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APPROVED

PROTOCOL TITLE: Transdisciplinary Approaches to Understanding Loneliness in Older Adults

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REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

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1.0 Study Summary

Study Title	Transdisciplinary Approach to Understanding Loneliness in Older Adults
Study Design	Multiphase mixed methods design; feasibility study
Primary Objective	Explore the biological, psychosocial, and environmental determinants of loneliness in older adults
Secondary Objective(s)	To obtain feasibility data to inform our understanding of the phenomenon of loneliness in older adults to support development of a larger transdisciplinary research proposal.
Research Intervention(s)/ Investigational Agent(s)	Not intervention research
IND/IDE #	N/A
Study Population	Older adults residing in Maple Knolls Communities, Cincinnati, OH
Sample Size	Aim 1: 10 participants Aims 2 & 3: 20 participants (same participants for both)
Study Duration for individual participants	Phase 1: 85 minutes Phase 2: 85 minutes
Study Specific Abbreviations/ Definitions	TDRP = Transdisciplinary Research Project

2.0 Objectives*

2.1 Describe the purpose, specific aims, or objectives.

This application represents a broad, transdisciplinary research project. The *primary objective* of this research is to improve our understanding of the phenomenon of loneliness, in light of dramatic societal changes and trends that have emerged in recent decades, through exploration of the biopsychosocial and environmental factors influencing loneliness in a group of older adults living in an urban environment. *The overarching methodology* is to approach loneliness from a *transdisciplinary perspective* using a *multiphase mixed methods research design*.

The project uses both inductive and deductive approaches to identify the interconnection of biopsychosocial and environmental contributors to the experience of loneliness for older adults through the following aims:

Aim 1. Explore the unique, "lived experience" of loneliness for older adults.

Aim 2. Understand the biological component of loneliness through analyses of the human gut microbiome and metabolite composition in older adults.

Aim 3. Evaluate the social and environmental interactions of older adults.

2.2 State the hypotheses to be tested.

Aim 1. No hypothesis. Research question: What is the lived experience of loneliness for older adults?

Aim 2. We hypothesize that the composition and abundance of microbiome flora will be distinct between persons experiencing loneliness and individuals not experiencing loneliness.

Aim 3. Older adults who score higher (more lonely) on the UCLA Loneliness Survey will report fewer and lower quality social and environmental interactions than older adults who score lower (less lonely).

3.0 Background*

3.1 Describe the relevant prior experience and gaps in current knowledge.

Loneliness is a complex and highly personal subjective condition[1] and a significant public health issue.[2] The factors leading to loneliness are diverse, complex, and unfortunately quite common.[3] These risks can be categorized into two types: internal (e.g., thoughts, perceptions) and external (e.g., environmental, social) factors.[4-6] The "internal" class of risks include: a diminished sense of belonging, emotional or psychological distress, cognitive/health impairment, a perceived lack of social support, emotionally distant relationships, membership in a minority group, and a lack of mobility.[3] External factors can include isolation stemming from lack of instrumental support (e.g., transportation, phones, internet access), a recent move to a new location, being unmarried, having infrequent contact with a social network, lack of diversity in network, and low participation in social activities.[7,8] A variety of risk factors render older adults especially vulnerable.[9-13] Although loneliness is recognized as an important public health concern,[2] a universal treatment for loneliness does not exist. Moreover, less effort has been placed on translation of decades of

theoretical research into practical guidance for service providers, particularly those caring for aging populations.

In order to support the well-being of older adults, it is essential to understand the social, psychological, and physical factors that influence the subjective consciousness of the individual. Indeed, the personal and unique qualities of loneliness can only be fully understood through comprehensive analysis of the underlying physical/biological factors. Traditionally, biological contributions to loneliness have been understudied in the literature, perhaps owing to the challenge of teasing apart the unique effects of social relationships on mood, physical symptoms, and overall functioning.[14] An important justification for considering the role of biology in the genesis and maintenance of loneliness is that older age is a complex, multidimensional construct comprised of biological, cultural, functional, psychological, and social elements. The biological component that we propose to investigate as part of Aim 2 of our project is the gut microbiota. Despite the growing evidence of its critical influence on mood,[15] mental,[16] and physical health,[17] the microbiome and associated metabolites have never been evaluated in the context of loneliness. We anticipate that the composition of the microbiome will be distinct between persons reporting loneliness, and individuals that do not experience loneliness.

A wealth of research in the past decade has led to an appreciation for the microbiome-gut-brain axis and an interconnected relationship between the composition of the commensal microbes in the gut and psychiatric disorders.[18-21] For example, patients suffering from Major Depression demonstrate reduced abundance of Firmicutes, and increased abundance of Bacteriodetes, Proteobacteria, and Actinobacteria.[22] At present, the biological underpinnings of loneliness remain largely unknown. To fill this gap, we will evaluate the gut microbiome composition among a group of older adults that self-report as lonely and a set that report as non-lonely.

As previously discussed, a key challenge to understanding loneliness in older adults is disentangling the effects of environmental variables on social interactions; determining how these social interactions influence mood; and how mood impacts biological functioning. Given that old age is a multidimensional construct (with biological, cultural, functional, psychological and social components), a comprehensive approach to assessing the unique experience of loneliness is essential. To our knowledge, there are no previous studies conducted to study the intersection of the biopsychosocial and environmental factors influencing loneliness through a transdisciplinary lens.

3.2 Describe any relevant preliminary data.

This will be a pilot study; therefore, there is no preliminary data available for our research.

3.3 Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge.

Our goal is to perform a transdisciplinary assessment of the biopsychosocial and environmental (BPSPE) factors influencing loneliness. Each of the factors we will explore, and more importantly, their various combinations, offers the potential for future targeted interventions. First, we propose to determine the salient psychosocial underpinnings of the unique, “lived experience” of loneliness through the eyes of individuals experiencing this phenomenon using phenomenological interviewing. Research within a phenomenological framework is aimed at understanding the lived experience of participants to capture the

essences of their combined stories to provide new insights and truths surrounding a particular phenomenon. Microbiome-based determination has a potential to influence the development of a new method for the diagnosis and treatment of loneliness. Finally, understanding the social and environmental interactions of older adults can help us further elucidate the social and environmental resources that support the health and well-being of older populations. The transdisciplinary approach we propose will mitigate conceptual ambiguity that has hampered our understanding of the unique, personal nature of loneliness. The long-term goal of this program of research is the future development of a precise, targeted, and effective approach to reducing loneliness in affected persons.

4.0 Study Endpoints*

4.1 Describe the primary and secondary study endpoints.

Primary study endpoint: Completion of interviews, data collection, and analysis of data from 20 participants.

4.2 Describe any primary or secondary safety endpoints.

Non-intervention, exploratory study; minimal risk to participants.

5.0 Study Intervention/Investigational Agent

5.1 FDA-Related, Select Applicable:

☐	Drugs or Biologics	The proposed research involves the administration of an article (e.g. drug, biologic, herbal preparation, dietary supplement, etc.) to a human where the article is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease or is intended to affect the structure or any function of the body. For both FDA and non-FDA approved article.
☐	Devices	Any research that involves the use of a device (medical or other devices, approved or investigational) to test the safety or effectiveness of the device or the device is the focus of the research. **Note:** This includes research that will use human samples to test the safety or effectiveness of a device.
☐	Data Collection	Any research that involves the collection of data or other results from individuals that will be submitted to, **OR** held for inspection by, the FDA. In general this would include research that involves any data that will be provided (in any form) to a pharmaceutical, medical device or biotech company.
☐	Specimens	Any research activity where specimens (of any type) from individuals, regardless of whether the specimens are identifiable, are used to test the safety or effectiveness of any device (medical or other devices, approved or investigational) and the information will be submitted to, or held for inspection by, the FDA.
☒	None of the Above	None of the above describes my research.

6.0 Procedures Involved*

6.1 Describe and explain the study design.

A multiphase, mixed methods design will be used to conduct this study.[23] In this design, the research team will combine the concurrent and/or sequential collection of quantitative and qualitative data sets over multiple phases of the study. Because of the multidimensionality of loneliness, we need to implement multiple phases of investigation in order to achieve each of our specific aims:

Phase 1 (Aim 1): Qualitative Phase: In this phase, in-depth phenomenological[24] interviews with participants will reveal the meaning of the lived experience of loneliness, providing unique, first-person insight into this phenomenon.

Phase 2 (Aims 2 & 3): Quantitative Phase: In this phase, a microbiome analysis will be conducted on stool specimens provided by participants who are lonely and not lonely in order to identify unique metabolites. Surveys will be used to record information on diet, medications, medical history, social interactions, and environmental interactions of participants, thus providing a comprehensive understanding of internal and external environmental influences on loneliness.

6.2 Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks.

Phase 1: Data Collection: Ten participants who self-report as currently experiencing loneliness will complete an 85 minute interview session with a researcher trained in interviewing. At the beginning of the interview session, the participant will complete the UCLA Loneliness Scale (Version 3)[25] (see UCLA Loneliness Scale Appendix 1) and a Demographic Form (see Demographic Form Appendix 2). In addition, individuals will complete a one-hour in-depth interview phenomenological interview in which they will be asked to describe the meaning of the lived experience of loneliness (see Appendix 3 Phenomenological Interview Guide). If at any point during the interview the participant becomes visibly tired, upset, or otherwise unable to complete the interview, or if the participant asks to halt the interview, the interview will be stopped.

Data Analysis: Audiotapes from the interviews will be transcribed into de-identified text documents and verified by the research team to ensure accuracy. Transcripts will be uploaded into MAXQDA Data Analysis Software package. Interpretive Phenomenological Analysis (IPA)[26] will be used to analyze the resulting transcripts and identify recurring patterns and emergent themes, within and across participant interviews.

Phase 2a: Sample collection: Ten participants will be enrolled in Phase 2. This group will consist of 10 individuals who self-report as currently lonely and 10 individuals who self-report as not currently lonely. Each of these individuals will self-collect stool and deposit it into a commode specimen collection system (Fisher Scientific). 1) Collection: Upon enrollment, participants will be given this specimen collection system and provided training in how to use. Once the specimen is collected, the participant will place the container on the back of their toilet and notify the research team of collection. Once notified, a member of the team will retrieve the sample for transport to the UC facility within 24 hours. Under aseptic conditions, all samples will be homogenized with a microspatula and separated into two roughly equivalent aliquots. Samples will then be flash frozen on dry ice, and stored at -80°C until extraction. 2) DNA extraction: extraction of nucleic acid from samples will be performed using 0.10 – 0.25 g of stool mixed with the

bacterial lysis buffer (including lysozyme and proteinase) using the Fecal DNA Isolation kit (MO Bio) for 10 minutes, and microbial DNA will be isolated by bead-beating for three minutes, and purified using a Qiagen DNA spin column. Purified extracts will be stored in TE buffer, and concentrations of all samples will be determined using a NanoDrop spectrophotometer, and stored at -20°C until further processing. 3) Shotgun metagenome sequencing: To prepare a library, ~1-5 μg of genomic DNA will be mechanically sheared and size-selected (~300-600bp) using a Covaris LE220 or S220 instrument. Shearing conditions will be carried out using Crimp-Cap microTubes with AFA fiber, according to the following conditions: temperature: 7-9°C; duty cycle: 20%; intensity: 5; cycles per burst: 200; time: 90 s. Fragmented DNA will be end-repaired and 3' adenylated, and ligated using Illumina proprietary adaptor sequences. Libraries will then be subjected to whole-genome sequencing using the Illumina MiSeq or HiSeq platforms.

Phase 2b: Participants who submit stool specimens will also complete an interview with a member of the research team. The interview will take place in a private setting of the participant's choice. At the beginning of the interview session, the participant will complete the UCLA Loneliness Scale (Version 3)[25] and a Demographic Form (Appendices 1 & 2). Each participant will also complete brief surveys to report 24-hour diet recall, medications, and medical history (See Appendices 4, 5, and 6). Participants will also be asked to respond to questions corresponding to the Lubben Social Network Scale (See Appendix 7) and to carry on a conversation to help fill-in the Ecomap Diagram analysis (See Appendix 8). Data Analysis: The data generated will be used to create a social-environmental profile of the participant's loneliness contributors. If at any point the participant becomes visibly tired, upset, or otherwise unable to complete the interview, or if the participant asks to halt the interview, the interview will be halted.

Transdisciplinary Analysis of Multiphase Design: A final stage of analysis will be used to integrate findings across each of the two phases of the study. The team will identify relevant connections between data collected across phases and then create unique loneliness profiles based on findings.

6.3 Describe:

1) *Procedures performed to lessen the probability or magnitude of risks.*

- The procedures related to this study pose no more than minimal risk to participants. Every effort will be made to maintain the confidentiality of participant information and research records related to this study. The University of Cincinnati, the Institutional Review Board (IRB), and other regulatory authority(ies) will be granted direct access to original research records for verification of the research study procedures or study data without violating confidentiality, to the extent permitted by applicable laws and regulations. The research team has experience and training in managing participant information during research studies and will follow HIPAA regulations. Only de-identified data will be disseminated in presentations or publications unless written permission is obtained from the study participant. Participant interviews will be digitally recorded and transcribed verbatim. All transcriptions will be verified for accuracy. Following verification of accuracy in transcripts, digital recordings will be destroyed. All data will be de-identified and assigned a unique identifier and stored on a secure HIPAA compliant file on OneDrive.

During interviews and other study-related activities, any participant who expresses discomfort, anxiety, or other health-related issues will be free to stop the interview process. Researchers will immediately notify Maple Knoll Communities staff and health care providers if a participant requires follow-up or care.

2) *All drugs and devices used in the research and the purpose of their use, and their regulatory approval status.*

No drugs nor devices will be used in the research.

3) *The source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)*

Table 1. Study Measures & Activities	
Measurement	**Project Phase**
Demographic Questionnaire	Phase 1 & 2
UCLA Loneliness Scale	Phase 1 & 2
Phenomenological Interview	Phase 1
Client Interview	Phase 2
Stool Sample	Phase 2
24-hour Dietary Recall	Phase 2
Medical History	Phase 2
Medications Form	Phase 2
Lubben Social Network Scale	Phase 2
Ecomap	Phase 2

6.4 What data will be collected during the study and how that data will be obtained?

Data collected will be aim-dependent:

Aim 1: a) Questionnaire – Demographic information; UCLA Loneliness Scale (Version 3); b) audio-recording of 1-hour phenomenological interview.

Aim 2: a) Questionnaires – 1) Demographic information; 2) 24-hr dietary recall; 3) Medical history; 4) Medications Form; b) Fecal sample for microbiome analysis.

Aim 3: a) Questionnaires – 1) UCLA Loneliness Scale (Version 3); 2) Lubben Social Network Scale; 3) Ecomap; filled in directly and through interview.

6.5 If there are plans for long-term follow-up *(once all research related procedures are complete),* what data will be collected during this period.

No long-term follow-up is planned. However, participants can indicate on the consent document if they wish to be contacted for future research projects.

6.6 For Humanitarian Use Device (HUD) uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

No HUD use.

7.0 Data and Specimen Banking*

7.1 If data or specimens will be banked for future use, describe where the specimens will be stored, how long they will be stored, how the specimens will be accessed, and who will have access to the specimens.

No specimens will be stored for future use.

7.2 List the data to be stored or associated with each specimen.

For each specimen, the associated data will be: 1) whole metagenome raw sequences and associated data, and 2) data associated with metabolite analyses based on short-chain fatty acid (SCFA) composition and abundance.

7.3 Describe the procedures to release data or specimens, including: *the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.*

All original samples and nucleic acid extracts will be destroyed once sequence and metabolite data are collected.

8.0 Sharing of Results with Subjects*

8.1 Describe whether results *(study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings)* will be shared with subjects or others *(e.g., the subject's primary care physicians)* and if so, describe how the results will be shared.

No individual results will be shared. At the completion of the study and after completion of data analysis, our team will return to Maple Knoll Communities and present an overview of our findings. These findings will be de-identified and will consist of themes and factors associated with loneliness identified as a result of our analysis.

9.0 Study Timelines*

9.1 Describe:

This study is expected to take one year to complete. See the table below for more details:

Table 2. Study Timeline (months)	**0-2**	**3**	**4-5**	**6-7**	**8-10**	**11-12**
Study Activity						
IRB approval & study start initiation						
Recruitment						
Aim 1: Interviews						
Aim 2: Microbiome Analysis						

Aim 3: Environmental & Social Network Assessment						
Data Analysis						
Dissemination						

1) *The duration of an individual subject's participation in the study.*

The duration of an individual's participation in the study will not be longer than 4 months, from time of enrollment to completion of data collection.

2) *The duration anticipated to enroll all study subjects.*

The anticipated duration for enrollment is two months. This includes the time from initial posting of information regarding the study and researcher informational sessions at Maple Knolls to the final enrollment of participants from the group of participants screened.

3) *The estimated date for the investigators to complete this study (complete primary analyses)*

The study will be concluded within 10 months of initial posting of information regarding voluntary participation.

10.0 Inclusion and Exclusion Criteria*

10.1 Describe how individuals will be screened for eligibility.

Individuals who express an interest in participating in the study will have an opportunity to ask questions and learn more about participation upon initiating contact with the study team. This contact will be either in-person at Maple Knoll Communities, or via telephone (see telephone script, Appendix 10). During that conversation, the entire study will be described to potential participants. They will be informed that consent to participate will in no way influence their standing at Maple Knoll. The consent will include information on the study investigators, study purpose, procedures, methods, participant rights, protection of human subjects, and contact information for the study staff. Consent will be required prior to data collection and will be obtained in conformity with standards of the University of Cincinnati Institutional Review Board (IRB).

10.2 Describe the criteria that define who will be included or excluded in your final study sample.

Inclusion Criteria

Participants will be eligible to participate if they are:

1) 65 years of age or older

2) Able to speak and read English

3) A resident of the independent living section of Maple Knoll Communities

4) Able and willing to provide informed consent for participation

5) Self-report currently experiencing loneliness (Phase 1 and ½ of Phase 2 participants)

Exclusion Criteria

Participants will be excluded if they are:

1) Critically ill and physically unable to participate

2) Cognitively impaired, as determined by a six-item screener derived from the Mini-mental state examination (MMSE).[27] This screening tool for cognitive impairment has been validated in diverse community populations (see Appendix 13 Six-Item Screener).

10.3 Indicate specifically whether you will include or exclude each of the following special populations: *(You may not include members of the above populations as subjects in your research unless you indicate this in your inclusion criteria.)*

1) *Adults unable to consent*

All individuals unable to provide verbal and written consent will be excluded from enrollment.

2) *Individuals who are not yet adults (infants, children, teenagers)*

Due to the purpose of the study, to understand loneliness in older adults, no participants younger than 65 years of age will be enrolled in the study.

3) *Pregnant women (a woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery)*

All women enrolled in the study will be over the age of 65 and therefore beyond reproductive age.

4) *Prisoners*

No prisoners will be enrolled in this study. All participants will be residents of Maple Knoll Communities.

11.0 Vulnerable Populations*

11.1 If the research involves individuals who are vulnerable to coercion or undue influence, describe additional safeguards included to protect their rights and welfare.

1) *If the research involves pregnant women, review "CHECKLIST: Pregnant Women (HRP-412)" to ensure that you have provided sufficient information.*
2) *If the research involves neonates of uncertain viability or non-viable neonates, review "CHECKLIST: Neonates (HRP-413)" or "HRP-414 – CHECKLIST: Neonates of Uncertain Viability (HRP-414)" to ensure that you have provided sufficient information.*

3) *If the research involves prisoners, review "CHECKLIST: Prisoners (HRP-415)" to ensure that you have provided sufficient information.*
4) *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children"), review the "CHECKLIST: Children (HRP-416)" to ensure that you have provided sufficient information.*
5) *If the research involves cognitively impaired adults, review "CHECKLIST: Cognitively Impaired Adults (HRP-417)" to ensure that you have provided sufficient information.*

None of the vulnerable populations listed above will be eligible for enrollment in the study.

12.0 Local Number of Subjects*

12.1 Indicate the total number of subjects to be accrued locally.

A total of 30 participants will be recruited from the independent living community.

12.2 If applicable, distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures *(i.e., numbers of subjects excluding screen failures.)*

Approximately 30 individuals will be screened for participation. Of this number, we will enroll 20 total participants for the project.

13.0 Recruitment Methods*

12.3 Describe when, where, and how potential subjects will be recruited.

Recruitment flyers [Appendix 9] will be posted in common areas of the Maple Knoll Communities and distributed in resident mailboxes.

Members of the research team will also hold two information sessions at Maple Knoll Communities in which they will be available to provide additional information regarding the research study.

12.4 Describe the source of subjects.

All participants recruited will be residents of Maple Knoll Communities independent living facility.

12.5 Describe the methods that will be used to identify potential subjects.

We will use a variety of strategies and convenience and snowball sampling to identify potential participants: 1) Interested individuals may call the number included on the Recruitment flyer [Appendix 9] in order to reach one of the PIs of the project. 2) Potential participants may approach a member of the research team during one of the two information sessions held at Maple Knoll Communities. 3) Finally, snowball sampling will be used, whereby participants who are enrolled in the study may refer interested friends for screening and potential enrollment.

12.6 Describe materials that will be used to recruit subjects. *(Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may*

submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

An IRB approved Recruitment Flyer [Appendix 9] will be posted in various open spaces accessed by Maple Knoll residents in the Independent Living section of the facility. In addition, flyers will be placed in resident mailboxes, per suggestion of Maple Knoll staff. Contact information will be provided on the flyer for anyone interested in learning more about the research study. A Telephone/In-person recruitment script has also been developed (see Appendix 10) to facilitate any telephone or in-person requests for information by potential participants.

12.7 Describe the amount and timing of any payments to subjects.

Each participant in Phase 1 and Phase 2 of the research study will receive a $40 gift card. These gift cards will be distributed at the beginning of the schedule private interview that is an activity of each phase. If a participant chooses to stop participation at any time prior to the completion of the interview, they will retain the full amount of payment.

14.0 Withdrawal of Subjects*

14.0 Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.

If a participant displays any indications of discomfort, illness, exhaustion, and/or confusion, data collection will be stopped immediately.

14.1 Describe any procedures for orderly termination.

Upon determination that a participant is not eligible to continue the study for any of the above identified reasons, all data collection will be ceased. The research team member will notify the appropriate personnel at the independent living community in order to ensure safety of the participant.

14.2 Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.

Participant's data will be removed from database. Study consent will be retained, and a page added that states that the participant withdrew.

15.0 Risks to Subjects*

15.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research.

There are minimal risks associated with participation in this study. Participants may experience short-term fatigue from completion of interviews and surveys. At any point during data collection, if a participant expresses fatigue the interview will stop and be rescheduled. There are no legal and economic risks associated with participation. Participants may become upset when discussing loneliness. Once again, if discomfort is expressed, the interview will be stopped.

15.2 If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.

N/A

15.3 If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.

N/A

15.4 If applicable, describe risks to others who are not subjects.

N/A

16.0 Potential Benefits to Subjects*

16.1 Describe the potential benefits that individual subjects may experience from taking part in the research.

Participants may benefit from being able to enjoy companionship during the interview process. Individuals who participate in interviews often relate that these experiences are positive as they allow them to express their view on loneliness and their social conditions.

16.2 Indicate if there is no direct benefit. Do not include benefits to society or others.

There are no direct benefits.

17.0 Data Management* and Confidentiality

17.1 Describe the data analysis plan, including any statistical procedures or power analysis.

Phase 1 –Audio recordings from 1-hour phenomenological interview will be assigned a participant key, de-identified, and then stored in a HIPPA compliant OneDrive file accessible only to members of the research team. The audio recordings will be transcribed, and any identifiers removed during this process. After verification of the original transcription, the original recording will be deleted. The transcripts and interview will be analyzed by researchers to create a "lived experience" profile for loneliness as experienced by older adults. The Demographic Questionnaire and completed UCLA Loneliness Scale will be scanned, assigned a participant key, and stored on a HIPPA compliant OneDrive file accessible only by members of the research team.

Phase 2a – 2a.1) Whole metagenome sequence analysis (taxonomic/functional profiling): We will use MetaPhlAn software to perform taxonomic profiling to determine the composition of gut microbial communities (Bacteria, Archaea, Eukaryotes and Viruses) based on the shotgun metagenomics sequencing data. This tool maps raw sequence reads to a database of predefined clade-specific marker genes and returns the taxonomic identity of each read cluster. After mapping reads to clade-specific marker genes, raw counts will be normalized to provide profiles of clade relative abundance and marker gene presence/absence. We will then use HUMAnN software (http://huttenhower.sph.harvard.edu/humann) to perform functional profiling of genes based on the KEGG database of gene families and pathways. Statistical Analysis: We will use principal component/coordinates analysis (SPSS software) to reveal the clustering and correlation patterns in the data between loneliness scales and relative abundance of each taxonomic rank. A p value <0.05 will be considered statistically significant. 2a.2) SCFA analysis: A panel of SCFAs and butyrate will be analyzed using gas chromatography-mass spectrometry (GC-MS or LC-MS). This analytical method is used to identify the constituent components of a test sample. Each test sample will be prepared from 1g of stool suspended in 2 ml of deionized water, and homogenized. This suspension will be centrifuged for 10 minutes at 10,000 x g. To the supernatant, we will add an internal standard, 4-methylvaleric acid solution. The supernatant will be analyzed through GC-MS or LC-MS. 2) Data analysis: We will use SPSS and Origin 9.0 software to correlate the

SCFA concentrations with loneliness scales and microbiota relative abundance. Both linear and no-linear correlations will be calculated using Pearson's and Spearman's coefficients.

Phase 2b – The Demographic Questionnaire, UCLA Loneliness Scale, 24-hour dietary recall, Medical History, Medications form, Lubben Social Network Scale and Ecomap will be scanned, assigned a participant key, and stored on a HIPPA compliant OneDrive file accessible only by members of the research team.

17.2 Describe the steps that will be taken to secure the data *(e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data)* during storage, use, and transmission.

All de-identified data will be stored on a HIPPA compliant OneDrive file accessible only by members of the research team. A key code will be generated for participants and all research data will be listed with a key, not the participant's name. All biological specimens (Phase 2) will be de-identified and stored under lock-and-key in a private freezer in the Department of Biology or Environmental Engineering, until use. Once processed, all tissues will be destroyed (see above). The study key and signed consent documents will be scanned and stored separately from any data. This information will be stored on a secure HIPAA compliant research server maintained by the UC College of Nursing CATER staff.

17.3 Describe any procedures that will be used for quality control of collected data.

Data from surveys will be double-entered and assessed for matching by case and variable. When a variable shows mismatch, the source document will be assessed, and the data entry error corrected. Audiotaped interviews will be transcribed by a transcription service. R. Lee (PI) will verify each transcript upon receipt of the document to ensure accuracy. For Aim 2, prior to sequencing, all nucleic acid extracts will be quality assessed at the Cincinnati Children's Hospital DNA Sequencing Core. Samples achieving an RIN/RQS value of 8+ will proceed to library generation. Those samples failing to meet this threshold will be discarded from further evaluation. Additionally, all sequencing analyses will be performed in triplicate and assessed for consistency of sequencing across different samples to control for inter-run variation.

17.4 Describe how data or specimens will be handled study-wide:

Phase 1 & 2: Paper data and consent documentation will be scanned and stored on the HIPPA compliant research server managed by the College of Nursing. After verifying documentation was saved, original paper document will be destroyed by shredding.

Audio recordings and electronic databases will be saved to the HIPPA compliant research server managed by the College of Nursing.

Phase 2: Specimens will be de-identified and assigned an index identifier to associate specimens to downstream microbiome sequencing and metabolite results. All subsequent data will be stored on encrypted servers through UC College of Arts and Sciences, and College of Engineering. Only research team members will have access to data and specimens. The project leaders will be responsible for receipt and transmission of specimens and data. Fecal samples will be securely transported from the partner facility to UC research facilities (A&S; Engineering) by a research team member in sterile IATA-approved transport containers. Data collected from the specimens will be stored for no more than three years following completion of the study. Once data is collected from stool samples, the remainder will be destroyed.

1) *How long the data or specimens will be stored?*

   De-identified data will be stored until completion of all data analysis and through a period of no longer than 3 years. After that, all data will be destroyed.

2) *Who will have access to the data or specimens?*

   Only approved members of the research team will have access to data or specimens.

3) *Who is responsible for receipt or transmission of the data or specimens?*

   The members of the research team identified to collect data or specimens will be responsible for transporting data or specimens back to the UC campus and the appropriate storage location, as described previously.

4) *How data or specimens will be transported?*

   Data from interviews and digital recordings will be transported in a lock box maintained by the researcher collecting the data. Specimens will be stored in an approved stool collection kit and transported packed in dry ice back to the lab at UC from Springdale, OH, a distance of approximately 20 miles.

18.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

This section is required when research involves more than Minimal Risk to subjects.

18.1 Describe*:*

1) *The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe. The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.*
2) *What data are reviewed, including safety data, untoward events, and efficacy data.*
3) *How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).*
4) *The frequency of data collection, including when safety data collection starts.*
5) *Who will review the data.*
6) *The frequency or periodicity of review of cumulative data.*
7) *The statistical tests for analyzing the safety data to determine whether harm is occurring.*
8) *Any conditions that trigger an immediate suspension of the research.*

Research does not involve more than minimal risk to participants.

19.0 Provisions to Protect the Privacy Interests of Subjects

19.1 Describe the steps that will be taken to protect subjects' privacy interests. *"Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.*

Participants will be allowed to select the private location for their interview with a trained member of the research team. At no time will any Maple Knoll Communities administrator or staff member be informed of a resident's participation in research activities unless there

is a medical emergency that develops during study activities. All data that is collected will be de-identified. A unique identifier will be assigned to each of the participants and noted on each data source for that participant. A key will be developed to record each participant's identifier. The key will be stored on a research server away from the data. Finally, any dissemination of study findings in the way of presentations or manuscripts will not include any personal identifiers, including the name of the facility.

19.2 Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. *"At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.*

By allowing the research participant to select their preferred location for all interviews the research team hopes to ensure a comfortable environment. Dr. Lee will be leading interviews with participants. She has extensive experience in conducting qualitative and mixed methods studies with vulnerable participants, and in conducting community-based participatory research in non-healthcare settings. Over the years, she has been able to develop expertise in facilitating interpersonal communication and facilitating 100% retention in each of her completed studies. If at any time a research participant is uncomfortable responding to a question, they will be informed to stop responding, notify the researcher, and they will move on to the next item. If the participant wishes to stop all questions, they will simply inform the researcher and the interview will stop.

19.3 Indicate how the research team is permitted to access any sources of information about the subjects.

The research team will only have access to information that is provided during interviews and through responses to surveys and questionnaires. No other information will be accessed.

20.0 Compensation for Research-Related Injury

20.1 If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

N/A

20.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury.

N/A

21.0 Economic Burden to Subjects

21.1 Describe any costs that subjects may be responsible for because of participation in the research.

Participants will not incur any economic burden in relation to participation in this study.

22.0 Consent Process

22.1 Indicate whether you will you be obtaining consent, and if so describe:

1) *Where will the consent process take place*

Steps will be taken to minimize coercion or undue influence during the process of obtaining informed consent will be followed in accordance with all applicable regulatory requirements. Consent will be obtained in conformity with standards of the

Institutional Review Board (IRB). The flyer and consent will include information on the study investigators, study purpose, procedures, methods, participant rights, protection of human subjects, and contact information for the study staff. Consent will be required prior to data collection

The consent process will take place in person in a private location. A copy of the completed consent document will be provided to the participant for their own records. Participants from the study may be eligible to participate in future studies related to loneliness in older adults. To obtain permission to re-contact these individuals for future studies, participants will be asked to provide contact information on the form, "Are you willing to be contacted about opportunities to participate in future studies?" [Appendices 11, 12]. Participants will be made aware that they are only agreeing to have the study's research personnel re-contact them to inform them of future projects. By completing the form they are NOT agreeing to participate in future projects.

2) *Any waiting period available between informing the prospective subject and obtaining the consent.*

There is no pre-determined waiting period between providing information and obtaining consent. Timing of this process will be tailored to meet the needs of the participant and to ensure adequate time to determine if they wish to enroll in the study.

3) *Any process to ensure ongoing consent.*

During all data collection activities of the study, participants will be reminded that they have the right at any time to stop participation in the study.

4) *Whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." If not, describe:*
   - *The role of the individuals listed in the application as being involved in the consent process.*
   - *The time that will be devoted to the consent discussion.*
   - *Steps that will be taken to minimize the possibility of coercion or undue influence.*
   - *Steps that will be taken to ensure the subjects' understanding.*

     The research team will be following SOP: Informed Consent Process for Research (HRP-090).

5) *The conditions under which you believe it would be appropriate to obtain ongoing consent from subjects.*

As this is a minimal-risk, non-intervention study, the research team does not anticipate participants choosing to terminate participation in the study. However, if at any time a participant appears to be upset by questions, or appears tired, the research team member will immediately stop study activities and make sure the participant still provides consent to continue.

Non-English Speaking Subjects

6) Indicate what language(s) other than English are understood by prospective subjects or representatives.

Participants recruited for the research study must be able to read and speak English.

7) If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

All enrolled participants must read and speak English as an inclusion criterion.

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

8) Review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure you have provided sufficient information for the IRB to make these determinations.

N/A

9) If the research involves a waiver the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations.

N/A

Subjects who are not yet adults (infants, children, teenagers)

10) Describe the criteria that will be used to determine whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. *(E.g., individuals under the age of 18 years.)*
    - *For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*
    - *For research conducted outside of the state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

N/A: All participants will be adults.

11) Describe whether parental permission will be obtained from:
    - *Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.*

- *One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.*

N/A

12) Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's general medical care.

N/A

13) Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent.

N/A

14) When assent of children is obtained describe whether and how it will be documented.

N/A

Cognitively Impaired Adults

15) Describe the process to determine whether an individual is capable of consent. *The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require children to sign assent documents.*

No participants enrolled in the research study will be cognitively impaired. Participants will be recruited from the population of Maple Knoll Communities independent living residents. Residents of the independent living program are monitored to ensure ability to live independently, including cognitive ability. Prior to administering consent, a member of the research team will administer a six-item screener [Appendix 13] derived from the Mini-mental state examination (MMSE).[27] This screening tool for cognitive impairment has been validated in diverse community populations. Any adult who does not achieve a satisfactory score on this screening will be excluded from participation in the study. Since these individuals do live independently, this information will be passed along to Maple Knoll representatives for further evaluation.

Adults Unable to Consent

16) List the individuals from whom permission will be obtained in order of priority. (E.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child.)
    - *For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative."*

- *For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Adults who are unable to consent are excluded from the study.

17) Describe the process for assent of the subjects. Indicate whether:
   - *Assent will be required of all, some, or none of the subjects. If some, indicated, which subjects will be required to assent and which will not.*
   - *If assent will not be obtained from some or all subjects, an explanation of why not.*
   - Describe whether assent of the subjects will be documented and the process to document assent. *The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.*

All adults enrolled in the study must be able to give consent.

Adults Unable to Consent

18) For HUD uses provide a description of how the patient will be informed of the potential risks and benefits of the HUD and any procedures associated with its use.

N/A

23.0 Process to Document Consent in Writing

23.1 Describe whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not, describe whether and how consent of the subject will be documented in writing.

Documentation of Consent will follow the written documentation of consent process.

23.2 If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

23.3 (If you will document consent in writing, attach a consent document. If you will obtain consent, but not document consent in writing, attach a consent script. Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. *You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)"to create the consent document or script.)*

See Appendices 11 and 12 – Consent for Participation – Group 1 and Consent for Participation – Group 2

24.0 Setting

24.1 Describe the sites or locations where your research team will conduct the research.

1) *Identify where your research team will identify and recruit potential subjects.*

Potential participants will be identified and recruited from the independent living section of Maple Knoll Communities, a senior living community located in Springdale, Ohio. Recruitment activities will take place in common areas of the facility accessed by independent living residents.

2) *Identify where research procedures will be performed.*

All research procedures and administration of consent will take place in a private setting of the participant's selection. The anticipated setting will be the private residence of the participant.

3) *Describe the composition and involvement of any community advisory board.*

There is no community advisory board participating in this project. The study team did meet with Maple Knoll staff during early stages of project development in order to determine the appropriateness of this population and facility. Important information regarding the setting and residents was shared with the team and incorporated in the protocol. Maple Knoll Communities administrators have reviewed the proposed project and provided a Letter of Support that is attached as Appendix 15.

4) *For research conducted outside of the organization and its affiliates describe:*
   - *Site-specific regulations or customs affecting the research for research outside the organization.*

     The administrative team at Maple Knoll Communities has reviewed the proposed research and granted their approval. The residents, by nature of their independent living agreement, have full say in whether or not to participate in the research. Maple Knoll Communities administrators will not be informed as to which residents are choosing to participate and which decline.

   - *Local scientific and ethical review structure outside the organization.*

     No scientific or ethical review structures in place.

24.2 *Select all applicable UC/UC Health Affiliated Research Sites:*

☐	Barrett Cancer Center (Including IV Therapies & Pancreatic Disease Clinic	☐	Medical Sciences Building
☒	College of Nursing	☐	Shriners Hospital
☐	Crossroads Center	☐	UC Gardner Neuroscience Institute
☐	Drake Center	☐	UCMC (Emergency Department, Inpatient, and Outpatient Units)
☐	Genome Research Institute (Reading Campus)	☐	UCMC (Emergency Department, Inpatient, and Outpatient Units)

☐	Hoxworth: Inpatient Unit	☐	UCMC NICU
☐	Hoxworth: Outpatient Clinics	☐	University of Cincinnati Physicians (UCP)
☐	Infectious Disease Clinic (Holmes-UC Health)	☐	University Pointe Surgical Hospital
☐	Infectious Disease Clinical Trial Unit (Holmes-UC)	☐	VA-Cincinnati Medical Center
☐	Kettering Laboratory	☐	West Chester Hospital
☐	Linder Center of Hope	☐	Other UC Health Affiliated Clinic
☐	Liver Transplant Clinic (Medical Arts Building)		

25.0 Resources Available

25.1 Describe the resources available to conduct the research:

Maple Knoll Communities houses approximately 219 potential participants in the independent living section of their facility. After distribution of informational recruitment flyers about voluntary participation in our study, we expect to screen approximately 50 residents who are interested in participation in the study. From this number, 20 will be selected in consultation with a Maple Knoll representative in order to ensure cognitive ability to participate.

Phase 1 & 2: Each PI involved in interviewing portions of the project is able to dedicate up to 12 hours per month (w/ up to 20 hours during the month of initial interviews) to conducting and completing the proposed research. Material support is provided by the UC Office of Research and on-going support of faculty effort through the College of Nursing, The College of Arts and Sciences, and the College of Engineering and Applied Sciences. The study key and scanned consent documents will be stored on a password protected and encrypted research drive maintained by the University of Cincinnati College of Nursing IT services, located in Procter Hall, through the Center for Academic Technology and Educational Resources (CATER). In addition, de-identified data will be shared between research team members through a shared file set up in a HIPAA compliant file on OneDrive. Dr. Lee has dedicated office space, laptop, and equipment to support her research activities. All team members will be briefed on each aspect of the scientific and technical components of the proposed work prior to participation. This includes adequate training in research procedures, protocols, and clarification of duties. In addition, the research team will continue holding weekly team meetings throughout the duration of the study.

Phase 2: Each PI is able to dedicate up to 12 hours per month to conducting and completing the proposed research. The Gross lab is located on the 7th floor of Rieveschl Hall on the main campus of the University of Cincinnati. The PI's main lab space is configured as an open lab concept (18' x 12', 216 sq. ft.), capable of supporting the research of at least 8 lab members. The Gross laboratory space includes four dedicated study carrels for laboratory members. The Gross lab houses a PC-format computer dedicated solely for use as a bioinformatic workstation running the current Mac operating system as well as the DNASTAR Lasergene software package, MS Office suite and various freeware programs. Routine laboratory software programs include the following: DNAStar; BioBam Blast2GO; ImageJ and FIJI (freeware); CLC Genomics Workbench. All computers have hard-wired access to the internet and the full digital resources of the University of Cincinnati Library system including electronic

journals, textbooks and other resources. The LAN environment at UC is 802.11N compliant, allowing Ethernet connections at a speed of 1 Gb. The Gross laboratory houses two Bio-Rad gradient thermocyclers, a C1000 and an S1000, each outfitted with independently running 2 x 48 well units. Additionally, we have a NanoDrop Lite (Thermo Fisher Scientific) spectrophotometer and a 96-well Bio-Rad CFX96 Real-Time PCR Instrument. Alongside a gel-dock station, we have a UVP Transilluminator, and a 2.6 cubic foot VWR Molecular Biology-grade incubator. Numerous resources relevant to this project include a departmental administrative team charged with various miscellaneous (i.e., administrative) operations helpful to the proposed work. All team members will be briefed on every aspect of the scientific and technical components of the proposed work prior to participation. This includes adequate training in research procedures, protocols, and clarification of duties.

We do not anticipate the need for medical or psychological resources as a result of participation in this study. However, should any participant indicate distress, either emotional or physical, the research team members will immediately notify medical staff at Maple Knoll Communities.

26.0 HIPAA

26.1 *26.0 If you will use hospital or other healthcare provider records, data from a research data repository or any other information maintained by a hospital, academic medical center or another healthcare entity, how will you gain access to this information?*

☒ Not using HIPAA-protected information for any research activities.

☐ Through a HIPAA Authorization signed by the participant (or their legally authorized representative).

☐ Requesting that the IRB approve a waiver of authorization in this application. **SUBMIT HIPAA WAIVER REQUEST FORM**.

☐ As a limited data set under a data use agreement.

27.0 Other Reviews

27.1 *Select applicable:*

☐ **Radiation Safety:** *The proposed research involves the research participants being exposed to radiation for research purposes. Note: This includes an increase of frequency of radiological imaging procedure and/or increase duration of clinically indicated radiological imaging procedures.*

☒ **Institutional Biosafety Committee:** *IBC Approval is required for research that will utilize any of the following: infectious agents, select agents (See "Selected Agents for IBC Review"), recombinant DNA or viral gene transfer vectors, select agents or toxins for human gene transfer or an agent (virus, bacteria, etc.) that has been genetically modified. Information regarding submission to the University of Cincinnati IBC can be found at: Institutional Biosafety Committee. The IRB must receive a copy of IBC approval prior to issuing final IRB approval.*

See Appendix 16 for Institutional Biosafety Committee Approval.

☐ **Infectious Agent:** *The proposed research involves an infectious agent that is administered to a human subject, or that involves a risk of accidental exposure to a member of the research team, other hospital staff or other patients in the hospital.*

27.2 CT.Gov Registration

☐ The PI is responsible for registration of this study on www.clinicaltrials.gov (If yes, contact the IND-IDE Assistance Program at (513) 558-0453).

27.3 Identify where funds are being held:

☐ Funds held in Sponsored Research Services for a Grant or Contract (funds are held internally at UC)

☒ Funds are from a UC department account (held internally at UC)

☐ Funds held in a Corporate account from a Contract (funds held externally at UC)

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Appendix 1

UCLA Version 3 Loneliness Scale

Instructions: The following statements describe how people sometimes feel. For each statement, please indicate how often you feel the way described by placing a check in the space provided. Here is an example: How often do you feel happy? If you never felt happy, you would check "never"; if you always feel happy, you would check "always."

	NEVER 1	RARELY 2	SOMETIMES 3	ALWAYS 4
*1. How often do you feel that you are "in tune" with the people around you?				
2. How often do you feel that you lack companionship?				
3. How often do you feel that there is no one you can turn to?				
4. How often do you feel alone?				
*5. How often do you feel part of a group of friends?				
*6. How often do you feel that you have a lot in common with the people around you?				
7. How often do you feel that you are no longer close to anyone?				
8. How often do you feel that your interests and ideas are not shared by those around you?				
*9. How often do you feel outgoing and friendly?				
*10. How often do you feel close to people?				
11. How often do you feel left out?				
12. How often do you feel that your relationships with others are not meaningful?				
13. How often do you feel that no one really knows you well?				
14. How often do you feel isolated from others?				
*15. How often do you feel you can find companionship when you want it?				
*16. How often do you feel that there are people who really understand you?				
17. How often do you feel shy?				
18. How often do you feel that people are around you but not with you?				
*19. How often do you feel that there are people you can talk to?				
*20. How often do you feel that there are people you can turn to?				

Scoring: Items that are asterisked should be reversed (i.e., 1 4, 2 3, 3 2, 4 1), and the scores for each item then summed together. Higher scores indicate greater degrees of loneliness. From Russell DW: UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure, *J Pers Assess* 66:20-40, 1996.

Demographic Form

Participant Name: _____ Date: _____

1. Gender: ☐ Female ☐ Male

2. Date of Birth: __ __ / __ __ __ / __ __ __ __
   d d m m m y y y y

3. Race ("X" ONLY one with which you MOST CLOSELY identify):

   ☐ American Indian or Alaska Native

   ☐ Asian

   ☐ Black or African American

   ☐ Native Hawaiian or Other Pacific Islander

   ☐ White

   ☐ More than one race

   ☐ Unknown or not reported

4. Ethnicity ("X" ONLY one with which you MOST CLOSELY identify):

   ☐ Hispanic or Latino

   ☐ Not Hispanic or Latino

   ☐ Unknown or not reported

Appendix 3

Guide for Phenomenological Interviews

Inquiry Guide for Recorded Interviews with Participants: Phase 1:

Research question guiding interview: What is the lived experience of loneliness for older adults?

Participants will be recruited for this phase of the study based on self-reporting of currently experiencing loneliness.

Phenomenological interviews will be semi-structured in nature. A semi-structured interview will allow for gathering of information related to the phenomenon of loneliness as it is situated in the lifeworld of the participant, both currently, and historically. This interview will be guided by these overarching questions:

1. Please describe for me your current experience with loneliness? Be as specific and detailed as possible.
2. How does loneliness currently impact your daily life?
3. Describe for me people, situations, or activities that make you feel lonely.
4. Describe for me people, situations, or activities help you feel less lonely.
5. Thinking back, describe for me other times in your life when you have been lonely.
6. At those times, what helped you become less lonely?
7. Is there anything else that you feel I should know about loneliness in older adults?

Remaining questions will follow the response of the participant. These will include prompts and probes and other questions intended to gain deeper reflection on significant information that is shared by the participant. Examples might include:

1. Tell me more about that.
2. How did you feel when that happened?
3. Could you give me an example of that?

Other techniques that will be used during the interview include silence, echoing the response of the participant, or reframing the response for greater clarification.

Appendix 4

24-Hour Dietary Recall

Participant Name: _____ Date: _____

A 24-hour dietary recall (24HR) is a structured interview intended to capture detailed information about all foods and beverages consumed by the respondent in the past 24 hours, most commonly, from midnight to midnight the previous day.

Appendix 5

Medications Form

Participant Name: _____ Date: _____

Medication	Indication	Dosage	Start Date	Stop Date	Ongoing?
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐
					☐

Appendix 6

Medical History

Participant Name: _____ Date: _____

Does the participant have a medical or surgical history, current or resolved, of any of the following?

MEDICAL HISTORY	Yes / No	Unknown	If Yes, Explain	Current / Resolved
1. Head, Eye, Ear, Nose, Throat	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
2. Respiratory	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
3. Cardiovascular	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
4. Gastrointestinal	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
5. Genitourinary	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
6. Musculoskeletal	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
7. Neurological	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
8. Endocrine-Metabolic	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
9. Blood/Lymphatic	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
10. Dermatologic	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
11. Psychiatric	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
12. Allergy	☐ Yes ☐ No	☐		☐ Current ☐ Resolved
13. Other, specify: _____	☐ Yes ☐ No	☐		☐ Current ☐ Resolved

Appendix 7

Lubben Social Network Scale

About: This scale is a self-report measure of social engagement including family and friends. There are two versions of this scale included; the short, 6 item scale and the 12 item scale. **Before using this scale, researchers are asked to fill out this permission form.

Items: 12 / 6

Reliability:
Internal reliability for the 12 item scale = .70
Internal reliability for the 6 item scale = .83
Reliability of the family questions = .84 - .89
Reliability of the non-kin questions = .80 - .82

Validity:
The Lubben Social Network Scale is correlates with mortality, all case hospitalization, health behaviors, depressive symptoms, and overall physical health.

Scoring:

	Less Social Engagement				More Social Engagement	
All questions	0	1	2	3	4	5

The total score is calculated by finding the sum of the all items. For the LSNS-R, the score ranges between 0 and 60, with a higher score indicating more social engagement. For the LSNS-6, the score ranges between 0 and 30, with a higher score indicating more social engagement.

References:

Lubben, J. (1988). Assessing social networks among elderly populations. *Family & Community Health: The Journal of Health Promotion & Maintenance, 11,* 42-52.

Lubben, J., Blozik, E., Gillmann, G., Iliffe, S., von Renteln Kruse, W., Beck, J. C., & Stuck, A. E. (2006). Performance of an abbreviated version of the Lubben Social Network Scale among three European Community–dwelling older adult populations. *Gerontologist, 46*(4), 503–513.

LUBBEN SOCIAL NETWORK SCALE – REVISED (LSNS-R)

FAMILY: Considering the people to whom you are related by birth, marriage, adoption, etc…

1. How many relatives do you see or hear from at least once a month?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

2. How often do you see or hear from the relative with whom you have the most contact?

0 = less than monthly 1 = monthly 2 = few times a month 3 = weekly 4 = few times a week 5 = daily

3. How many relatives do you feel at ease with that you can talk about private matters?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

4. How many relatives do you feel close to such that you could call on them for help?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

5. When one of your relatives has an important decision to make, how often do they talk to you about it?

0 = never 1 = seldom 2 = sometimes 3 = often 4 = very often 5 = always

6. How often is one of your relatives available for you to talk to when you have an important decision to make?

0 = never 1 = seldom 2 = sometimes 3 = often 4 = very often 5 = always

FRIENDSHIPS: Considering all of your friends including those who live in your neighborhood…

7. How many of your friends do you see or hear from at least once a month?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

8. How often do you see or hear from the friend with whom you have the most contact?

0 = less than monthly 1 = monthly 2 = few times a month 3 = weekly 4 = few times a week 5 = daily

9. How many friends do you feel at ease with that you can talk about private matters?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

10. How many friends do you feel close to such that you could call on them for help?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

11. When one of your friends has an important decision to make, how often do they talk to you about it?

0 = never 1 = seldom 2 = sometimes 3 = often 4 = very often 5 = always

12. How often is one of your friends available for you to talk to when you have an important decision to make?

0 = never 1 = seldom 2 = sometimes 3 = often 4 = very often 5 = always

LUBBEN SOCIAL NETWORK SCALE – 6 (LSNS-6)

FAMILY: Considering the people to whom you are related by birth, marriage, adoption, etc…

1. How many relatives do you see or hear from at least once a month?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

2. How many relatives do you feel at ease with that you can talk about private matters?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

3. How many relatives do you feel close to such that you could call on them for help?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

FRIENDSHIPS: Considering all of your friends including those who live in your neighborhood

4. How many of your friends do you see or hear from at least once a month?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

5. How many friends do you feel at ease with that you can talk about private matters?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

6. How many friends do you feel close to such that you could call on them for help?

0 = none 1 = one 2 = two 3 = three or four 4 = five thru eight 5 = nine or more

Appendix 8

The Ecomap Diagram Form

Family Name: _____

Date Completed: _____

Completed By: _____

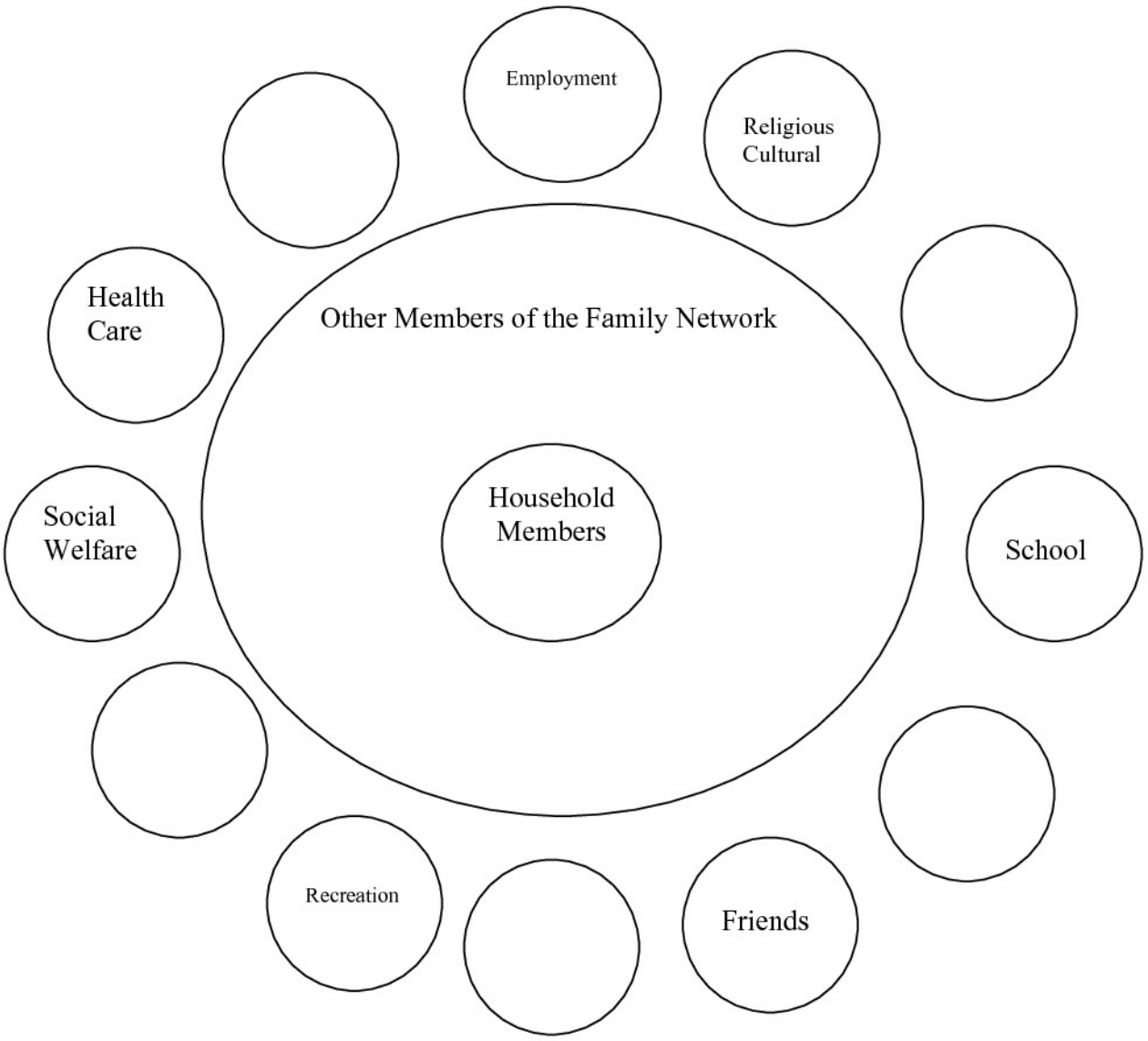
Family Address: _____

Strong Connection _____

Tenuous Connection ----------

Stressful Connection __/___/__/

Flow of Resources ⟷



Adapted from the *Special Needs Adoption Curriculum*, Spaulding for Children, 1991

college of nursing

UNIVERSITY OF Cincinnati

PARTICIPANTS NEEDED

Transdisciplinary Approaches to Understanding Loneliness in Older Adults

What is the purpose of this research study?

The purpose of this study is to better understand loneliness in older adults. We want to find out what it's like to be lonely. We also want to see if there are things you eat or things in your personal and social environments that increase or decrease your loneliness.

Who will be in this research study?

About 20 residents of Maple Knoll Communities who are interested in the topic of loneliness will be in this study. There will be two groups in this study, with 10 people in each.

What will you be asked to do in this research study, and how long will it take?

Everyone in this study will fill out a survey about loneliness. People in Group 1 will be asked to take part in a private interview lasting about 85 minutes. This interview can be in your home, or in another private area at Maple Knoll.

People in Group 2 will be asked to meet privately to give us a stool specimen for analysis. They will be asked to take part in a private interview lasting about 85 minutes. This interview can be in your home, or in another private area at Maple Knoll.

What will you get because of being in this research study?

Each person who is in the study will receive a $40 gift card in appreciation of your time.

Who do you contact?

To learn more about this research, contact Dr. Rebecca Lee at 513-558-5498 or by email at rebecca.lee@uc.edu.

In-Person or Telephone Script
Transdisciplinary Approaches to Understanding Loneliness in Older Adults

Hello _____,

My name is _____ (investigator will announce him or herself to potential participant). I am talking with you about a research study called: **Transdisciplinary Approaches to Understanding Loneliness in Older Adults**

Have you seen our flyer at Maple Knoll?

If they say yes, they have seen the flyer "Would you like for me to tell you about the study?"

If they say no, show them the flyer. Then, say, "Would you like for me to tell you about the study?"

In this study, we are asking Maple Knoll residents to help our team understand more about loneliness in older adults. People who agree to participate will take a survey on loneliness. They will then be asked to select one of two groups to be in for the study. We will have 10 people in each group.

Group 1 will include 10 people who are currently lonely, based on the survey. Each person in this group will meet privately with a member of our research team to talk about what it's like to be lonely. Your interview will last about 85 minutes. You will receive a $40 gift card if you are in this group.

Group 2 will include 10 people – 5 who are not currently lonely and 5 who are currently lonely, based on the survey. These people will be asked to give us a sample of their stool for analysis. In addition, they will meet privately with a member of the research team to fill out information on their diet, medical history, medications, activities, and social connections. You will receive a $40 gift card if you are in this group.

Taking part in this study is completely up to you. It is completely voluntary, and you can withdraw at any time.

Does this sound like something that you would be interested in?

If you are interested, we will give you more details about the study, and see if you are eligible to participate.

When is a good time for us to contact you? Thank you for your interest in our study.

If you have questions about this study, you may contact

- Dr. Rebecca Lee, 513-558-5498, Rebecca.lee@uc.edu

If you are not interested, we understand. We will not contact you again. If you change your mind, please contact Dr. Rebecca Lee.

- Dr. Rebecca Lee, 513-558-5498, Rebecca.lee@uc.edu

Thank you for letting us explain our study. Please contact us if you have further questions.

- Dr. Rebecca Lee, 513-558-5498, Rebecca.lee@uc.edu

Adult Consent Form for Research – Group 1: Phenomenological Interviews
University of Cincinnati
Department: College of Nursing
Principal Investigators: Rebecca Lee, Zvi Biener, Joshua Gross, Maobing Tu

Title of Study: Transdisciplinary Approaches to Understanding Loneliness in Older Adults

Introduction:
You are being asked to take part in a research study. Please read this form carefully and ask questions about anything that you do not understand. This research is sponsored by the University of Cincinnati (UC) Office of Research.

Who is doing this research study?
The persons in charge of this research study are Dr. Rebecca Lee (UC College of Nursing), Dr. Zvi Biener and Dr. Joshua Gross (UC College of Arts & Science), and Dr. Maobing Tu (UC College of Engineering and Applied Science). There may be other people on the research team helping at different times during the study.

What is the purpose of this research study?
The purpose of this study is to gain a better understanding of loneliness in older adults.

Who will be in this research study?
About 20 older adults who are residents of Maple Knoll Communities will take part in the overall study. There will be two groups of participants – 10 residents in group 1 and 20 residents in groups 2. You are being asked to participate in Group 1.

What will you be asked to do in this research study, and how long will it take?
If you are eligible, you will be asked to take part in a private, in-depth interview with a member of the research team. This interview will take place in person at a location of your choosing, such as your home. The interview will last about 85 minutes. You will be asked about:

- your age, gender, race, and your background
- your health and well-being
- what it is like for you to live with loneliness

Are there any risks to being in this research study?
Some questions may make you feel uncomfortable. You can refuse to answer any questions that you don't want to answer. The risk is not expected to be more than you would have in daily life.

Are there any benefits from being in this research study?
You will probably not get any benefit from taking part in this study. But, being in this study may help us develop better ways of helping older adults reduce loneliness in the future.

What will you get because of being in this research study?
You will be paid to take part in this study. You will receive a $40 gift card at the beginning of

our interview appointment.

Do you have choices about taking part in this research study?
If you do not want to take part in this research study you may simply not participate. Your participation in this study is completely voluntary. You may withdraw at any time. You will still receive your $40 payment for participation even if you stop the interview early.

How will your research information be kept confidential?
The interview with you will be conducted in a private location of your choice. The interview will be audiotaped. Audiotapes will be erased as soon as they are transcribed or checked for accuracy. Your name will not be used on any typed transcripts or data collection forms. A study ID number will be used instead of your name. Your name and contact information will be stored separately from the transcripts and research forms. All data will be kept on a password-protected computer, password-protected secure OneDrive, or research drive at the University of Cincinnati, or in locked file cabinets. Within 3 years after the study is over, all research data will be de-identified. Your information will be kept confidential, unless authorities have to be notified about abuse or immediate harm that may come to you or others. If you have a health issue, you will be encouraged to contact a healthcare provider. In an emergency, a healthcare provider or the emergency medical system may be contacted on your behalf. Agents of the University of Cincinnati may inspect study records for audit or quality assurance purposes.

What are your legal rights in this research study?
Nothing in this consent form waives any legal rights you may have. This consent form also does not release the investigator, the University of Cincinnati, the institution, or its agents from liability for negligence.

What if you have questions about this research study?
If you have any questions or concerns about this research study, you should contact Dr. Rebecca Lee at 513-558-5498, Rebecca.lee@uc.edu. If you would like further information mailed to you after the study is over, please contact Dr. Lee. The UC Institutional Review Board reviews all research projects that involve human participants to be sure the rights and welfare of participants are protected. If you have questions about your rights as a participant, complaints and/or suggestions about the study, you may contact the UC IRB at (513) 558-5259. Or, you may call the UC Research Compliance Hotline at (800) 889-1547, or write to the IRB, 300 University Hall, ML 0567, 51 Goodman Drive, Cincinnati, OH 45221-0567, or email the IRB office at irb@ucmail.uc.edu.

Do you HAVE to take part in this research study?
No one has to participate in this study. Refusing to take part will NOT cause any penalty or loss of benefits that you would otherwise have. You may start and then change your mind and stop at any time. To stop being in the study, you should tell Dr. Rebecca Lee 513-558-5498, Rebecca.lee@uc.edu. BY TAKING PART IN THIS RESEARCH YOU INDICATE YOUR CONSENT FOR YOUR ANSWERS TO BE USED IN THIS RESEARCH STUDY.

Agreement:
I have read this information and have received answers to any questions I asked. I give my consent to participate in this research study. I have received a copy of this signed and dated consent form to keep.

Participant Name (Please Print): _____

Participant Signature: _____ Date: _____

PLEASE RETURN THE ORIGINAL AND KEEP THE COPY OF THIS INFORMED CONSENT FORM FOR YOUR REFERENCE.
>>>>> ***SEE NEXT PAGE FOR ADDITIONAL QUESTIONS*** >>>>>

Are you willing to be contacted about opportunities to participate in future studies?

_____ No

_____ Yes:

Name: _____

Phone number(s): _____

Best time to reach you? _____

Email address(s): _____

Thank you.

Adult Consent Form for Research – Group 2: Microbiome Analysis & Interview
University of Cincinnati
Department: College of Nursing
Principal Investigators: Rebecca Lee, Zvi Biener, Joshua Gross, Maobing Tu

Title of Study: Transdisciplinary Approaches to Understanding Loneliness in Older Adults

Introduction:
You are being asked to take part in a research study. Please read this paper carefully and ask questions about anything that you do not understand. This research is sponsored by the University of Cincinnati (UC) Office of Research.

Who is doing this research study?
The persons in charge of this research study are Dr. Rebecca Lee (UC College of Nursing), Dr. Zvi Biener and Dr. Joshua Gros (UC College of Arts & Science), and Dr. Maobing Tu (UC College of Engineering and Applied Science). There may be other people on the research team helping at different times during the study.

What is the purpose of this research study?
The purpose of this study is to gain a better understanding of loneliness in older adults.

Who will be in this research study?
About 30 older adults who are residents of Maple Knoll Communities will take part in the overall study. There will be two groups of participants – 10 residents in group 1 and 20 residents in groups 2. You are being asked to participate in Group 2.

What will you be asked to do in this research study, and how long will it take?
If you are eligible, you will be asked to collect a stool sample for the research team in a container that we will give you. You will then take part in a private interview with a member of the research team to complete some information sheets. This interview will take place in person at a location of your choosing, such as your home. The interview will last about 85 minutes. You will be asked about:

- your age, gender, race, and your background
- your health, well-being, and medical history
- your food intake prior to collecting the stool sample
- your environmental interactions
- your social connections with friends and family

Are there any risks to being in this research study?
Some questions may make you feel uncomfortable. You can refuse to answer any questions that you don't want to answer. The risk is not expected to be more than you would have in daily life.

Are there any benefits from being in this research study?
You will probably not get any benefit from taking part in this study. But, being in this study may

help us develop better ways of helping older adults reduce loneliness in the future.

What will you get because of being in this research study?
You will be paid to take part in this study. You will receive a $40 gift card at the beginning of our interview appointment.

Do you have choices about taking part in this research study?
If you do not want to take part in this study you may simply not participate. Your participation in this study is completely voluntary. You may withdraw at any time. You will still receive your $40 payment for participation even if you stop the interview early.

How will your research information be kept confidential?
The interview with you will be conducted in a private location of your choice. Your name will not be used on any data collection forms. A study ID number will be used instead of your name. This number will also be used to identify your stool sample. Your name and contact information will be stored separately from any research forms. All data will be kept on a password-protected computer, password-protected secure OneDrive, or research drive, at the University of Cincinnati, or in locked file cabinets. Within 3 years after the study is over, all research data will be de-identified and destroyed. Your information will be kept confidential, unless authorities have to be notified about abuse or immediate harm that may come to you or others. If you have a health issue, you will be encouraged to contact a healthcare provider. In an emergency, a healthcare provider or the emergency medical system may be contacted on your behalf. Agents of the University of Cincinnati may inspect study records for audit or quality assurance purposes.

What are your legal rights in this research study?
Nothing in this consent form waives any legal rights you may have. This consent form also does not release the investigator, the University of Cincinnati, the institution, or its agents from liability for negligence.

What if you have questions about this research study?
If you have any questions or concerns about this research study, you should contact Dr. Rebecca Lee at 513-558-5498, Rebecca.lee@uc.edu. If you would like further information mailed to you after the study is over, please contact Dr. Lee. The UC Institutional Review Board reviews all research projects that involve human participants to be sure the rights and welfare of participants are protected. If you have questions about your rights as a participant, complaints and/or suggestions about the study, you may contact the UC IRB at (513) 558-5259. Or, you may call the UC Research Compliance Hotline at (800) 889-1547, or write to the IRB, 300 University Hall, ML 0567, 51 Goodman Drive, Cincinnati, OH 45221-0567, or email the IRB office at irb@ucmail.uc.edu.

Do you HAVE to take part in this research study?
No one has to participate in this study. Refusing to take part will NOT cause any penalty or loss of benefits that you would otherwise have. You may start and then change your mind and stop at any time. To stop being in the study, you should tell Dr. Rebecca Lee 513-558-5498,

Rebecca.lee@uc.edu. BY TAKING PART IN THIS RESEARCH YOU INDICATE YOUR CONSENT FOR YOUR ANSWERS TO BE USED IN THIS RESEARCH STUDY.

Agreement:
I have read this information and have received answers to any questions I asked. I give my consent to participate in this research study. I have received a copy of this signed and dated consent form to keep.

Participant Name (Please Print): _____

Participant Signature: _____ Date: _____

PLEASE RETURN THE ORIGINAL AND KEEP THE COPY OF THIS INFORMED CONSENT FORM FOR YOUR REFERENCE.
>>>>> ***SEE NEXT PAGE FOR ADDITIONAL QUESTIONS*** >>>>>

Are you willing to be contacted about opportunities to participate in future studies?

_____ No

_____ Yes:

Name: _____

Phone number(s): _____

Best time to reach you? _____

Email address(s): _____

Thank you.

Appendix 13

MMSE Six-Item Screener

1. I would like to ask you some questions that ask you to use your memory. I am going to name three objects. Please wait until I say all three words, then repeat them. Remember what they are because I am going to ask you to name them again in a few minutes. Please repeat these words for me: APPLE—TABLE—PENNY. (Interviewer may repeat names 3 times if necessary but repetition not scored.)

Did patient correctly repeat all three words?	Yes	No
	Incorrect	Correct
1. What year is this?	0	1
2. What month is this?	0	1
3. What is the day of the week?	0	1
What were the three objects I asked you to remember?		
4. Apple =	0	1
5. Table =	0	1
6. Penny =	0	1

Appendix 15

mapleknoll
COMMUNITIES

11100 Springfield Pike
Cincinnati, OH 45246
Tel 513.782.2400 **Fax** 513.782.8301
mkcommunities.org

October 14, 2019

Rebecca C. Lee, PhD, RN, PHCNS-BC, CTN-A
University of Cincinnati College of Nursing
PO Box 210038
Cincinnati, OH 45221-0038

Dear Dr. Lee:

I am pleased to provide this letter in support of your Transdisciplinary Research team's research study entitled *A Transdisciplinary Approach to Understanding Loneliness in Older Adults.* The proposed project represents an innovative approach to better understanding the phenomenon of loneliness in older adults from a biopsychosocial and environmental perspective. You and your team members, Dr. Joshua Gross, Dr. Zvi Biener, and Dr. Maobing Tu, are welcome to partner with our community and its residents on this important work.

Maple Knoll Communities, Inc. is a nationally recognized leader in the care and support of older adults. Founded in 1848 and located in Cincinnati. Ohio, we are a non-profit senior healthcare services provider. Maple Knoll Communities, Inc. includes the exceptional retirement communities of Maple Knoll Village and the Knolls of Oxford, Maple Knoll Outreach Services for Seniors, three affordable HUD Senior Living Residences, Village Home Health and Hospice, WMKV 89.3 and 89.9 FM Radio Station, a Montessori Child Center, and the Hemsworth Wellness Center. As Vice President of Marketing, Communications and Development, I oversee occupancy, advertising, publicity and fundraising efforts for our organization. Our residents range in age from 62-106 and live in Independent Living, Assisted Living and Skilled Nursing.

As the identified community partner for this study, we pledge our ongoing support of the proposed project, serving as a resource for the research team. Participants for this research will be recruited from the population of residents who live independently in our community. You and your fellow research team members previously completed an orientation to our facility, touring the grounds and meeting with members of our staff to present your project and receive our input and suggestions. Your team will continue to receive our support as you engage with any residents who choose to participate in this study. While research team members will work independently with individuals who enroll in the study to schedule private interviews in their residences, we will be available to assist should you identify the need for additional resources or support for any of the study participants.

We are pleased to be a part of this collaborative, transdisciplinary endeavor to enhance the health and well-being of older adults by identifying factors that increase the risk for loneliness. In addition, we recognize that the factors identified through this research hold the potential to inform future interventions.

mapleknoll
COMMUNITIES

11100 Springfield Pike
Cincinnati, OH 45246
Tel 513.782.2400 **Fax** 513.782.8301
mkcommunities.org

Upon completion of your work, your team is welcome to present an overview of your findings to our residents and staff.

We look forward to future joint endeavors made possible through the important partnership forged through this pilot project.

Sincerely,

Megan Gresham-Ulrich

Megan Gresham-Ulrich
Maple Knoll Communities, Inc.
Vice President of Marketing, Communications and Development
11100 Springfield Pike
Cincinnati, OH 45246
Tel: 513.782.2423
Cell: 513.312.2546
Fax: 513.782.4324
http://www.mapleknoll.org

Instructions For Stool Specimen Collection

****Before you collect your specimen, please place all gel packs in your freezer for at least 12 hours. ****

Specimen should be collected no more than 24 hours before your clinic visit.

STEP 1. Raise the toilet seat. Place the stool collection frame on the back of the toilet bowl (see Figure 1). All four corners of the collection frame should be supported by the toilet bowl. Place collection bowl in frame (see Figure 2).

Figure 1

Figure 2

STEP 2. Place toilet seat down (see Figure 3). Do **not** urinate into the collection container*. Deposit your stool directly into the collection container.
If accidental urination occurs, discard the stool and collect a new sample using the second (back-up) container provided.

Figure 3

STEP 3. After collecting your specimen, remove the container from the frame (see Figure 4). Place the container on a flat surface and firmly press the lid closed (see Figures 5 and 6).

Figure 4

Figure 5

Figure 6

STEP 4. Place the closed container into the Ziploc bag (see Figure 7) and seal the bag.


Figure 7

STEP 5. Discard collection frame in trash.

STEP 6. Package your specimen immediately following the instructions below. Write the date and time of collection on the outer box label, and bring it in with you for your baseline sampling visit or re-sampling visit. Your specimen may be stored in the Styrofoam box with gel packs (see below) up to a maximum of 24 hours, prior to your clinic visit.

Stool Packaging Instructions

1. Place all seven gel packs in your freezer (see Figure 1). Do not collect your specimen until the gel packs have been in your freezer for at least 12 hours.

FIGURE 1

2. Remove the gel packs from your freezer and place two of the gel packs in the bottom of the Styrofoam box (see Figure 2).

FIGURE 2

3. Place the sealed Ziploc bag containing your stool specimen on top of the two frozen gel packs in the Styrofoam container (see Figure 3).

FIGURE 3

4. Place four of the frozen gel packs around the specimen container so that the container is completely surrounded (see Figures 4 and 5).

FIGURE 4

FIGURE 5

5. Place one gel pack on top of the container (see Figure 6).

FIGURE 6

6. Place the Styrofoam lid on the Styrofoam container (see Figure 7) and close cardboard box.

FIGURE 7

7. Using the tape dispenser provided, seal the middle of the box and both sides of the box (see Figures 8 and 9).

FIGURE 8

FIGURE 9

8. Bring the box with you to your sample collection appointment. [Note: Subject ID# and body site-specific, pre-printed clinic label will be applied to the container at the time of provision to the subject]

7.3.3.5 Specimen Receipt

When subject arrives in the clinic for the specimen collection visit, the stool collection container should be retained in the Styrofoam box with the gel packs while being transported to the clinical lab.

Appendix 16

Institutional Biosafety Committee
The University of Cincinnati
Biosafety Office
Mail Location: 0767
Phone (513) 558-6182
(513) 558-6355
email: inbiocom@ucmail.uc.edu

IBC APPROVAL – NOTIFICATION

Principal Investigator: Maobing Tu **IBC #:** 19-03-25-01

Protocol Title: Loneliness and human gut microbiome and metabolites project

IBC Review: 04/04/19 **IBC Approval:** 05/10/19 **Protocol Expiration**: 05/10/22

Approved Items: *in vitro* Human stool

The Principal Investigator is responsible for implementing and ensuring that laboratory and clinical personnel follow the safe work practices described in this protocol as well as the policies and procedures found in the biological laboratory safety manual (http://researchcompliance.uc.edu/Biosafety/biomanual.aspx).

Persons under 18 years of age (except under some circumstances) are not allowed in University of Cincinnati (UC) laboratories where hazardous substances (biological, chemicals, radioactive etc.) are present. Under NO circumstances shall infants, toddlers, or children too young to understand safety training be permitted in UC laboratories (http://www.ehs.uc.edu/Advisories/Advisory_21_0.PDF).

The University of Cincinnati is required to report certain incidents involving recombinant or synthetic nucleic acid research to the NIH/OSP. To ensure timely and appropriate follow-up and to comply with federal reporting requirements, Principal Investigators shall immediately report exposures and releases involving biohazards and/or recombinant or synthetic nucleic acid materials to the Biosafety Office.

Any changes in this protocol, such as inclusion of agents or change in procedures, must be submitted to the IBC as an amendment for approval.

*This protocol will expire 3 years from its **initial** approval date.*

This approval is restricted to items within the IBC purview (recombinant or synthetic nucleic acid and other biological hazardous materials).

Gary E. Dean, PhD
IBC Chairman

Marcia Espinola, DVM, MS, CBSP
Biosafety Officer