTICS

Cohort	Time	N	Mean	SD
Cohort 1	M1	17	3.853	0.520
Cohort 1	M9	17	3.794	0.402
Cohort 1	M18	17	4.000	0.537
Cohort 2	M1	17	3.833	0.283
Cohort 2	M9	17	3.608	0.553
Cohort 2	M18	17	3.873	0.576

As far as the means are concerned, whenever they reflect some change, this is minimal in size. The high standard deviation however also indicates that individuals within each cohort deviate from its mean, to a high extent suggesting that effects could highly vary throughout individual cases.

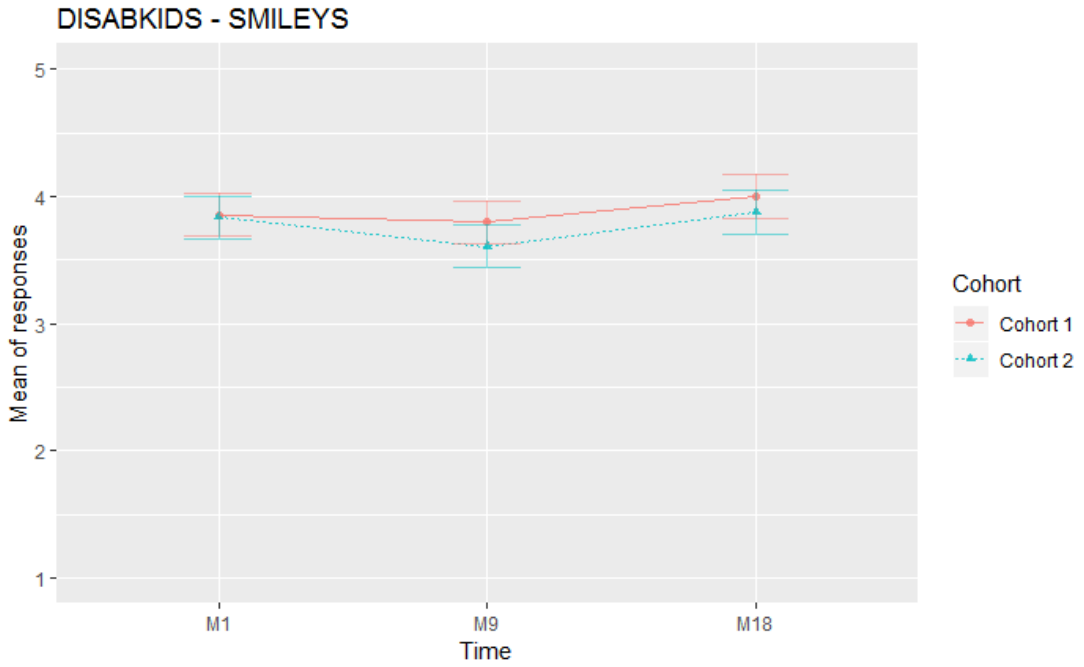


FIGURE 4: EFFECT OF THE INNOVCARE PILOT ON THE QUALITY OF LIFE OF PATIENTS OVER TIME (DISABKIDS-SMILEY)

Paradoxically, the means of the first cohort worsens between M1 and M8 (after the intervention), which would indicate that the intervention had adverse effects, contrary to what was expected. The scores specifically drop from 3.85 (71.324) to 3.79 (69.853). The effects however were not statistically significant, as follows from the ANOVA results below. Furthermore, the scores of the second cohort, which did not receive the intervention during this period, also dropped to a slightly higher degree than the first cohort: from 3.833 (70.833) to 3.608 (65.196). Nevertheless, this difference was also not statistically significant as can also be seen by the overlapping error bars. On the contrary, the means of both cohorts increased in the period, where the second cohort received the intervention and the first cohort did not (Month 09 to Month 18). However, neither increase was statistically significant.

TABLE 10: ANOVA RESULTS - DISABKIDS – SMILEYS

	DFn	DFd	SSn	SSd	p	η_G [241]
Intercept	1	32	1493.727	7.255	0.000*	0.985
Cohort	1	32	0.315	7.255	0.247	0.014
Time	2	64	0.955	15.739	0.152	0.040
Cohort:Time	2	64	0.121	15.739	0.782	0.005

As can be seen in Table 11 below, Mauchly's test for sphericity does not reject the null-hypothesis that there is no difference in variances for all pairwise group comparisons. Therefore the ANOVA results are reliable.

TABLE 11: MAUCHLY'S TEST FOR SPHERICITY - DISABKIDS - SMILEYS

Effect	W	p
Time	0.875	0.125
Cohort:Time	0.875	0.125

2.3.5.1.2 DCGM-12 (SHORT VERSION)

As in the cases of the aforementioned quality of life measurement instruments, the ones of the DCGM-12 (Short Version) display a similar pattern. Effects are barely notable in terms of size and after the intervention not always positive changes are tracked. Although a bit lower than in the case of the previous quality of life measures, the standard deviation is still considerably high and again points at a high variation and thus possibly qualitatively different effects among the different cases. Also in this case there seem to be no significant effects.

TABLE 12: DCGM-12 DESCRIPTIVE STATISTICS

Cohort	Time	N	Mean	SD
Cohort 1	M1	24	2.510	0.450
Cohort 1	M9	24	2.560	0.384
Cohort 1	M18	24	2.485	0.364
Cohort 2	M1	28	2.510	0.401
Cohort 2	M9	28	2.518	0.338
Cohort 2	M18	28	2.441	0.324

[41] Generalized eta squared - effect size statistic for repeated measures designs as recommended by R. Bakeman (Bakeman, 2005).

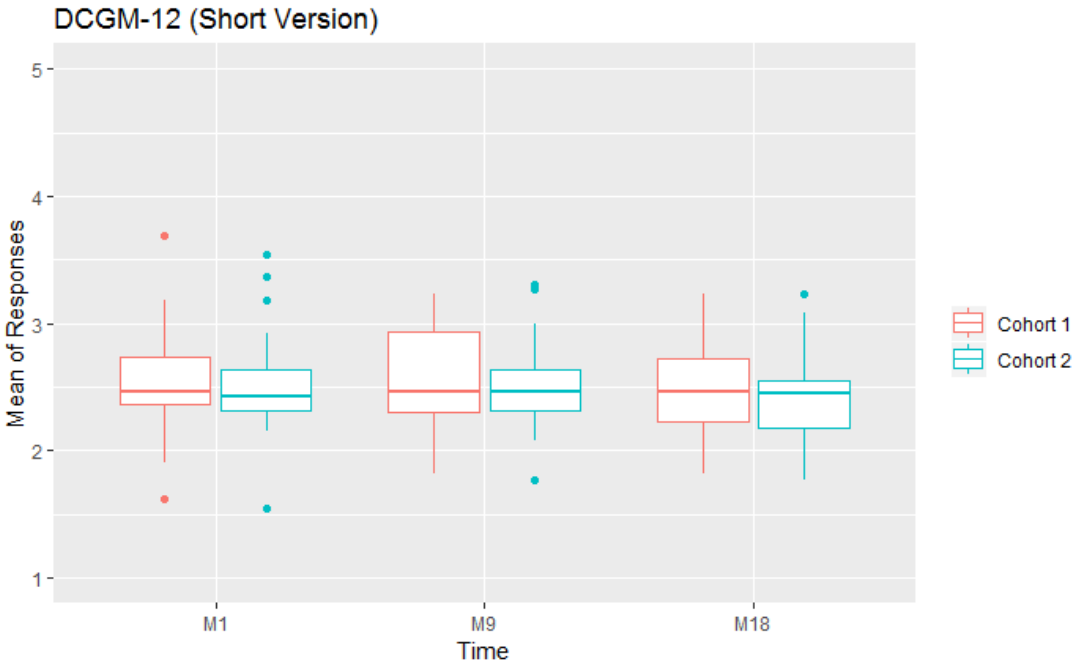


FIGURE 5: DISTRIBUTION OF SCORES OF THE DCGM-12 TOOL

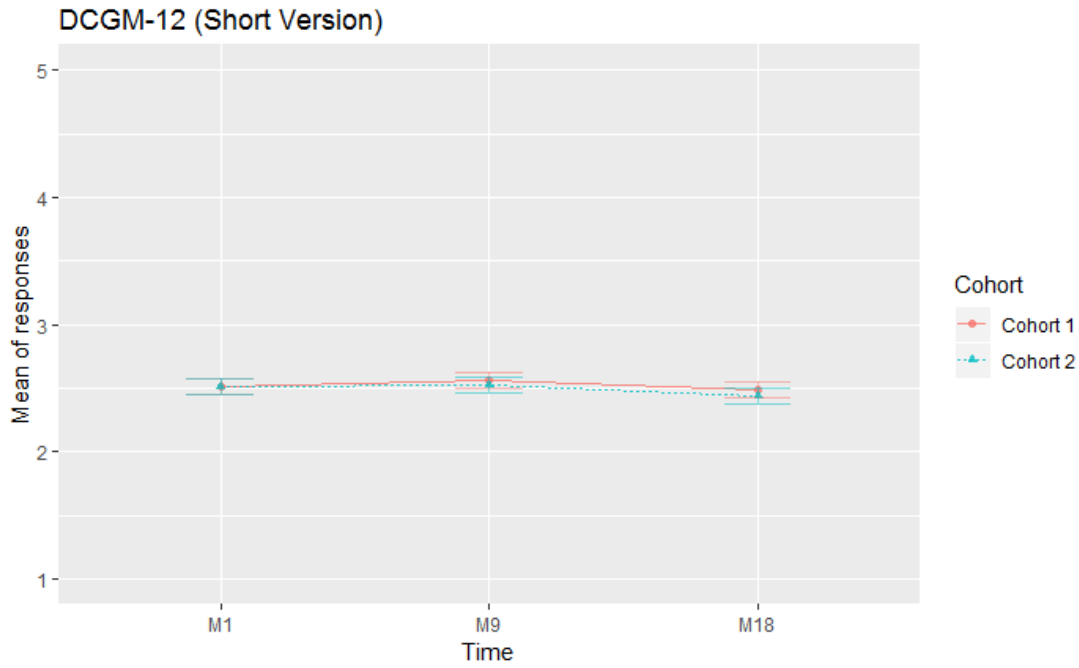


FIGURE 6: EFFECT OF THE INNOVCARE PILOT ON THE QUALITY OF LIFE OF PATIENTS OVER TIME (DCGM-12)

TABLE 13: ANOVA RESULTS DCGM-12 (SHORT VERSION)

	DFn	DFd	SSn	SSd	p	η_G[42]
Intercept	1	50	972.548	16.117	0.000*	0.979
Cohort	1	50	0.032	16.117	0.754	0.001
Time	2	100	0.152	5.247	0.240	0.007
Cohort:Time	2	100	0.016	5.247	0.856	0.001

TABLE 14: MAUCHLY'S TEST FOR SPHERICITY - DCGM-12 (SHORT VERSION)

Effect	W	p
TimePoint	0.865	0.028*
Cohort:TimePoint	0.865	0.028*

As can be seen in
Table 14, Mauchly's test for sphericity also in this case rejects the null hypothesis of no difference in variances for all pairwise group comparisons. Therefore the ANOVA results are not reliable and the Greenhouse-Geisser and Huynh-Feldt sphericity corrections are performed. As their respective p values seen in Table 15 suggest, when accounting for the sphericity violation, the estimated effects remain statistically insignificant.

TABLE 15 SPHERICITY CORRECTIONS -"DCGM-12 (SHORT VERSION)"

Effect	GG ε[43]	p.GG.[44]	HF ε[45]	p.HF.[46]
TimePoint	0.881	0.241	0.911	0.241
Cohort:TimePoint	0.881	0.830	0.911	0.837

In part, a general least squares as well as a linear mixed effects model are fitted to the data.

2.3.5.1.3 EQ-5D-Y

The boxplots below suggest that the medians of both cohorts lie close to each other, with a minor shift of the second cohort's median in M18. Also the medians of both cohorts slightly increase in M9, with that of the first cohort being minimally higher. At first glance one could wish to interpret this as an indication of a positive intervention effect – since always the cohorts that received treatment have better responses – however the size effect is minimal as is it is contradictory to the results collected by the first quality of life measurement instruments as presented above.

[42] Generalized eta squared - effect size statistic for repeated measures designs as recommended by R. Bakeman (Bakeman, 2005).
[43] Greenhouse-Geisser epsilon value; epsilon being a measure of departure from sphericity
[44] Greenhouse-Geisser p-value
[45] Huynh-Feldt epsilon value; epsilon being a measure of departure from sphericity
[46] Huynh-Feldt p-value

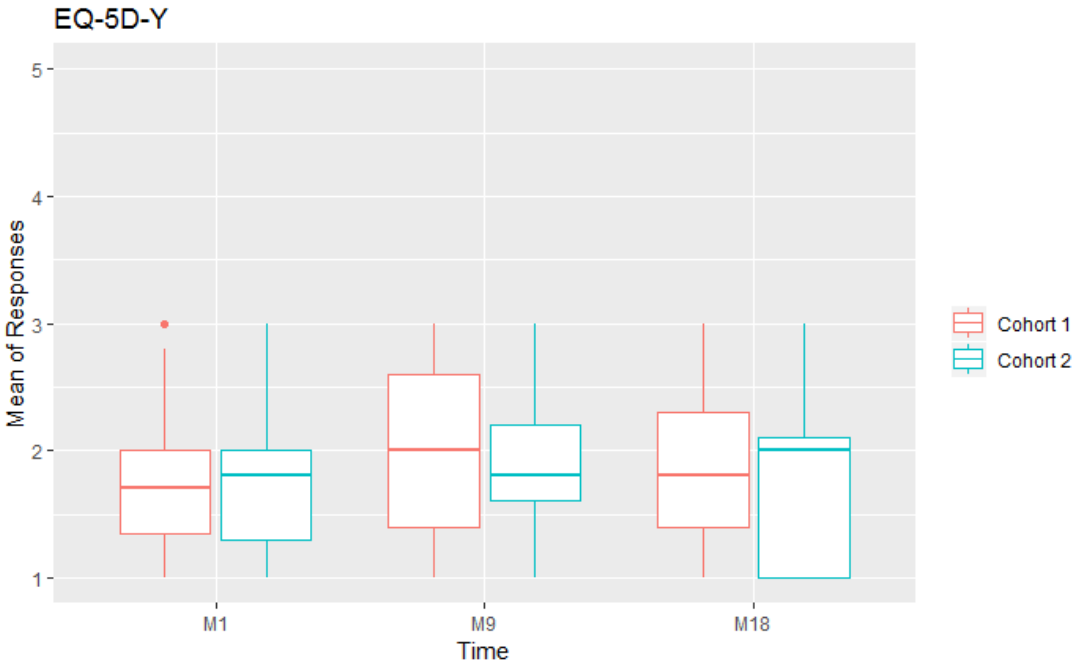


FIGURE 7: DISTRIBUTION OF SCORES OF THE EQ-5D-Y TOOL

TABLE 16: EQ-5D-Y DESCRIPTIVE STATISTICS

Cohort	Time	N	Mean	SD
Cohort 1	M1	24	1.792	0.625
Cohort 1	M9	24	1.967	0.653
Cohort 1	M18	24	1.892	0.675
Cohort 2	M1	27	1.756	0.567
Cohort 2	M9	27	1.924	0.587
Cohort 2	M18	27	1.785	0.627

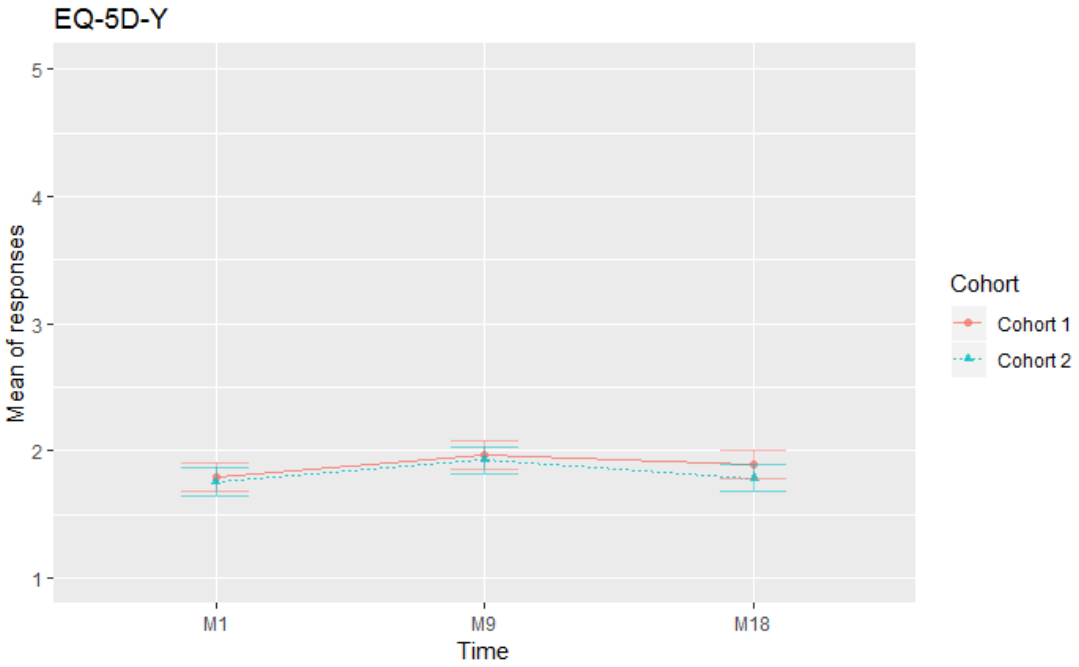


FIGURE 8: EFFECT OF THE INNOVCARE PILOT ON THE QUALITY OF LIFE OF PATIENTS OVER TIME (EQ-5D-Y)

As far as the means are concerned, these also display ambiguous movements across both cohorts. In M9, the mean for the first cohort has a small increase, which is in line with the median movement. The second cohort however displays decreased means after intervention in M18, falling from 1.92 (23.102) to 1.785 (19.630). Again, the size of the effect is itself are barely noteworthy and as in the case of the first DISABKIDS-SMILEY, the standard deviation that large, again indicates that individuals within each cohort deviate to a high extent from its mean, suggesting that effects could highly vary throughout individual cases.

As above, the ANOVA results confirm that none of the differences are statistically significant.

TABLE 17: ANOVA RESULTS EQ-5D-Y

	DFn	DFd	SSn	SSd	p	η_G [247]
Intercept	1	49	523.224	42.283	0.000*	0.902
Cohort	1	49	0.145	42.283	0.683	0.003
Time	2	98	0.765	14.555	0.081	0.013
Cohort:Time	2	98	0.038	14.555	0.879	0.001

As can be seen in Table 18, Mauchly's test for sphericity however rejects the null hypothesis that there is no difference in variances for all pairwise group comparisons. Therefore the ANOVA results are not reliable and the Greenhouse-Geisser and Huynh-Feldt sphericity corrections are performed. As their

[47] Generalised eta squared - effect size statistic for repeated measures designs as recommended by R. Bakeman.

respective p values seen in Table 19 suggest, when accounting for the sphericity violation, the estimated effects remain statistically insignificant.

TABLE 18 MAUCHLY'S TEST FOR SPHERICITY - "EQ-5D-Y"

Effect	W	p
TimePoint	0.682	0.000*
Cohort:TimePoint	0.682	0.000*

TABLE 19 SPHERICITY CORRECTIONS -"EQ-5D-Y"

Effect	GG ε[48]	p.GG.[49]	HF ε[50]	p.HF.[51]
TimePoint	0.759	0.097	0.778	0.096
Cohort:TimePoint	0.759	0.822	0.778	0.827

2.3.5.2 Direct objectives of the INNOVCare pilot : According to the patients

2.3.5.2.1 EFFICACY OF THE INNOVCARE TRIAL ON THE WHOLE

As described in Chapter 2.2.9 above, to measure the efficacy of the intervention in general, seven of the eight outcome variables described in Chapter 2.2.4 above were combined to create an index. The one outcome variable that was excluded was the one concerning disease-related peer-to-peer learning. The question related to this variable was only addressed to those participants who said that they were in contact with other people in a similar situation as themselves; therefore the sample size for this item was considerably smaller as with the other seven outcome variables.

In essence the INNOVCare pilot was made up of two trials: the control trial and the intervention trial. In the control trial the participants continued on with 'treatment as usual'; this means that during this time, they did not receive the support of the case managers. For the first cohort, this was during the last nine months of the pilot, while for the second cohort; this was during the first nine months of the trial. On the contrary, in the intervention trial was the period where the participants were under the care and support of a case manager that had been assigned to them. For the first cohort, this was during the first nine months of the intervention, while for the second cohort this was during the last nine months of the intervention (see Table 20 below).

TABLE 20: THE CONTROL AND INTERVENTION TRIAL MAKING UP THE INNOVCARE PILOT BY COHORT

	Month 1 to Month 9	Month 9 to Month 18
Control trial	2nd cohort	1st cohort
Intervention trial	1st cohort	2nd cohort

[48] Greenhouse-Geisser epsilon value; epsilon being a measure of departure from sphericity
[49] Greenhouse-Geisser p-value
[50] Huynh-Feldt epsilon value; epsilon being a measure of departure from sphericity
[51] Huynh-Feldt p-value

To determine any changes that may have occurred as a result of the INNOVCare pilot on the index created, a two-way mixed ANOVA was run on the statistical software SPSS. The assumptions of a two-way mixed ANOVA were duly checked[52].

Data are mean ± standard deviation unless otherwise stated. Considering the first cohort in the two trials; control and intervention trials, there was a significant two-way interaction between treatment and time, $F(1,23) = 49.902$, $p<.001$. Likewise, the second cohort also had a significant two-way interaction between treatment and time, $F(1,25) = 27.977$, $p<.001$. In the paragraphs below, the simple effects of treatment and time for each of the cohorts will be presented.

2.3.5.2.1.1 BETWEEN-GROUPS

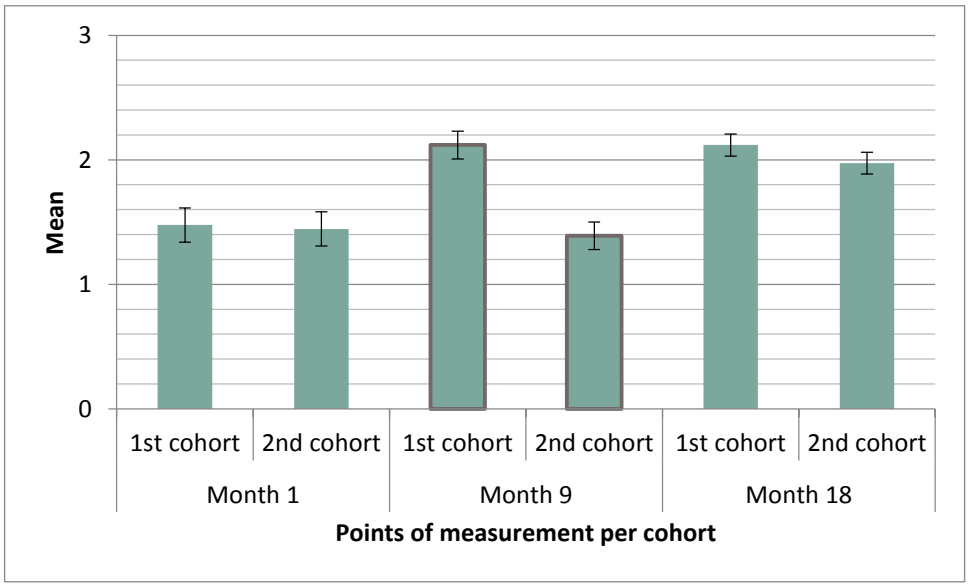
Independent-samples t-tests were conducted to determine whether the mean efficacy of the INNOVCare pilot differed between the two cohorts at the three measurement points. A significant difference was only expected at the second measurement point, after nine months of intervention, where the first cohort had received the intervention and the second cohort continued as usual (Chapter 2.3.5, expectation 1b). For the first and third measurement points, no significant difference between the groups was expected (Chapter 2.3.5, expectation 1a). The first measurement was conducted before the pilot had commenced, while the third measurement was conducted after both cohorts had received the intervention. 24 patients from the first cohort completed all measurements; while in the second cohort this number was 26. In total, there were three outliers, as assessed by the box plots: one in the first cohort at the first two measurement points and two in the second cohort at the first measurement and one in the second and third measurement points. As only three outliers in total were detected, they were left in the analysis. The results of the independent t-tests will be compared with the non-parametric equivalent, the Mann-Whitney U test[53] which is not as affected by outliers as independent-

[52] 1. Continuous dependent variable: The indices created were measured at a continuous level
2. Two within-subject factors where each of the two factors consists of two or more categorical levels: The first within-subject variable is 'treatment' which is a categorical variable with two levels 'control' and 'intervention'. The other within-subjects factor is 'time' which has two categories the 'pre' and the 'post'. For the first cohort the 'pre' measurement is that at Month 1 and the 'post' that at Month 9. For the second cohort the 'pre' is the measurement at Month 9 and the 'post' is that at Month 18.
3. One between-subjects factor measured which with two or more categories: 'cohort' is the between-subjects factor with two categories
4. No significant outliers in any cell of the design: There were no outliers, as assessed by examination of studentized residuals for values greater than +/-3
5. The dependent variable should be normally distributed for each cell of the design: Efficacy of the INNOVCare pilot (the index of the direct objectives) was normally distributed ($p>.05$) except in the second cohort at the end of the intervention trial ($p=0.025$) and at the beginning of the control trial ($p=0.34$), as assessed by Shapiro-Wilk's test of normality on the studentized residuals. As ANOVAs are considered to be fairly robust to deviations of normality (Maxwell & Delaney, 2004) no transformations of the data were performed and the analysis was carried on with the data as they were
5. The variances of the differences between levels should be equal: Since there are only two levels of the within-subject variables, sphericity is automatically assumed (Field, 2013, p. 561).

[53] Due to the violations of the assumptions of the independent-samples t-tests with regard to outliers and normality of variance, a Mann-Whitney U test was also run to determine whether the results from the two tests

samples t-tests. All the data for the first cohort as assessed by the Shapiro-Wilks test was normally distributed; for the second cohort the first and third measurements were not normally distributed as according to the Shapiro-Wilk test with p values of 0.034 and 0.025 respectively. As the sample sizes in each group are nearly equal, differing by just two cases, this violation was not expected to affect the results of the t-test ((Maxwell & Delaney, 2004) and (Shadish, et al., 2002), and as a result, the test was carried on regardless. There was homogeneity of variances, as assessed by Levene's test of homogeneity of variances at all measurement points except the second (p=0.830, 0.023 and 0.607 respectively). As a result of this violation, the scores based on Welch's t-test were interpreted.

At the first measurement, the first cohort had a mean score of 1.476 ±0.5 while the second had a mean score of 1.445 ±0.5; the mean difference of 0.031 was not statistically significant (95% CI, -0.24 to 0.31), t(46.790)=0.228, p=0.821. In the second measurement the first cohort had a mean score of 2.119 ±0.3 while the second cohort had a mean score of 1.390 ±0.5; the mean difference of 0.729 was statistically significant (95% CI, 0.51 to 0.95), t(40.288)=6.625, p<0.001. Like the first measurement, the third measurement did not demonstrate a statistically significant difference between the groups (95% CI, -0.03 to 0.322), t(47.978)=1.672, p=0.101, the mean score for the first cohort was 2.119 ±0.3 while that of the second was 2.043 ±0.3.



[54]

FIGURE 9: DIFFERENCES BETWEEN COHORTS BY MEASUREMENT POINTS OF THE INNOVCARE EFFICACY INDEX

differ sufficiently to warrant different conclusions. The results of the Mann-Whitney U test in this case were essentially the same as that from the independent-samples t-test . Distribution of the INNOVCare index score for both cohorts was similar, as assessed by visual inspection. Median score for the first cohort for the three measurements was 1.43, 2.00 and 2.07 respectively. For the second cohort the same was: 1.29, 1.36 and 1.86. The first measurement U=293, z=-0.372, p=0.7 and the third measurement U=210, z=-2.005, p=0.05 were not statistically significantly different while the second measurement, just like with the independent-samples t-test was: U=61, z=-4.897, p<0.001.

[54] For ease of interpretation, significant differences are signalled by highlighted bars throughout this report.

2.3.5.2.1.2 WITHIN-GROUPS

2.3.5.2.1.2.1 1ST COHORT

A two-way repeated measures ANOVA was run to determine the efficacy of the INNOVCare pilot on the first cohort over time. Analysis of the studentized residuals showed that there was normality, as assessed by the Shapiro-Wilk test of normality and no outliers, as assessed no studentized residuals were greater than ± 3 standard deviations. Sphericity was assumed as both within-subjects variables had only two levels. After determining that there was a statistically significant interaction between the intervention and time (see paragraph above), simple main effects were run.

As expected, there was a statistically significant difference in the mean efficacy of the INNOVCare intervention at the beginning of the intervention trial for the first cohort compared to the end. The mean was 0.640 (95% CI, -0.481 to 0.799) points higher at the end of the intervention trial as opposed to the beginning of the intervention trial, a difference that was statistically significant, $F(1,24) = 69.113$, $p<0.001$.

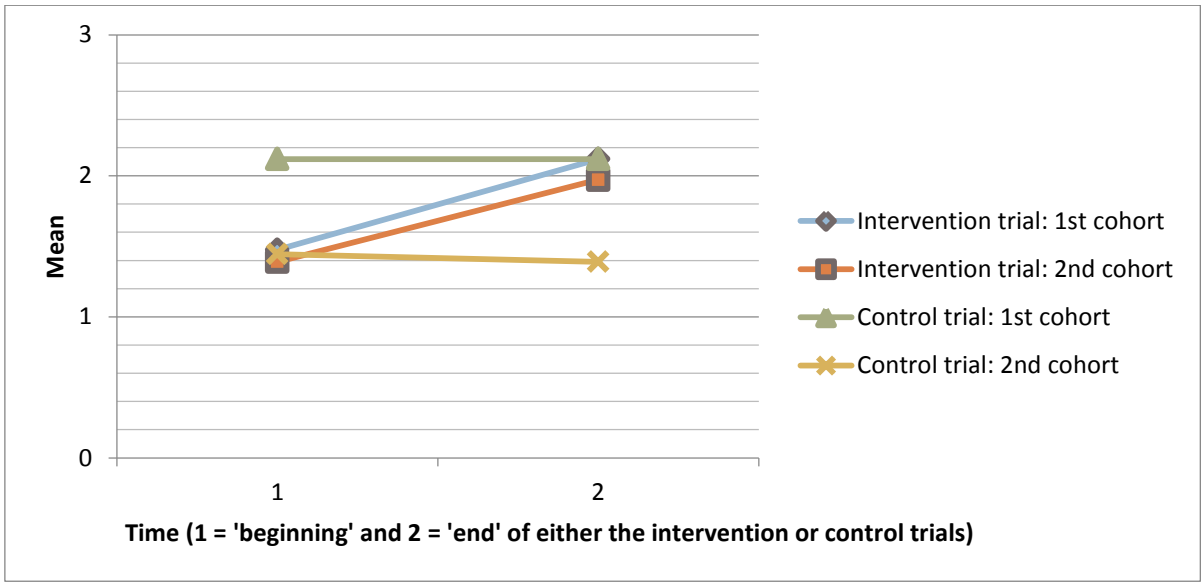
During the control trial, there was no statistically significant effect of time on the efficacy of the INNOVCare pilot, $F(1,24) = 0.000$, $p=1$; in fact the mean remained exactly the same, with the standard deviations being slightly higher at the end of the control trial. This indicates that the first cohort, which had received the intervention during the first phase of the intervention, was able to sustain the effects of the intervention at least nine months after the INNOVCare pilot.

2.3.5.2.1.2.2 2ND COHORT

A two-way repeated measures ANOVA was run to determine the efficacy of the INNOVCare pilot on the second cohort over time. Analysis of the studentized residuals showed that there were no outliers as no studentized residuals were greater than ± 3 standard deviations. Normality as assessed by the Shapiro-Wilk test of normality determined that the scores at the end of the intervention trial and the beginning of the control trial were not normally distributed with, p values of 0.025 and 0.034. As ANOVAs are considered to be fairly robust to deviations of normality (Maxwell & Delaney, 2004), no transformations of the data were performed and the analysis was carried on with the data as they were. Sphericity was assumed as both within-subjects variables (treatment and time) had only two levels. After determining that there was a statistically significant interaction between the intervention and time (see paragraph above), simple main effects were run.

As according to expectation 2d in Chapter 2.3.5 above, although the mean slightly declined by 0.055, there was no statistically significant effect of time on the efficacy of the INNOVCare pilot, $F(1,25) = 0.774$, $p=0.387$ during the control trial of the second cohort.

During the intervention trial on the other hand, a significant improvement was expected (expectation 2b in Chapter 2.3.5) and subsequently observed. The mean was 0.598 (95% CI, -0.440 to 0.756) points higher at the end of the intervention trial for the second cohort than at the beginning, a difference that was statistically significant, $F(1,26) = 60.253$, $p<0.001$.



[55]

FIGURE 10: EFFICACY OF THE INNOVCARE PILOT AT THE INTERVENTION AND CONTROL TRIALS BY COHORT

2.3.5.2.1.3 SYNOPSIS

Looking at the results presented in Chapter 2.3.5.2.1 above, all in all, it can be concluded that the INNOVCare pilot was effective in achieving its main objectives: Increasing level of knowledge of patient's condition, their rights as patients and available social health and social services; improving their ability to manage their own care as well as to communicate about their condition including symptoms, medical examinations and treatments; improved coordination among providers as well as understanding and acceptance in the community. Although the first cohort improved slightly more than the second cohort in the intervention trial, this difference of 0.042 was not statistically significant. Furthermore, these results show that the effects of the intervention could be retained for at least nine months after the end of the trial (see Chapter 2.3.5.2.1.2.1).

The following sections will look at how far the INNOVCare trial was able to reach each of its individual goals listed in Chapter 2.2.4 above. Unlike the analysis above based on the index created for the efficacy of the INNOVCare intervention, the sections below will look at the eight objectives of the intervention individually. As each of the eight items was measured at an ordinal level, hence violating one of the main assumptions of parametric tests, instead of implementing the different parametric tests conducted in the previous sections, their non-parametric equivalents will be used here.

[55] For ease of interpretation, significant differences are signalled by highlighted marker points throughout this report.

2.3.5.2.2 KNOWLEDGE ON DISEASE OR CONDITION

2.3.5.2.2.1 BETWEEN-GROUPS

A Kruskal-Wallis test[56] was conducted to determine whether there were differences between the first (n=24) and second (n=26) cohorts in their level of information about their condition/disease at the three measurement points. Distributions of the scores for this variable were similar for both groups at the first and last measurement but not at the second measurement, as assessed by visual inspection of the respective boxplots. Median scores were statistically significantly different only for the second measurement. An inspection of the means suggests, after having received the intervention, the first cohort (mean rank=33.33) was significantly more informed about their condition/disease than the second cohort (mean rank=18.27), $X^2(1)=16.866$, p<0.0001.

TABLE 21: KNOWLEDGE OF DISEASE/CONDITION: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	1	1.42	24.33	1	0.321	0.548
	2nd cohort	26	1	1.58	26.58			
Month 9	1st cohort	24	2	2.17	33.33	1	16.866	<0.001
	2nd cohort	26	1	1.46	18.27			
Month 18	1st cohort	24	2	2.21	25.21	1	0.036	0.850
	2nd cohort	26	2	2.23	25.77			

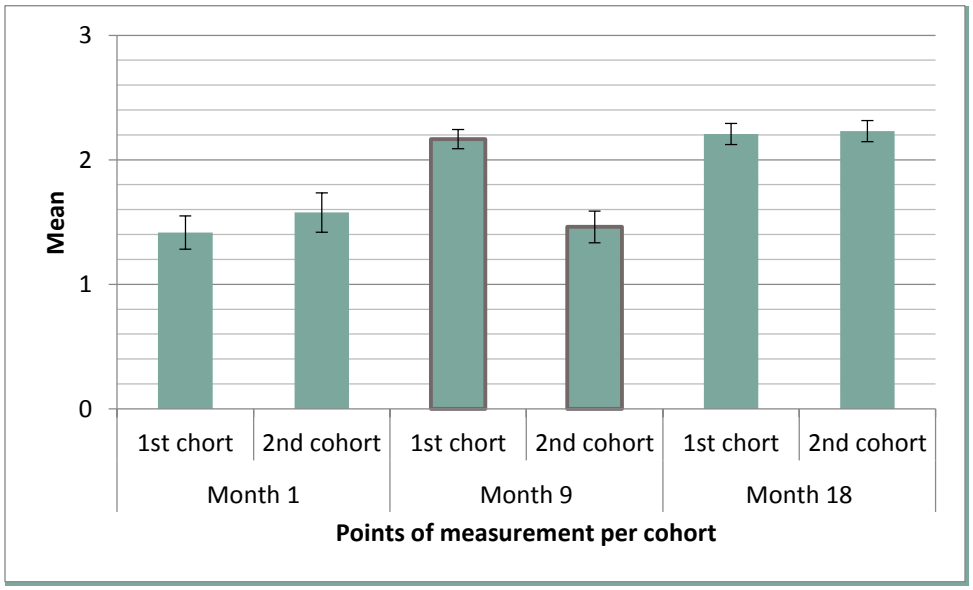


FIGURE 11: DIFFERENCES BETWEEN-COHORTS IN KNOWLEDGE OF DISEASE/CONDITION BY MEASUREMENT POINTS

[56] The Kruskal-Wallis test is the non-parametric equivalent to the one-way independent-samples ANOVA

2.3.5.2.2.2 WITHIN-GROUPS

The Friedman's test[57][58] was run to determine, whether the mean of each of the two cohorts with regard to their knowledge about their disease differed significantly over the three measurement points. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. As according to the expectations in Chapter 2.3.5, when comparing the differences within-groups, a significant difference is only expected during the intervention periods: For the first cohort this was between the first and the second measurement and for the second cohort this was between the second and the third measurements. In addition, after both cohorts received the intervention (after 18 months), the scores are expected to be significantly different to those at the beginning of the trial (Month 1). As can be seen especially by the p values in the table below, all these expectations were met. By inspecting the means, the second cohort improved slightly more than the first cohort in the intervention trial. However, this difference was not statistically significant.

TABLE 22: KNOWLEDGE OF DISEASE/CONDITION: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig.)	M9 to M18 p value (Adj. Sig.)	M1 to M18 p value (Adj. Sig.)
1st cohort (n=24)	Month 1	1	1.42	2	29.391	<0.001	0.004	1.000	0.003
	Month 9	2	2.17						
	Month 18	2	2.21						
2nd cohort (n=26)	Month 1	1	1.58	2	26.062	<0.001	1.000	<0.001	0.007
	Month 9	1	1.46						
	Month 18	2	2.23						

[57] The Friedman's test is considered the non-parametric equivalent for the one-way repeated measures ANOVA
[58] Distributions of the scores for this variable were compared for each group at the three points in time and were similar, assessed by visual inspection of respective histograms.

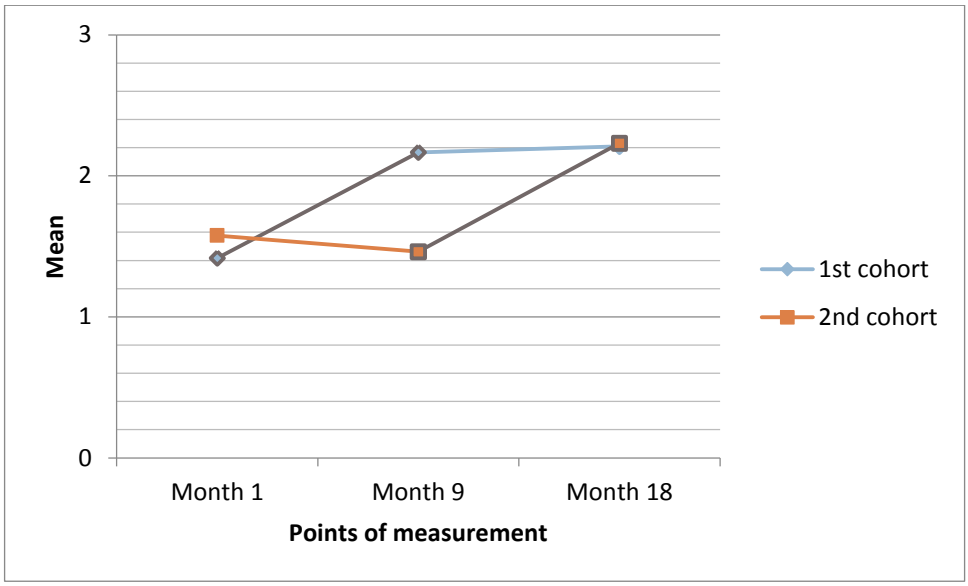


FIGURE 12: DIFFERENCES WITHIN-COHORTS IN KNOWLEDGE OF DISEASE/CONDITION BY MEASUREMENT POINTS

2.3.5.2.3 UNDERSTANDING OF RIGHTS AS PATIENTS

2.3.5.2.3.1 BETWEEN-GROUPS

To compare whether the two cohorts differed in their level of understanding of their rights as patients over the three measurements, a Kruskal-Wallis test was run[59]. Just as expected (see expectation 1 in Chapter 0), the scores of the two cohorts only differed significantly at the second measurement after the first cohort had received the intervention for the previous nine months while the second cohort had not yet received the support of the case managers: $X^2(1)=28.751$, $p<0.001$. The mean rank (36.44) for the first cohort was significantly higher compared to that of the second cohort (Mean rank=15.4) at this measurement point. For easier interpretation, an inspection of the means suggests that after receiving the intervention, the first cohort rated the relevant questionnaire item with a score of about 1.34 higher than the second cohort; considering that the answer option was based on a four-point Likert scale, this difference is quite meaningful.

[59] Distributions of the scores for this variable as assessed by visual inspection of relevant boxplots were only similar for the third measurement.

TABLE 23: UNDERSTANDING OF RIGHTS AS PATIENTS: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	1	1.13	25.88	1	0.041	0.840
	2nd cohort	26	1	1.08	25.15			
Month 9	1st cohort	24	2	2.38	36.44	1	28.751	<0.001
	2nd cohort	26	1	1.04	15.40			
Month 18	1st cohort	24	2	2.33	25.33	1	0.009	0.925
	2nd cohort	26	2	2.35	25.65			

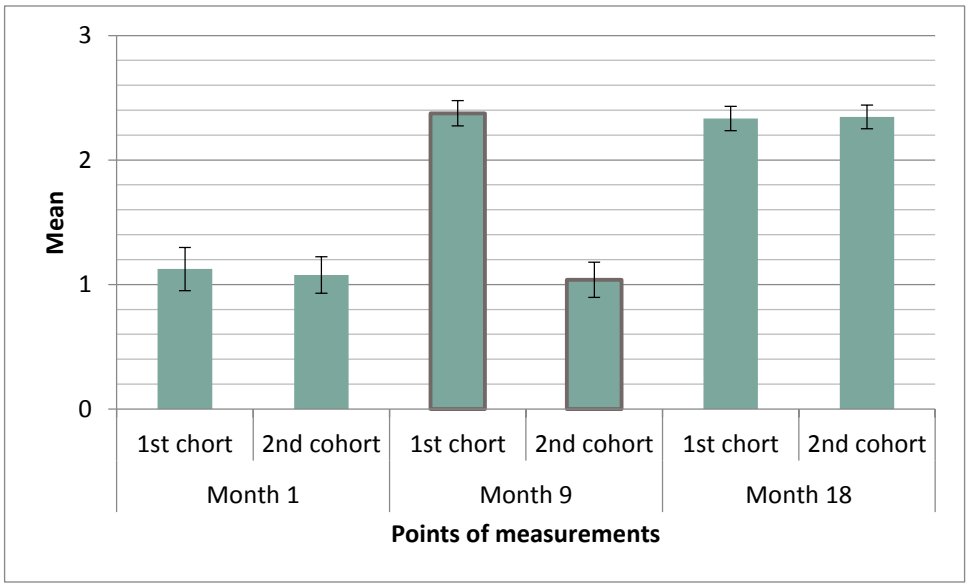


FIGURE 13: DIFFERENCES BETWEEN-COHORTS IN UNDERSTANDING OF RIGHTS BY MEASUREMENT POINTS

2.3.5.2.3.2 WITHIN-GROUPS

To determine the change in the patients' level of understanding of their rights over the 18 month lifetime of the INNOVCare pilot the Friedman test was conducted for each cohort separately. The expectation was that there would be a significant improvement from the beginning to the end of the intervention trials for each cohort (first cohort: Month 1 to Month 9 and second cohort: Month 9 to Month 18) as well as for both cohorts, from the beginning of the pilot to the end (Month 1 compared to Month 18) (see expectation 2 in Chapter 0). Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons and just as expected, for both cohorts there was a significant improvement in their level of understanding of their rights during the intervention trials as well as comparing the beginning to the end of the pilot. Inspecting the means differences for both cohorts during the intervention trials, the first cohort improved by 1.25 compared to 1.31 by the second cohort. The difference of 0.06 in both groups was not statistically significant, hence disallowing the assumption that one cohort improved to a much greater extent than the other.

TABLE 24: UNDERSTANDING OF RIGHTS AS PATIENTS: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig)	M9 to M18 p value (Adj. Sig)	M1 to M18 p value (Adj. Sig)
1st cohort (n=24)	Month 1	1	1.13	2	36.133	<0.001	<0.001	1.000	<0.001
	Month 9	2	2.38						
	Month 18	2	2.33						
2nd cohort (n=26)	Month 1	1	1.08	2	38.456	<0.001	1.000	<0.001	<0.001
	Month 9	1	1.04						
	Month 18	2	2.35						

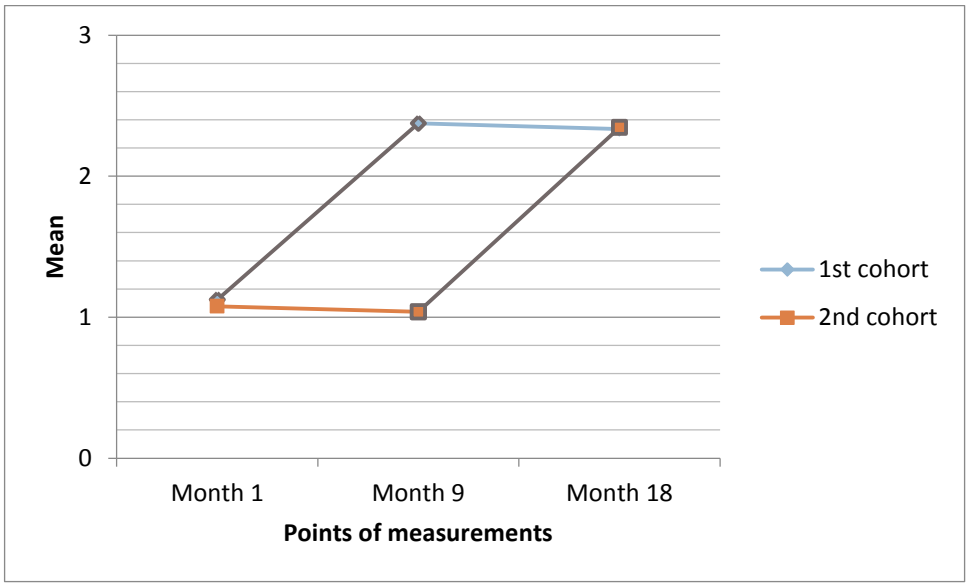


FIGURE 14: DIFFERENCES WITHIN-COHORTS IN UNDERSTANDING OF RIGHTS BY MEASUREMENT POINTS

2.3.5.2.4 KNOWLEDGE ON AVAILABLE HEALTH AND SOCIAL SERVICES

2.3.5.2.4.1 BETWEEN-GROUPS

With regard to the goal of broadening the participants' knowledge on the health and social services available to them, an analysis of the group differences using the Kruskal-Wallis test[60], observed, as expected, group differences only at the second measurement point: $X^2(1)=31.557$, $p<0.001$. Worth noting, there was a slight difference between the group means in the first measurement (Mean difference=0.25), one of which was not statistically significant (p=0.151). The mean rank of the first

[60] Distributions of the relevant scores were not similar for all groups at the different points in time, as assessed by a visual inspection of the relevant box plots.

cohort was 36.94 compared to 14.94 of the second cohort at Month 9. An examination of the means[61] showed that compared to the second cohort, the assessment of this variable by the first cohort at the end of their intervention trial, was about 1.37 higher. For a four-point Likert scale this change is quite significant.

TABLE 25: KNOWLEDGE ON AVAILABLE HEALTH AND SOCIAL SERVICES: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	1	1.17	28.04	1	2.064	0.151
	2nd cohort	26	2	0.92	23.15			
Month 9	1st cohort	24	2	2.29	36.94	1	31.557	<0.001
	2nd cohort	26	1	0.92	14.94			
Month 18	1st cohort	24	1	2.25	24.63	1	0.252	0.615
	2nd cohort	26	2	2.31	26.31			

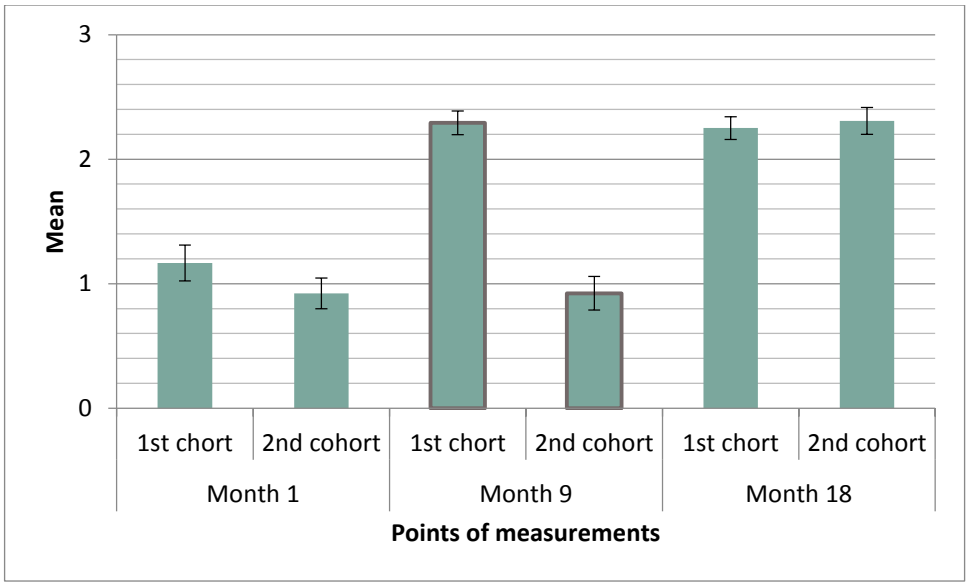


FIGURE 15: DIFFERENCES BETWEEN-COHORTS IN KNOWLEDGE OF AVAILABLE SERVICES BY MEASUREMENT POINTS

2.3.5.2.4.2 WITHIN-GROUPS

The level of participants' knowledge of services available to them from both cohorts was significantly different over the three measurement points. For the first cohort this was: $X^2(2)=39.337$, $p<0.001$ and for the second cohort: $X^2(2)=40.177$, $p<0.001$ as according to the Friedman's test. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. For the first cohort the level of knowledge about services was significantly different between the first and the second measurement

[61] Although an examination of the means with regard to ordinal variables is not proper, the results of this examination have been provided to ease interpretation.

(p<0.001) as well as between the first and third measurements (p<0.001). For the second cohort, the level of knowledge of services was significantly higher at the third measurement compared to the first (p<0.001) and second measurements (p<0.001). During the intervention trials alone for each of the two cohorts, the first cohort improved by a mean of 1.12 while the second cohort improved by 1.39. The different rate of improvements between the two cohorts was not statistically significant (p=0.211).

TABLE 26: KNOWLEDGE ON AVAILABLE SERVICES: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig)	M9 to M18 p value (Adj. Sig)	M1 to M18 p value (Adj. Sig)
1st cohort (n=24)	Month 1	1	1.17	2	39.337	<0.001	<0.001	1.000	<0.001
	Month 9	2	2.29						
	Month 18	2	2.25						
2nd cohort (n=26)	Month 1	1	0.92	2	40.177	<0.001	1.000	<0.001	<0.001
	Month 9	1	0.92						
	Month 18	2	2.31						

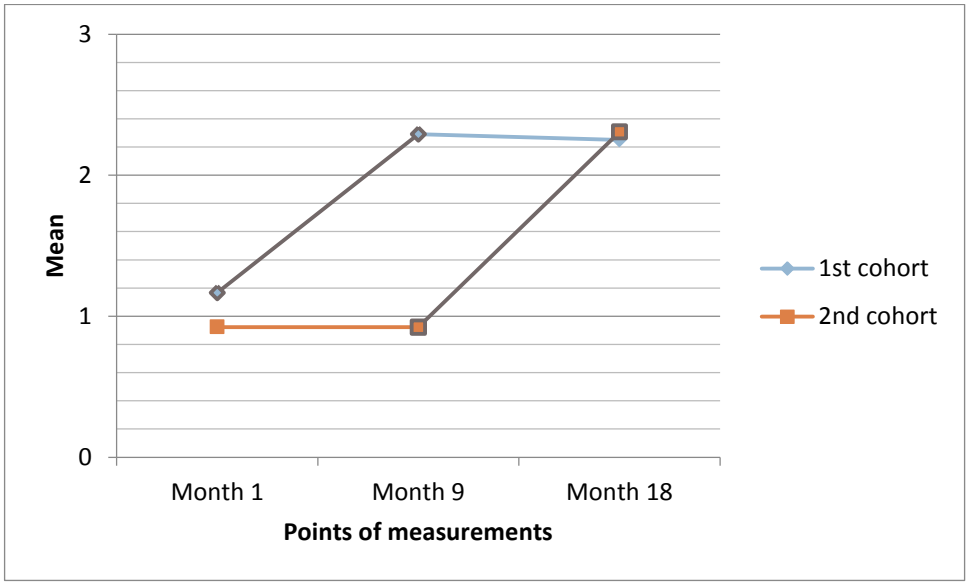


FIGURE 16: DIFFERENCES WITHIN-COHORTS IN KNOWLEDGE ABOUT AVAILABLE SERVICES BY MEASUREMENT POINTS

2.3.5.2.5 ABILITY OF SELF-MANAGEMENT OF CARE

2.3.5.2.5.1 BETWEEN-GROUPS

A Kruskal-Wallis test[62] was run to determine if there were differences in the ability of the participants to manage their own care between the two cohorts over the three measurement points. At the first measurement the mean rank of the second cohort (26.35) was slightly higher than that of the second cohort (Mean rank=24.58); however, this difference was not statistically significant: $X^2(1)=0.209$, p=0.648. At the second measurement, after the first cohort had received the intervention, its mean rank (27.90) was somewhat higher than that of the second cohort (Mean rank=23.29). The mean difference of 0.27 was not statistically significant: $X^2(1)=1.420$, p=0.233. At the third measurement, the mean rank of the second cohort (27.42) was higher than that of the first cohort (Mean rank=23.42). The mean difference between the two cohorts was 0.23 and also not statistically significant: $X^2(1)=1.176$, p=p.278. Hence considering the goal of increasing the participants' ability to manage their own care, there were no group differences suggesting that the INNOVCare pilot was less effective in reaching this goal than the direct goals previously described in this report.

TABLE 27: ABILITY OF SELF-MANAGEMENT OF CARE: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	1	1.21	24.58	1	0.209	0.648
	2nd cohort	26	2	1.31	26.35			
Month 9	1st cohort	24	2	1.54	27.90	1	1.420	0.233
	2nd cohort	26	1	1.27	23.29			
Month 18	1st cohort	24	1	1.58	23.42	1	1.176	0.278
	2nd cohort	26	2	1.81	27.42			

[62] Distribution of the relevant scores was similar for both groups at all points in time, as assessed by visual inspection of relevant box plots.

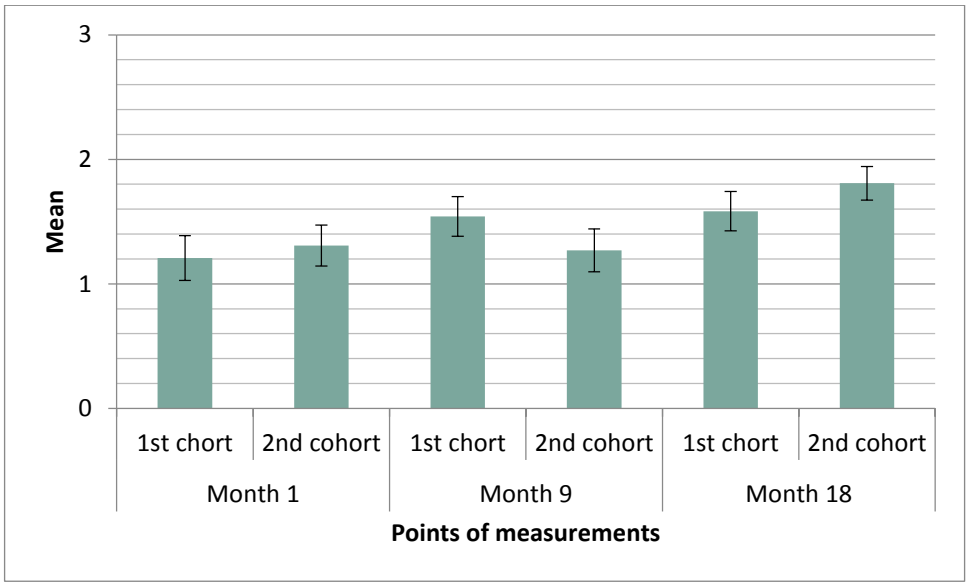


FIGURE 17: DIFFERENCES BETWEEN-COHORTS IN ABILITY TO MANAGE OWN CARE BY MEASUREMENT POINTS

2.3.5.2.5.2 WITHIN-GROUPS

To determine whether there were differences in the ability of the participants to manage their own care in each cohort over the pilot duration, a Friedman test was carried out for each of the two cohorts separately. In the first cohort, the ability of the patients to manage their own care was statistically different during the three measurement points: X2(2)=9.500, p=0.009. However, pairwise comparisons performed with a Bonferroni correction for multiple comparisons did not exhibit pairs of measurement point comparisons that were significantly different. This is likely due to the loss of power with the Bonferroni tests, which are quite conservative, as well as weak changes observed in this variable. The patients' ability to manage their own care increased during the intervention trial, from the first measurement (*Mdn*=1) to the second measurement (*Mdn*=2), but the differences were not statistically significant (p=0.389).

The second cohort's ability to manage their own care was also significantly different over the three measurement points as according to the Friedman test: X2(2)=14.250, p=0.001. Pairwise comparisons with a Bonferroni correction for multiple comparisons revealed that the ability of the participants of the second cohort to manage their own care increased significantly (p=0.038) during the intervention trial, from the second measurement (*Mdn*=1) to the third (*Mdn*=2).

These results suggest that the INNOVCare pilot was more effective in improving the patients' ability to manage their own care during the second phase of the intervention compared to the first. This could be due to learning effects of the case managers.

TABLE 28: ABILITY TO MANAGE OWN CARE: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig)	M9 to M18 p value (Adj. Sig)	M1 to M18 p value (Adj. Sig)
1st cohort (n=24)	Month 1	1	1.21	2	9.500	0.009	0.389	1.000	0.250
	Month 9	2	1.54						
	Month 18	2	1.58						
2nd cohort (n=26)	Month 1	1	1.26	2	14.250	0.001	1.000	0.038	0.066
	Month 9	1	1.40						
	Month 18	2	1.70						

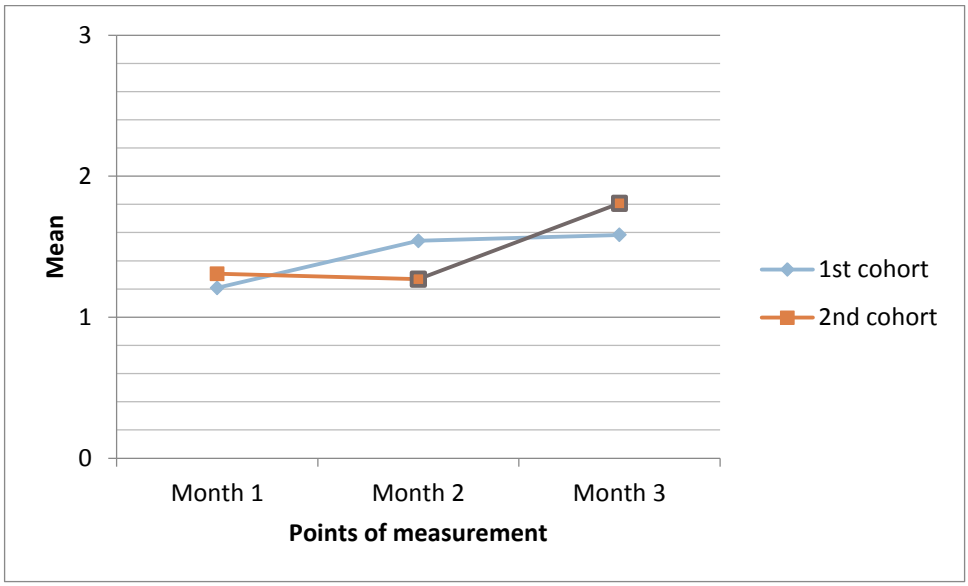


FIGURE 18: DIFFERENCES WITHIN-COHORTS IN ABILITY TO MANAGE OWN CARE BY MEASUREMENT POINTS

2.3.5.2.6 COMMUNICATION SKILLS

2.3.5.2.6.1 BETWEEN-GROUPS

Investigating the difference between cohorts in communication skills over the three measurement points, a Kruskal-Wallis H test[63] demonstrated a significant difference only at the second measurement, as according to the expectations listed in Chapter 2.3.5 point 1: $X^2(1)=12.611$, $p<0.001$. At Month nine, the mean rank of the first cohort was 32.08 compared to 19.42 for the second cohort. In terms of mean, this translated to 0.63 mean difference; therefore, after the intervention the first cohort was likely to indicate that their communication skills were about 0.63 points higher than the second cohort.

[63] Distribution of the relevant scores was were similar for both groups at all points in time, as assessed by visual inspection of relevant box plots.

TABLE 29: COMMUNICATION SKILLS: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	2	1.92	28.21	1	2.065	0.151
	2nd cohort	26	2	1.65	23.00			
Month 9	1st cohort	24	2	2.17	32.08	1	12.611	<0.001
	2nd cohort	26	1.50	1.54	19.42			
Month 18	1st cohort	24	2	2.08	25.54	1	0.001	0.978
	2nd cohort	26	2	2.08	25.46			

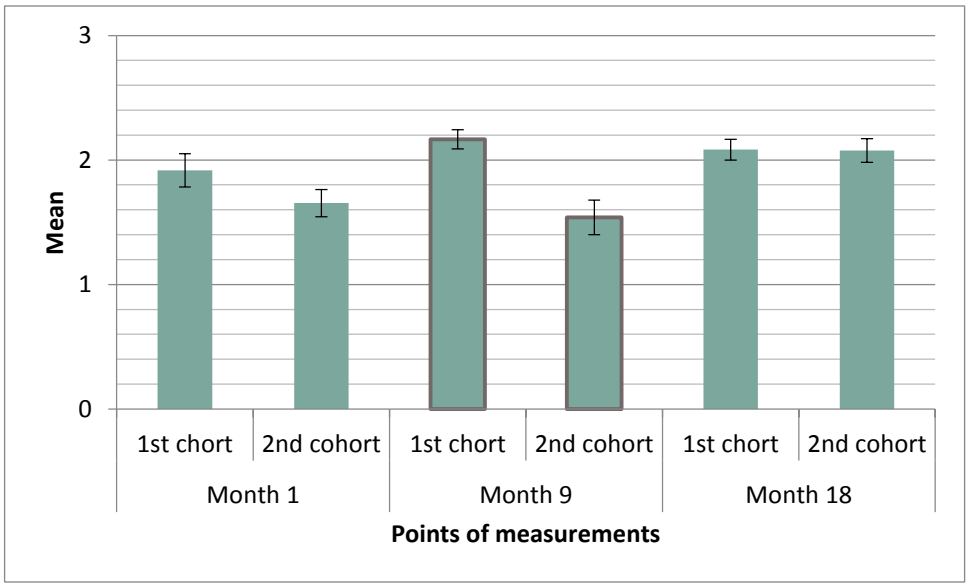


FIGURE 19: DIFFERENCES BETWEEN-COHORTS IN COMMUNICATION SKILLS BY MEASUREMENT POINTS

2.3.5.2.6.2 WITHIN-GROUPS

The development in communication skills within the cohorts over the intervention period as assessed by the Friedman test revealed that although there was an improvement in the scores of the first cohort during the intervention trial: from the first measurement (M=1.92) to the second measurement (2.17), this change was not statistically significant: $X^2(2)=5.091$, p=0.078. Worth noting is that at the first measurement, the mean (1.92) and median (2) of the first cohort for this variable was highest in comparison to the rest of the outcome variables.

However, the difference in communication skills of the second cohort over the 18 month pilot duration was statistically significant: X2(2)=15.520, p=<0.001. Pairwise comparisons with a Bonferroni correction for multiple comparisons revealed that only the improvement in communication skills in the intervention trial; from the first measurement (Mdn=1.5 and Mean=1.54) to the second measurement (Mdn=2 and Mean=2.08) was statistically significant (p=0.025). This result suggests that the intervention was more successful in improving the communication skills of the participants during the second phase of the intervention.

TABLE 30: COMMUNICATION SKILLS: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig)	M9 to M18 p value (Adj. Sig)	M1 to M18 p value (Adj. Sig)
1st cohort (n=24)	Month 1	2	1.92	2	5.091	0.078	NA	NA	NA
	Month 9	2	2.17						
	Month 18	2	2.08						
2nd cohort (n=26)	Month 1	2	1.65	2	15.520	<0.001	1.000	0.025	0.157
	Month 9	1.5	1.54						
	Month 18	2	2.08						

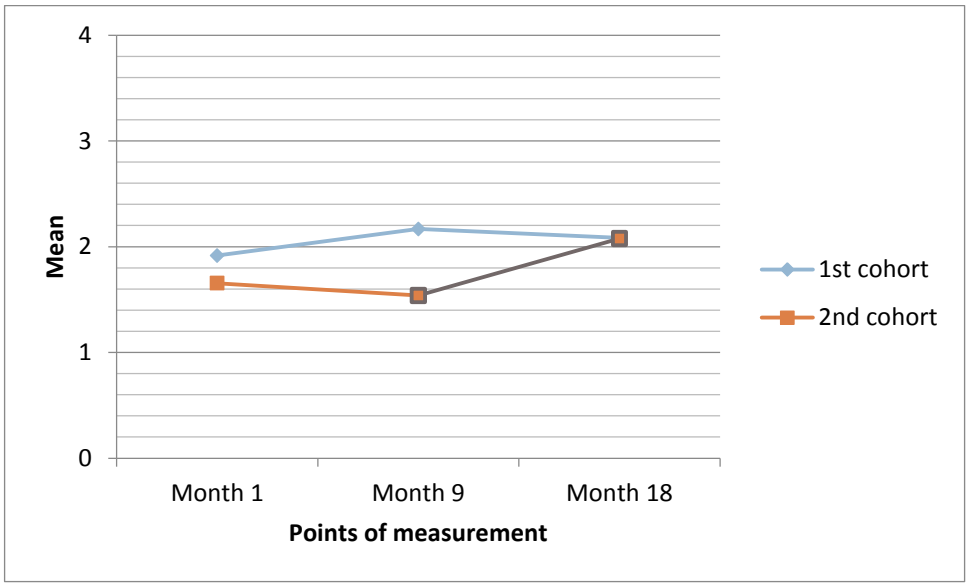


FIGURE 20: DIFFERENCES WITHIN-COHORTS IN COMMUNICATION SKILLS BY MEASUREMENT POINTS

2.3.5.2.7 DISEASE-RELATED PEER-TO-PEER LEARNING

Like previously mentioned in this report, only those participants that indicated that they were in contact with a people in a similar situation as themselves were probed further about how these relationships are instrumental to their wellbeing. In the first cohort, at the first measurement, six people indicated that they were in contact with other people in a similar situation, however only five of these participants completed the subsequent measurements. At the second and third measurement points, this number increased to 10; which could indicate that the INNOVCare intervention through the case managers connected four other participants with other people either suffering with the same or similar rare disease as them.

At the beginning of the INNOVCare pilot 11 of the participants in the second cohort pointed out that they were already in contact with other people in a similar situation. At the second measurement this number was 10. One of the participants who previously indicated that s/he was in contact with other people in a similar situation, did not complete the subsequent questionnaires while two participants

who had indicated the same at the first measurement, indicated at the second measurement that they were no longer in contact with that person. This could be due to many reasons including the loss of contact or erroneous entries at the first measurement. The latter reason is rather unlikely as the data underwent a check before analysis to identify unreliable entries. At the same time, one person who had previously indicated that s/he was not in contact with a person in a similar disposition as well as one person who did not indicate previously whether s/he was in contact with a person in a similar condition, indicated at the second measurement that they had contact with another person in this situation. After receiving the intervention after nine months of the start of the INNOVCare pilot, 19 people in total indicated that they were in contact with a person in a similar condition as themselves. This meant that during the INNOVCare intervention, it was possible to bring nine people, who had indicated at the second measurement that they were not in contact with other people in a similar situation as themselves in touch with such people.

Unfortunately due to the formulation of the question it is not possible to decipher how many people in a similar situation, one is in contact with and whether it was possible during the duration of the intervention to bring those who had indicated being in touch with other people during the previous measurements in contact with additional people.

TABLE 31: NUMBER OF PEOPLE IN CONTACT WITH PEOPLE IN A SIMILAR SITUATION BY COHORT (PATIENT)

	Month 9	Month 9	Month 18
1st cohort	6	10	10
2nd cohort	11	10	19

The follow-up question to the one presented above, involved asking the participants where they saw the advantages of being in contact with peers. The options included: For an accurate medical diagnosis, information about prescription drugs, a recommendation for a doctor or a specialist, emotional support and a quick solution to an everyday problem.

1. For an accurate medical diagnosis

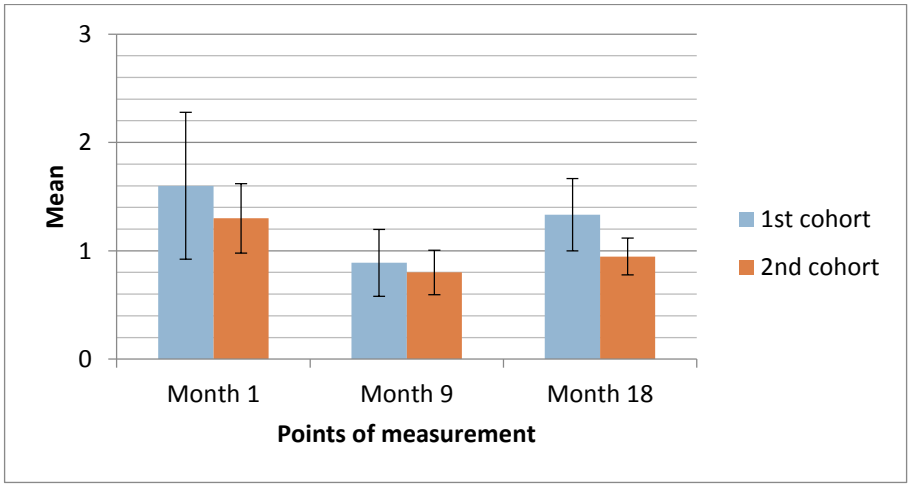


FIGURE 21: DEPENDENCE OF PARTICIPANTS ON THEIR PEERS FOR AN ACCURATE MEDICAL DIAGNOSIS BY COHORT

2. Information about prescription drugs

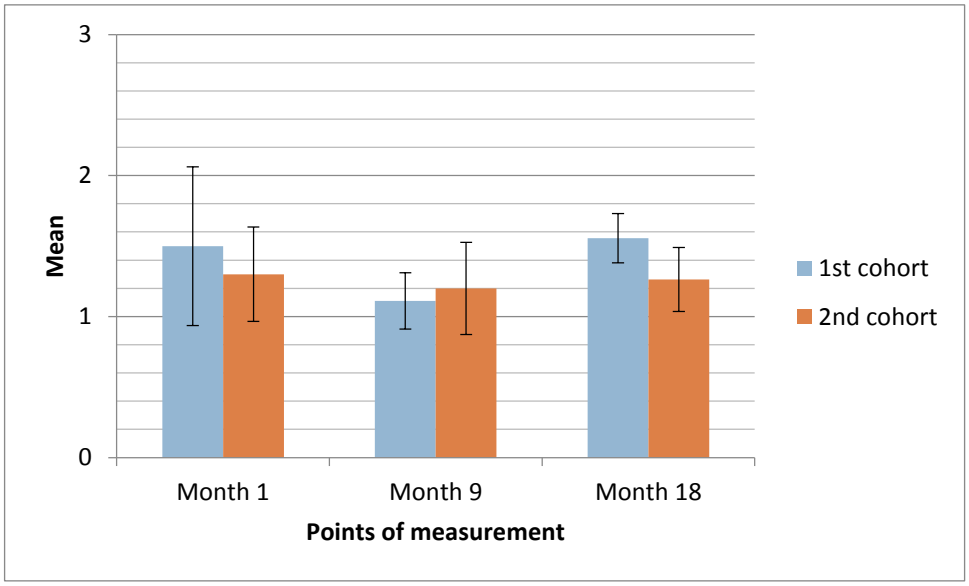


FIGURE 22: DEPENDENCE OF PARTICIPANTS ON THEIR PEERS FOR INFORMATION ABOUT PRESCRIPTION DRUGS BY COHORT

3. A recommendation for a doctor or a specialist

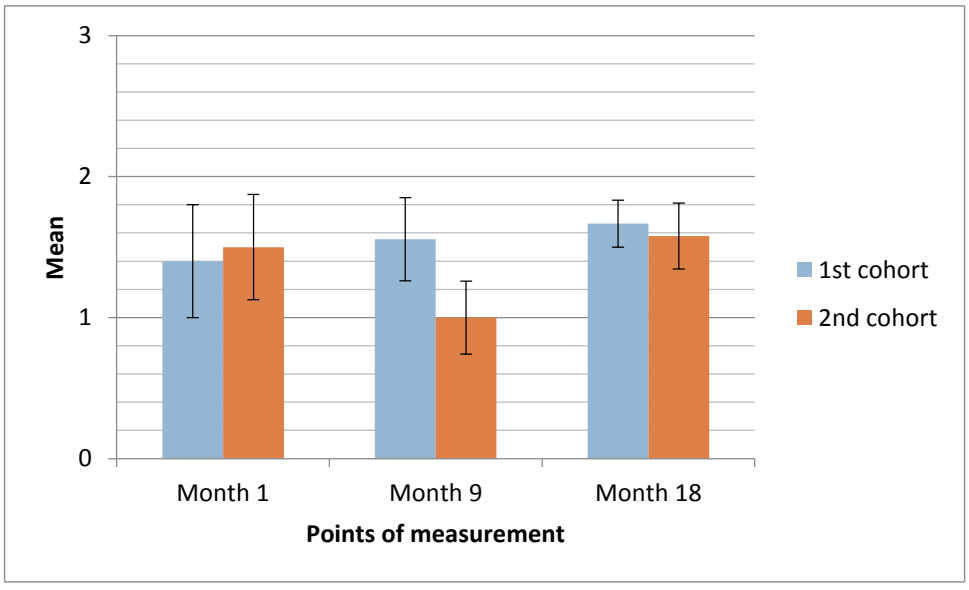


FIGURE 23: DEPENDENCE OF PARTICIPANTS ON THEIR PEERS FOR RECOMMENDATION FOR A DOCTOR OR A SPECIALIST BY COHORT

4. Emotional support

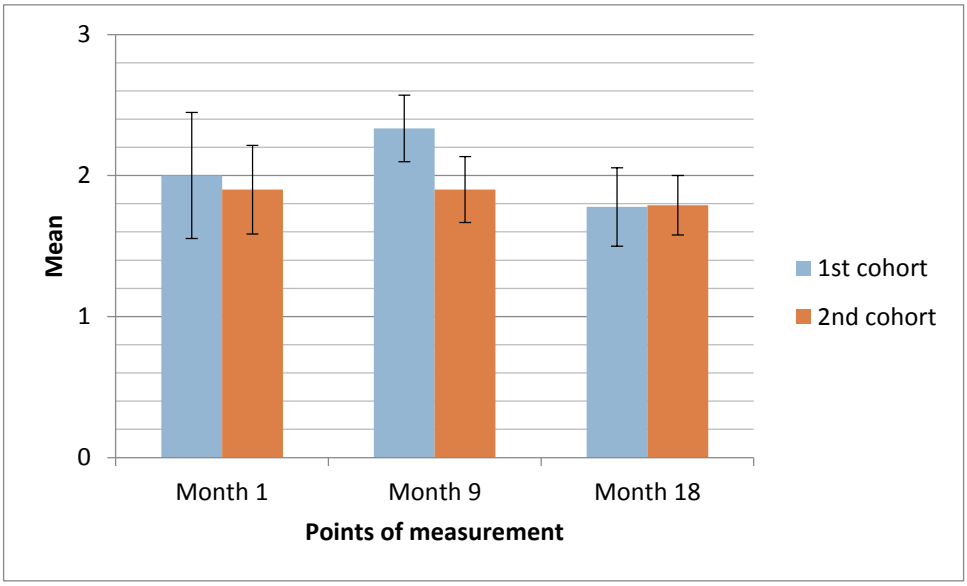


FIGURE 24: DEPENDENCE OF PARTICIPANTS ON THEIR PEERS FOR EMOTIONAL SUPPORT BY COHORT

5. A quick solution for an everyday issue

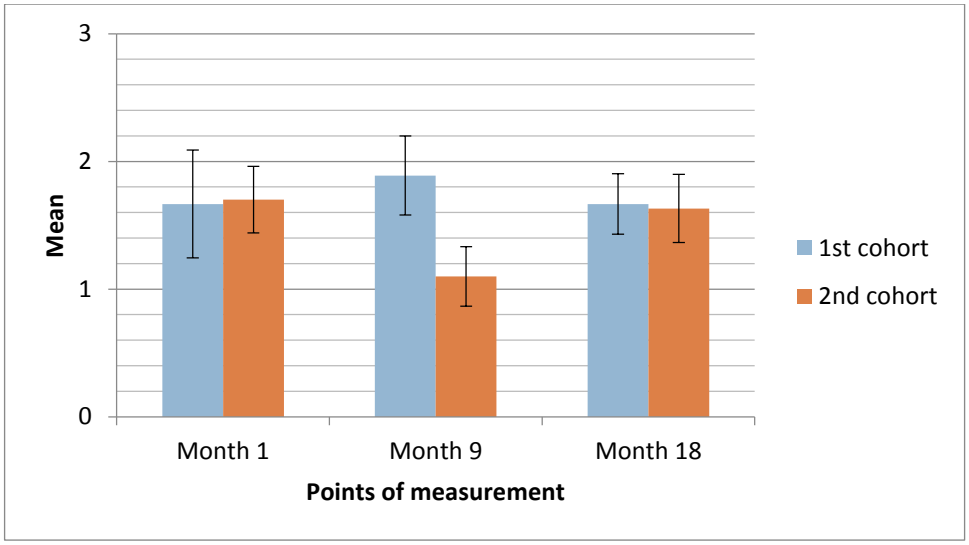


FIGURE 25: DEPENDENCE OF PARTICIPANTS ON THEIR FOR A QUICK SOLUTION FOR AN EVERYDAY ISSUE BY COHORT

The graphs above present how the participants rated[64] each of the five benefits of being in contact with peers by cohort over time. Just as expected and backed up by the findings of the PewResearchCentre

[64] Here, the means are used for easier interpretation although they are not considered very precise for ordinal variables.

(Fox, 2011), the benefit of 'emotional' support was the highest rated with the mean falling in the realm of 'fairly much' in as far as how much the participants depend on other people in a similar situation as themselves. This was followed by dependence for 'a quick solution to an everyday medical problem'. Depending peers for 'an accurate medical diagnosis' and for 'information on prescription drugs' were the lowest rated.

Although based on the information about whether the participants were in contact with other people in a similar situation over time indicated that the INNOVCare intervention contributed in people who were not in contact with other people in a similar situation to get in touch with such people, none of the between-groups and within-groups differences were statistically significant for the items above. This could be due to the reduced sample size or the inability of the intervention to make any changes in this relation over nine months intervention trial.

2.3.5.2.8 COORDINATION AMONG PROVIDERS

2.3.5.2.8.1 BETWEEN-GROUPS

One of the aims of the INNOVCare pilot was to support and encourage the different stakeholders that provide support for rare and complex disease patients to work better together, thus decreasing the burden to the rare patient and his or her family. Considering the differences for the variable relating to coordination of care among providers between cohorts which are expected to be significant at the second measurement point, just after the first cohort has completed the intervention and the second cohort was about to start, the results reflected these expectation based on the Kruskal-Wallis H test[65]. At Month nine, the mean rank for the second cohort was 31.21 compared to 20.23 for the second cohort. This difference was statistically significant: $X^2(1)=7.907$, p=0.005. The mean difference equated to 0.67 suggesting that after the intervention, participants were likely to score the item with 0.67 points higher or more readily that the different people caring and treating them work well together to give them the best care and support.

TABLE 32: COORDINATION AMONG PROVIDERS: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	2	1.71	25.85	1	0.30	0.862
	2nd cohort	26	1.5	1.69	25.17			
Month 9	1st cohort	24	2	2.21	31.21	1	7.907	0.005
	2nd cohort	26	1	1.54	20.23			
Month 18	1st cohort	24	2	2.13	25.98	1	0.061	0.805
	2nd cohort	26	2	2.08	25.06			

[65] Distributions of the relevant scores were not similar for all groups in the first and second measurement but similar in the third measurement by inspection of relevant box plots.

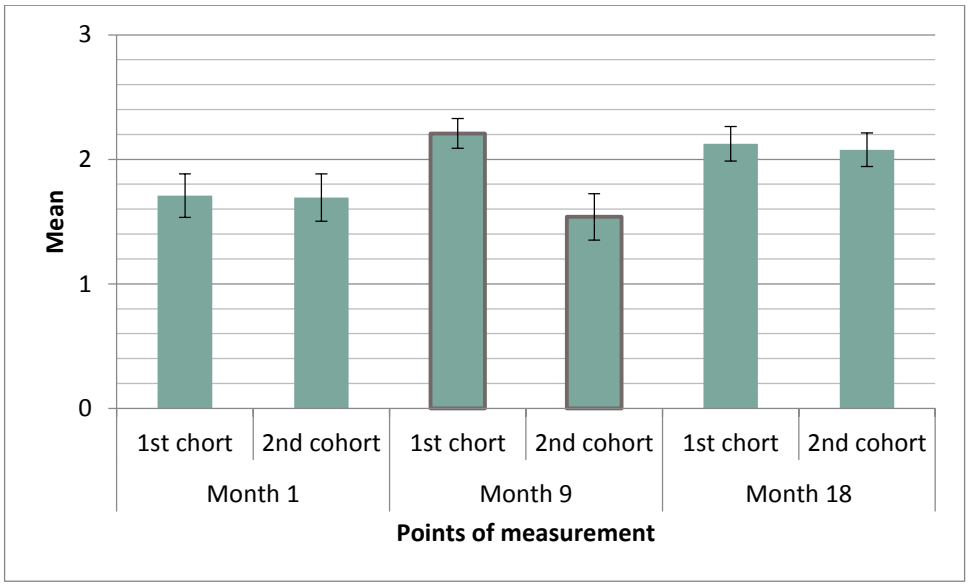


FIGURE 26: DIFFERENCES BETWEEN-COHORTS IN COORDINATION AMONG PROVIDERS BY MEASUREMENT POINTS

2.3.5.2.8.2 WITHIN-GROUPS

A Friedman test was run to determine whether there were differences in the participant's perception of the coordination of care among providers over time for each cohort. The omnibus statistic reported that both cohorts had significant differences within-groups: For the first cohort: $X^2(2)=14.000$, p=0.001 and for the second cohort: $X^2(2)=9.640$, p=0.008. Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. However none of the comparisons delivered a statistically significant difference. The difference of the measurements for both cohorts during the intervention trials were only significant one-tailed. The first cohort p=0.091 (Asym. 2-tailed) and the second cohort p=0.095 (Asym. 2-tailed). Considering the study was an experiment, it is anyway associated with directed hypothesis. In this case, that the perception of the participants towards the level of coordination among providers increased from the beginning to the end of each trial period. This is however only a weak difference with a Kendall's W coefficient of concordance of 0.292 for the first cohort and 0.185 for the second cohort.

TABLE 33: COORDINATION AMONG PROVIDERS: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig)	M9 to M18 p value (Adj. Sig)	M1 to M18 p value (Adj. Sig)
1st cohort (n=24)	Month 1	2	1.71	2	14.000	0.001	0.091	1.000	0.250
	Month 9	2	2.21						
	Month 18	2	2.13						
2nd cohort (n=26)	Month 1	1.5	1.69	2	9.640	0.008	0.995	0.095	0.716
	Month 9	1	1.54						
	Month 18	2	2.08						

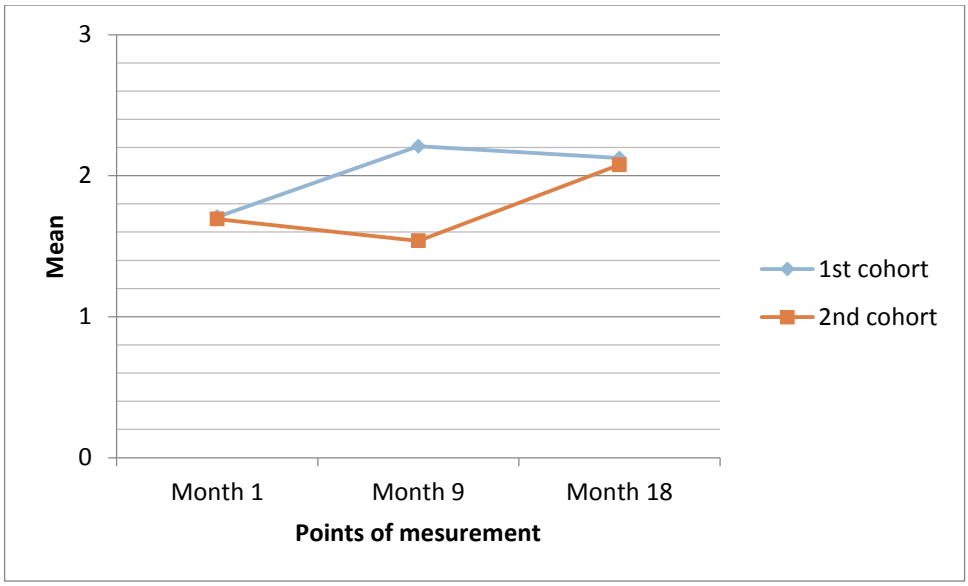


FIGURE 27: DIFFERENCES WITHIN-COHORTS IN COORDINATION OF CARE AMONG PROVIDERS BY MEASUREMENT POINTS

2.3.5.2.9 UNDERSTANDING AND ACCEPTANCE IN THE COMMUNITY

2.3.5.2.9.1 BETWEEN-GROUPS

A Kruskal-Wallis H test[66] was run to determine if there were differences in the participants' perception regarding their understanding and acceptance in the community between the two cohorts. Median scores were not statistically different between the cohorts at any of the three measurement points: Months one: $X^2(1)=0.155$, p=0.694; Month nine: $X^2(1)=0.516$, p=0.473 and $X^2(1)=0.112$, p=0.738.

TABLE 34: UNDERSTANDING AND ACCEPTANCE IN THE COMMUNITY: BETWEEN-GROUPS

		n	Median	Mean	Mean rank	Degrees of freedom	H test statistic	p value
Month 1	1st cohort	24	2	1.79	24,77	1	0.155	0.694
	2nd cohort	26	2	1.88	26.17			
Month 9	1st cohort	24	2	2.08	26.79	1	0.516	0.473
	2nd cohort	26	2	1.96	24.31			
Month 18	1st cohort	24	2	2.21	24.90	1	0.112	0.738
	2nd cohort	26	2	2.27	26.06			

[66] Distributions of the respective scores were similar for all groups at all points in time except for the first measurement as assessed by visual inspection of boxplots.

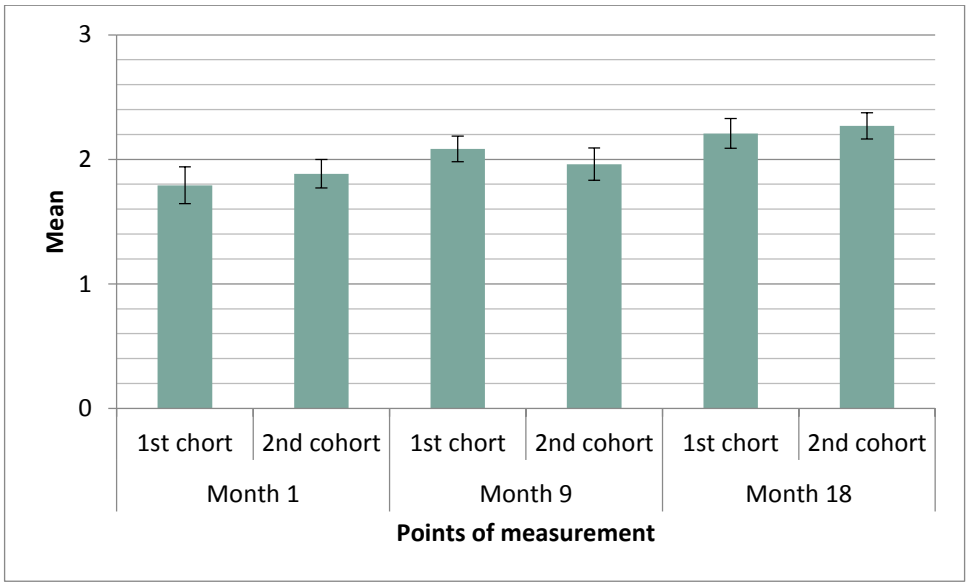


FIGURE 28: DIFFERENCES BETWEEN-COHORTS IN UNDERSTANDING AND ACCEPTANCE IN THE COMMUNITY BY MEASUREMENT POINTS

2.3.5.2.9.2 WITHIN-GROUPS

To determine if the participants' impression of whether the people who are in regular contact with them (the community) e.g. at school, work understand and accept their condition over time, a Friedman test for each cohort was carried out separately. The results for both cohorts indicated that the participants' perception in this matter was significantly different at the different measurement points: First cohort – $X^2(2)=12.235$, p=0.002 and second cohort – X^2 (1)=9.500, p=0.009. To determine which pairs of time points had significantly different perceptions, pairwise comparisons with a Bonferroni correction for multiple comparisons were run. None of the pairings was significantly different from one another. This contradiction in the results indicated that the effect of the intervention was rather weak and hence was lost in the Bonferroni calculations as this test is quite conservative. As a result, one can conclude that the INNOVCare intervention had only marginal effects on the perception of the participants by the community around them.

TABLE 35: UNDERSTANDING AND ACCEPTANCE IN THE COMMUNITY: WITHIN-GROUPS

		Median	Mean	Degrees of freedom	X^2	p value	M1 to M9 p value (Adj. Sig)	M9 to M18 p value (Adj. Sig)	M1 to M18 p value (Adj. Sig)
1st cohort (n=24)	Month 1	2	1.79	2	12.235	0.002	0.447	1.000	0.130
	Month 9	2	2.08						
	Month 18	2	2.21						
2nd cohort (n=26)	Month 1	2	1.88	2	9.500	0.009	1.000	0.249	0.133
	Month 9	2	1.96						
	Month 18	2	2.27						

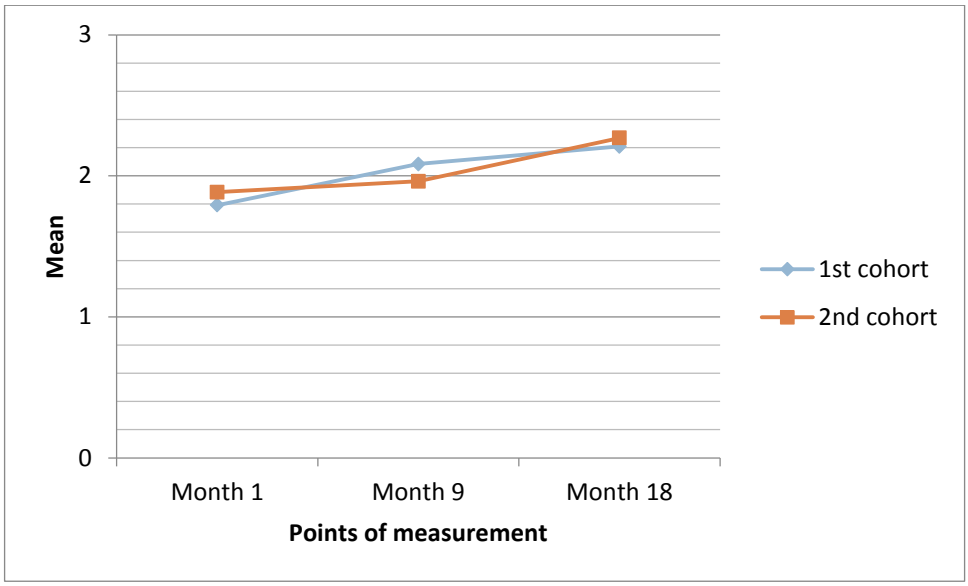


FIGURE 29: DIFFERENCES WITHIN-COHORTS UNDERSTANDING AND ACCEPTANCE IN THE COMMUNITY BY MEASUREMENT POINTS

2.3.5.2.10 SUMMARY OF THE OUTCOME VARIABLES FROM THE PATIENT DATASET

TABLE 36: SUMMARY OF THE OUTCOME VARIABLES FROM THE PATIENT DATASET: BETWEEN-GROUPS

Outcome variable	Cohort	n	Mean	Mean rank	X^2	p
Knowledge on disease or condition	1st cohort	24	2.17	26.58	16.866	<0.001*
	2nd cohort	26	1.46	33.33		
Understanding of rights as patients	1st cohort	24	2.38	36.44	28.751	<0.001*
	2nd cohort	26	1.04	15.4		
Knowledge on available health and social services	1st cohort	24	2.29	36.94	31.557	<0.001*
	2nd cohort	26	0.92	14.94		
Ability of self-management of care	1st cohort	24	1.54	27.9	1.42	0.233
	2nd cohort	26	1.27	23.29		
Communication skills	1st cohort	24	2.17	32.08	12.611	<0.001*
	2nd cohort	26	1.54	19.42		
Disease-related peer-to-peer learning	1st cohort	24				
	2nd cohort	26				
Coordination among providers	1st cohort	24	2.21	31.21	7.907	0.005*
	2nd cohort	26	1.54	20.23		
Understanding and acceptance in the community	1st cohort	24	2.08	26.79	0.516	0.473
	2nd cohort	26	1.96	24.31		

TABLE 37: SUMMARY OF THE OUTCOME VARIABLES FROM THE PATIENT DATASET FOR THE 1ST COHORT (N=24): WITHIN-GROUPS

Outcome variable	Measurement point	Median	Mean	X^2	p	Kendall's W	M1-M9 (p)	M1-M18 (p)
Knowledge on disease or condition	Month 1	1	1.42	29.391	<0.001*	0.612	0.004*	0.003*
	Month 9	2	2.17					
	Month 18	2	2.21					
Understanding of rights as patients	Month 1	1	1.13	36.133	<0.001*	0.753	<0.001*	<0.001*
	Month 9	2	2.38					
	Month 18	2	2.33					
Knowledge on available health and social services	Month 1	1	1.17	39.337	<0.001*	0.820	<0.001*	
	Month 9	2	2.29					
	Month 18	2	2.25					
Ability of self-management of care	Month 1	1	1.21	9.500	0.009*	0.198	0.389	0.250
	Month 9	2	1.54					
	Month 18	2	1.58					
Communication skills	Month 1	2	1.92	5.091	0.078			
	Month 9	2	2.17					
	Month 18	2	2.08					
Disease-related peer-to-peer learning	Month 1							
	Month 9							
	Month 18							
Coordination among providers	Month 1	2	1.71	14.000	0.001*	0.292	0.091	0.250
	Month 9	2	2.21					
	Month 18	2	2.13					
Understanding and acceptance in the community	Month 1	2	1.79	12.235	0.002*	0.255	0.447	0.130
	Month 9	2	2.08					
	Month 18	2	2.21					

TABLE 38: SUMMARY OF THE OUTCOME VARIABLES FROM THE PATIENT DATASET FOR THE 2ND COHORT (N=26): WITHIN-GROUPS

Outcome variable		Median	Mean	X^2	p	Kendall W	M9-M18 (p)	M1-M18 (p)
Knowledge on disease or condition	Month 1	1	1.58	26.062	<0.001*	0.501	<0.001*	0.007*
	Month 9	1	1.46					
	Month 18	2	2.23					
Understanding of rights as patients	Month 1	1	1.08	38.456	<0.001*	0.74	<0.001*	<0.001*
	Month 9	1	1.04					
	Month 18	2	2.35					
Knowledge on available health and social services	Month 1	1	0.92	40.177	<0.001*	0.773	<0.001*	<0.001*
	Month 9	1	0.92					
	Month 18	2	2.31					
Ability of self-management of care	Month 1	1	1.26	14.250	0.001*	0.274	0.038*	0.066
	Month 9	1	1.40					
	Month 18	2	1.70					
Communication skills	Month 1	2	1.65	15.520	<0.001*	0.298	0.025*	0.157
	Month 9	1.5	1.54					
	Month 18	2	2.08					
Disease-related peer-to-peer learning	Month 1							
	Month 9							
	Month 18							
Coordination among providers	Month 1	1.5	1.69	9.640	0.008*	0.185	0.095	0.716
	Month 9	1	1.54					
	Month 18	2	2.08					
Understanding and acceptance in the community	Month 1	2	1.88	9.500	0.009*	0.183	0.249	0.133
	Month 9	2	1.96					
	Month 18	2	2.27					

2.3.5.2 Direct objectives of the INNOVCare pilot: According to the patients' family members

2.3.5.2.1 BETWEEN-GROUPS

The results in Chapter 2.3.5.1 above, represent the results of the analysis of the patient dataset. For each patient, a family member who was most involved or knowledgeable in the patient 'care, also completed a questionnaire at the same three measurement points. The questions to the social impact of the intervention were similar to those completed by the patients. It was not a proxy questionnaire, that is, the family members did not complete the statements on behalf of the participants, but rather, completed the questionnaires in terms of how they viewed their own knowledge of the specific items. For example with regards to the main item covering the knowledge of condition/disease the patients were asked: 'How informed do you currently feel about your condition?' while the family members were asked: 'How informed do you currently feel about the condition of the person you care for?'

For each of the outcome variables that have been presented for the patients under Chapter 0 in detail, a Kruskal-Wallis H test[67] was performed on the family dataset to determine whether there were differences between groups at the three measurement points. 55 family members of the patients in the first cohort completed the questionnaire. This was true for 48 family member of the patients allocated to the second cohort. Distribution of scores of the index created to represent the efficacy of the intervention from seven of the eight outcome variables for both were not similar for all groups, as assessed by inspection of respective box plots.

According to the expectations listed in Chapter Outcomes and Estimationpoint one, at the first and third measurements, statistically significant differences between the cohorts were not expected. The Kruskal-Wallis test on these two measurements was conducted and just as expected, none of the outcome variables bore statistically significant changes at these two measurements. Especially with regard to the first measurement, these results which show that the distribution of scores between both cohorts were similar at the first measurement, confirms that the randomisation procedure had worked and both cohorts were at a similar stand at the beginning of the intervention.

The third measurement at Month 18 was taken after both the cohorts had received the intervention: The first cohort during the first nine months of the intervention and the second cohort during the last nine months of the 18 month intervention period. The lack of statistically significant differences in the outcome variables at this measurement point when comparing the two cohorts, suggests that the gain from the intervention in both groups was similar. Also that during the last nine months of the intervention, when the first cohort was not receiving the intervention, the effects of the intervention that they had received earlier, was sustained and did not wear out significantly. From such an intervention, such a lasting effect is normally aimed for.

As anticipated, the differences between cohorts were only statistically significant at the second measurement when the intervention trial for the first cohort had just ended and that for the second

[67] Due to very unbalanced groups, respective non-parametric tests were conducted to avoid violating the assumptions of the parametric equivalents caused by this unevenness.

cohort was just about to start. Table 39 below shows the results of the Kruskal-Wallis test at the second measurement point (Month 9). Unlike in the analysis of the patients' data that revealed a statistically significant group change in all outcome variables except in the ability to independently manage own care and in the understanding and acceptance in the community, the results of the family questionnaire show statistically significant group differences for all outcome variables (all p values are below the statistical significance threshold of 0.05). The effect of the intervention on the individual outcome variables also differed slightly to the analysis of the patient data. This can be interpreted by the differences between mean ranks as well as by the h statistic (X^2). As with the data from the patients, the effect of the intervention was felt most with regards to the items: Increased knowledge on condition/disease, rights and services. The order of importance for the patients and their families of the effectiveness of the intervention was interchanged for increased knowledge on rights and on services. The patients' knowledge on rights increased slightly more on rights than on services. For the family members, the reverse was true. The rest of the outcome variables were ranked in the same order by both the patients and their families. The table below also provides the median for each of the cohorts for each of the outcome variables. For easier interpretation, the means for each cohort for each outcome variables are also presented in the table below.

TABLE 39: BETWEEN-GROUPS ANALYSIS OF THE OUTCOME VARIABLES AT MONTH 9 BASED ON THE FAMILY DATASET

Outcome variable	Cohort	n	Mean	Median	Mean rank	X^2	p
Knowledge on disease or condition	1st cohort	55	2.38	2	65.01	29.180	<0.001
	2nd cohort	48	1.65	2	37.09		
Understanding of rights as patients	1st cohort	55	2.47	2	67.94	38.740	<0.001
	2nd cohort	48	1.46	1	33.74		
Knowledge of available health and social services	1st cohort	55	2.42	2	67.19	34.247	<0.001
	2nd cohort	48	1.31	1	34.59		
Ability of self-management of care	1st cohort	55	2.27	2	59.66	11.267	0.001
	2nd cohort	48	1.81	2	43.22		
Communication skills	1st cohort	55	2.35	2	62.39	19.351	<0.001
	2nd cohort	48	1.73	2	40.11		
Disease-related peer-to-peer learning	1st cohort	55					
	2nd cohort	48					
Coordination among providers	1st cohort	55	2.11	2	62.01	15.284	<0.001
	2nd cohort	48	1.52	1	40.53		
Understanding and acceptance in the community	1st cohort	55	2.09	2	56.87	4.716	0.03
	2nd cohort	48	1.83	2	46.42		

2.3.5.2.2 WITHIN-GROUPS

Looking at the changes within each cohort over time, according to the expectations in Chapter 2.3.5, point 2 above, statistically significant changes were expected at each of the intervention trials for each cohort: For the first cohort, from Month one to Month nine and for the second cohort, from Month nine to Month 18. In addition there was a high likelihood that the difference in the performance of each cohort at the beginning of the intervention, at Month one, compared to at the end of the intervention, at Month 18 was statistically significantly different.

For each cohort and for each outcome variable, the Friedman test was conducted to ascertain these expectations. The test determined that there was a statistically significant difference in the performance of each cohort in all the outcome variables over the duration of the INNOVCare pilot (see column labelled 'p' in Table 40 and Table 41 below: all the p values are below the significance threshold of 0.05).

Having detected these statistically significant differences, pairwise comparisons with a Bonferonni correction for multiple comparisons were conducted to determine where exactly these differences were i.e. from which measurement to which measurement. As explained preciously, for the first cohort, this was expected between Month 1 and Month 9 and Month 1 and Month 18. For the second cohort the same was expected from Month 9 to Month 18 and Month 1 to Month 18.

During the control trials, (first cohort: between Month 9 and Month 18; second cohort: between Month 1 and Month 9), no significant differences were detected. This means that in the case of the first cohort, one can conclude that, nine months after receiving the intervention, the effects of the intervention were still upheld. For the second cohort, this lack of statistically significant difference during the control trial indicates the unlikelihood of outside factors having affected the INNOVCare trial and therefore the changes that were visible after having received the intervention can be attributed to the INNOVCare intervention.

Table 40 and Table 41 below display the changes of each cohort over the three measurement points (columns: X^2 and p) as well as the effect size of the differences (Kendall's W); Table 40 represents the changes in the first cohort while Table 41 represents the changes in the second cohort. The last two columns represent the significance levels of each of the two pairs of scores where a statistically significant difference was expected. The differences during the control trials are not displayed.

With regards to the first cohort, although the Friedman test reported statistically significant changes in all the outcome variables over the 18 Month intervention period, due to the conservative nature of the Bonferroni tests that were conducted to determine where exactly the differences were detected, the pairwise comparisons for two outcome variables were not statistically significant: Communication skills and understanding and acceptance in the community. For the former, communication skills, the changes were just short of being statistically significant in a two-tailed test (p=0.066); they would have likely been statistically significant if a one-tailed p value was taken which is typical for directed hypothesis like in such trials; that an improvement in the communication skills of the participants is anticipated from the beginning of the intervention to the end. For the latter outcome variable, increase understanding and acceptance in the community, the Friedman test being statically significant but the insignificant pairwise comparisons suggests that these changes achieved were relatively small.

The within-groups analysis for the second cohort revealed similar differences. However, worth noting, the improvements within the second cohort seem higher than those in the first cohort by inspection of the Kendall W statistic with the exception of the impact of the INNOVCare intervention on the ability of the participants to independently manage their care; which had a higher improvement in the first cohort. As observed in the first cohort, the Friedman test detected a statistical difference in the measurements of the second cohort on the outcome variable relating to increasing understanding and acceptance in the community over the three measurement points; however the pairwise comparisons were not significant. In this case as well, these results suggest that the INNOVCare intervention made strides in changing this aspect of the community, however its impact was only marginal. The fact that the pairwise comparisons for the outcome variable on communication skills detected significant changes within this cohort compared to the first cohort, suggests a learning effect of the case managers; being able to instil better communications in the participants of the second cohort likely through their experience with the first cohort.

TABLE 40: WITHIN-GROUPS ANALYSIS OF THE OUTCOME VARIABLES FOR THE 1ST COHORT (N=55) BASED ON THE FAMILY DATASET

Outcome variables	Measurement points	Median	Mean	X^2	p	Kendall's W	M1-M9 (p)	M1-M18 (p)
Knowledge on disease or condition	Month 1	2	1.80	47.226	<0.001	0.429	<0.001	0.001
	Month 9	2	2.38					
	Month 18	2	2.35					
Understanding of rights as patients	Month 1	2	1.53	72.605	<0.001	0.660	<0.001	<0.001
	Month 9	2	2.47					
	Month 18	2	2.45					
Knowledge on available health and social services	Month 1	2	1.55	58.639	<0.001	0.533	<0.001	<0.001
	Month 9	2	2.42					
	Month 18	2	2.38					
Ability of self-management of care	Month 1	2	1.87	27.630	<0.001	0.251	0.008	0.045
	Month 9	2	2.27					
	Month 18	2	2.20					
Communication skills	Month 1	2	2.04	17.043	<0.001	0.155	0.066	0.458
	Month 9	2	2.35					
	Month 18	2	2.24					
Disease-related peer-to-peer learning	Month 1							
	Month 9							
	Month 18							
Coordination among providers	Month 1	2	1.71	26.378	<0.001	0.240	0.023	0.040
	Month 9	2	2.11					
	Month 18	2	2.07					
Understanding and acceptance in the community	Month 1	2	1.80	14.179	0.001	0.129	0.21	0.121
	Month 9	2	2.09					
	Month 18	2	2.13					

TABLE 41: WITHIN-GROUPS ANALYSIS OF THE OUTCOME VARIABLES FOR THE 2ND COHORT (N=48) BASED ON THE FAMILY DATASET

Outcome variables	Measurement points	Median	Mean	X^2	p	Kendall W	M9-M18 (p)	M1-M18 (p)
Knowledge on disease or condition	Month 1	2	1.65	53.835	<0.001	0.561	<0.001	<0.001
	Month 9	2	1.65					
	Month 18	2	2.40					
Understanding of rights as patients	Month 1	1	1.35	66.578	<0.001	0.694	<0.001	<0.001
	Month 9	1	1.46					
	Month 18	2	2.44					
Knowledge on available health and social services	Month 1	1	1.35	62.783	<0.001	0.654	<0.001	<0.001
	Month 9	1	1.31					
	Month 18	2.5	2.50					
Ability of self-management of care	Month 1	2	1.79	17.383	<0.001	0.181	0.032	0.037
	Month 9	2	1.81					
	Month 18	2	2.25					
Communication skills	Month 1	2	1.83	25.910	<0.001	0.270	0.005	0.150
	Month 9	2	1.73					
	Month 18	2	2.29					
Disease-related peer-to-peer learning	Month 1							
	Month 9							
	Month 18							
Coordination among providers	Month 1	1.5	1.63	31.818	<0.001	0.331	<0.001	0.007
	Month 9	1	1.52					
	Month 18	2	2.08					
Understanding and acceptance in the community	Month 1	2	1.83	14.026	0.001	0.146	0.124	0.109
	Month 9	2	1.83					
	Month 18	2	2.17					

With regards to peer-to-peer learning, during the intervention trials of both cohorts, 10 people in each cohort were able to engage with other people in a similar situation as themselves.

TABLE 42: NUMBER OF PEOPLE IN CONTACT WITH PEOPLE IN A SIMILAR SITUATION BY COHORT (FAMILY)

	Month 9	Month 9	Month 18
1st cohort	29	39	38
2nd cohort	23	24	34

Whereas patients depended most on other people in a similar situation for emotional support, by the end of the pilot, family members were more likely to rely more on such people for recommendations for doctors and specialists followed by for emotional support and a quick solution to an everyday problem.

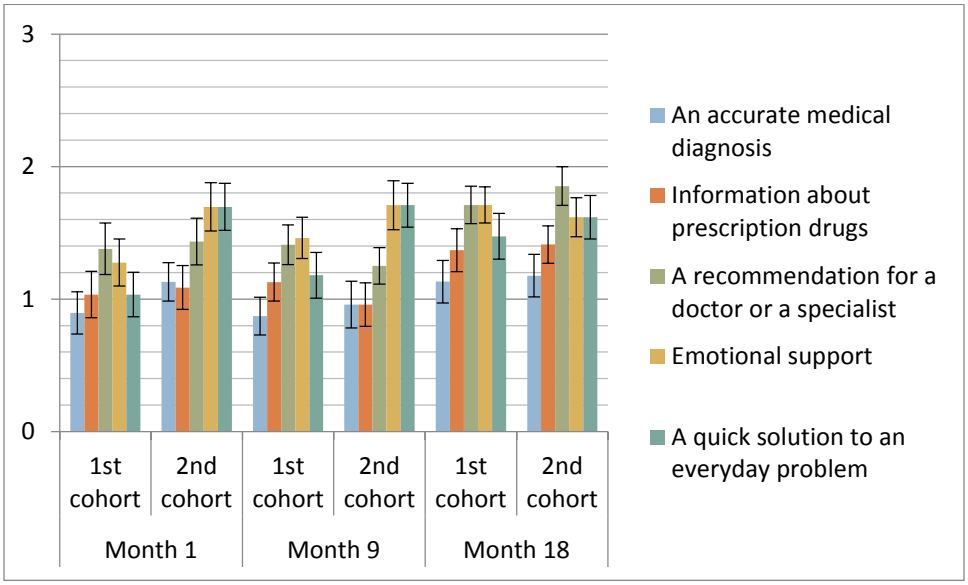


FIGURE 30: DEPENDENCE OF PARTICIPANTS ON THEIR PEERS BY COHORT (FAMILY)

2.3.6 ANCILLARY ANALYSES

The section below presents selected subgroup analyses based on the quality of life measurements as well as the index created to measure the efficacy of the INNOVCare intervention.

2.3.6.1 Overarching goal of the intervention: improvement in Quality of life

In order to further explore the potential relationship between measured responses related to the health related quality of life of the patients and the treatment, a general least squares – gls() – as well as a linear mixed effects model – lme() – were fitted to the data, with the difference that contrary to the ANOVA, they considered an autocorrelation component in the residuals, specified as an autoregressive model. Since the results of the ANOVA on the gls() and the lme() are near-identical, only the results of the linear mixed effects model are reported. Also applying this method, no significant effects could be identified. Furthermore, for each of the three different quality of life measurement instruments, the data visualizations from part 2.3.5.1 were repeated such that they include the sex dimension. However, due to the small sub-sample sizes when grouping by sex/gender, these only serve as a visualization of the different outcomes and no further exploration was undertaken in seeking possible statistical significance.

2.3.6.1.1 DISABKIDS – SMILEYS

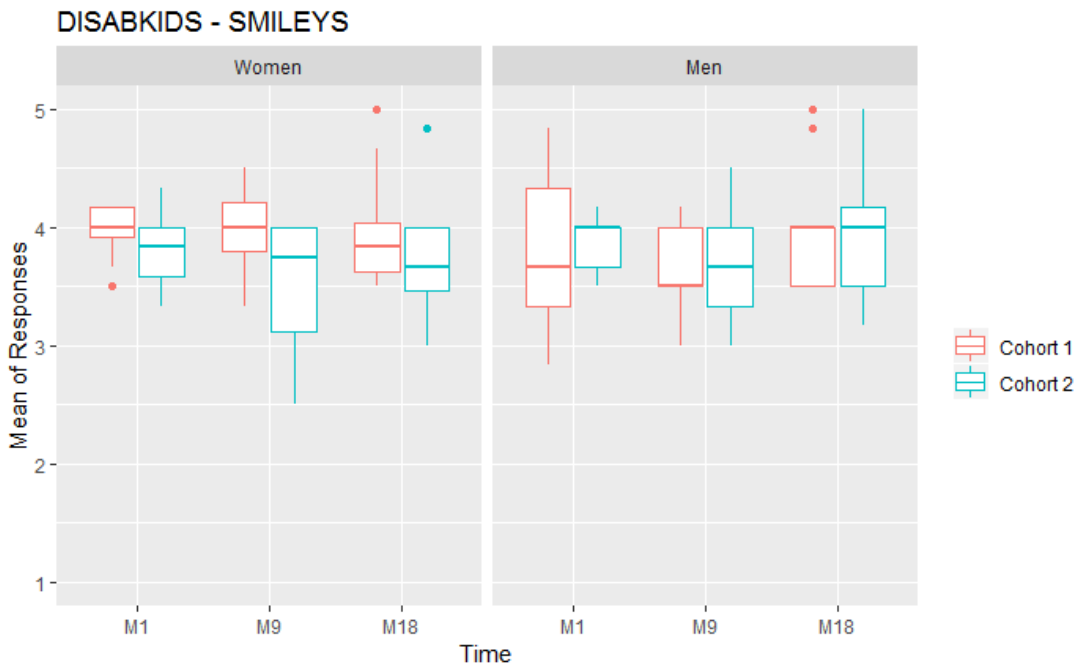


FIGURE 31: DISTRIBUTION OF SCORES OF THE DISABKIDS-SMILEY TOOL BY GENDER

TABLE 43: LINEAR MIXED EFFECTS MODEL – DISABKIDS - SMILEYS

	Value	Std.Error	DF	t value	p value
(Intercept)	3.853	0.102	64	37.960	0.000*
Cohort2	-0.020	0.144	32	-0.137	0.892
Time M9	-0.059	0.144	64	-0.409	0.684
Time M18	0.147	0.196	64	0.751	0.455
Cohort2:TimeM9	-0.167	0.204	64	-0.819	0.416
Cohort2:TimeM18	-0.108	0.277	64	-0.389	0.698

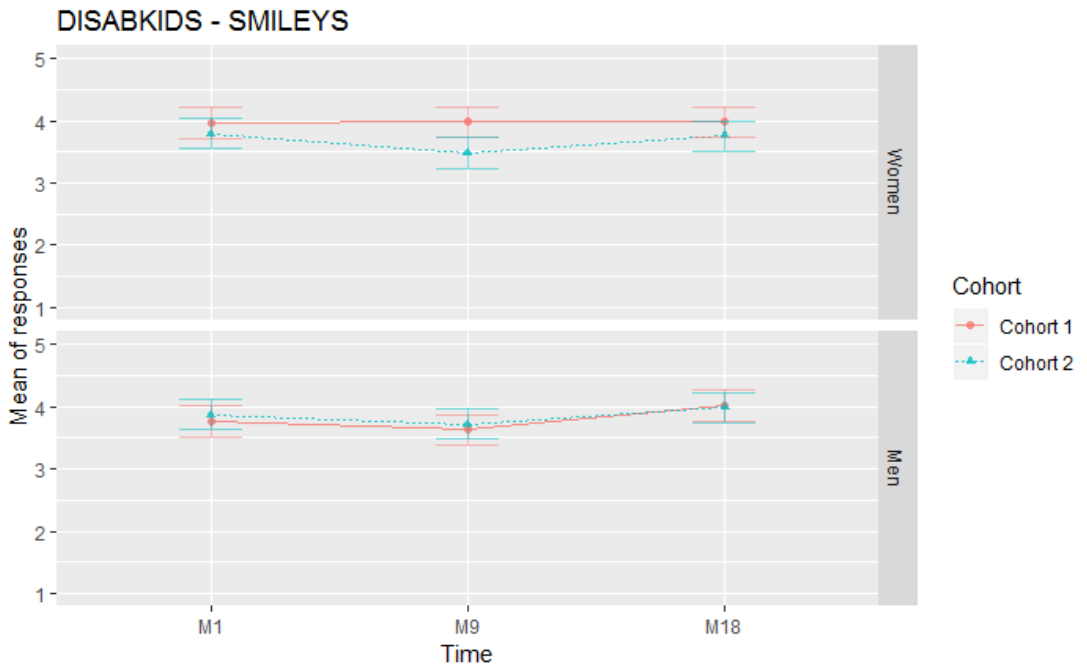


FIGURE 32: EFFECT OF THE INNOVCARE PILOT ON THE QUALITY OF LIFE OF PATIENTS OVER TIME (DISABKIDS-SMILEY) BY GENDER

2.3.6.1.2 DCGM-12 (SHORT VERSION)

FIGURE 33: DISTRIBUTION OF SCORES OF THE DCGM-12 TOOL BY GENDER

TABLE 44: LINEAR MIXED EFFECTS MODEL -DCGM-12 (SHORT VERSION)

	Value	Std.Error	DF	t value	p value
(Intercept)	2.510	0.087	100	28.986	0.000*
Cohort2	0.000	0.118	50	0.002	0.998
Time M9	0.051	0.065	100	0.782	0.436
Time M18	-0.024	0.077	100	-0.320	0.750
Cohort2:TimeM9	-0.043	0.088	100	-0.483	0.630
Cohort2:TimeM18	-0.044	0.104	100	-0.427	0.671

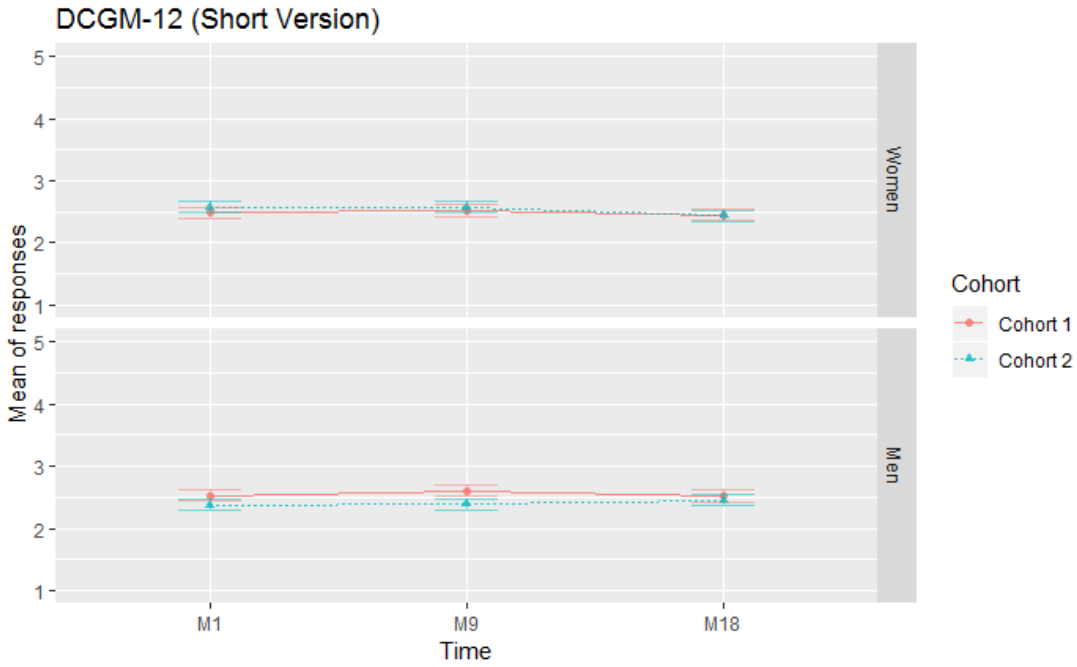


FIGURE 34: EFFECT OF THE INNOVCARE PILOT ON THE QUALITY OF LIFE OF PATIENTS OVER TIME (DCGM-12) BY GENDER

2.3.6.1.3 EQ-5D-Y

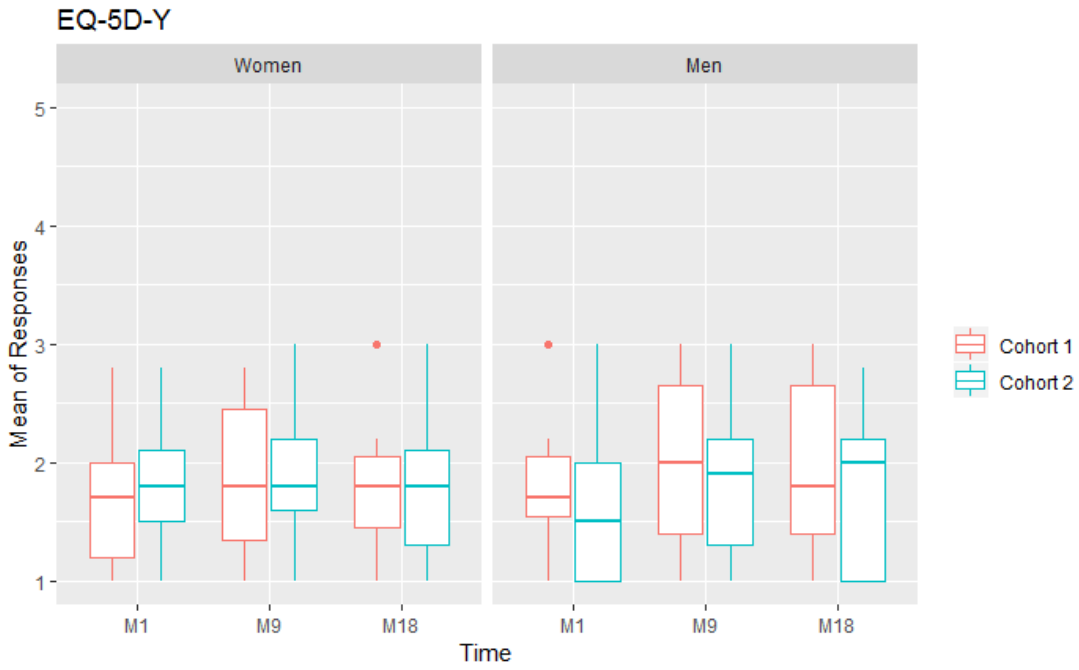


FIGURE 35: DISTRIBUTION OF SCORES OF THE EQ-5D-Y TOOL BY GENDER

TABLE 45 LINEAR MIXED EFFECTS MODEL - "EQ-5D-Y"

	Value	Std.Error	DF	t value	p value
(Intercept)	1.792	0.121	98	14.753	0.000*
Cohort2	-0.036	0.167	49	-0.216	0.830
Time M9	0.175	0.120	98	1.456	0.148
Time M18	0.100	0.131	98	0.764	0.447
Cohort2:TimeM9	-0.006	0.165	98	-0.039	0.969
Cohort2:TimeM18	-0.070	0.180	98	-0.391	0.696

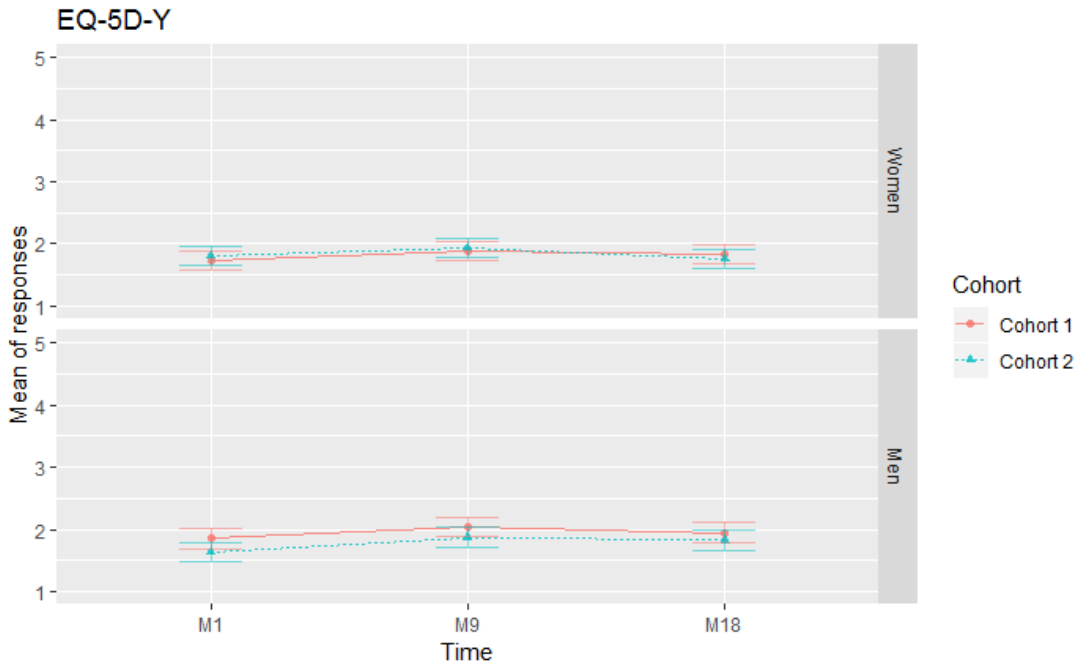


FIGURE 36: EFFECT OF THE INNOVCARE PILOT ON THE QUALITY OF LIFE OF PATIENTS OVER TIME (EQ-5D-Y) BY GENDER

2.3.6.2 Efficacy of the INNOVCare trial on the whole: Patients' perspective

2.3.6.2.1 NORO BENEFICIARIES VERSUS EXTERNAL PATIENTS

As previously explained in this report, participants who were at the same time beneficiaries of NoRo were automatically included in the sample. 78.5% of this group of participants was under the age of 18. The patient 8+ and patient SOLO questionnaires (see Table 2) , which included the items to measure the social impact of the INNOVCare pilot was to be completed by participants aged 8 and above who had the cognitive ability to do so. Of the 50 participants from both cohorts who completed these questionnaires only eight participants who were at the same time beneficiaries of NoRo or former beneficiaries of NoRo completed them (n=3 in the first cohort and n=5 in the second cohort). As a result of this low number, subgroup analysis was not logical. As a result of the sample composition for the patient questionnaire, it cannot be determined whether the INNOVCare intervention benefitted external participants or participants affiliated with NoRo more.

TABLE 46: EFFICACY OF THE INNOVCARE INTERVENTION ON NORO BENEFICIARIES VS. EXTERNAL PATIENTS BY COHORT[68] (PATIENT PERSPECTIVE)

		n	Median	Mean difference [69]	Mean rank	Degrees of freedom	H test statistic	p value
1st cohort	External	21	0.71	0.65	12.69	1	0.124	0.725
	NoRo	3	0.57	0.57	11.17			
2nd cohort	External	21	0.71	0.63	14.36	1	1.395	0.238
	NoRo	5	0.57	0.40	9.90			

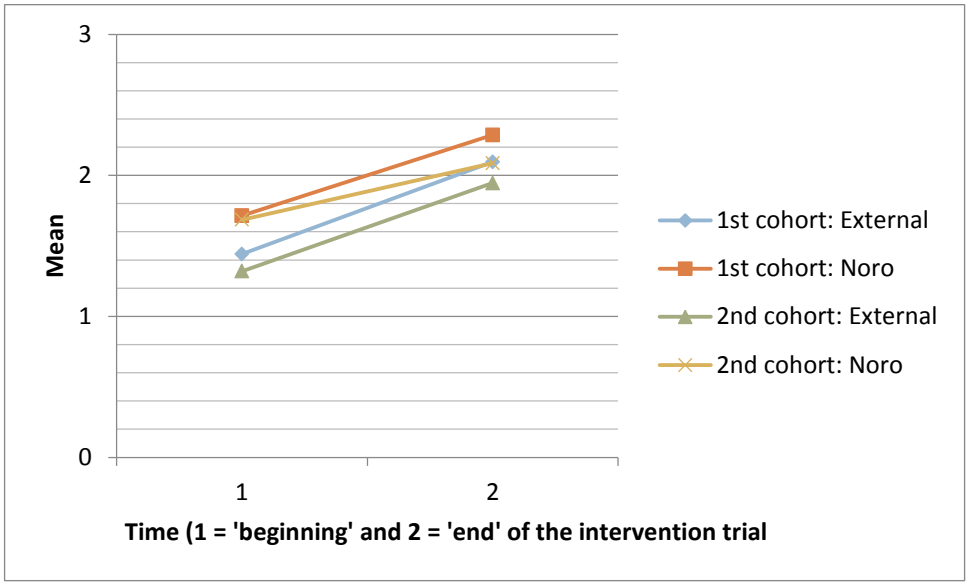


FIGURE 37: EFFICACY OF THE INNOVCARE INTERVENTION ON NORO BENEFICIARIES VS. EXTERNAL PATIENTS BY COHORT (PATIENT PERSPECTIVE)

2.3.6.2.2 AGE GROUP

All the 50 participants who completed the items of the questionnaire comprising of the social impact of the INNOVCare pilot were aged over 18. 70% of the participants in both cohorts combined were between the age of 18 and 59 at the start of the intervention and the rest were above 60. A Kruskal-Wallis H test was conducted to determine whether the INNOVCare pilot was more effective on specific age groups. The participants were divided into two age groups: 18 to 59 (n=45; n=17 for the first cohort

[68] A Kruskal-Wallis H Test was run to determine if there were differences in the performance of NoRo (n=21) and external patients (n=3) from the first cohort during the intervention trial. Distributions of the scores were not similar for both groups at both points in time as assessed by inspection of respective box plots. The mean rank of the scores was not statistically significantly different between groups for both cohorts: first cohort: $X^2(1)=0.124$, p=0.725 and second cohort:$X^2(1)=1.395$, p=0.238

[69] The mean difference signifies the difference between the means at the beginning of the intervention trial and the end.

and n=18 for the second cohort) and 60+ (n=15; n=7 for the first cohort and n=8 for the second cohort). The gains scores[70] for each age group within each cohort were evaluated. The distribution of the gain scores of the first cohort was similar across the categories of age group, as assessed by the visual inspection of relevant box plots. The distribution for the second cohort was dissimilar.

For the first cohort, median scores were not statistically significantly different between the different levels of age group: $X^2(1)=0.004$, p=0.949. On the other hand, the median scores of the second cohort were statistically significantly different at the different levels of the same variable: $X^2(1)=12.262$, p<0.001. This suggests that possibly due to the learning effects of case managers, in the second phase of the intervention, where the second cohort received the intervention, the INNOVCare pilot benefitted participants who were 60 or older more than at the start of the pilot.

TABLE 47: EFFICACY OF THE INNOVCARE INTERVENTION ON DIFFERENT AGE GROUPS BY COHORT (PATIENT PERSPECTIVE)

		n	Median	Mean difference	Mean rank	Degrees of freedom	H test statistic	p value
1st cohort	18-59	17	0.57	0.65	12.44	1	0.004	0.949
	60+	7	0.71	0.63	12.64			
2nd cohort	18-59	18	0.29	0.40	10.03	1	12.262	<0.001*
	60+	8	1.00	0.98	21.31			

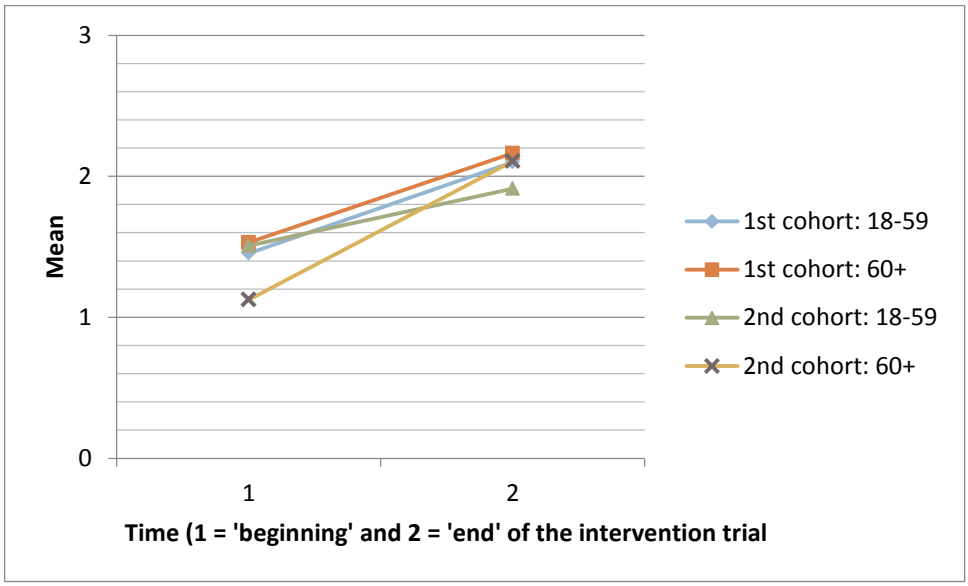


FIGURE 38: EFFICACY OF THE INNOVCARE INTERVENTION ON DIFFERENT AGE GROUPS BY COHORT (PATIENT PERSPECTIVE)

[70] The term 'gain score' refers to the mean differences.

2.3.6.2.3 GENDER

Just like in the full sample of the INNOVCare pilot (n=120), the ratio of females to males among the 50 patients who completed the social impact section of the questionnaire was 54.5% to 45.5%. However, this division was different among the cohorts[71] only considering those 50 participants who were examined in the following analysis: The ratio of females to males in the first cohort was 50% to 50%; for the second cohort this ratio was: 73.1% to 26.9% signifying that females were overrepresented in the latter.

A Kruskal-Wallis H test[72] was performed to determine the difference in the efficacy of the intervention according to gender for each cohort. The gain scores in both cohorts were not significantly different between genders: First cohort: $X^2(1)=0.042$, p=0.838 and the second cohort: X^2 (1)=0.449, p=0.503. Although, the mean rank of the male participants is marginally higher in the second cohort (Mean rank=15.14) than in the first cohort (Mean rank=12.21), this difference of gain scores for the male participants between cohorts was not statically significant.

TABLE 48: EFFICACY OF THE INNOVCARE INTERVENTION ON DIFFERENT GENDERS BY COHORT (PATIENT PERSPECTIVE)

		n	Median	Mean difference	Mean rank	Degrees of freedom	H test statistic	p value
1st cohort	Female	12	0.71	0.65	12.79	1	0.042	0.838
	Male	12	0.57	0.63	12.21			
2nd cohort	Female	19	0.55	0.71	12.89	1	0.449	0.503
	Male	7	0.67	0.57	15.14			

[71] In the first cohort of the final INNOVCare sample the ration of females to males was:50.8% to 49.2%. That for the second cohort was 58.3% to 41.7%. The difference in composition of the two cohorts in terms of gender was not statistically significant (Tschank & Handler, 2017, p. 60)

[72] Distribution of the gain scores for all groups as assessed by a visual inspection of the boxplots determined that they were not similar.

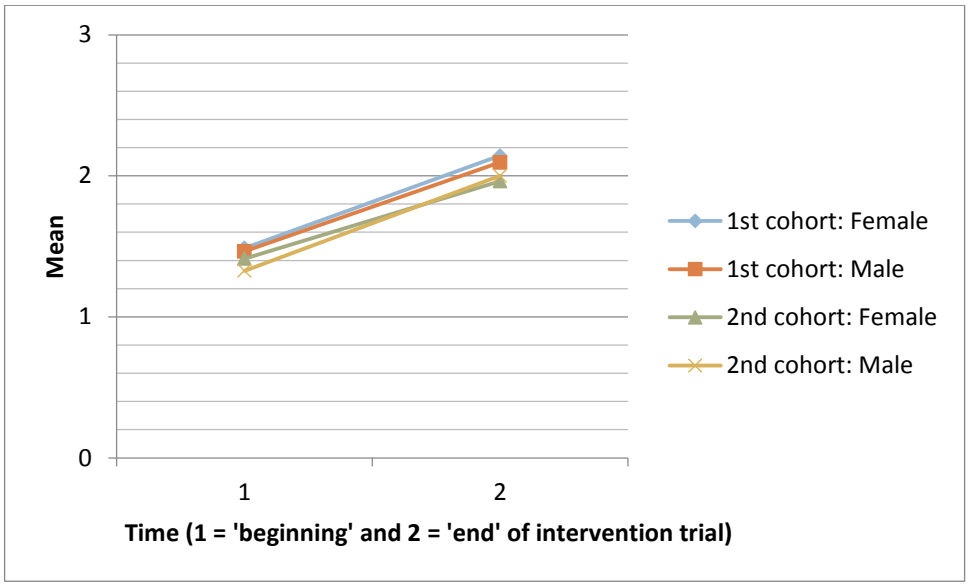


FIGURE 39: EFFICACY OF THE INNOVCARE INTERVENTION ON DIFFERENT GENDERS BY COHORT (PATIENT PERSPECTIVE)

2.3.6.2.4 LOCATION OF THE PARTICIPANTS

The total sample of the INNOVCare pilot included 71.9% of people living in urban areas and 28.1% living in rural areas. Differentiated by cohort, the trend was similar: First cohort 73.8% of participants lived in urban areas and 26.2% in rural areas. For the second cohort, this ratio was 70% to 30%. Considering just the participants whose data was available for all the outcome variables of the INNOVCare pilot (n=50), the proportion of the total number of participants was 52% to 48% (urban to rural) and according to cohort 58.3% to 41.7% (first cohort) and 46.2% to 53.8%(second cohort). This shows that the participants living in rural areas were overrepresented in comparison with the total sample.

To determine whether the INNOVCare pilot had a differentiated effect on people living in urban areas compared to those living in rural areas, a Kruskal-Wallis test[73] war run for each cohort separately. This analysis revealed statistically significant differences in gain scores between the participants living in urban and rural areas within the first cohort during the intervention trial. The participants living in rural areas seem to have benefitted more from the intervention having had a mean rank of 16.35 compared to 9.75 for the participants living in urban areas: $X^2(1)=5.172$, p=0.023. Like in the first cohort, the mean rank for the participants of the second cohort living in rural areas (15.00) was higher than that of those living in urban areas (Mean rank=11.75), however, the difference in gain scores between the two groups was not statistically significant: $X^2(1)=1.187$, p=0.276. The difference in the gain scores of people living in either urban areas or in rural areas was not statistically different between cohorts. This therefore suggests that the INNOVCare intervention had a stronger effect on people living in rural areas.

[73] Distributions of the gain scores were similar for participants living in urban and rural areas in the first cohort but not similar for all groups in second cohort inspection of respective box plots.

TABLE 49: EFFICACY OF THE INNOVCARE INTERVENTION ON PEOPLE LIVING IN DIFFERENT LOCATIONS BY COHORT (PATIENT PERSPECTIVE)

		n	Median	Mean difference	Mean rank	Degrees of freedom	H test statistic	p value
1st cohort	Urban	14	0.57	0.48	9.75	1	5.172	0.023*
	Rural	10	0.86	0.87	16.35			
2nd cohort	Urban	12	0.50	0.49	11.75	1	1.187	0.276
	Rural	14	0.79	0.66	15.00			

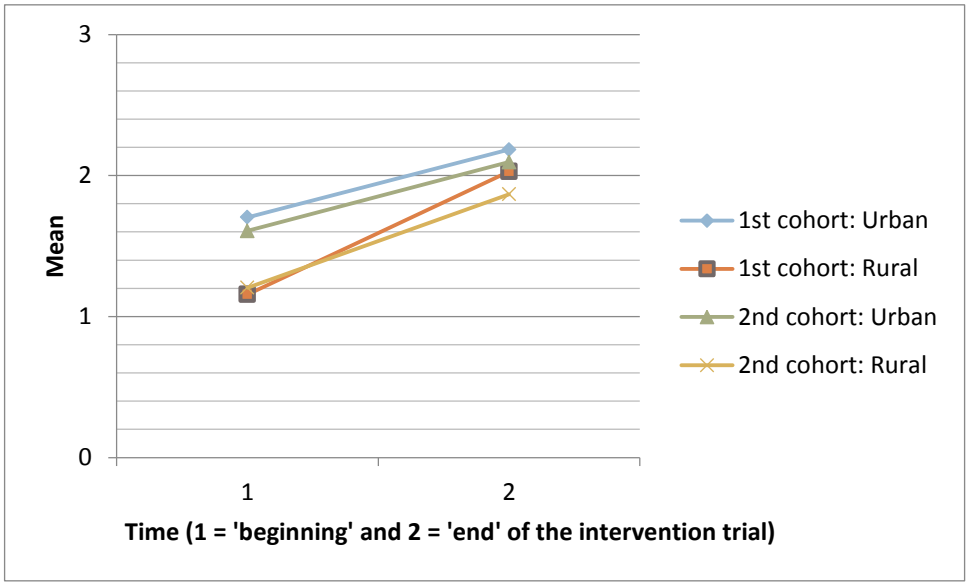


FIGURE 40: EFFICACY OF THE INNOVCARE INTERVENTION ON PEOPLE LIVING IN DIFFERENT LOCATIONS BY COHORT (PATIENT PERSPECTIVE)

2.3.6.2.5 DEGREE OF DISABILITY

The level of disability of the participants considered for the following analysis, as can be seen by Figure 42 below, does not mirror that of the total INNOVCare sample (see Figure 41). Nevertheless, comparative analyses to decipher whether people with varying degrees of disability were affected differently by the INNOVCare intervention were carried out. However, the interpretation of results of further analyses should be handled with caution.

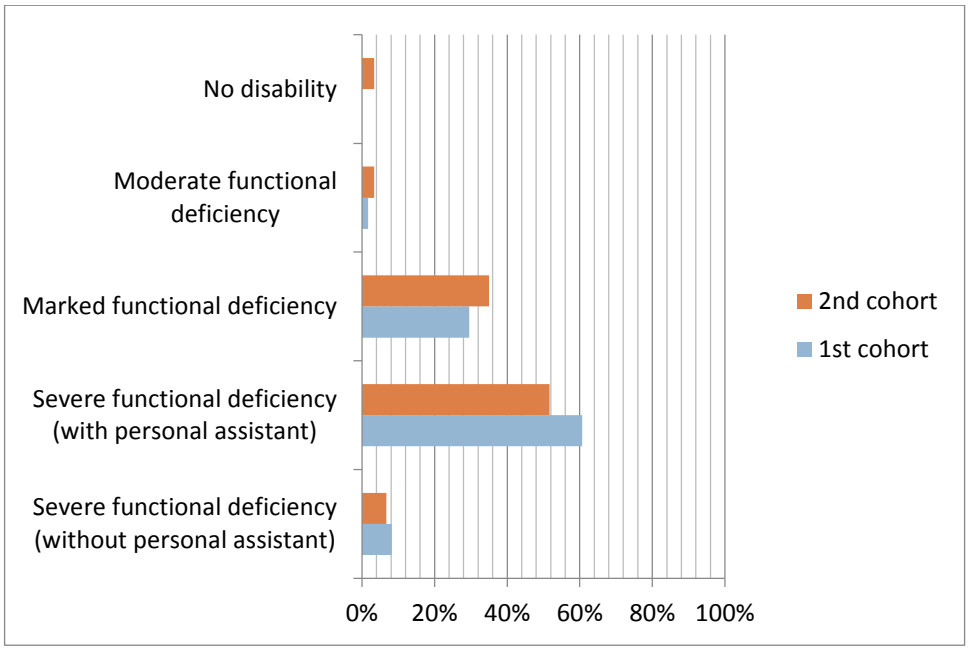


FIGURE 41: DISTRIBUTION OF LEVEL OF DISABILITY OVER THE WHOLE INNOVCARE SAMPLE (N=120)

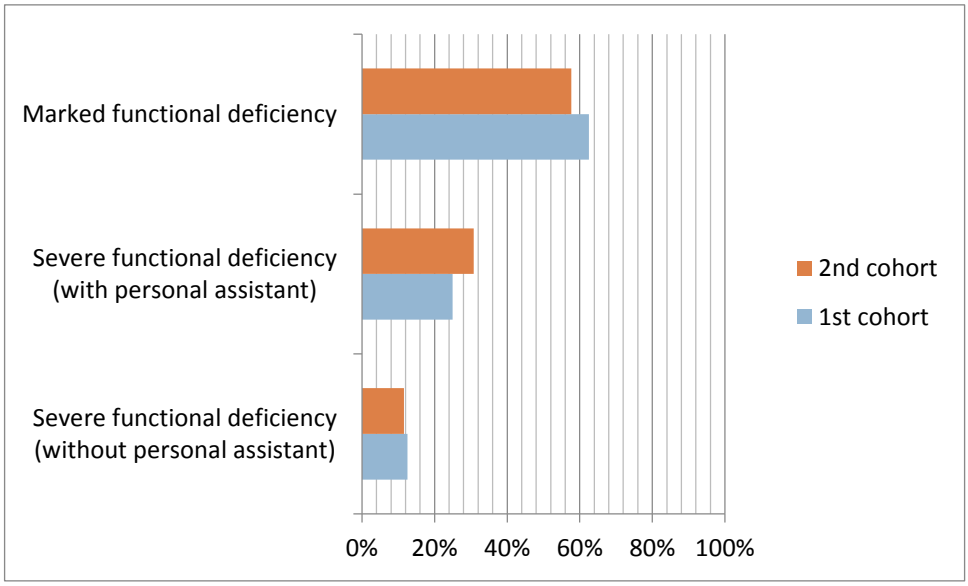


FIGURE 42: DISTRIBUTION OF LEVEL OF DISABILITY IN THE SAMPLE CONSIDERED FOR ANALYSIS (N=50) (FAMILY)

For the purpose of analysis a new variable was created that represented participants with 'severe' functional disability with and without a personal assistant in one category and participants with 'marked' functional disability in another. Based on a Kruskal-Wallis H test[74], the two gain differences of these levels of disability within each cohort were tested. In both cohorts, the intervention does not

[74] Distributions of the gain scores were not similar for all groups as assessed by inspection of respective box plots.

seem to have been received to different intensities by either participants with marked or severe disabilities in both cohorts: First cohort $X^2(1)=0.565$, p=0.452 and second cohort $X^2(1)=0.175$, p=0.675.

TABLE 50: EFFICACY OF THE INNOVCARE INTERVENTION ACCORDING TO LEVELS OF DISABILITY BY COHORT (PATIENT PERSPECTIVE)

		n	Median	Mean difference	Mean rank	Degrees of freedom	H test statistic	p value
1st cohort	Marked	15	0.71	0.69	13.33	1	0.565	0.452
	Severe	9	0.57	0.57	11.11			
2nd cohort	Marked	15			14.03	1	0.175	0.675
	Severe	11			12.77			

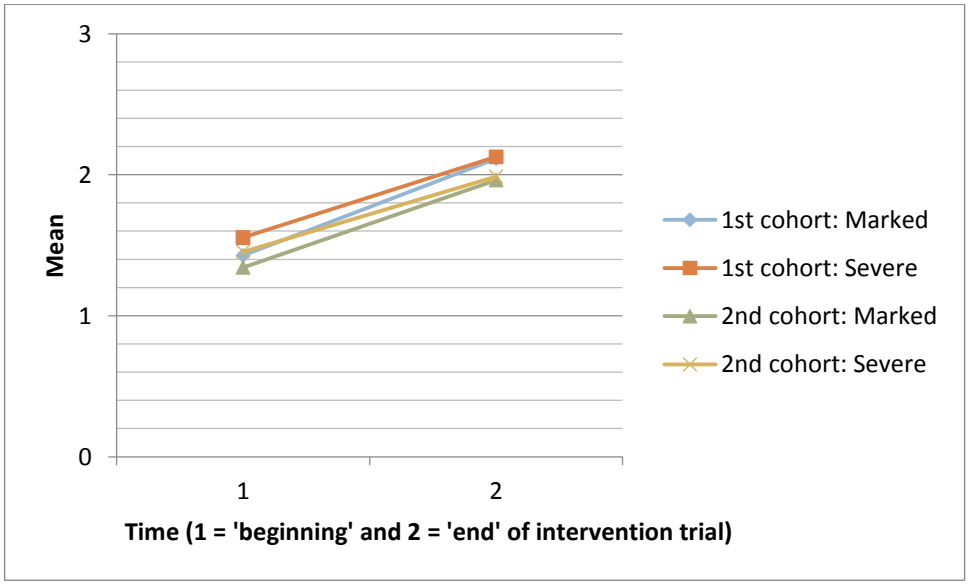


FIGURE 43: EFFICACY OF THE INNOVCARE INTERVENTION ACCORDING TO LEVELS OF DISABILITY BY COHORT (PATIENT PERSPECTIVE)

2.3.6.3 Efficacy of the INNOVCare trial on the whole: Family perspective

In an attempt to decipher on which groups of participants the INNOVCare pilot had the highest impact, like with the patient data, the family data underwent subgroup analyses on the following variables: Noro beneficiaries versus external patients', age, gender, location of the patients and their families as well as the patients' degree of disability.

These analyses showed that the INNOVCare pilot, especially in the second phase of the intervention, had the highest impact on external patients ($X^2(1)=10.140$, p=0.001) as well as people living in rural areas ($X^2(1)=8.150$, p=0.004). These results are consistent with the composition of the pilot participants in as far as the majority of participants, who were at the same time receiving services from NoRo, lived in urban areas (about 91%). On the other hand, the majority of the external patients lived in rural areas (about 54%).

In addition, there were indications, that older people, 60 years and above, benefitted most from the pilot (first cohort: $X^2(2)=5.778$, p=0.056 and second cohort: $X^2(1)=5.161$, p=0.076).

The pilot does not seem to have affected the different genders (first cohort: $X^2(1)=1.073$, p=0.300 and second cohort: : $X^2(1)=0.301$, p=0.532) or people with varying degrees of disability (first cohort: : $X^2(1)=1.237$, p=0.539 and second cohort: : $X^2(1)=1.177$, p=0.555) any differently.

TABLE 51: SUBGROUP ANALYSIS OF FAMILY DATA

Subgroup variable	Cohort	Grouping	n	Mean difference	Median	Mean rank	df	X^2	p
Noro beneficiaries versus external patients	1st cohort	External	22	0.66	0.57	31.43	1	1.712	0.191
		NoRo	33	0.46	0.43	25.71			
	2nd cohort	External	18	0.79	0.86	32.75	1	10.140	0.001*
		NoRo	30	0.40	0.43	19.55			
Age group of patient	1st cohort	Under 18	30	0.51	0.43	28.25	2	5.778	0.056**
		18-59	18	0.40	0.36	22.94			
		60+	7	1.02	1.14	39.93			
	2nd cohort	Under 18	26	0.48	0.43	22.33	2	5.161	0.076**
		18-59	15	0.51	0.43	23.13			
		60+	7	0.88	1.00	35.50			
Gender	1st cohort	Female	27	0.62	0.57	30.26	1	1.073	0.300
		Male	28	0.47	0.43	25.82			
	2nd cohort	Female	22	0.57	0.64	25.86	1	0.391	0.532
		Male	26	0.53	0.43	23.35			
Location of the participant	1st cohort	Urban	43	0.48	0.43	25.59	1	4.525	0.033*
		Rural	12	0.76	0.79	36.63			
	2nd cohort	Urban	34	0.45	0.43	20.82	1	8.150	0.004*
		Rural	14	0.80	0.86	33.43			
Degree of disability	1st cohort	No to moderate	1	0.14	0.14	10.50	2	1.237	0.539
		Marked	16	0.56	0.43	28.25			
		Severe	38	0.54	0.43	28.36			
	2nd cohort	No to moderate	4	0.64	0.57	28.13	2	1.177	0.555
		Marked	12	0.45	0.29	20.96			
		Severe	32	0.57	0.57	25.38			

2.3.7 HARMS

At the development stage of the INNOVCare evaluation design, any harms to the participants as well as measures to overcome them were considered in detail (see Tschank, et al., 2017, chapter 4.5). In general, due to the non-invasive nature of the intervention and the fact that case management as an approach has been tried and tested in different fields and widely proven as advantageous, any harms to the participants directly caused by the INNOVCare intervention were considered rather unlikely or rather insignificant (see Tschank, et al., 2017, chapter 4.5).

2.4 DISCUSSION

4.2.1 LIMITATIONS

One of the key limitations of the study was the ability of the participants to complete the questionnaires; especially the sections relating to the social impact of the trial. All participants above the age of 8 were foreseen to complete the Patient 8+ or Patient SOLO questionnaires. However, in practical terms, during implementation of the measurement tools, it was not possible for the majority of the participants under the age of 18 to complete these questionnaires; hence they completed the quality of life instruments alone. Since this affected mostly the participants who at the same time were beneficiaries of NoRo, who were mostly under the age of 18, subgroup comparison of the patient data was difficult due to very dissimilar group sizes (2.3.6.2). Although this could result in potential bias of the results, the comparison of the patient data to the family data presents a relatively balanced picture, as the response rate of the family questionnaire was comparatively high.

According to the analysis presented in this report, the intervention does not seem to have had a significant change in the quality of lives of the participants. This could be due a number of reasons including that the measurement instruments used were possibly not sensitive enough to register any changes or that for such a goal, there may have been a lag between treatment and effect; that the changes would only become visible to the participants and measurable after some time. Having measured the first cohort nine months after receiving the intervention, suggests that if the INNOVCare intervention helped to increase the quality of life of the patients and their families, then this change would become measurable a least more than nine months afterwards. At the same time, one should consider that quality of life can only be affected indirectly, needs a considerably long time to improve (therefore possibly a longer intervention period) and is also affected by several dimensions which cannot be influenced by the intervention for example type of disease and degree of disability.

Another limitation regarding the quality of life instruments was that due to confusion in application of the instruments, quite a number of participants who should have completed the DISABKIDS-SMILEY instrument, were issued the DCGM-12 instrument at the first measurement then the DISABKIDS-SMILEY instrument at the subsequent measurements. This mistake in data collection therefore reduced the sample size that could be compared in all three measurements. Only those participants who completed the same instruments at all three measurement points were compared. This means that those that completed the wrong instrument at the first measurement were excluded from the analysis therefore reducing power considerably.

About 20% of the participants initially selected to take part in the study were non-takers; which would eventually reduce the statistical power as sample size was based on power calculations. However to counterbalance this situation and maintain the statistical power, 25 new participants were sampled and randomised relatively early on in the process.

From the analysis of the individual outcome variables, it can be deduced that the intervention was able to make a stronger impact on some of the dimensions e.g. informing the patients and their families on their condition, rights and services but weaker on other dimensions like increasing the patients' and their families' ability to independently manage their own care; supporting coordination of care among providers and increasing understanding and acceptance in the community. There were indications in the areas that the intervention did not have a strong impact and that there had already been some improvements. A longer intervention duration may have been able to elicit stronger positive changes in these areas.

4.2.2 GENERALISABILITY

As regards to content, the findings of this study can be generalised to at least the whole rare disease patients and their families in the county of Salaj in Romania; but also possibly to the whole population of rare disease patients in Romania as the contexts here are probably very similar to those of the INNOVCare pilot sample. Also, the different legislations, which play a central role in the Romanian health and social systems, as seen by the qualitative analysis of the efficacy of the INNOVcare trial, are the same.

The findings in this report are based on the design and analysis of an individual pilot trial in a very specific context with a special group of participants. Nonetheless, the methods of this study have been well documented, not just in this report but in other related reports like the methodology report (Tschank, et al., 2017) and the technical report on random sampling and random allocation (Tschank & Handler, 2017). This thorough documentation was aimed to provide other studies wishing to implement such studies in different settings with a working template.

4.2.3 INTERPRETATION

The main aim of the INNOVCare trial was to improve the quality of life of the patients and their families. Analysis of the quality of life measures implemented in this study (DISABKIDS-SMILEY, DCGM-12 and EQ-5D-Y) show that the INNOVCare intervention did not have a significant impact on this aspect. Inspections of the means during the intervention trials provide different results. In some cases, the mean increased as expected; in others, the change was in the opposite direction to the one expected. Nevertheless, these changes were very small (between -0.08 to 0.27) and were not statistically different within-groups or between the cohorts. Considering the complexity of quality of life and the fact that it is mainly influenced by medical dimensions like type of disease and degree of disability which cannot be influenced by an non-medical intervention such as case management and that it can only be affected indirectly, it is not surprising that the INNOVCare intervention did not manage to make a significant impact on it.

Regarding the direct objectives of the INNOVCare trial, which were specifically targeted by the INNOVCare intervention, the findings suggest that the INNOVCare intervention was successful in

achieving all its set objectives but impacting the individual outcomes to different degrees. The results of the analysis of the index created from seven of the eight objectives of the intervention show that the score for both cohorts statistically significantly improved during the intervention trials. Furthermore, during the control trial, the score of the second cohort did not change significantly, suggesting that outside factors such as other interventions that the participants might have been receiving simultaneously or anticipation or spillover effects did not significantly affect the intervention and thus between-groups analyses would provide an accurate representation of the impact of the intervention. The control trial for the first cohort took place between Month nine and Month 18, after the participants in this group had already received the intervention. The main expectation of the analyses of scores between these two measurements was to examine whether the treatment effects were short-term or whether they lasted at least nine months after the intervention. Based on the evidence that the scores for this cohort did not change significantly during the control trial, it can be derived that the treatment effects of the INNOVCare intervention were not short-term, but rather could be sustained for at least nine months after the intervention.

Looking at the individual goals, the intervention seems to have had the highest impact on increasing the level of information of the patients and their families regarding their condition/disease, rights and available social and health care services. The patients from both cohorts felt the highest impact was in their knowledge of health and social care services available to them, followed by their rights as patients and their condition. The expansion in the level of information on these three aspects also registered the highest impact for the family members; however in a slightly different sequence. The effect of the INNOVCare intervention for the family members was felt highest with regards to increasing their information stand on the rights of the patients followed by the available health and social care services and finally about their rights.

In terms of the effect of the INNOVCare intervention on the participants' communication skills, in the patients' dataset, improvements were detected in both the between-groups and within-groups analyses but to a lesser degree than those items (see previous paragraph) related to information. However, over time, the changes were only statistically significantly different for the second cohort. The differences in the first cohort over time were just short of being statistically significant ($p=0.078$ two-tailed). A one-tailed significance test, which is consistent with such a study with a directed hypothesis, would have been below the significance threshold. This suggests that during the first phase of the INNOVCare trial, the case managers were able develop the patients' communication skills but only marginally. Possibly due to the experience gained during their work with the first cohort, they had gained skills to better train the participants on their communication and hence the stronger detection of a difference within the second cohort. Another explanation for this result is the fact the first cohort's mean (1.92) and median (2) for the respective item was already somewhat higher than that of the second cohort (Mean=1.65 and *Mdn*=1.5) at the beginning of the intervention trial. With a four-point answering scale from 0: 'not at all' to 3: 'very well', the possibility of change is limited. The consequence of the INNOVCare pilot on the communication skills of the patients' families resulted in similar results. Both between-groups and within-groups analyses demonstrated a significant improvement in the communication skills of the family members. Both cohorts delivered statistically significant improvements in the communication skills of the family members during the intervention trial (within-groups analyses); but the changes in the second cohort were more distinct than those of the first. This could again be explained by the learning effect of the case managers.

The learning effect of the case managers was further visible with regard to the goal of empowering the patients and their families to independently manage all aspects of their care. The analysis of the patients' data reported insignificant group differences at the second measurement point, contrary to what was expected. Nevertheless, analyses of each cohort over time presented significant improvements in the ability of the patients' to manage their own care. The improvement of the second cohort was slightly higher than that of the first; a difference that was not statistically significant. With regard to the family members, their empowerment to independently manage the care of the person they care for was higher than that of the patients in that both the between-groups and within-groups analyses resulted in significant improvements. On the contrary to the patients, the improvement in the first cohort was slightly higher but not statistically higher than in the first cohort on assessment of the effect sizes.

The two goals of the intervention that did not directly involve the patients or their families; namely: increasing and supporting coordination among providers as well as understanding and acceptance in the community were the least affected by the intervention in comparison to the other goals; nevertheless, positive, statistically significant changes were still observed by both the patients and their families. Between and within-groups analyses of the patient data showed significant improvements in the coordination of different stakeholders that are involved in the patients' care. Nevertheless, although the omnibus within-groups tests reflected a significant difference in each of the two cohorts over time with regard to this item, the pairwise comparisons in both groups were only significant for a one-tailed comparison. This implies that although the INNOVCare intervention managed to impact some changes on the network of providers in the region of Salaj, these improvements were only minimal. Similarly, the family members were of the opinion through both the between-groups and within-groups that the INNOVcare intervention improved the coordination among providers to a higher degree than the patients, but at the same time the treatment effect was not ranked as highly as those for example involving expanding knowledge on key factors important to people suffering from rare and complex diseases and their carers. The family members of the patients allocated to the second cohort marked higher improvements than in the first; just as the patients.

The case managers running the INNOVCare intervention also made it their goal to improve the understanding and acceptance of the community regarding people living with complex and rare disorders and the challenges they faced. They did this through for example raising awareness of teachers in schools. The between-groups analysis of the patients' data did not bear any significant differences between the groups after the first cohort had received the intervention. Nevertheless, the within-groups analyses signalled differences in both cohorts over the three measurement times. The subsequent pairwise comparisons, however, did not yield any significant differences between the time pairings of both cohorts. This suggests that although the intervention made progress in raising the community's awareness as demonstrated by the omnibus within-group analyses, these changes were only minimal. The analysis of the family data provided a similar picture with the only difference that the between-groups analysis were also significant. The omnibus within-groups analyses were statistically significant; whereas the pairwise comparisons were not. A longer intervention duration or / and targeted activities may have positively affected both the understanding and acceptance of the community and also coordination among providers.

With regards to peer-to-peer learning, analysis of both the patient and family datasets show that the intervention initiated contact between the patients and their families with people in a similar situation;

be it suffering from the same disease or similar disease or caring for such a person. These contacts can be very valuable in terms of emotional support and tips and tricks of coping with the situation among others.

Furthermore, subgroup analyses of both datasets suggested that the intervention was most impactful on: People who were not at the same time beneficiaries of NoRo, people living in rural areas and people aged 60 or above.

3. QUALITATIVE ANALYSIS

For each cohort, each case manager completed a document that detailed which organisations she had contacted in a bid to solve the needs of the patients and their families. This data was received and analysed at two points in time and built the basis for the visualisation of the Ego-network for each case manager for each period (the first nine months and the last nine months).

Additionally each of the case managers was interviewed at two points in time with both the network picture and an interview guideline (see Annex 6.3 and 6.4) forming the basis. Aim of the interviews was to discuss the individual networks in detail and to qualitatively monitor the progress of the intervention. These interviews were qualitatively analysed. As a result, this part of the report strongly reflects the experiences and the points of view of the case managers.

3.3 THE NETWORKS OF THE CASE MANAGERS: 1ST AND 2ND PHASE OF THE INNOVCARE PILOT

According to detailed records of contacts of each case manager with organisations or individuals essential in meeting the INNOVCare pilot participants' needs, individual Ego-networks were developed. The single nodes represent the different persons or organisations contacted. The colour of the nodes and lines refer to the type of organisation[75]. The size of the nodes depicts the duration that the case manager has been in contact with that person or organisation; the bigger the node the longer the duration of contact. The thickness of the lines demonstrate the frequency of communication during the intervention periods; the thicker the line the more frequent the contact.

3.3.5 CASE MANAGER 1

In the first phase of the intervention, case manager 1 had frequent contact especially with public organisations, NGOs and private service providers (see Figure 44). In the second period, case manager 1's contacts were very similar to period 1 (see Figure 45). However, some new institutions were also engaged e.g.: General Directorate for Public Domain Administration, Anca Maries, Territorial Pension Authority and Charcot Marie Tooth Association[76]. Furthermore, comparing the networks of both periods for this case manager, it is visible that, especially, the contacts to public institutions to organisations in the medical field grew.

[75] Colour codes: black – medical institutions, purple – NGOs, pink – educational institutions, blue – public institutions, green – private providers, grey – SRL and businesses, orange – professional organisations
[76] A short description of each of the organisations is provided in section 3.1.5 of this report.

3.1.1.1 Phase 1 (Month 1 to Month 9)

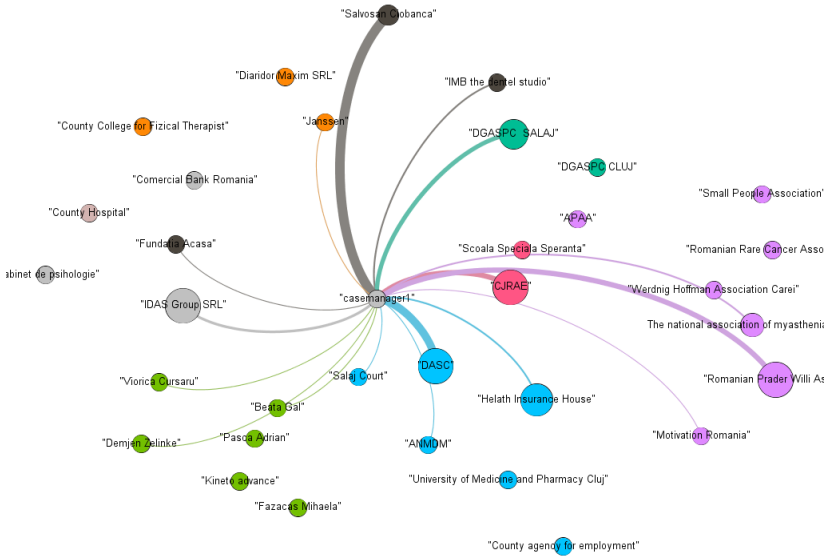


FIGURE 44: CASE MANAGER 1'S NETWORK DURING THE FIRST NINE MONTHS OF THE INTERVENTION

3.1.1.2 Phase 2 (Month 9 to Month 18)

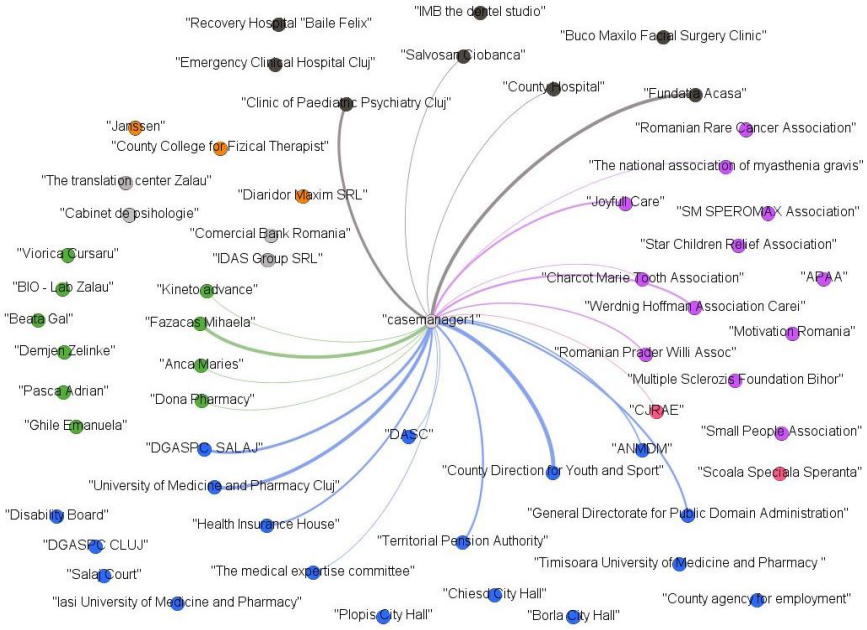


FIGURE 45: CASE MANAGER 1'S NETWORK DURING THE LAST NINE MONTHS OF THE INTERVENTION

3.1.2 CASE MANAGER 2

As an experienced social worker, case manager 2 had already built a rapport with many persons and organisations before the start of the intervention. Nevertheless, with passing time, some people that she personally knew were no longer in their position. Therefore, in her new role as a case manager, for some organisations, she just had to refresh the contacts, for others, she had to establish new contacts. In period 1, frequent communication was especially with the public and NGO sectors (see Figure 46). This is also true for period 2, but additionally, contacts with medical institutions and private providers were more frequent than in period 1 (see Figure 47).

3.1.2.1 Phase 1 (Month 1 to Month 9)

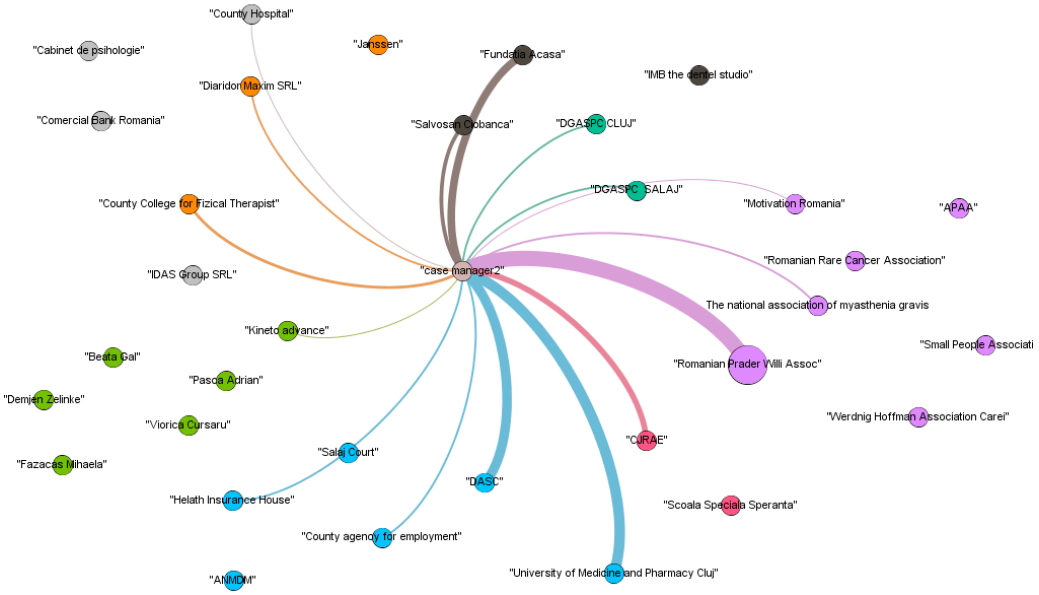


FIGURE 46: CASE MANAGER 2'S NETWORK DURING THE FIRST NINE MONTHS OF THE INTERVENTION

3.1.2.2 Phase 2 (Month 9 to Month 18)

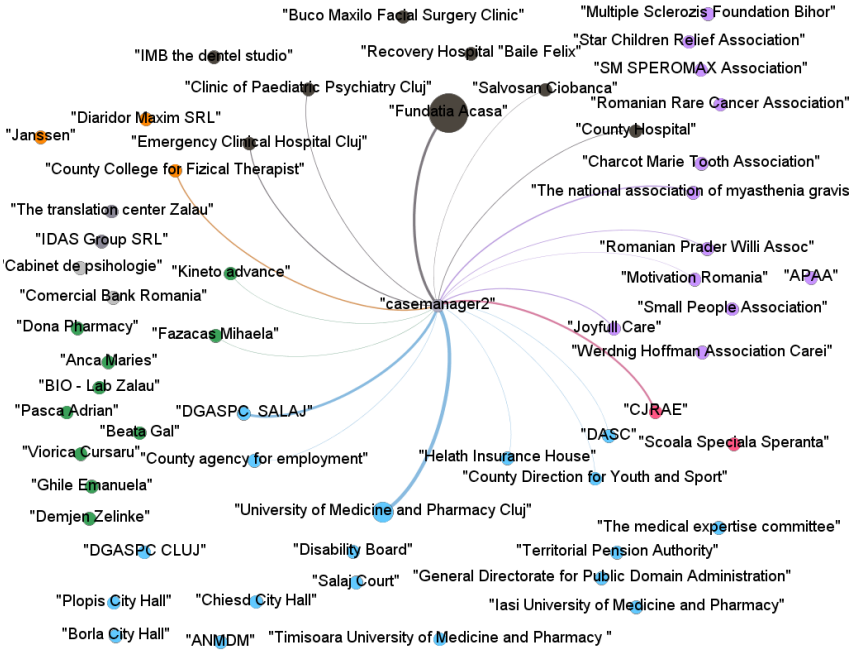


FIGURE 47: CASE MANAGER 2'S NETWORK DURING THE LAST NINE MONTHS OF THE INTERVENTION

3.1.3 CASE MANAGER 3

In period 1, case manager 3 had the most contact with the NGO sector, followed by private service providers and public institutions (see Figure 48). In period 2 her network grew considerably and additionally, the frequency of contacts with medical institutions increased (see Figure 49).

3.1.3.1 Phase 1 (Month 1 to Month 9)

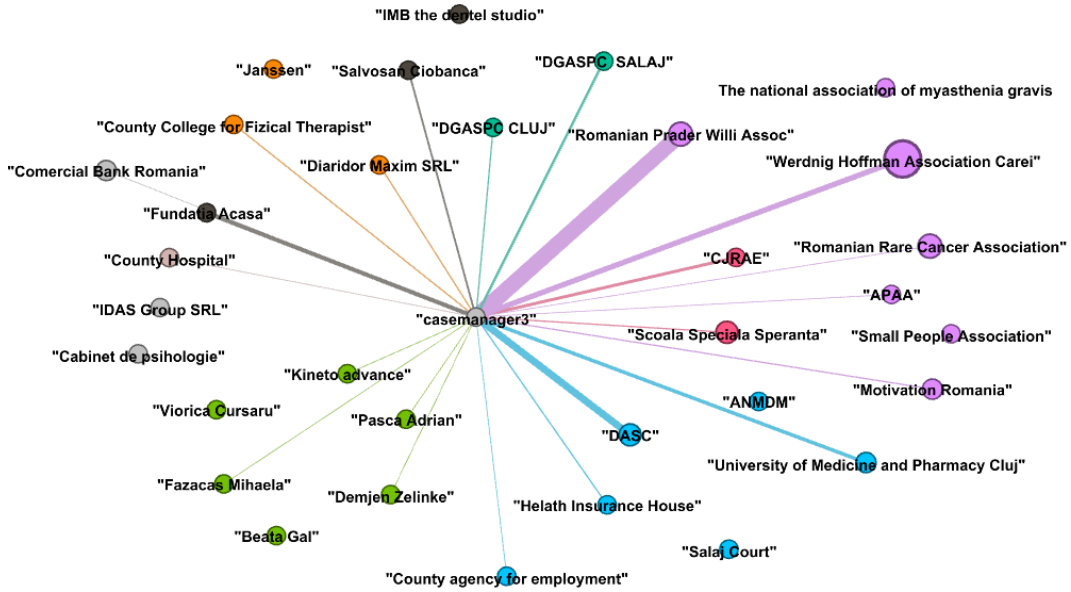


FIGURE 48: CASE MANAGER 3'S NETWORK DURING THE FIRST NINE MONTHS OF THE INTERVENTION

3.1.3.2 Phase 2 (Month 9 to Month 18)

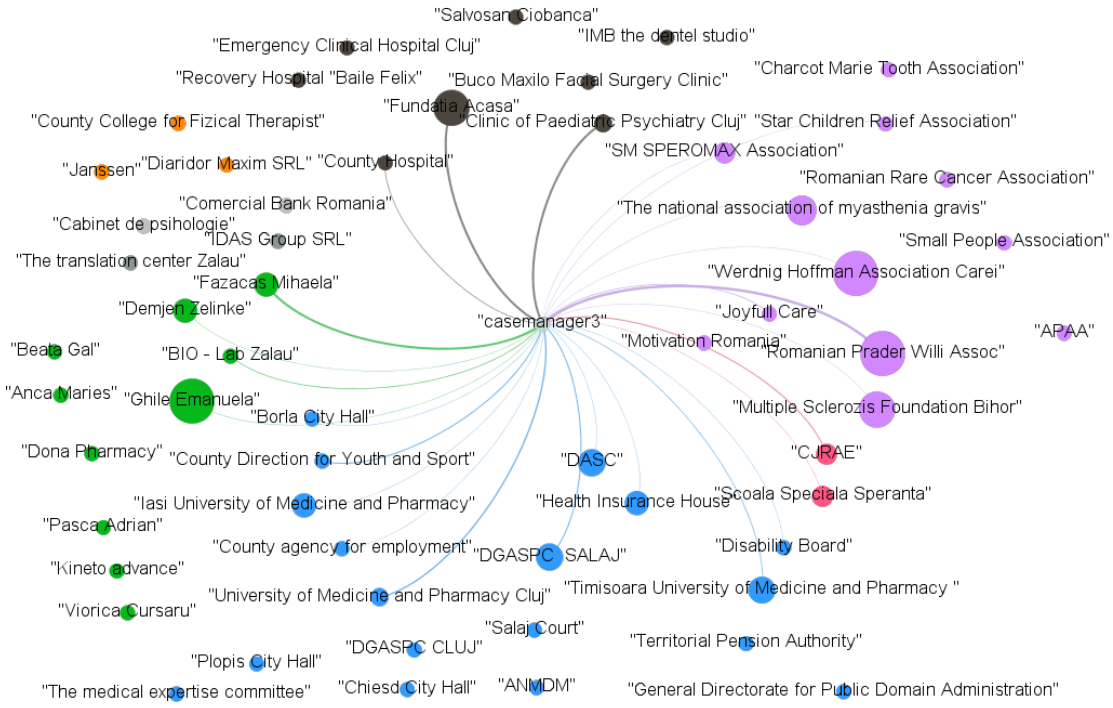


FIGURE 49: CASE MANAGER 3'S NETWORK DURING THE LAST NINE MONTHS OF THE INTERVENTION

3.1.4 CASE MANAGER 4

In period 1, most frequent contacts for case manager 4 were with the NGO, the public and the educational sectors. There were no contacts at all with private service providers (see Figure 50). Compared with period 1, her network grew significantly in period 2. There were more frequent contacts with the public and the NGO sectors and also contacts in the medical field and with private service providers were established (see Figure 51).

3.1.4.1 Phase 1 (Month 1 to Month 9)

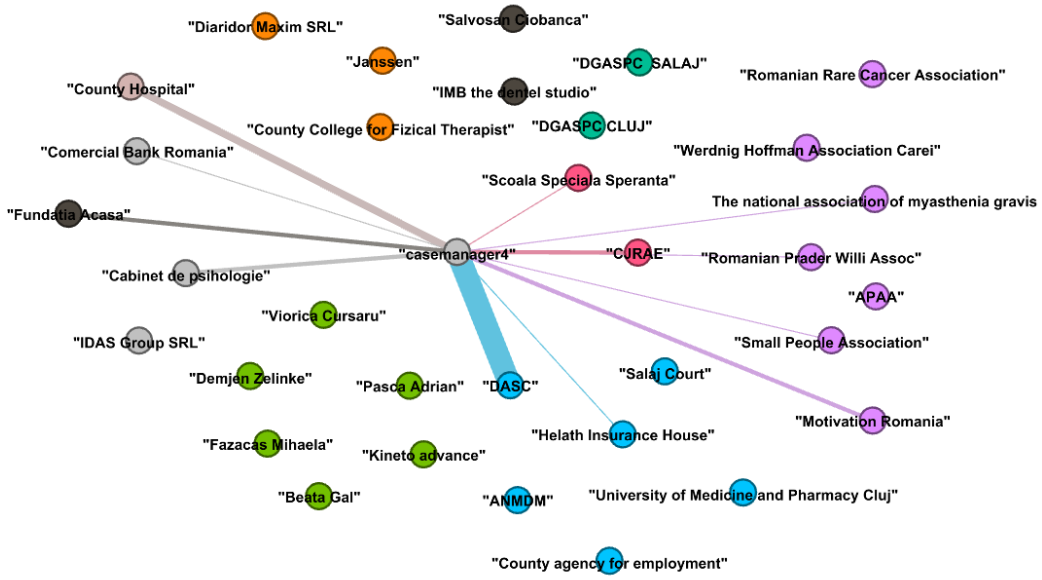


FIGURE 50: CASE MANAGER 4'S NETWORK DURING THE FIRST NINE MONTHS OF THE INTERVENTION

3.1.4.2 Phase 2 (Month 9 to Month 18)

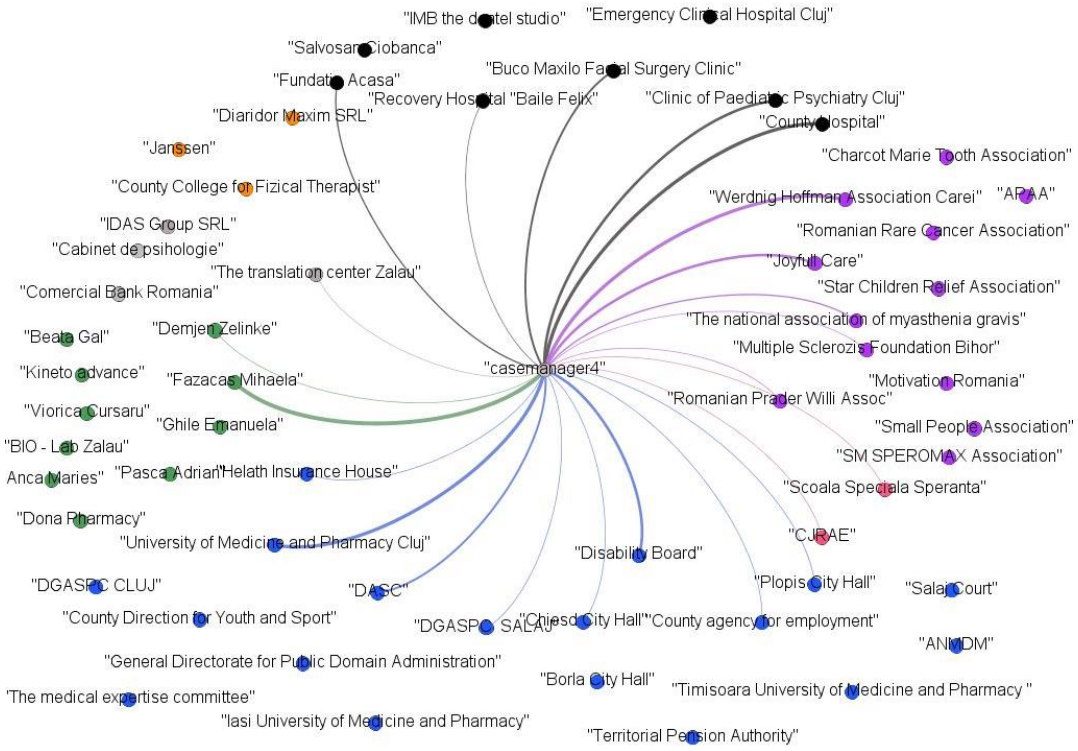


FIGURE 51: CASE MANAGER 4'S NETWORK DURING THE LAST NINE MONTHS OF THE INTERVENTION

3.1.5 LIST OF INSTITUTIONS/CONTACTS

3.1.5.1 Public institutions

- **Adults' disability board** is the public commission that issues the certificate for the degree of disability for adults. For persons above the age of 18, the certificate is issued for life and does not need to be renewed. However, in case the health status of the patient changes, the certificate can be reviewed and if necessary, the level of disability accordingly adapted.
- **ANMDM –** Is the **national agency for medicines and medical devices** under the Ministry of Health. It was contacted in the framework of the INNOVCare pilot for example to find out about a treatment that is not available in Romania for people under 16.
- **Children's Disability Board** is part of the general directorate for social assistance and childhood protection. It issues the certificate for degree of disability to people under the age of 18. The certificate for children is only valid for one year, which means that it has to be renewed every year.
- **City halls:**
  - Borla city hall
  - Chiesd city hall: Engaged community assistants who were receiving case management training. During the INNOVCare pilot, these community assistants already acted as an intermediary between the case managers and the patients because they are local. If

the case manager could not reach the patient directly, then the community assistant was requested to follow up on the patient.
    - Plopis city hall
- **County agency for employment** was contacted for example regarding jobs and conditions for employment or benefits for people with disabilities.
- **County direction for youth and sport** is under the Ministry for youth and sports, which has its representative in every county. Due to a change in legislation, it offered summer camps for children and adults with disabilities for free in 2018.
- **DASC** is the **directory of communitary social assistance in Zalau**. It belongs to the city council and has more or less the same responsibilities as DGASPC, but on city level. DASC is funded by the city council whereas DGASPC is funded by the county council, but they provide different kinds of procedures to certify a citizen's disability level. All the cities in the county have this service. They have to follow a standard procedure to help the general directorate to get a comprehensive picture of the patients' situation. A social worker conducts the first part of the process including the social interview which the beneficiary needs to undergo to obtain the medical certificate. When all necessary documents have been gathered, these are forwarded to the general directorate where the rest of the procedures are finalised. Only the general directorate can issue the certificates of disability.
- **DGASPC Cluj = General directorate of social assistance and child protection Cluj**
- **DGASPC Salaj = General directorate of social assistance and child protection Salaj**: The DGASPCS's are part of the county council and run the commissions for certifying disabilities according to the law for protection of people with disabilities.
- **General Directorate for Public Domain Administration:** This institution was contacted to obtain free parking cards for people with disabilities
- **Health insurance house** is a public institution that pays for medical services and medical devices. Many NGOs offering services to people with disabilities and rare and complex disease patients have a contract with the health insurance house enabling them to provide their services at no direct cost to the patient.
- **Iasi University of Medicine and Pharmacy** offers some medical treatments and tests
- **Salaj Court:** For legal problems for example issues of child support in a case in the INNOVCare pilot where the parents were divorced
- **The medical expertise committee**
- **Territorial Pension Authority**
- **Timisoara University of Medicine and Pharmacy** is a public medical school that offers different services to patients
- **University of medicine and pharmacy in Cluj is** a public medical school and has a genetic department.

3.1.5.2 NGOs

- **APAA - Association of Autoimmune Disease Patients:** Patient association
- **Association of Mastocytosis patients:** Patient association
- **Charcot Marie Tooth Association**: This is a patient association established only in 2018. INNOVCare pilot participants with Charcot Marie Tooth disease have been put in contact with this organisation.

- **Joyful Care is a** new association in Zalau that offers home services e.g. kineto-therapy or electro-simulation. The organisation presented itself at NoRo in January or February 2018 kick-starting the cooperation with NoRo.
- **Motivation Romania** is an association that supports people in wheelchairs. They have a contract with the health insurance house. Motivation Romania tells the patient which wheelchair they need and directs them to a specific department / or person at the health insurance house to complete the paperwork. The health insurance house then covers the costs for the chair. However, Motivation Romania does not take over the procedure and communication with the health insurance house.
- **Multiple Sclerosis association Bihor** is a patient association from Oradia, 120 km away from Zalau. They have annual meetings and offer group support for patients.
- **The Romanian Prader Willi association (APWR, NoRo centre)** provides a day care centre for children with rare diseases and autistic spectrum disorders as well as group activities for specific diseases.
- **Romanian rare cancer association:** Patient association
- **Small people association** is a patient association supporting children with cancer.
- **SM SPEROMAX association** is a patient association that aims to increase the quality of life among people affected by multiple sclerosis.
- **Star children relief association** is an association that provides summer camps for patients with Downs syndrome**.**
- **The national association for myasthenia gravis** is a patient association for the myasthenia gravis disease. The association offers telephone support, counselling and advice on medicine and doctors. They connect patients with the same disease in the same city. The association had organised a support group for this disease at NoRo during the INNOVCare pilot.
- **Werdning Hoffman association** is an association for neurological diseases, located in Carei, and organises a summer camp for patients with neurological problems each summer**.**

3.1.5.3 Hospitals/ medical institutions

- **Buco maxilo facial surgery clinic** is a dentist in Cluj. According to the case managers, he is the only dentist willing to work with children with 'problems' i.e. with disabilities.
- **Clinic of paediatric psychiatry Cluj**
- **County hospital** or **Spitalul Judetean Zalau** is the public hospital in Zalau. During the INNOVCare pilot, it was contacted for medical needs of the patients e.g. blood tests, appointments with neurologists etc.
- **Emergency clinical hospital Cluj**
- **Fundatia ACASA** is an NGO that runs a hospital. They have a rehabilitation centre and they focus on physical therapy. They have a contract with the health insurance house and can therefore provide their services for free.
- **IMB dentel studio** is a dental clinic. Children, especially those with disabilities have a problem going to dentists because they often cannot stay still for treatment and therefore require general anaesthesia. The clinic was contacted to find out whether they do general anaesthesia. Unfortunately such a service is not available in Zalau.
- **Recovery hospital Baile Felix is** a public hospital. It is located in Bihor, 120 km from Salaj.

- **Salvosan Ciobanca** is a private hospital. It provides some health services at no extra cost for patients because they have a contract with the health insurance house, which is the institution that pays medical evaluations and rehabilitation services for the patients.

3.1.5.4 Private Service Providers

- **Anca Maries** is a therapist
- **Beata Gal** is a psychologist
- **Bio-Lab Zalau** is a laboratory and provides blood analysis.
- **Demjen Zelinke** is a physical- and kinetotherapist who also offers the service in the patients' homes. He used to work at NoRo.
- **Dona Pharmacy**
- **Ghile Emanuela is a speech therapist**
- **Kineto Advance o**ffers different therapies such as Kinetotherapy, Vojta therapy, Schroth therapy, electrotherapy and medical massages.
- **Mihaela Fazacas** is a psychologist. The funding mechanisms in Romania changed during the INNOVCare intervention, specifically during the second phase. The local government used to pay for different services for the patients e.g. accessing the NoRo day-care centre. Meanwhile, local government has changed the criteria and processes for these payments. To access NoRo services, patients now need an assessment by a psychologist and one by a psychiatrist. Mihaela Fazacas is one of the local psychologists providing that evaluation for beneficiaries at NoRo, who comprised of half of the INNOVCare pilot particpants.
- **Pasca Adrian** is a therapist.
- **Viorica Cursaru** is the president for Myeloma Euronet Romania. She represents the patients with multiple Myeloma.

3.1.5.5 Educational institutions

- **CJRAE** is the county centre for resource and educational assistance in Zalau; the school inspectorate. It assigns children to public and special education schools after an evaluation of the child. If a child is assigned to a 'mass' school, even if they have special education needs, the law in Romania gives them some financial benefits. There is also the possibility to bring a special education teacher to the class especially for that child. Furthermore CJRAE provides the permission for children with disabilities to start school or delay starting school. Commonly, compulsory schooling in Romania starts at age six, but if the child has disabilities CJRAE is able to delay starting school by a year. Instead, the child attends kindergarten one year longer.
- **Scoala Speciala Speranta** or **CSEI** is a special education school for children with special needs in Zalau.

3.1.5.6 Others (Training and consulting firm, SRL, bank, professional organisation)

- **Commercial bank Romania**
- **County college for physical therapists** is a new organisation that started a few months before the INNOVCare pilot. They have connections with all the physical therapists able to work for difficult patients in the county. In order to provide these services privately, one needs to be part of this college and be recognised by them.

- **Cabinet de psihologie** is a professional organisation that regulates the profession of psychologists, certifies and coordinates their continuous qualification programme and solves litigation cases.
- **Diaridor** is a private company which hires people with disabilities.
- **IDAS Group SRL (= Camelia Arion)** is a private institution which offers counselling for writing project proposals e.g. for funding agricultural (incl. animal husbandry) ventures.
- **Janssen** is a pharma representative.
- **The translation centre Zalau** is a translation company that officially translates documents from different languages. This was needed for example for the official translation of a patient's diagnosis documents which were in German Romanian.

3.1.6 CHANGES IN THE NETWORK AND DURATION OF CONTACTS

During the first phase of the intervention the networks of the case managers grew. At the beginning of the intervention the networks of case managers were rather small compared to their networks after the first phase of the intervention.

One case manager reports that she could establish contacts with public institutions, which she did not have before as her former responsibilities mostly covered collaboration with NGOs. Another case manager pointed out that she already knew all organisations relevant for her patients in the INNOVCare project, but she had no specific contact there. This changed in the first weeks of the pilot as she called the organisations and looked for contacts that were helpful for solving her patients' needs. Another case manager was completely new to the world of rare diseases and therefore all connections were new.

Strengthening already existing contacts also played a key role in the capacity of the case manager to meet the needs of the participants. Especially with NGOs, many contacts had already been established prior the start of the intervention. These connections were also supportive in finding new contacts; as the contact persons redirected the case managers according to the specific needs of the patients. As a result, refreshing old contacts helped the case managers to build their networks further.

During the second phase of the intervention, changes in the case manager's networks were minimal as most of the necessary contacts had already been established during the first phase of the pilot. Nevertheless, also in the second phase new connections were created where needed to meet the needs of the patients. This was especially true for the medical part of the networks as quite a number of patients needed genetic testing. None of the participants in the first cohort required this during the first phase of the intervention. Also contacts with public institutions increased due to changes in legislation. Social benefits had been increased and therefore patients had a lot of new questions. The NoRo centre *'has a name in Zalau'* and contacts soon knew about the new case management service. As a result, it was quite easy to contact different institutions: *'It was enough to say "hi I am from NoRo centre" – 'ah ok, ok. The one with the case management?' – "yes the one with the case management".'*

3.1.7 FREQUENCY OF COMMUNICATION

3.1.7.1 Reasons for strong/frequent contacts

According to the network analyses, in the first period of the intervention, the frequency of communication was highest with the NGO sector. Also communication with private service providers was very frequent. This can be explained by the needs of patients on the one hand and by the strong connections that the case managers already had to the different NGOs in the county on the other hand. An important reason for getting in contact with NGOs was to give patients more support and empower them as many of the NGOs involved were patient organisations. This involves the importance of sharing experiences with others and learning how fellow patients are living well despite their condition. Furthermore NGOs and private service providers offer the whole spectrum of services like rehabilitation, psychological consultancy, etc. Private services are often of high quality, often better located, there have more and better doctors and they are free for the patients (because the institutions have contracts with local authorities). Specialised services are mostly provided by private organisations and only very rarely offered by public institutions. Compared to public providers, they are described as far more 'relaxed', when it comes to decisions etc. On the contrary, public service providers offer often less quality services and have long waiting lists. In general, there are many services potentially available at no cost to patients in Romania, but provision remains well below the demand: *You need like 100% and you have [services] for free like 30%. But it is better than nothing because a lot of families cannot afford to pay for these services.'*

Frequent contacts with public institutions have mostly been established for legal procedures, e.g. certification for the degree of disability or applications for wheelchairs: '*You have to go first of all to the doctor, the doctor can prescribe the necessity of wheelchair and you go to a public institution to put a lot of papers together and make the application and they will provide the wheelchair.'*

In the second phase, the frequency of communication with the different parts of the network was in generally similar to the first phase, with one exception – the frequency of communication with the medical sector was higher. Contacts mostly concerned the searching for results of genetic tests and, due to changes in the legislation and social benefit, obtaining genetic testing or medical diagnosis.

In general case managers perceived it as difficult to stay in contact with organisations from the public and the medical sectors. Both types of organisations were found to be too busy to have frequent contact. Medical institutions tend only to see the medical part of the case and public institutions are understaffed. NGOs and private institutions are in general more open to the needs of disabled persons or persons with complex medical problems.

3.1.7.2 Facilitating factors for good relationships

There are a few factors that facilitate a good relationship. First, it is important that case managers or their organisation already cooperated with the respective organisations. This means that they understand how NoRo works and with which patients. They already know their needs and they are open-minded.

Another supporting factor is collaboration with already existing networks, e.g. the community support network or the national alliance of rare diseases, as well as organisations of the case managers' personal networks. Representatives of those organisations generally already know about the project and the work of the case managers. They understand needs and challenges associated to rare diseases. These contacts also make it easier if necessary to escalate a problem higher up the hierarchy to solve it.

Furthermore, having a specific contact person in each organisation is considered helpful. If this person cannot provide immediate help, they are normally able to redirect the case manager to the person in charge.

A facilitating factor in working with private institutions is that there are generally fewer levels of hierarchy than in the public sector.

In general case managers found it was much easier to establish and maintain good relationships in the second phase of the intervention. On the one hand, case managers already knew most of the relevant contacts. On the other hand, for new contacts they already knew exactly where to go, which questions to ask and who to talk to.

3.1.7.3 Difficulties in establishing good connections

Case managers found it difficult to establish good connections with organisations that they had not been in contact with before, because such organisations did not know NoRo and it was felt that they lacked an understanding of the patients that NoRo works with; namely, rare and complex disease patients. This meant that case managers had to individually present their cases in detail to respective members of such organisations to be able to get the support and assistance they needed.

This was especially true for most of the public institutions that had had nothing to do with rare diseases before: *'You don't know how to ask to receive the answer you want.'* This became easier during the project as they gained experience.

There were also difficulties to get patients in touch with organisations that were not based in Salaj through the phone or through email. Especially for older people, this was a barrier because they found communication over the phone not very easy and sometimes were reluctant to talk to people remotely whom they could not see. The solution found in one case was talking on Facebook, which seemed easier for patients.

3.1.8 ORGANISATIONS MISSING IN THE NETWORK

In the first phase of the intervention, medical service providers and schools were mostly absent in the networks of the case managers. The need for cooperation with special schools only emerged later as some patients had difficulties integrating into class and the case manager provided support talking to the headmaster/-mistress, the teachers and providing information on the disease. In general case managers saw a need to increase contacts and collaborations with schools and initiated an awareness raising campaign in February 2018.

But also some connections to public institutions could not be established during the first nine months of the intervention, e.g. with the county public healthcare department that has an advisory function in connection with health care services at county level. They were later integrated into the community support network[77] and support their work, but the case managers did not initially have direct contact. They employ community nurses who work in the villages, which could be an option to continue the work started in the INNOVCare project.

According to the case managers, the picture was quite balanced in the second phase of the intervention and there were almost no organisation missing. One remark referred to integrating more home services of therapists but there was only one (Joyful Care) available to work with the case managers in the county.

3.1.9 EXCHANGE OF INFORMATION BETWEEN CASE MANAGERS

Exchange of information between case managers took place in regular team meetings that took place approximately once a week. At these meetings they reviewed cases and shared their ideas and contacts: '*I think this was very good for us. Because for example, the examples with the genetic; to find out if the children also have the disease of the parents was a common idea. I thought about it and discussed with the girls [other case managers] and the girls said 'do this, if you can, do it, because it is good for the patient to know.'*

The case managers learnt from each other and updated each other also on new developments, e.g. new legislation. Sharing of contacts and information was especially important as each case manager had different competencies and connections and by sharing them, they could use synergies. Many organisations and associations that are helpful for patients are not based in Zalau, but on national level. Hence, if one case manager had already established contact with such an organisation, it made it easier for this case manager, who already has a trusted relationship working with them, to connect the other case managers with this organisation directly.

Exchange between case managers was not only about sharing ideas, information and contacts, but they also talked about problems in their work and of their patients and about ways of coping with these challenges emotionally.

3.1.9.1 Utilisation of resources from NoRo

The utilisation of resources from NoRo at large was seen as a great advantage for the case managers. They appreciated the wide knowledge, networks and support of management staff such as NoRo's founder and director Dorica Dan and also the assistant manager Zsuzsa Almasi. They were known to have far-reaching higher-level connections to institutions and service providers and were also involved in organising awareness raising campaigns: '*the director knows the director'*. Dorica also coached one case

[77] The community network was established by NoRo with the support of the city council of Salaj by bringing together care providers, payers, patient and disability organisations in Salaj and also other community services or community support.

manager on ways to present the problems of her patients in such a way that they appeared manageable and surmountable to the counterparts.

Furthermore, the direct access to the medical staff of NoRo was useful (therapists, psychiatrists etc.) to get information on the medical history of the patients, on services available in the county and on their contacts. Needs of patients were regularly discussed by the case manager and the therapists together, which lead to possible solutions for the patients and their families.

3.1.10 COMMUNITY SUPPORT NETWORK

According to the case managers the community support network had a positive impact on the case managers. They felt more informed and had the certainty that patients received high quality help. When meeting with the community support network, case managers clarified questions, talked about problems and signalled the issues they observed working in the field. The community network provided case managers as well as patients, who were also present at these meetings, with a contact person in each organisation who already knew the project. This lead to more openness in the relationship and facilitated the willingness to help: *'I can be more open if I know that I have this network. It is also a very important resource for our work.'*

3.2 The INNOVCare Intervention

3.2.1 DESCRIPTION OF WORK AS A CASE MANAGER WITH THE PATIENTS AND THEIR FAMILIES IN THE FRAMEWORK OF THE INNOVCARE PROJECT

The case managers describe their role in the INNOVCare pilot as being manifold involving for example:

- Research on different kinds of diseases to be prepared to inform the patients and their families and answer related questions;
- Review the patients' history including medical history regarding for example services previously accessed;
- Informing themselves of services that may be useful in solving the patients' and their families current needs;
- Informing the patients and their families about:
  - Their rights as patients
  - The services available to them
- Providing counselling to the cases especially those with disabilities;
- Investigating the needs of the patients and their families which requires the ability to ask the right questions particularly because at the beginning, some of the cases were not aware of their needs;
- Prepare the action plan together with the patient and their family based on the needs analysis as well as the research of possible solutions for example relevant services and through discussions with other case managers;
- Contacting the organisations identified in the action plan in an attempt to solve the needs of the participants e.g. getting information about the procedures, making appointments etc. by phone or in person;
- Guiding and supporting the patient and their family in fulfilling the tasks identified for them in the action plan;

- Identifying and adding new needs into the action plan as they arise;
- Through these activities, to empower the patients and their families to be more independent and more capable of managing their own care.

Referring to their individual role descriptions, it became visible that every case manager interprets her role and tasks differently, which also depended on the needs of the patients. Below are some paraphrased excerpts of some of the case managers' perception of their roles:

One case manager described that at the beginning of the intervention she spent a lot of time reading up about rare diseases in order to have an idea of how to talk to the patients and what kind of information and services they needed. She talked to each case and made a plan together with the patient and the family. She then tried to find out what kinds of services had been accessed before and then she searched for information to solve the patient's needs. She also noticed that many, especially the ones living in the rural areas, were not aware about their legal rights and what services they can access. The older ones had not been to a medical evaluation for a long time. She then presented the information to the case and chose the institution or services to contact.

Another case manager describes her work as providing counselling for people with disabilities, which means that she talks with the patients about their needs. She has to find the right questions to discover these needs because often, patients are not aware that they have needs with which the case manager can help with. Then they make a list of all needs and write the action plan together. She discusses the action plan with the other case managers and then goes back to the patients to suggest organisations. If they agree she proceeds to contact and talk to the institutions, by phone or in person. Furthermore she guides and supports the patients in fulfilling the tasks. During the whole process, if they have questions about the disease, rights etc. the case manager provides them with these. When new needs arise, they are added into the action plan. The final goal of the case management services is to empower the patients.

Another case manager stated that she always started with the evaluation of needs by doing a normal interview with the patient. By doing this she realised the needs of the patients, e.g. information about procedures and the law on rights of people with disabilities and rights of patients in Romania. The first step is then to inform the patients about these issues and about the services available in these areas. In the next two to four meetings the available services are discussed in detail and it is decided together with the patient where to go and in which order.

One of the case managers also explained that on top of trying her best to meet the needs of the patients and their families through performing the tasks listed above, she always tried to go beyond her role as a case manager to bring a 'little' joy to her clients. For example, based on her previous experience and by asking people in her network with experience in occupational therapy for tips, she could help two of her clients whose disease was regressing to gain the ability to eat independently by teaching them some exercises that they could perform at home alone. This proved successful as by the end of the intervention, they were able to feed themselves and at the same time increased the job satisfaction of the case manager.

Some general remarks regarding the work as a case manager in the framework of the INNOVCare project are:

- The work with the cases started very slowly because patients were not aware that they had needs at all or were not capable of explaining their needs.
- At the beginning of the intervention it was important to make the participants understand that they have needs by asking e.g. 'How do you think I can help you?' Also a relationship of trust had to be developed. Over time, patients gained trust and they realised they have needs.
- Counselling is an important pillar of the case management, which is not depicted in the network pictures.
- There is also work in the background. E.g. one case manager mentioned that she reads about the respective disease beforehand to help the patients to better understand the disease and to be able to teach them how to communicate about the disease. Another example is discussions with the other case managers on the best options for the patients.

3.2.2 NUMBER OF CASES

On average one case manager cared for 13 - 15 cases. There were a number of drop outs, e.g. due to relocation from the region (see the participant flow diagrammes for the exact number and reasons for drop-out 2.3.1). Case managers stated that the number of cases per case manager for the duration of time and resources available was exactly right.

3.2.3 NEEDS OF PATIENTS

Most of the patients who were not from Salaj County needed at home services. Not all of them had the possibility to come to Zalau and not all of them were able to pay for home services. The case managers organised admission to hospitals and rehabilitations, psychological consultation when needed and appointments with medical specialists. Furthermore patients and their families received information on their rights and information on access to services (e.g. therapies, supports groups etc.). In this sense case managers coordinated interactions of parents with service providers and supported them in legal issues.

Another main need that the case managers identified was communication skills. A lot of patients were not able to communicate properly about their conditions, needs etc. Finally, beneficiaries were counselled about their situation. This was not just provided for patients but also for parents and siblings. In some cases, group counselling was organised for them.

In the second phase of the intervention needs of the patients were slightly different. This can be explained by the different problems of the new patients, different problems in the family and how they managed to cope with their issues.

One focus was on medical needs: medical evaluations, genetic testing and access to treatments. Other needs were informing and supporting patients about procedures necessary to receive different treatments or medical evaluations, putting patients in contact with other patients with the same disease, putting them in contact with organisations, getting places in summer camps and counselling.

The counselling aspect was connected with visiting patients at home and not seeing them only in the NoRo centre. Counselling could not be done at the centre, because there patients were involved in other activities and the centre does not provide adequate capacity to talk about patients' issues confidentially. Furthermore, in the context of home visits, other needs can become visible.

It became obvious that patients living in rural areas have specific needs. Some communities are isolated and the coverage of care and service is inadequate, and patients have become accustomed to coping on a very poor level. Often it seems like: *'they don't have anything. They don't have a certificate, they haven't seen a doctor for a long time, they haven't seen anybody. They just get some money and they don't want to do more. They are somehow satisfied with what they have.'* Case managers saw a need to make these very marginalised clients aware of their situation and help them realise there are possibilities to improve their situation The same was true also for patients who had already lost faith that their situation could be improved. However, case managers were aware that it was important to never try to convince people of their needs, but to be there, to listen to them and to sensitively raise their awareness, but also their level of coping with the situation.

Besides these leading needs detailed above, the patients and their families also had other requirements like organisation of in summer camps, accomplishment of criteria for special education schools, needing translation of diagnosis documents, accessing bank credits, access to the labour market etc. The individual network pictures of each case manager provide a complete overview of the patients' needs by the organisations contacted.

3.2.4 SOLVING THE NEEDS OF THE PATIENTS

A central part of case managers' role was to act in a patient-centered way. Depending on the specific needs of the patients, they directed them to services and institutions. They tried to improve coordination and communication among different actors and services involved, also drawing on the community support network.

A particular objective was to enhance patients' ability for self-management, to independently find solutions for their needs. This requires information about the disease, rights and services. Increasing patients' capabilities in this way was all the more important since the intervention was only available for nine months due to the project's duration. However, case managers did not always consider this limited time sufficient to empower all patients to self-coordinate their treatment or care.

In general, for people living in Zalau, solutions could be found more easily since services were locally available. For patients living in rural areas this was considerably more difficult. Some had no transport to come to Zalau frequently, but others refused to come. Extending the coverage of health and social services to rural areas, through mobile or remote delivery where possible, was not possible so far and remains a challenge well beyond the scope of case management service alone.

In some cases case management was not only about finding solutions for the patients' needs, but also about helping the family cope with their overall situation. This sometimes generated some creativity and a view beyond immediate needs: *'One of the joy that I could bring to her was during one of my visits, I could bring one of my friends who is working for a national radio – I don't know how we started the conversation but she had said to me I know this guy and he is from Zalau and I like him so much and I want to meet him and I said ok I will bring him for you because at least this I can do for you to make you feel better. There were also some law problems and I asked some people from the general directorate, how they can empower the mother to get the money (…) and we managed to do it. She can paint very*

well and my friend [from the national radio] brought someone else to maybe buy some of her paintings and help her financially.'

3.2.5 TIME DEDICATED TO EACH CASE AND DETERMINING THE INTENSITY OF WORK

Time dedicated to each case was officially calculated at one day per month per case (which meant five meetings/calls for each case). In general there were at least two face-to-face meetings per patient. However, time really spent per case was reallocated by case managers depending on the patients and their needs. Some patients dropped into the NoRo centre from time to time; others were squeezed into the schedule if they needed urgent support.

For some patients, more time had to be spent on counselling at the beginning, especially in the cases of very resigned clients who had lost confidence that anything could be changed. In these cases, case managers had to both build the confidence of the patients in possible improvements and win their trust. Only then could the case managers start with what they considered their 'real work' of problem-solving and with involving their network.

In a few other cases, where patients had found workable accesses to services and solutions already, case managers could step into the core of their role right from the start. The intensity of the work depended on the type of problems patients came up with. For some problems, such as information questions, a call or email was sufficient, but others required face-to-face meetings and comprehensive support, such as organising appointments, writing emails and letters on their behalf regarding their financial situation etc. But even if their current needs were addressed already in a first meeting, patients benefitted from counselling afterwards.

3.2.6 DETERMINING THE ACHIEVEMENT OF GOALS

For achieving the goals of the intervention, the case managers had a dedicated plan; the action plan. However, a few of the plans were modified throughout the intervention. In general the goal was that patients were to have more information about the disease, rights and services etc., which would increase their resources and ability to self-manage. This was specified and achievements of the goals determined in agreement with the patients.

Even after the intervention for the first cohort of patients had ended after nine months, communication with some patients was still ongoing when the project team conducted the interviews with the case managers, some time after their intervention period. One case manager explicitly told her patients to be sure to get in touch if after the end of the intervention they needed further assistance.

One case manager elaborated on the evaluation procedures of the project in a personalised way: In the second phase of the interventions she asked all her patients to write her a letter in the last meeting and tell her what she did well and what she did not do so well. She promised patients to only open the letters when she had received all of them for reasons of anonymity. She wanted to use this opportunity to reflect and learn from her own work or mistakes. She was pleased with the feedback which noted only limited dissatisfaction and goals were achieved that had been set at the beginning of the intervention.

However, nine months intervention was not sufficient time for all patients and families, especially not for those in very depraved and also remote situations with multiple and accumulated problems.

3.2.7 WELL WORKING ASPECTS

Case managers considered it crucial to get a more comprehensive picture of their patients' and families' situation by visiting them at home. Patients were more open and felt more comfortable there than at NoRo or other places. This was seen as a main aspect that worked well during the intervention, also adding a dimension to case managers' previous work roles based at NoRo. Although it was time-consuming, home visits to patients living outside of Zalau was considered as especially important, because many of were generally isolated and having someone 'to talk to' was beneficial in itself.

Case managers found that the counselling part of the intervention was also working very well. This was part of most case managers' previous work roles before the pilot.

Another well working aspect was the empowerment of the patients. Case managers defined their roles as facilitators, enabling patients to manage themselves as much as possible. Yet, being there for the patients and focusing on the patients' needs was also seen as positive. Even for patients who had to recover confidence and trust in outside help, in the end it worked well to focus on providing concrete solutions and continually communicating and negotiating with the patients. Support in administrative procedures was also successful and appreciated, because case managers had the relevant contacts and knew the relevant people.

Individual case management provided much more time for the patients and their needs than previous counselling and advice offers at NoRo. Now, trust relationships could be established with patients, which had not always been possible during 'normal' social work.

In building their networks, case managers found that especially the collaboration with the NGOs was working well. For already established contacts, the bond was made stronger and also new contacts were established.

3.2.8 CHALLENGES AND NOT WELL WORKING ASPECTS

A considerable challenge for the case managers was that services are not distributed equally in the region. For example schooling for special needs and paradoxically, home visits by therapists are only available in Zalau. Families in the country and the surrounding villages often do not have the resources to travel to access the services. Case managers thus were searching for services and people who would go to the villages but this requires more multi-level improvements. The department of public health is now offering the services of local community nurses, which could contribute to filling the gap, and NoRo is trying to help integrate case management training and functions into their role.

Another challenge is a lack of services for adults as opposed to children, especially in at-home services. This means, adults are often put on waiting lists. However, even when there are services available, such as rehabilitation services, some older patients are not willing to use them because they do not want to leave their homes for two weeks in a row.

Another challenge was the legislation. Especially access to treatment – meaning the availability of medicine in Romania – is an obstacle. In some cases, treatments were available, but could only be accessed if the patient was over 16 years. In this case the only solution was to buy the treatment from outside of Romania. Recent changes in legislation implemented by local authorities had the effect that some patients were no longer able to receive services they needed for free. To solve the legislation problem, the case managers helped their patients to fight for their rights and provided some advocacy. They informed themselves about the local laws and legislations, wrote numerous letters and provided their patients support and information to empower them. The difficulties with legislation are closely related to the bureaucracy in Romania: *'it is very difficult because we don't have developed electronic systems to make these things easier. You have to go there and talk to two or three people until you get to the right person.'*

A further difficult topic was the employment of people with disabilities as companies don't have the necessary facilities. To solve this issue, legislation should encourage companies to employ people with disabilities.

As reflected in the quantitative analysis which shows that there were only marginal improvements in the participants' ability to manage their own care (especially in the second cohort), the interviews with the case managers revealed that patients and their families often did not believe sufficiently in their own capabilities to solve their needs. According to the case managers' view, there is a group of patients that would need this service on a long-term basis to become more independent in this respect. The recently established new law for social assistance requires local authorities to hire one case manager for each 50 disabled people in the municipality. In the region, NoRo will build on the INNOVCare experience and learning materials to train them in the future and include them in the community support network.

Focusing on the establishment of the networks the building of connections with the medical part was a challenge. It often seemed to case managers that medical services in the region are not very open towards the individual needs of patients – which may be due to the sector's general shortages in staff and resources.

3.2.9 DIFFERENCES BETWEEN CASE MANAGEMENT SERVICE AND PREVIOUS TASKS/OFFERS FOR PATIENTS AND THEIR FAMILIES

The most significant difference between case management and the previous work of the case managers (who had been social workers in the NoRo centre, responsible for the NoRo helpline, and one was a therapist) was caused by the task of home visits, which offered a new perspective to the case managers. They could investigate educational needs, social needs and medical needs and they felt closer to the patients. Compared to working on the telephone helpline, *'When you have direct contact with a person, everything is very different. You can see how big the problem is and you are more involved in the work. You have to search; you have to work a lot.'*

Working as a social worker for the day care centre meant a lot of paperwork for local authorities, justifying the money spent and providing explanations why patients needed a special service. There was not much time for individual counselling, and therefore the relationship with patients was more distanced. Case managers were now doing more hands-on immediate 'helping' work with their clients and both they and the clients appreciated the time available for this and found that the case

management had a large positive impact on patients. Compared with working as a therapist, this case manager found it a significant difference that case management does not only focus on the patients, but on the whole family.

Finally, case management required case managers to connect with more specialists of diverse disciplines. They widened their contacts and learned for the future where to point the patients, having a variety of options depending on their respective problems.

Beside the positive differences there are is also one negative difference between case management and case managers' previous work. Sometimes they found it more difficult to stop thinking about the problems of patients and found they took problems home with them: *'(…) There were times when I would go home and I was crying, because it was hard to see how many problems one person has and I think I am ok, I don't have any problems, but this person is really suffering.'* The common challenge of case-based work in social services, to retain empathy while maintaining some professional detachment, emerges here as well, and learning and reflecting on this balancing also requires time, organisational and peer-to-peer support.

3.2.10 CONTACTS WITH PARTICIPANTS FROM THE 1ST COHORT AFTER THE INTERVENTION

Officially the last of five meetings with each patient was the ending point of the intervention. From the practical side, the intervention ended when the needs of the patients were met. However, there were cases that were more work intense and others were not so complex. All case managers left their phone numbers and told the patients to contact them by phone if they needed anything after the intervention period. As NoRo is a centre for rare diseases and disabilities there is always the possibility to contact them if patients need help. One case manager mentioned: *'For them it's not over and for me the same. I am in touch with them. From the day care centre, I see them when they come to the therapies and we talk. When they have something to ask they ask. I don't say 'it's the end of the project, we can't talk anymore.'* But even if case managers maintained availability by phone, trying to help patients by e.g. redirecting them or giving them information etc. the comprehensive support including home visits stopped after the nine months. Besides asking for contacts and information, a few patients were found to call the case managers without a specific need, but mainly to have someone listen to them.

In contrast to patients that contacted the case managers after the intervention, there was also one case that contacted her/his designated case manager before the start of the intervention. This case was assigned to the 2nd cohort and was in urgent need of a genetic testing. Therefore the case manager agreed to support him already before the starting of the second phase of the intervention as planned.

3.2.11 INDEPENDENT MANAGEMENT OF CARE BY PATIENTS THROUGH SUPPORT OF CASE MANAGEMENT

On the question to what extent patients had been able to achieve sufficient self-management skills to handle their care and social needs, opinions of the four case managers differ. On the one hand, there is the perception that this goal has been met and that the majority of the patients (and especially their families) were able to confidently manage their own care after the intervention. However, case managers found that often quite capable patients and their families had too little trust in themselves to do this alone and needed a sense of empowerment that they were able to manage their own care. For this, they needed a back-up just in case, which is the reason why case managers assured them they could call them

when they needed help. One case manager mentioned that she tried to reach the goal of independent management of care through 'trial': E.g. she would sit next to the patient or their families and tell them – *'you need to get a blood test, what do you do? – call the hospital for an appointment'*. Then while she was sitting next to them, they called the hospital and made the appointment for themselves while she was supporting them and giving them pointers.

On the other hand, this does not apply for all of them. Older people especially were expected to still have problems in managing their lives and care, exacerbated by rural isolation. However, they now know they have someone to ask for help. Some case managers also thought that the patients and their families would be able to independently manage their needs if they were faced with a similar need in the future, however, they were not confident this would be the case if they were faced with a completely different need; in this case they would need someone like the case manager for guidance.

3.2.12 WAS THE 9 MONTHS INTERVENTION PERIOD ENOUGH?

The nine months' intervention period delivered considerable positive results but case managers observed that it was not sufficient for all cases. For example, it was problematic for patients who were waiting for results of genetic testing, which took a long time and therefore left no time for an individually suitable intervention and follow-up. Others needed more and continuous guidance.

If a new need arose at the end of the intervention period or even afterwards, case managers were somewhat frustrated that they were not able to help the patients sufficiently: '*I think this has to be a continuous job. If after one year someone has to come back with something else, I can help them again.'* It is seen as important to be able to support people when they come back with a new need. However, for patients with few needs, with good support from their family, or with educated parents who are informed and looking for treatments on their own, the intervention period of nine months turned out to be sufficient.

3.2.13 CONCLUSIONS BY CASE MANAGERS

In general, case managers perceived their new roles as a difficult, but at the same time an important and satisfying job. Case managers had the impression that cases in the second phase of the intervention were easier to manage and had fewer problems. This may reflect their increasing experience and learning they gained during working with the first cohort. One area of learning was how to discover what problems patients had. This required asking patients in a specific way to find out, in situations where patients often did not realise they had problems and these could be addressed.

There are some more differences when comparing the first and second cohort. During this time legislation was changing and case managers realised that patients and their families were not well informed. Staying informed and navigating the legal side of social services is a common task for professional social workers, but patients and their families usually are not trained for this activity.

Summing up, case management is seen as a very important and successful tool by the case managers: *'Case management could be one solution in helping as a guidance and support in finding out what are the most immediate needs and to organise. I hope every disabled could get a case manager, especially for rare diseases it's a necessity from my point of view.'*

4. NETWORK ANALYSIS: THE NETWORKS OF SERVICE PROVIDERS

One of the goals of the INNOVcare intervention was to increase the coordination among different services. All organisations the case managers had been in contact with during the two phases of the pilot were surveyed at two times during the project with the aim of finding out about the contacts between these organisations and their change in time. The first online survey was conducted in December 2017 and January 2018 and included questions on the degree of contacts before the start of the INNOVCare intervention at the end of 2016 and after the first phase of the intervention at the end of 2017. It was completed by 31 organisations. The second online survey was conducted in August and September 2018 and included questions on the degree of contacts after the second phase of the intervention in 2018. This survey was completed by 40 organisations.

In the following section, the networks of organisations are illustrated for each time of measurement. Colours of the nodes refer to the type of organisations[78] and the thickness of the lines refer to the degree of contacts (the thicker the line, the stronger the contact).

[78] black – medical institutions, purple – NGOs, pink – educational institutions, blue – public institutions, green – private providers, grey – SRL and businesses, orange – professional organisation

4.1 Assessment of cooperation between services 2016 (before first phase of intervention)

In 2016, contacts between organisations were mainly visible within individual sectors, especially the NGO sector, the public sector and also the sector of private service providers. The data suggests that cross-sectoral contacts that existed in 2016 were mainly between NGOs and public organisations and NGOs and private service providers. Other cross-sectoral coordination was minimal (see Figure 52).

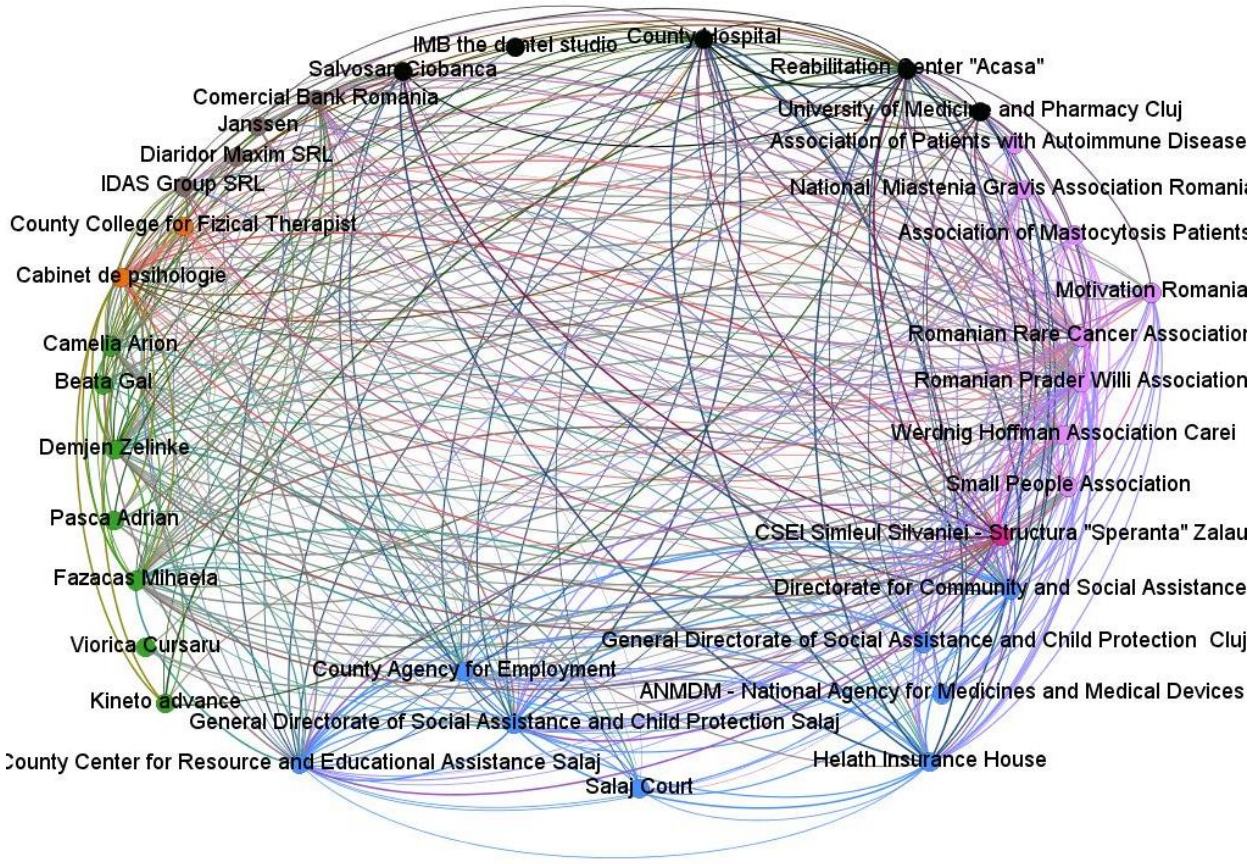


FIGURE 52: NETWORK OF SERVICE PROVIDERS IN 2017

4.2 Assessment of cooperation between services 2017 (first phase of intervention)

In 2017 the degree of contact seems to have become stronger as the lines are thicker. There are still a lot of contacts within the different sectors, but also between NGOs and public organisations, NGOs and private service providers but also between NGOs and medical institutions (see Figure 53).

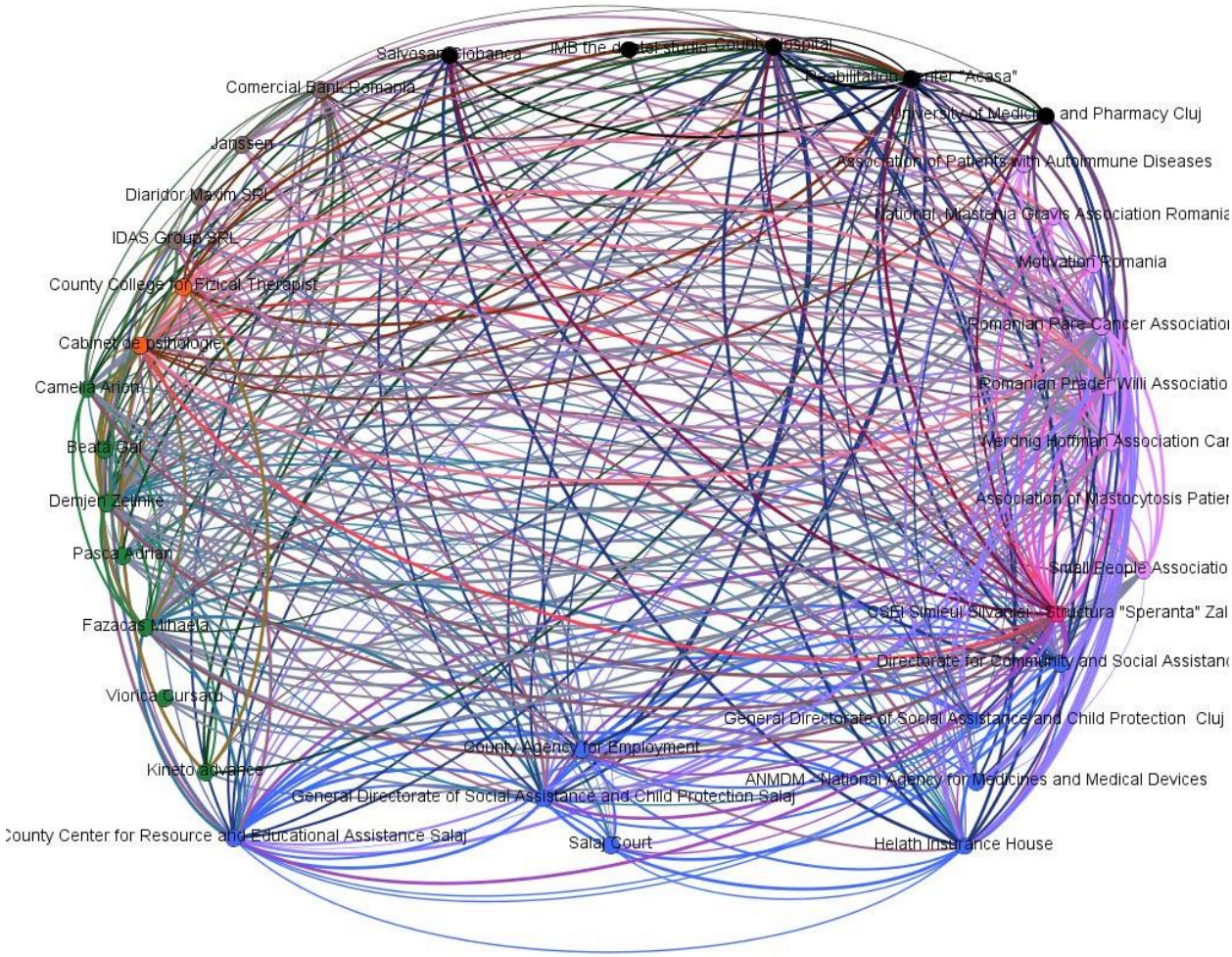


FIGURE 53: NETWORK OF SERVICE PROVIDERS IN 2017

4.3 Assessment of cooperation between services 2018 (second phase of intervention)

In 2018 the network of organisations became denser and the number of lines grew. Again, within the different sectors are tight, but also cross-sectoral communication increased. Especially contacts with the public sector, but also with the medical sector increased with all types of organisations. Still, it can be seen that the NGO sector has the densest network.

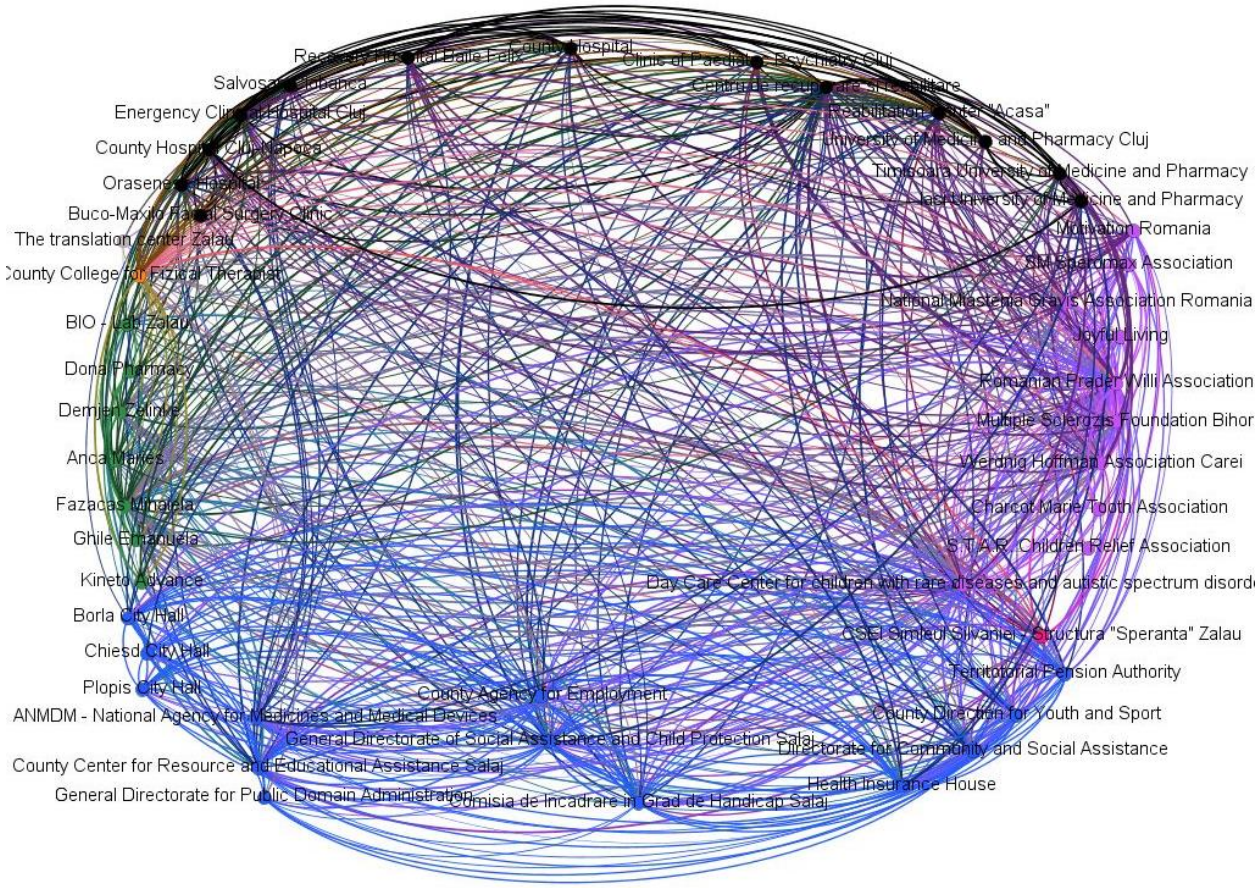


FIGURE 54: NETWORK OF SERVICE PROVIDERS IN 2018

In summary, the networks of organisations grew and became denser in the course of the INNOVcare intervention. Especially the NGO-sector appears to have a special role as in every year most contacts are originating from their side. It may be concluded that this sector, consisting of disability-related and disease-specific organisations and representing patients' interest has the most needs and reasons to contact social and health services, articulate and advocate patients' interest and support improvements of health and social service delivery. It is thus in a position to catalyse improvements in service coordination, integrated and patient-centred care well beyond the segment of rare diseases.

5. CONCLUSIONS AND RECOMMENDATIONS

All in all, based on the findings of this report as well as the very few numbers of dropouts, the INNOVCare pilot was a success; in some aspects more than others. During the nine months of intervention it was possible to significantly improve the patients' and their families' knowledge on services, rights and disease. Strides were made to improve the participants' and their families' ability to manage their care independently. At the level of the community and the stakeholders involved in the patients care and support, advances were made to increase awareness and forge coordination respectively. A longer intervention duration or a shift in the focus of the intervention to implement interventions particularly targeting the community including the providers could have led to increased effects. The results of the network analysis show that the networks of the case managers definitely grew. As a result, indirectly, so did the networks of the patients and their families increasing their resources to independently manage their own care.

Below some of the main reflections and recommendations regarding the INNOVCare trial are presented:

- The results of the quantitative, qualitative and network analysis of the INNOVCare pilot suggest that the nine months intervention duration was a good start; in that depending on the participants' needs, it was adequate. However, for others with more complex needs, it may have been too short.
    - As a result, one recommendation is to have and keep this case management service without time restrictions to allow those with complex needs to be assisted to the point that they are able to independently manage their care. Although the participants were thoroughly informed about conditions of the pilot especially in terms of duration, after the intervention many of them did not feel confident enough in 'taking over' from the case managers. This problem was solved by the case managers taking initiative and offering the participants support if necessary. Future studies or implementations of such an intervention could initiate a gradual end phase to empower the participants to be independent.
    - Such a fixed position would also help patients with new needs, who are unsure of how to go about them to get a consultation.
    - Furthermore, this point of contact would be able to keep the patients and their families up to date in case of changes in legislation.
    - The qualitative interviews with case managers revealed that some of the patients and their families who benefitted from the intervention were not confident about taking control of their care. Knowing that there is support when needed, might increase their confidence in this respect.
- As the findings of this study have revealed, there has also been a learning effect for case managers. A longer duration of service provision would therefore not only benefit the patients and their families but it would also increase the case manager's skills therefore being able to offer the service more effectively.
- According to the interviews with the case managers, their role although very satisfying was sometimes a burden because they found themselves 'taking their clients problems with them at home'. To support the case managers to implement their work more effectively, some form of support such as professional supervision could be introduced.

- Projects requiring such a comprehensive evaluation should consider not only enough time to plan and implement the study but also enough time for the analysis and recommendation.
    - Enough time before the start of the intervention would ensure that the intervention is well planned and data collection tools are developed and well tested to ensure that they also function in the test population. In the case of INNOVCare, the questionnaires underwent a number of cognitive pretesting but based on the low numbers of patients who could complete the questionnaire, more pretests and also pretests in Romania would have possibly enabled tailoring the instruments to the test population better.
    - With the pilot ending at the end of July 2018 and the project ending in September 2018, there was very limited time for analysis of the data and dissemination of the results. Considering the vast amount of data collected, targeted analysis for the purpose of dissemination would have been possible.
    - Should the project duration have been longer or should the possibility of a follow-up project be available, follow-up analysis could have been conducted to determine whether the intervention had an impact on the quality of life of the patients and their families. This is because there is a chance that there is a lag for such effects to develop and become measurable.
- The evaluation instruments were based on the self-assessment of participants. The inclusion of objective measures or 'hard facts' would have enabled validation of the results and possible compatibility with other regions and countries.

Chapters 3.2.8 and 3.2.13 of the qualitative analysis of this report, goes into details about content-related suggestions such as availability of home-based care that the rare and complex disease patients, especially those living in rural areas need.

6. ANNEXES

6.1 R Markdown document

innovcare_documentation.html

The R Mardown document can be accessed through the following link:

6.2 Intensity of communication between the case manager and service providers

			Number of contacts					Mode of contact to providers		
		n[79]	Mean[80]	Median	Mode	Case specific	For all cases	Face-to-Face	Telephone	Email
Case manager 1	Phase 1	15	3.67	4	4	55	5	48 (10 to 60 Minutes)	6 (15 to 20 minutes)	1
	Phase 2	16	3.93	4	3	59	0	21 (10 to 45 minutes)	36 (10 to 30 minutes)	2
Case manager 2	Phase 1	25	2.52	2	1	63	7	46 (15 to 60 Minutes)	17 (10 to 20 minutes)	0
	Phase 2	13	4.85	5	6	63	0	47 (15 to 60 Minutes)	16 (10 to 20 minutes)	0
Case manager 3	Phase 1	15	7.00	7	7	105	8	81 (15 to 80 Minutes)	24 (10 to 80 Minutes)	0
	Phase 2	14	4.21	4	4	59	1	22 (20 to 120 minutes)	38 (20 to 70 Minutes)	0
Case manager 4	Phase 1	14	2.07	2	2	29	6	22 (30 to 90 minutes)	7 (15 to 60 minutes)	0
	Phase 2	13	4.46	4	4	58	1	37 (30 to 120 minutes)	21 (20 to 45 minutes)	0

[79] The maximum number of participants under a single case manager was 15. In this column some of the values are higher than this because in some cases where many participants under different case managers had the same need, one case manager contacted service providers not only for her cases but also those of other case managers with similar needs.

[80] The column 'mean' represents the average number of providers that were contacted to solve the needs of each case. The median and mode is extracted from the same information.

6.3 Interview guideline: Phase 1

1. **Discussion of the individual networks of the case managers:**
    a. Thinking about your professional network, what has changed during the first phase / the first 9 months of the intervention?

    b. Size of the nodes (Duration of contact):
        i. Have you established new connections that you did not have before the INNOVCare project?
            1. With which organisations?
            2. Why these organisations? E.g. based on the needs of the cases?
            3. How did you come into contact with these organisations?
        ii. Have you strengthened or refreshed old contacts?

    c. Thickness of the lines (frequency of communication):
        i. Why do you have such strong connections with organisations such X, Y and Z compared to A, B and C / or why do you contact organisations such X, Y and Z so much more frequently than organisations such as A, B and C?
        ii. What factors facilitate the good relationship with these organisations?
        iii. With which organisations or which kinds of organisations is it more difficult to establish a good connection? Why is this so?

    d. *Colour of the node (types of organisation)*:
        i. You seem to have more contact with X types of organisation e.g. private over public. Why is this so? E.g. is it based on the needs of your cases / your pre-existing contacts / quality of service etc.?

    e. Which organisations are missing in your network and should be integrated as well?
        i. Why are they still missing?
        ii. Why should they be integrated?
        iii. How are you planning to integrate them?

    f. How does the exchange of information between the four case managers take place? E.g. are there team meetings?
        i. How often?
        ii. Do you share contacts?
        iii. How do you utilise the resources from NoRo e.g. other colleagues working on the project like Dorica and Zsuzsa or those not working on the project like therapists, physicians etc.?

    g. Has the community support network being created by NoRo together with the county of Salaj affected your work so far? In what way?

2. **The INNOVCare Intervention:** Please describe your work with the patients and their families in the framework of the INNOVCare project / please describe your work as a case manager / what

does your role as a case manager involve / What are the goals of the case management service you offer?

a. How many cases (patients and their families) are you taking care of?

b. Where are they located? Do they come to the NoRo centre or do you go to them?

c. What kinds of needs do they have?

d. How do you go about finding a solution for these needs?

e. How much time do you dedicate to each case?

f. What are the considerations involved in determining the intensity of your work with them?

g. How do you determine if and when the goals have been reached?

h. What aspects of the intervention are working really well and why?

i. What aspects are not working so well and why?
    i. What challenges have you faced in the implementation of the first phase (the first 9 months) of the intervention?

    ii. What solutions did you implement to overcome these challenges?

j. If you think about your previous work at NoRo, how does the case management service you offer differ from your previous tasks or offers for the patients and their families?

3. AOB

6.4 Interview guideline: Phase 2

1. **Discussion of the individual networks of the case managers:**
    a. Thinking about your professional network, what has changed during the second phase / the second 9 months of the intervention?

    b. Size of the nodes (Duration of contact):
        i. Have you established new connections that you did not have before the INNOVCare project?
            1. With which organisations?
            2. Why these organisations? E.g. based on the needs of the cases?
            3. How did you come into contact with these organisations?
        ii. Have you strengthened or refreshed old contacts?

    c. Thickness of the lines (frequency of communication):
        i. Why do you have such strong connections with organisations such X, Y and Z compared to A, B and C / or why do you contact organisations such X, Y and Z so much more frequently than organisations such as A, B and C?
        ii. What factors facilitate the good relationship with these organisations?
        iii. With which organisations or which kinds of organisations is it more difficult to establish a good connection? Why is this so?

    d. *Colour of the node (types of organisation)*:
        i. You seem to have more contact with X types of organisation e.g. private over public. Why is this so? E.g. is it based on the needs of your cases / your pre-existing contacts / quality of service etc.?

    e. Which organisations are missing in your network and should be integrated as well?
        i. Why are they still missing?
        ii. Why should they be integrated?
        iii. How are you planning to integrate them?

    f. How does the exchange of information between the four case managers take place? E.g. are there team meetings?
        i. How often?
        ii. Do you share contacts?
        iii. How do you utilise the resources from NoRo e.g. other colleagues working on the project like Dorica and Zsuzsa or those not working on the project like therapists, physicians etc.?

    g. Has the community support network being created by NoRo together with the county of Salaj affected your work so far? In what way?

2. **The INNOVCare Intervention:** Please describe your work with the patients and their families in the framework of the INNOVCare project / please describe your work as a case manager / what does your role as a case manager involve / What are the goals of the case management service you offer?
    a. How many cases (patients and their families) are you taking care of?
    b. Where are they located? Do they come to the NoRo centre or do you go to them?
    c. What kinds of needs do they have?
    d. How do you go about finding a solution for these needs?
    e. How much time do you dedicate to each case?
    f. What are the considerations involved in determining the intensity of your work with them?
    g. How do you determine if and when the goals have been reached?
    h. What aspects of the intervention are working really well and why?
    i. What aspects are not working so well and why?
        i. What challenges have you faced in the implementation of the first phase (the first 9 months) of the intervention?
        ii. What solutions did you implement to overcome these challenges?
    j. If you think about your previous work at NoRo, how does the case management service you offer differ from your previous tasks or offers for the patients and their families?

3. **Which patients of the first cohort contacted you after the nine months? Why those and not the others?**

4. **The participants from the 1st cohort:**
    a. What was the ending point of the first phase of the intervention?
    b. How did the participants take it?
    c. Did some participants contact you even after the intervention?
    d. How many? Which patients of the first cohort contacted you after the nine months?
    e. Why those and not the others?
    f. How did you support them?

5. **Would you say that through your support made it possible for the participants to independently manage their own care?**

6. **Was the 9 month intervention period enough?**

7. AOB

7. OTHER INFORMATION

Registration: Registration number for pilot trial and name of trial registry
Protocol: Where the pilot trial protocol can be accessed, if available (other docs e.g. methodology report, technical report etc.)
Funding: Where the pilot trial protocol can be accessed, if available
Ethical approval: Ethical approval or approval by research review committee, confirmed with reference number

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