

PROVIDE: VIDEO BASED PATIENT REPORTED OUTCOMES FOR SANFILIPPO DISEASE: A NEW AND INNOVATIVE APPROACH TO RECORD AND MEASURE DISEASE POST GENE THERAPY.

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INTRODUCTION

Sanfilippo type A (MPS IIIA) leads to early-onset neurodegeneration and premature death. Presentation includes delayed speech and behaviour problems or features of autism. Parents of children with MPS IIIA report that clinic-based assessments do not fully capture the scope of patients' abilities or the real-world disease burden and may miss documenting potential treatment effects.

This study has developed a home-based method for capturing outcomes for MPS IIIA, as a means to monitor the onset and evolution of disease hallmarks remotely and in a non-invasive way that is suitable for children. Defined video captures were chosen based on identified gaps in clinic-based measures and personalized features identified by caregivers.

To address the methodological challenges of this small, heterogeneous population, the team designed a longitudinal parallel study to collect patient-specific home-based video data and qualitative interviews with caregivers to supplement the data from Lysogene's Phase 2/3 gene therapy trial (AAVance) in MPS IIIA.

METHODS

Caregivers of patients enrolled in the AAVance trial collect video data of patients doing specific daily life activities at baseline and follow-up timepoints throughout the clinical trial (3, 6, 12, 18, and 24 months post-treatment) through a secure smart phone mobile application.

Video assessments focus on several hallmarks of MPS IIIA progression, including inability to self-care, lack of engagement with environment, progressively abnormal gait, social withdrawal, lack or loss of communication or speech, hyperactivity, disrupted sleep, and evidence of distress without apparent cause.

In addition to standardized activities, caregivers record videos of patients' newly acquired abilities or abilities which have significantly changed in quality throughout the study. Caregivers participate in qualitative interviews to provide context for videos and discuss any changes observed during specified intervals.

Activity videos will be reviewed and scored by expert clinicians using both Clinical Global Impression of Severity (CGI-S) and Clinical Global Impression of Change (CGI-C) scales at the completion of the study.

Caregiver interviews and clinician-rated videos will inform the patient-specific disease trajectories for each hallmark, which will be compared with natural history.

Table 1: Video assessments collected during the study at baseline and follow-up

Category	Disease Hallmark	Video Assessment
Videos of Daily Living	Inability to self-care	Eating
	Lack of engagement with environment	Playing with iPad game, book or toy
	Progressively abnormal gait	Walking
	Social withdrawal	Playing with sibling/friend
	Lack or loss of communication or speech	Speaking/Communicating
	Hyperactivity	Video of child exhibiting typical levels of hyperactivity
Videos of Events	Disrupted sleep	Video of child during night waking
	Distress episodes	Video of child during distress episode
	Any new ability/meaningful change	Video of child demonstrating new ability/change

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RESULTS

To date, 17 caregiver/patient dyads of MPS IIIA participants ranging in age from 12 to 65 months, at time of enrollment into the AAVance study, have elected to participate in this parallel study.

Participating families come from eight different countries, capturing observational data on 9 male and 8 female study subjects.

Figure 1: PROVide App main menu

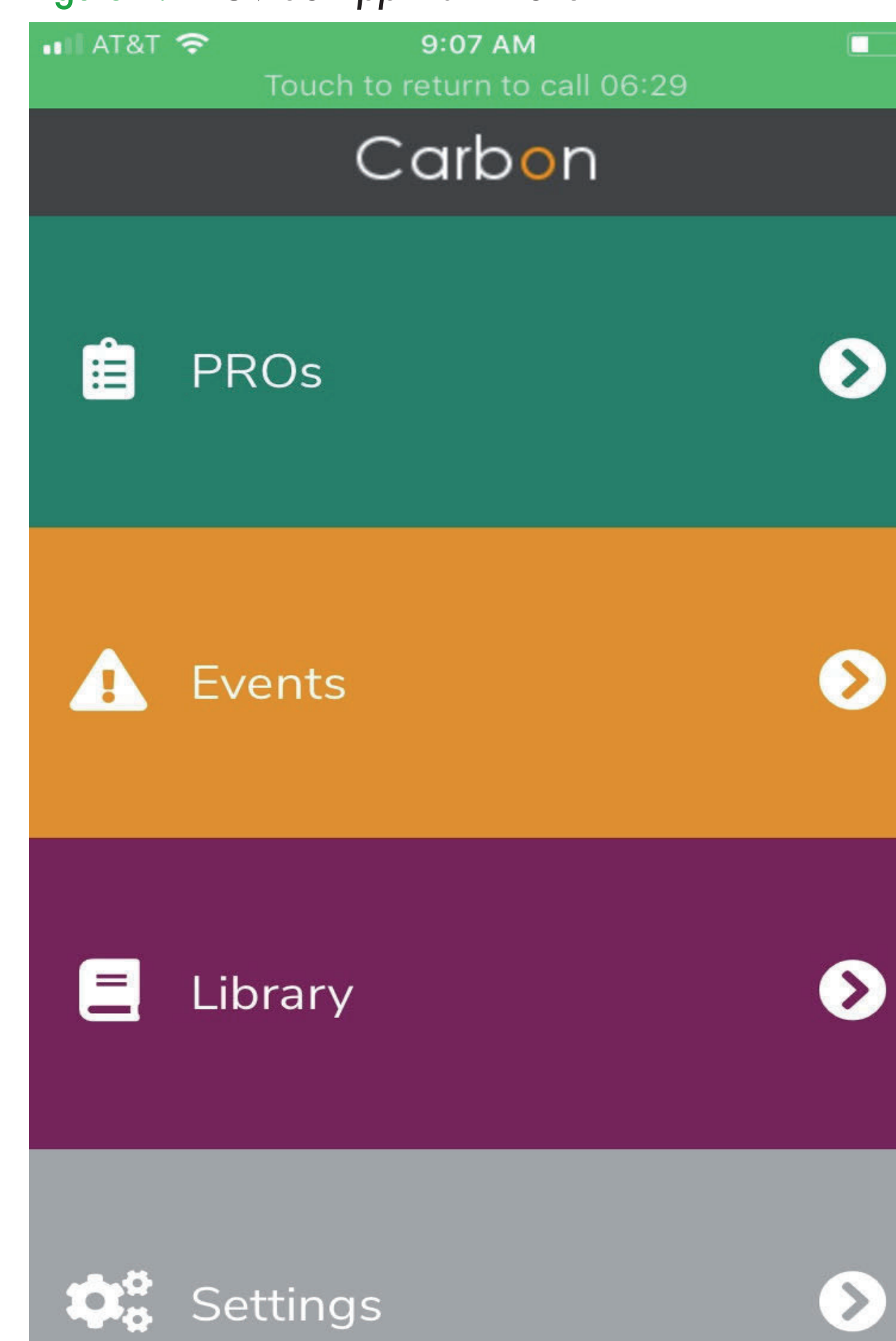


Figure 2: PROVide App menu for Videos of Daily Living

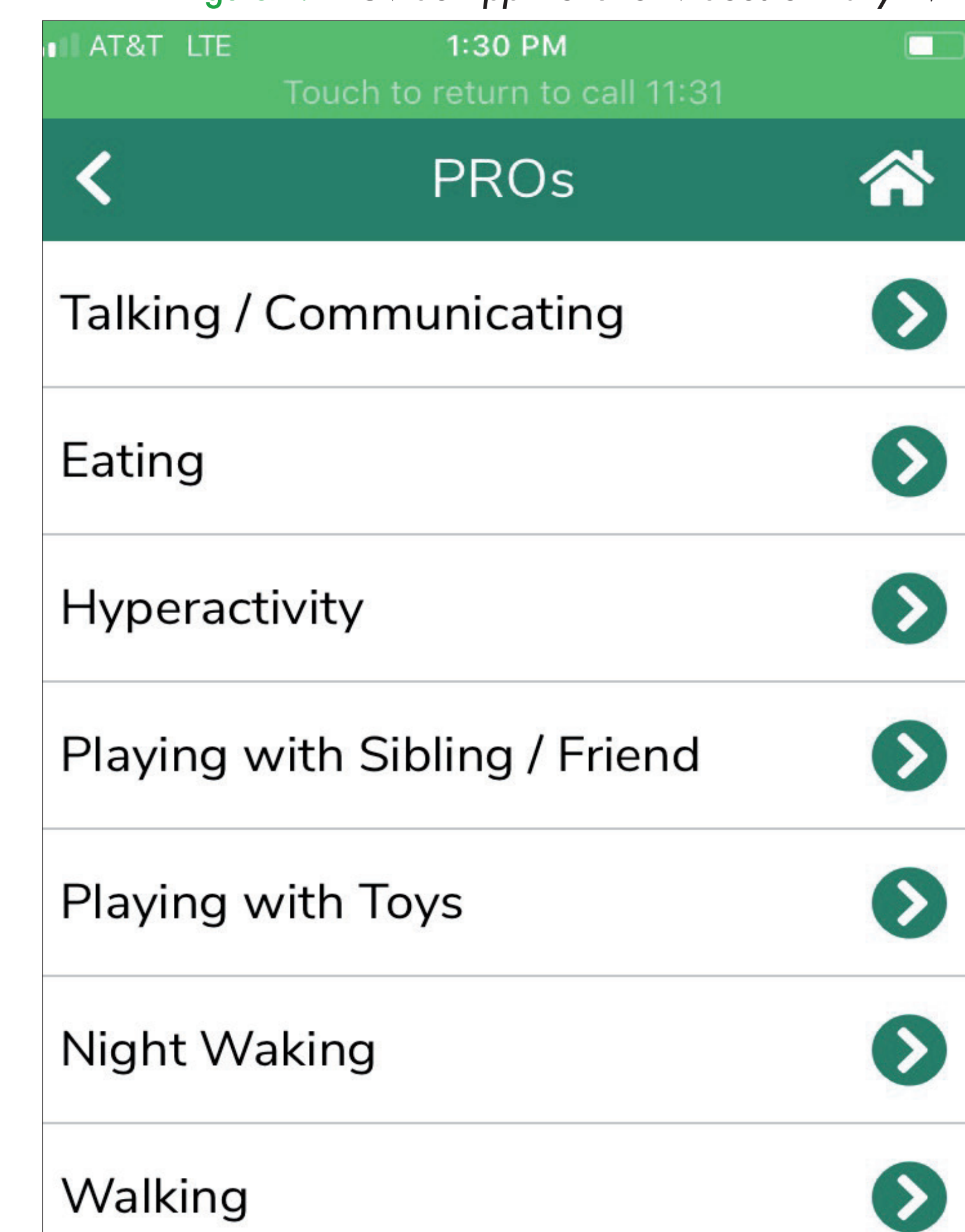


Figure 3: PROVide App description of Distress Episode

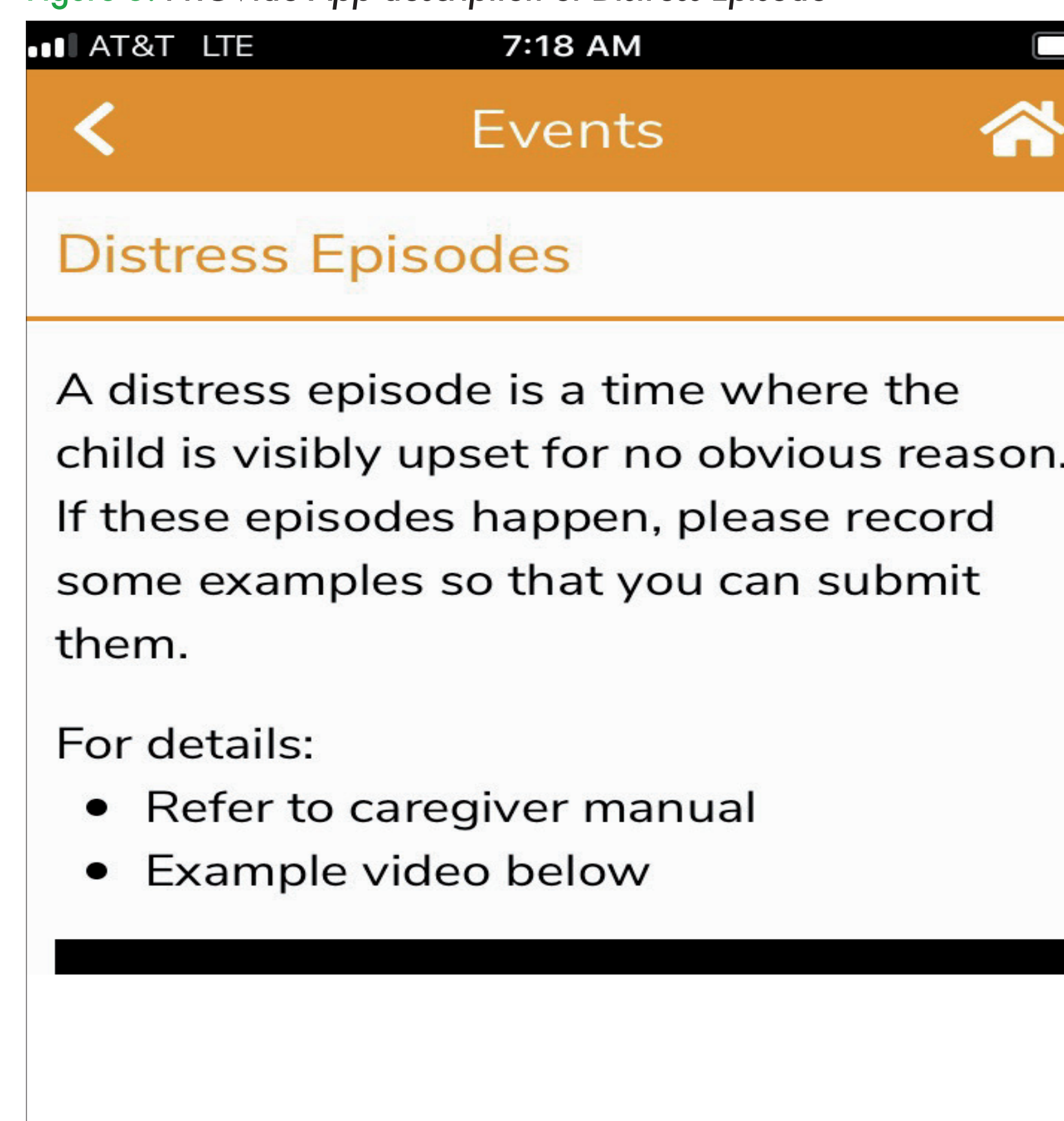
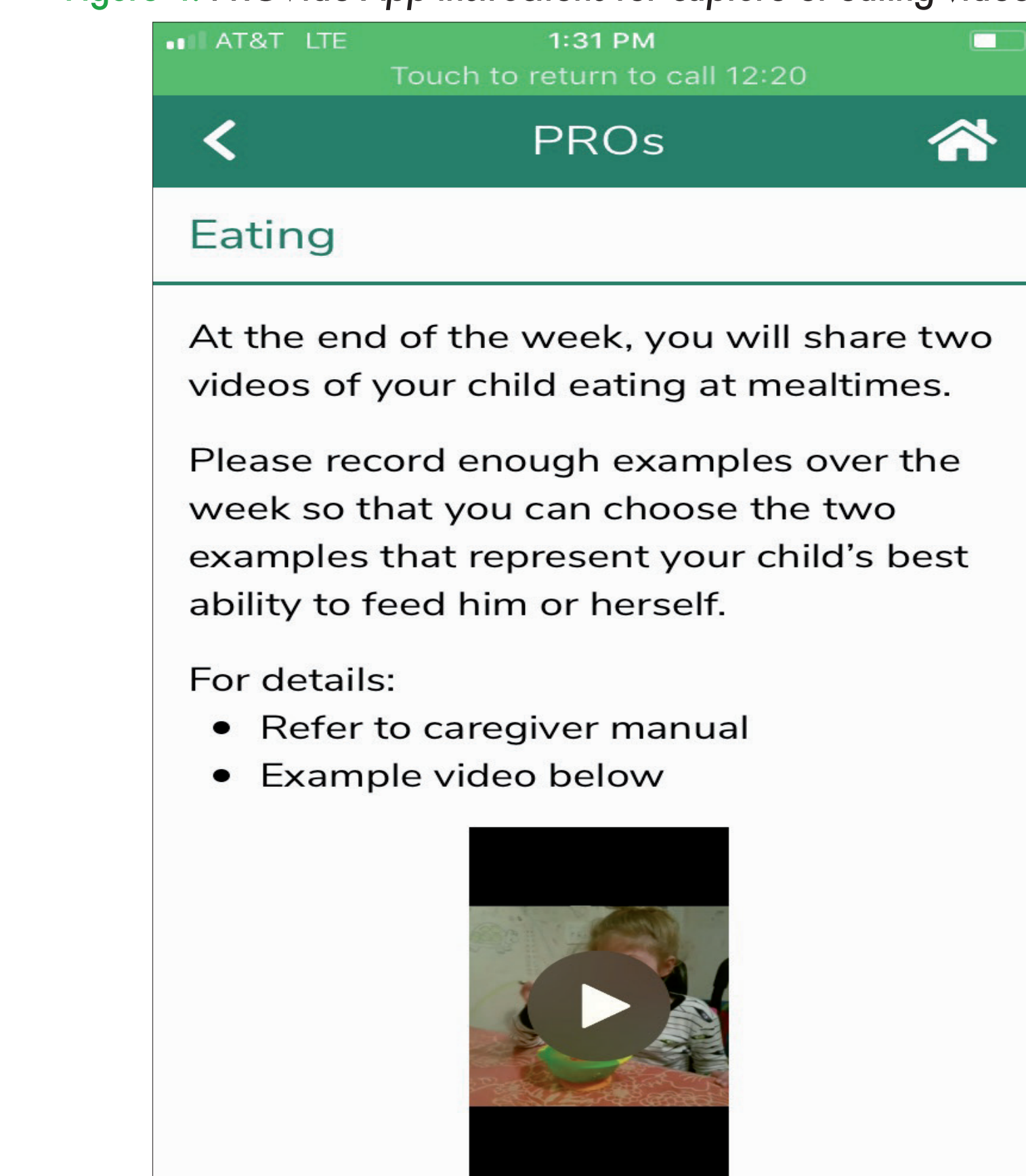


Figure 4: PROVide App instructions for capture of eating videos



INTERIM CONCLUSIONS

- 320 + videos have been recorded and shared by the caregivers to date.
- Qualitative interviews provide key information for interpreting videos
 - baseline patient trajectory
 - context for the videos is needed for proper interpretation
- Video and context allows capture of subtle but meaningful incremental changes
 - quality of interactions in real world setting, smoothness of movement, speech clarity and disfluency, etc.
- Feasible for longer term monitoring of real-world functioning and patient status.

ACKNOWLEDGEMENTS

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