COVER PAGE

PROTOCOL AND ANALYSIS PLAN FOR:
Relieving the Burden of Psychological Symptoms Among Families of Critically Ill Patients with COVID-19

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Background

The prevalence of psychological symptoms such as anxiety, depression, and acute stress is high among families of critically ill patients. The medical care of an ICU patient may be negatively impacted if these symptoms interfere with a family member assuming the role of surrogate decision maker. Mental health disorders such as complicated grief and post-traumatic stress disorder (PTSD) among families may also develop in the months after the patient is discharged from the ICU, which has been referred to Post-Intensive Care Syndrome-Family.[1] Psychological symptoms negatively affect the family member's quality of life and may hamper his or her ability to act as a caregiver of the patient who is recovering from critical illness.[2]

In March 2020, Rush University Medical Center, along with most healthcare systems, adopted a hospital-wide no visitation policy to limit the spread of COVID-19. Previously, families of Rush ICU patients were encouraged to visit and be active participants in the patient's medical care. This type of "family engagement," which was our standard of care, is believed to help reduce the risk of developing Post-Intensive Care Syndrome-Family.[3]

For the last year, my research group has been enrolling families in a clinical trial evaluating the impact of providing them with daily written summaries of ICU rounds on their experience (NCT03969810). Using validated instruments, we have measured symptoms of anxiety, depression, and acute stress among family members at multiple time points during the ICU stay. During the hospitalization, families also participated in interviews dealing with their experiences. Compared to the 96 family members who were enrolled prior to the COVID-19 pandemic, the 88 family members who have been enrolled during the COVID-19 pandemic were more likely to develop clinically significant depressive symptoms (27% vs. 13%, p=0.03 for difference) and tended to develop clinically significant acute stress symptoms (61% vs 48%, p=0.11 for difference). There were similar levels of clinically significant symptoms of anxiety before and during the COVID-19 pandemic (42% vs. 35%, p=0.43 for difference) (manuscript in preparation). It is likely that restrictions on family visitation and challenges with communication during the COVID-19 pandemic contributed to the high psychological symptom burden among family members during this time period.

The best practices for clinicians to engage with family members in times when they cannot visit their loved ones in the ICU are poorly understood. It is unclear the degree to which families of

COVID-19 patients continue to have psychological symptoms after the patient is discharged and how these symptoms may be impacting quality of life and the patient's recovery. For family members who develop mental health disorders, it is likely that many do not seek out professional help. To address these gaps in knowledge, we propose the following three specific aims.

1. To determine the extent to which families of COVID-19 patients have psychological symptoms 3-6 months after the patient was discharged from the hospital. We will reconsent family members who participated in our initial study during the COVID-19 pandemic. We will conduct one phone interview and use validated instruments to determine the prevalence of anxiety, depression, and post-traumatic stress disorder.

2. To determine the characteristics of ICU care delivery during the COVID-19 pandemic that were associated with the development of psychological symptoms among families. To achieve this goal, we analyze phone interviews conducted during and after the hospitalization. We compare themes among families who developed psychological symptoms to those who did not.

3. To determine whether a trauma-focused cognitive behavioral therapy intervention helps reduce the burden of symptoms among family members with psychological symptoms. We will pilot a program in which family members with clinically significant psychological symptoms will be offered up to six phone/video counseling sessions with mental health professionals. To determine the effect of this therapy, we will conduct phone interviews and use validated instruments to determine the prevalence of anxiety, depression, and post-traumatic stress disorder after the intervention.

Methods

Enrollment

Surrogates of ICU patients with COVID-19 who were enrolled in the study "ICU Rounding Summaries for Families of Critically Ill Patients" (19042604-IRB01) will be approached to participate in a follow-up study dealing with their mental health after patient discharge. We will email and call surrogates to describe the project and provide an informed consent form for them to review.

Inclusion criteria

- The patient's surrogate was enrolled in "ICU Rounding Summaries for Families of Critically Ill Patients" (19042604-IRB01) and the patient had COVID-19
- The patient has been discharged from the hospital

Exclusion criteria

- None

Intervention

Part 1- Post-ICU discharge survey and Interview

Upon enrollment in this post-ICU discharge follow-up study, the subject (surrogate of the ICU patient) will complete a survey dealing with the patient's course since Rush discharge

1. Is the patient still alive?

    a. If deceased, did the patient pass away at Rush or after discharge from Rush?
    b. If alive, is the patient at home?
        i. If at home, for how long? Is he/she receiving home health services?
2. If the patient did not pass away at Rush, did the patient spend time in a rehabilitation hospital, nursing home, or long-term acute care hospital after discharge from Rush?
3. Is the patient currently having any of the following symptoms (check all that apply).
    a. Fatigue
    b. Trouble Breathing
    c. Difficulty speaking
    d. Difficulty eating
    e. Difficulty thinking or paying attention
    f. Pain or discomfort
    g. Anxiety
    h. Depressed mood
    i. Difficulty moving or walking
    j. Difficulty performing activities of daily living such as dressing or bathing
4. Have you used mental health services since the time the patient was admitted?
5. What is your overall impression of mental health services (choices ranging from very unhelpful to very helpful)

Subjects will be asked to complete the 1) Critical Care Family Needs Inventory (CCFNI) questionnaire, 2) Hospital Anxiety and Depression Scale (HADS), and 3) Impact of Events Scale Revised (IES-R) questionnaire. (**Appendix)**

Subjects will participate in a 30-minute phone interview with a psychologist. The psychologist will review the subject's responses to the above surveys and ask follow-up questions (**Appendix)**. The psychologist will ask how the subject has been coping with any psychological symptoms (i.e. anxiety, depression, post-traumatic stress)

The psychologist will describe different types of interventions for people coping psychological symptoms and assess the subject's interest in pursuing any of them.

We will not begin Part 2 until 10 subjects have completed "Part 1- Post-ICU discharge survey and Interview." We will review survey responses and interview transcripts for the first 10 subjects. Based on responses will determine the type(s) of support interventions that will be offered for subjects in this study. An amendment to the study protocol will be made at this time.

Part 2 - Post-ICU psychological intervention
Subjects with clinically significant psychologist symptoms based on either their survey or interview responses will be invited to participate in 6-week trauma-focused intervention with a psychologist.

The program will be brief and delivered online to test the acceptability and feasible of the program, and to gather a preliminary estimate of effect size. We will pilot a group-based intervention (n =3-5) online over Zoom and deliver the intervention across six sessions outlined below. Sessions will last 60-75 minutes depending on participant questions and discussion.

Experiential exercises will be drawn from Acceptance and Commitment Therapy, a related contemporary cognitive behavioral treatment (Hayes, Strosahl, & Wilson, 2012). Some commentary of Viktor Frankl's (1985) work on meaning making will be made in group discussion. Activity scheduling worksheets from Martell, Dimijian and Herman-Dunn (2013) will be used for out of session homework.

We plan two phases for the study. The first phase, sessions 1-3, focus on introducing the model of behavioral activation and guide the participants to identify activities that will being pleasant, meaningful, or offer a sense of accomplishment and mastery. The first session aims to normalize diverse responses to health-related stress and loss by introducing the behavioral model of depression, and the rationale for behavioral activation. In the second session participants then clarify their values, so that they can begin scheduling pleasant and/or meaningful activities in the third session. These activities are tailored based on each participant's individuals goals, priorities and values. The second phase, sessions 4-6, aims to reinforce and sustain positive gains made via behavioral activation and pleasant activity scheduling. Session 4 offers suggestions for problem-solving ways to overcome unhelpful avoidance, a transdiagnostic vulnerability that sustains a number of emotional and psychiatric disorders. Session 5 offers suggestions for overcoming rumination including instruction in mindfulness, and attentional techniques that help participants attend to the outcomes and experiences of the pleasant activities they engage in. Session 6 concludes the program, and guides participants to consider plans to maintain commitment to pleasant activities.

Prior to beginning the intervention and at the completion of the intervention, surrogates will complete the 1) Hospital Anxiety and Depression Scale (HADS), and 2) Impact of Events Scale Revised (IES-R) questionnaire.

At the completion of the intervention, subjects will participate in another 30-minute phone interview with a study investigator. The study investigator will review the subject's responses to the above surveys and ask follow-up questions. The study investigator will ask how the subject has been coping with any psychological symptoms (i.e. anxiety, depression, post-traumatic stress).

All interviews will be audio recorded and transcribed. Two members study staff will review the transcriptions and use thematic content analysis to determine the types of psychological symptoms that are present and the reason(s) they may be present.

<u>Outcomes</u>

Part 1- Post-ICU discharge survey and Interview

- Critical Care Family Needs Inventory (CCFNI) questionnaire, a 14-question instrument with each question scored 1-4
- Hospital Anxiety and Depression Scale (HADS), 14-questions each question scored on 0-3 scale**.**
- Impact of Events Scale Revised (IES-R) questionnaire (measure of PTSD symptoms). This instrument contains 22 questions scored on 0–4 scale.

- Qualitative analysis of interview to determine the prevalence and reason(s) for psychological symptoms

Part 2- Post-ICU discharge survey and Interview

- Each subject's post-intervention HADS score relative to pre-intervention HADS score
- Each subject's post-intervention IES-R score relative to pre-intervention IES-R score
- Qualitative analysis of interview to determine the prevalence and reason(s) for psychological symptoms and effectiveness of the intervention.

When analyzing subject responses, we will account for the following variables

- Whether the patient is deceased or not
- Length of time since hospital discharge
- Whether the subject received mental health services on their own or not
- Whether the subject received daily written summaries in the ICU or not

Statistical Analysis

We expect ~100 subjects to meet inclusion criteria. We expect ~70 to complete Part 1 (Post-ICU discharge survey and Interview). We will determine the prevalence of psychological symptoms and opinions on ICU care by reviewing survey responses and interview recordings. We expect ~30 to complete Part 2 (Post-ICU discharge survey and Interview). We compare pre- to post-intervention survey responses for each subject using a paired t-test. Part 2 will be considered a pilot study. We will use the results to plan a future, adequately powered study.

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Appendix - Critical Care Family Needs Inventory (CCFNI) questionnaire

1. *Do you feel that the best possible care is being given to the patient?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
2. *Do you feel that the hospital personnel care about the patient?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
3. *Have the explanations given to you about the patient's condition been in terms that you can understand?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
4. *Do you feel that you have been given honest information about the patient's condition and progress?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
5. *Do you understand what is happening to the patient and why things are being done?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
6. *Have the staff members been courteous to you?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
7. *Have any of the staff members shown interest in how you are doing?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
8. *Do you believe that someone will call you at home with any major or significant change in the patient's condition?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
9. *Have the hospital personnel explained the equipment being used?*
   1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
10. *I am very satisfied with the medical care the patient receives.*
    1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
11. *There are some things about the medical care the patient receives that could be better.*
    1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
12. *Do you feel comfortable visiting with the patient in the intensive care unit?*
    1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
13. *Is the waiting room comfortable?*
    1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time
14. *Do you feel alone and isolated in the waiting area?*
    1. Almost all of the time 2. Most of the time 3. Only some of the time 4. None of the time

Hospital Anxiety and Depression Scale (HADS),

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:

Total score: Depression (D) _____ Anxiety (A) _____

0-7 = Normal

8-10 = Borderline abnormal (borderline case)

11-21 = Abnormal (case)

Impact of Events Scale Revised (IES-R) questionnaire

INSTRUCTIONS: Below is a list of difficulties people sometimes have after stressful life events. Please read each item, and then indicate how distressing each difficulty has been for you DURING THE PAST SEVEN DAYS with respect to _____ _____(event) that occurred on _____(date). How much have you been distressed or bothered by these difficulties?

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Any reminder brought back feelings about it	0	1	2	3	4
2. I had trouble staying asleep	0	1	2	3	4
3. Other things kept making me think about it.	0	1	2	3	4
4. I felt irritable and angry	0	1	2	3	4
5. I avoided letting myself get upset when I thought about it or was reminded of it	0	1	2	3	4
6. I thought about it when I didn't mean to	0	1	2	3	4
7. I felt as if it hadn't happened or wasn't real.	0	1	2	3	4
8. I stayed away from reminders of it.	0	1	2	3	4
9. Pictures about it popped into my mind.	0	1	2	3	4
10. I was jumpy and easily startled.	0	1	2	3	4
11. I tried not to think about it.	0	1	2	3	4
12. I was aware that I still had a lot of feelings about it, but I didn't deal with them.	0	1	2	3	4
13. My feelings about it were kind of numb.	0	1	2	3	4
14. I found myself acting or feeling like I was back at that time.	0	1	2	3	4
15. I had trouble falling asleep.	0	1	2	3	4
16. I had waves of strong feelings about it.	0	1	2	3	4
17. I tried to remove it from my memory.	0	1	2	3	4
18. I had trouble concentrating.	0	1	2	3	4
19. Reminders of it caused me to have physical reactions, such as sweating, trouble breathing, nausea, or a pounding heart.	0	1	2	3	4
20. I had dreams about it.	0	1	2	3	4
21. I felt watchful and on-guard.	0	1	2	3	4
22. I tried not to talk about it.	0	1	2	3	4

INTERVIEW GUIDE

Prepping for the interview

- **Review the above information**
- **Adopt an empathic stance.** Use open-ended questions to elicit large themes. Clarifying and close-ended questions can be used to narrow themes. Use reflective statements, and paraphrasing to let the participant know you're listening. Use your tone of voice to convey interest and empathy.

The Interview

- Ask for consent to record the interview to aid in note taking.
- Introduce yourself, and remind participants that this stage of the study involves an interview. Encourage participants to be open and forthcoming, and remind them that the information they provide may be useful for supporting other surrogates in the future.
- Tell the participant that the interview focuses on his/her experience during two periods – 1) while his/her loved one was hospitalized at Rush and 2) the time since his/her loved one was hospitalized at Rush.

(The questions are organized to elicit general observations, negative aspects of the ICU experience, and then to elicit positives. This order was chosen for two-reasons. First, to end the interview on a more "positive" tone. Second, to prompt participants to home in on aspects that could be addressed on the coaching intervention phase of the study)

Questions about your ICU experience

- What are your thoughts about your experience with the ICU?
- What are your thoughts about the ways the COVID-19 pandemic affected your experience in the ICU?
- What about your ICU experience was difficult?
    - Were there aspects of ICU care i.e lack of visitation, issues with communication? Were there external factors i.e job loss, family situation?
    - Did you have added responsibilities to other family members while your loved one was in the ICU
- What was most useful for coping?
- Refer to survey responses <u>during</u> ICU stay that stood out, ask to elaborate

Questions about your post-ICU experience

- Tell me how life has been after ICU discharge (note if the patient is alive or not)
- What are your thoughts about the ways the COVID-19 pandemic affected your experience *after* ICU discharge.
- What about your experience has been difficult after ICU discharge?
    - When asking this question, review whether the patient is now at home and/or is having ongoing symptoms
    - Have you had added responsibilities to other family members since your loved one was in the ICU
- What has been most useful for coping?

    - When asking this question, review whether the subject has sought out help from a mental health provider
    - When asking this question, review whether the subject was in the daily email update group or control group. Has the subject referenced the summaries after ICU discharge?
- Refer to survey responses *after* ICU stay that stood out, ask to elaborate
- Going forward, what resources would help you or others in similar situations recover from your experience with the ICU?

Assess interest in a support intervention.

- Refer to whether the subject has sought out help from a mental health provider
    - Has this been helpful? Why or why not
- Refer to the subject's impression of the helpfulness of mental health.
    - Why might it be helpful or unhelpful
- Use the subject's responses to the *whole* interview to suggest possible types of support interventions and gauge the subject's interest (we are expecting about half of the subjects who complete this interview to complete the support intervention)

Thank the participant for their participation. Is there anything else you would like us to know?